Factors affecting anticipatory grief in family carers of people living with Motor Neurone Disease:

The role of MND symptomatology

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Abstract

Caring for someone living with Motor Neurone Disease (MND) can be emotionally, psychologically and physically demanding. Due to the nature of disease progression, family carers are often confronted with continuous changes and losses, leading to the phenomenon of anticipatory grief (AG). Currently, studies focusing on carer AG are limited. Thus, the present research project focuses on identifying key factors that affect AG in this population to better support carers and inform future interventions and research.

A mixed-methods approach was used to address the research questions. Firstly, a systematic review was conducted to identify the current knowledge about factors associated with MND carers' grieving processes, including anticipatory, post-death and prolonged grief disorder. Results identified some factors associated with carer AG which were particular important in this population, such as the knowledge of MND, the uncertainty and unpredictability of the disease, absence of emotional acceptance and presence of emotional avoidance. The findings demonstrated that most of the literature targeted post-death and prolonged grief disorder and there was limited research on AG with no quantitative studies exploring factors associated with this phenomenon. To overcome this gap in the literature, the further exploration of factors affecting AG was considered crucial.

The second study used a qualitative methodology. Interviews were conducted with current MND carers about their experiences of changes and losses during the trajectory of the disease and how they coped emotionally with new circumstances. Three themes were generated, and findings suggested that carers transit an emotional journey during the progression of the disease, which starts with great destabilisation when diagnosis is conveyed, followed by the adaptation to continuous changes and losses and finally acceptance of the new reality. Different coping strategies that best work for carers to overcome these changes and losses were also revealed, including knowing (or not) about the disease, receiving formal and informal support and focus on the present moment.

To further understand carer AG, the third study explored the impact of various disease- and carer-related factors, which were devised from previous literature as potential

predictive factors of AG, including disease severity, behavioural changes, relationship closeness, familism and hours of care provided. The findings suggested that MND symptoms (i.e., disease severity and behavioural changes) have the greatest impact on carer AG.

The final study focused on exploring the moderating role of psychological inflexibility between MND symptoms and carer AG. Results demonstrated that while psychological inflexibility, disease severity and behavioural symptoms are associated with carer AG, psychological inflexibility does not serve as a moderator of the relationship between MND symptoms and AG.

This thesis has shown that MND symptoms, along with changes and losses, are the primary predictors and causal factors of carer AG. Additionally, carer-related and contextual factors have been identified as potential influencers of the intensity of grieving emotions. The findings highlight the interplay among factors contributing to carer AG, suggesting areas that may require targeted interventions and future research to better support emotionally carers of people living with MND.

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List of abbreviations

AAQ-II	Acceptance and Action Questionnaire-II
ACT	Acceptance and Commitment Therapy
AG	Anticipatory grief
ALS	Amyotrophic lateral sclerosis
ALSFRS-R	ALS Functional Rating Scale Revised
ALS-FTD	Amyotrophic lateral sclerosis-frontotemporal dementia
CGS	Caregiver Grief Scale
FC	Family carer
FS	Familism Scale
GAD-7	General Anxiety Disorder Scale
HCP	Healthcare professionals
MiND-B	Motor Neurone Disease Behavioural Instrument
MMCGI	Marwit and Meuser Caregiving Grief Inventory
MMCGI-SF	Marwit and Meuser Caregiving Grief Inventory-Short Form
MND	Motor Neurone Disease
MNDA	Motor Neurone Disease Association
NICE	National Institute of Clinical Excellence
NNUH	Norfolk and Norwich University Hospital
OECD	Organisation for Economic Cooperation and Development
PHQ-9	Patient Health Questionnaire
PGD	Prolonged Grief Disorder
PG-12	Prolonged Grief Disorder Questionnaire
PG-13	Prolonged Grief Disorder Diagnostic Tool
PIC	Participant Information Centre
PPIE	Patient and Public Involvement and Engagement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
pwMND	People living with Motor Neurone Disease
RCS	Relationship Closeness Scale
UK	United Kingdom
US	United States

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Declaration

Not part of this thesis has been submitted for any other degree or qualification at this or other institution.

Author contributions

I was responsible for the design of the studies and formulation of the research questions, data analyses, interpretation and writing up of all chapters of this thesis and dissemination of the results.

Oral and Poster presentations arising from this thesis

Trucco, A. P., Khondoker, M., Kishita, N., Backhouse, T., Meuser, T., & Mioshi, E. *Does carer psychological inflexibility moderate the relationship between MND symptomatology and emotions associated with carer anticipatory grief?*
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International Symposium on ALS/MND, 2023. Basel, Switzerland [Oral presentation].

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European Network for the Cure of ALS meeting, 2023. Barcelona, Spain [Poster presentation].

Trucco, A. P. *Factors influencing anticipatory grief in family carers of people living with MND – research project.*
Universidad Autónoma de Madrid, Madrid; Hospital Carlos III, Madrid; Hospital Clinic, Barcelona and Hospital de Figueres, Cataluña, 2023. Spain [Oral presentation in Spanish].

Trucco, A. P. *The emotional journey of family carers currently supporting people living with Motor Neurone Disease.*
Norfolk MND Care & Research Network, 2023. Online meeting [Oral presentation].

Trucco, A. P. *Exploring the various factors affecting grief in family carers of people living with MND.*
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Trucco, A. P., Backhouse, T., Mioshi, E., & Kishita, N. *A systematic review of factors associated with grief in informal carers of people living with Motor Neurone Disease*. International Symposium on ALS/MND, 2022. Online conference. [Poster presentation].

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MND Association ENCOURAGE Event, 2022. Northampton, UK [Oral presentation].

Trucco, A. P., Khondoker, M., Kishita, N., Backhouse, T., & Mioshi, E. *Factors affecting anticipatory grief: do severity of the disease and behavioural changes predict anticipatory grief in family carers of people living with MND?*
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Scientific publications arising from this thesis

Trucco A. P., Backhouse, T., Kishita, N. & Mioshi, E. (2023). Factors associated with grief in informal carers of people living with Motor Neuron Disease: a mixed methods systematic review. *Death Studies, 48*(2), 103-107. https://doi.org/10.1080/07481187.2023.2191351 (Chapter 2)

Trucco, A. P., Mioshi, E., Kishita, N., Barry, C. & Backhouse, T. (2023). Navigating an emotional journey: A qualitative study of the emotional experiences of family carers currently supporting people living with Motor Neurone Disease. *Palliative & Supportive Care*. [Advance online publication]. https://doi.org/10.1017/S147895152300158X (Chapter 3)

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Trucco, A. P., Khondoker, M., Kishita, N., Backhouse, T., Meuser, T. & Mioshi, E. (2024). Does carer psychological inflexibility moderate the relationship between Motor Neurone Disease symptomatology and carer anticipatory grief emotions? [Submitted for publication]. (Chapter 5)

Structure of the thesis

Chapter 1 offers the reader a general introduction including the rationale for the thesis, and definitions of the main terms used throughout the text.

Chapter 2 introduces the reader to a systematic review of the literature on the factors affecting grieving processes (anticipatory grief, post-death grief, prolonged grief disorder) in informal carers of people living with Motor Neurone Disease.

Chapter 3 explores qualitatively the experiences of losses and changes of family carers currently supporting people living with Motor Neurone Disease, and the coping strategies they find helpful to use during the trajectory of the disease.

Chapter 4 investigates how Motor Neurone Disease symptoms and carer-related factors impact on carer anticipatory grief. This study uses a quantitative approach.

Chapter 5 explores the role of psychological inflexibility as a potential moderating factor in the relationship between Motor Neurone Disease symptoms (i.e., disease severity and behavioural changes) and carer anticipatory grief.

Chapter 6 provides a general discussion of the thesis, integrating all the results reported in the different studies encompassing this thesis.

The context in which this PhD project was situated

This PhD project was embedded in a larger research project called *"Factors affecting family carers' wellbeing in Motor Neurone Disease — FACTOR-MND"*, which was sponsored by the University of East Anglia, Norwich, UK. FACTOR-MND was a non-funded project, and led by Prof Eneida Mioshi, primary supervisor of this thesis.

The FACTOR-MND project, aiming to explore factors impacting on current carers of people living with Motor Neurone Disease (MND)'s psychological wellbeing, using a quantitative approach, received ethical approval from the West Midlands - Black Country Research Ethics Committee (UK) [IRAS 281943, REC reference number: 20/WM/0185] in July 2020. It involved the collection of data within the UK through a comprehensive survey which included diverse measures pertaining to carer wellbeing. The recruitment of the study and data collection had not yet commenced at the time that I started my PhD research project in February 2021.

From February 2021 onwards, I took leadership of the FACTOR-MND project, modifying it to suit my PhD project, with support from my PhD supervisory team. I led the dissemination of the project, participant recruitment, data collection and administration of documents and tasks. As I refined my own PhD research project, I led, prepared and submitted four different amendments to the original protocol of FACTOR-MND to include a novel research question to investigate the factors impacting on MND carer anticipatory grief, a measure to assess anticipatory grief in carers, integrate a qualitative study into the project, and extend recruitment strategies.

Concerning the qualitative study, I framed the rationale, research questions, methodology and topic guide to explore carers' experiences of losses and changes and designed the material for study dissemination. In addition, I prepared the ethics to obtain approval to disseminate the quantitative study (survey) from the FACTOR-MND project in English speaking countries from the Faculty of Medicine and Health Sciences Research Ethics Subcommittee from the University of East Anglia (UK) [ETH2223-0204]. Subsequently, I designed the study material for recruitment purposes in United States (US) and Australia.

I updated the pre-existing survey to include the anticipatory grief measure. In addition, I also updated it to add a section to invite UK participants to share their contact details if they expressed interest in participating in the qualitative study. Furthermore, I incorporated pertinent information (e.g., crisis helpline numbers) for potential participants in other English-speaking countries, like United States and Australia.

The PhD research project was funded by MND Scotland, UK.

All relevant documents can be found as supplementary material in the appendices section.

Patient and public involvement and engagement meetings

In an effort to ensure the relevance and comprehensiveness of this research project, I engaged in Patient and Public Involvement and Engagement (PPIE) meetings with carers and stakeholders. These collaborative meetings were pursued and designed to incorporate the perspectives and insights of individuals affected by Motor Neurone Disease (MND), and those connected to MND, fostering a dynamic exchange and contribution of ideas.

PPIE meetings with family carers of people living with MND

I met with one current carer and one former carer to gain their insights on conducting an interview with family carers currently supporting people living with MND aiming to delve into their experience of anticipatory grief.

As a result of this meeting, carers recommended not using the term grief during the interview, as it could potentially evoke strong emotions and feelings and some individuals would find it distressing due to the traditional concept of grief related to death. Instead, they suggested employing more open-ended questions that allowed for an exploration of their experiences of losses and changes without directly labelling grief. This valuable insight from the meeting guided the adjustment of the interview topic guide in the qualitative study of this thesis (Chapter 3).

PPIE meetings with healthcare professionals

I met with healthcare professionals from the Norfolk and Norwich University Hospital NHS Foundation Trust (NNUH), United Kingdom (UK), to discuss best dissemination strategies for the project. These meetings were held with the MND nurse coordinator, physiotherapist, MND neurologist and MND palliative care doctor (all members of the Norfolk MND Care and Research Network). Following these discussions, it was decided that the NNUH was going to act as a Participant Identification Centre (PIC) for the purpose of supporting the research project's recruitment. Additionally, I was invited to actively

participate in MND clinics where we would present the research study to family carers of people living with MND attending these clinics.

Accordingly, following the same approach, I met twice with healthcare professionals from Sheffield Teaching Hospitals NHS Foundation Trust, UK, who also agreed to act as a PIC site for recruitment purposes.

PPIE meetings with coordinators from MND carers' support groups

I engaged in regular meetings with the Head of Regional Care Partnerships – Central and West, affiliated with the Motor Neurone Disease Association in the UK. The primary focus of these meetings was to explore effective avenues for disseminating the research study for recruitment purposes among family carers of people living with MND in the UK. The discussions were very productive as suggestions and recommendations on approaching carers attending carers' groups were highlighted. In addition, the Head of Regional Care Partnerships facilitated connections with local coordinators from various branches across the UK organising carers' support groups.

Consequently, I initiated contact with these local coordinators from MND local branches, convening meetings prior to attending carers' support groups (online and face-to-face). The purpose of these meetings was to decide on dates for presenting the PhD project at support groups and collaboratively plan how the presentation of the project should be conducted and agree upon appropriate terms and language to use with carers.

For a full list of recruitment strategies please see the supplementary material in the appendices section.

Chapter 1: General Introduction

In this thesis, the term Motor Neurone Disease (MND) has been employed as the umbrella term to encompass various phenotypes of the disease (explained in following paragraphs), consistent with the terminology used in the United Kingdom (UK). Specifically, Amyotrophic Lateral Sclerosis (ALS) has been recognised as the most prevalent phenotype under the MND classification. It is worth noting that certain studies and classification systems mentioned in this thesis, such as the Strong criteria, may utilise ALS as the umbrella term (adopted in countries such as United States and Canada), and in these cases the ALS term has been retained for consistency with the referenced studies.

Motor Neurone Disease

Motor Neurone Disease is a neurodegenerative, progressive disease, affecting primarily the upper motor neurones (neurones projecting from the cortex to the brainstem and the spinal cord) and lower motor neurones (neurones projecting from the brainstem or spinal cord to the muscles), leading to advancing motor and extra-motor symptoms and plausible behavioural and cognitive changes (Hardiman et al., 2017).

There is no cure for MND to date and the life expectancy is 2-3 years from symptom onset (Kiernan et al., 2011). Research indicates that MND typically manifests during middle age, with sporadic ALS showing onset between 58 to 63 years, while familial ALS tends to appear between 40-60 years of age (Ingre et al., 2015). MND has been found to be more common in men than women, with studies reporting a male: female ratio of 1.5:1 (Burchardt et al., 2022), and an increase in the proportion of females with ALS in older groups (Manjaly et al., 2010).

MND exhibits significant clinical heterogeneity, varying on the age of onset, different sites of onset, including limb and bulbar onset, distinct rates of progression and diverse survival outcomes (Ravits, 2014). Classification of MND is difficult due to its diverse nature and clinical manifestations (Rutter-Locher et al., 2016) and can be variable depending on the criteria applied. Within each classification system, a range of sub-phenotypes and clinical trajectories can be observed (Hardiman et al., 2017). Traditional MND phenotypes are based

on the extent of upper and lower motor neurone involvement. The four primary phenotypes distinguished by the site of origin and the severity of neurological involvement include amyotrophic lateral sclerosis (ALS), progressive bulbar palsy, progressive muscular atrophy, and primary lateral sclerosis (Statland et al., 2015). Other categorisations consider factors such as the site of onset (spinal or bulbar), diagnostic certainty following El Escorial (and Airlie house) criteria (Brooks et al., 2000; van den Berg et al., 2019), neurophysiological features following the Awaji criteria (Carvalho & Swash, 2009) and pattern of heritability (sporadic or familial disease).

Although epidemiological studies on MND have been published, current worldwide MND prevalence and incidence have been difficult to report, as studies looking into this include different years, locations and MND phenotypes. The Global Burden of Disease, Injuries and Risk Factor study, collecting data from 204 countries from 1990 to 2019, estimated that there were 268,673 prevalent cases of MND and 63,700 incident cases of MND worldwide in 2019 (Park et al., 2022). Studies investigating MND epidemiology in the United Kingdom (UK), reported an average crude incidence rate of 2,16/100,000 person-years, and an incidence of 1,61/100,000 person-years after being age- and sex-adjusted (Opie-Martin et al., 2021). Additionally, it was found that MND incidence in England was 5,69/100,000 person-years when age-standardised to the UK 2011 census (Burchardt et al., 2022).

MND Symptomatology

The heterogeneity of MND may suggest variable sites of disease onset, differences in prognosis, disease progression and symptom manifestation (Walhout et al., 2018).

From a motor-symptom perspective, people living with MND (pwMND) with predominantly upper motor neurone symptoms, present spasticity and weakness; conversely, lower motor neurone symptoms include fasciculations, cramps and muscle wasting. The initial presentation of the disease varies among patients; 60%-80% of cases will present with limb-onset disease (muscles weakness of the limbs), 25-30% with bulbar-onset disease (characterised by dysarthria and dysphagia) and up to 5% of patients present with

respiratory symptoms (characterised by breathlessness). People living with MND will experience progressive disability and dependency to carry out activities of daily living and functional impairment leading to worsening paralysis of voluntary muscles until death occurs (Arora & Khan, 2023; Hardiman et al., 2017).

While the primary symptoms of MND have traditionally been associated to motor dysfunction, the significant occurrence of non-motor symptoms and the advances in the genetics of MND, including the discovery of a hexanucleotide repeat expansion in C9orf72, have led to the redefinition of MND as a neurodegenerative and multisystem disorder rather than merely a neuromuscular condition. With the introduction of the Strong criteria in 2008 (Strong, 2008) and its subsequent revisions and updates (Strong et al., 2009, 2017) it has been well-established that at least 50% persons living with MND will develop behavioural and cognitive symptoms, with 15% of them developing a concurrent diagnosis of frontotemporal dysfunction, leading to the continuum of ALS-frontotemporal spectrum disorder (ALS-FTSD). It has been reported that behavioural and cognitive manifestations increase with disease progression, these changes are heterogenous (Crockford et al., 2018; Finsel et al., 2023; McHutchison et al., 2024), and can precede motor symptoms (Mioshi, Caga et al., 2014). Additionally, the National Institute of Clinical Excellence (NICE) in the UK, acknowledges that cognitive and behavioural symptoms may precede motor dysfunction and emphasises the importance of continually monitoring these changes (NICE, 2016).

The presence of behavioural symptoms in MND, including neuropsychiatric symptoms, has gained attention during the past decades. A previous systematic review of behavioural changes in MND, summarising data of published studies until 2011 (Raaphorst et al., 2012) and a recent scoping review, investigating behavioural symptoms in MND from 2011 to February 2024 (Trucco, Backhouse & Mioshi, 2024) have reported a wide range of changes in behaviour present in pwMND. These include apathy, disinhibition, loss of sympathy and empathy, emotional lability, perseverative, stereotyped or compulsive behavior, irritability, rigidity, hyperorality, altered food preference and loss of insight. Although apathy has been reported to be the most frequent behavioural symptom occurring in 50% of patients in past studies (Lillo et al., 2011; Woolley et al., 2011), it has been suggested that disinhibition might be broader and more recurrent than it has been reported

(Trucco, Backhouse & Mioshi, 2024). Despite the increasing recognition and awareness of behavioural changes within this population, notably, none of the MND classification systems, such as El Escorial or Awaji criteria, have yet incorporated the cognitive or behavioural symptoms, prevalent to a significant degree in pwMND.

People living with MND can present with cognitive dysfunction. Extensive research has explored and elucidated the cognitive decline and dysfunction in this population. Cognitive impairment has been typified by executive dysfunction, deficits in social cognition and verbal fluency, language dysfunction and memory deficits (Abrahams et al., 2000), with verbal fluency emerging as the most consistently observed cognitive change (Abrahams, 2023).

Other non-motor symptoms experienced by pwMND have also been found in the literature, including gastrointestinal issues, disturbed sleep, problematic saliva, low mood and sexual dysfunction (Beswick et al., 2024).

Alongside the motor, behavioural and cognitive manifestations experienced by pwMND, findings from a collaborative study across nine European countries aiming to investigate the burden experienced by pwMND, revealed that the overall quality of life was deemed acceptable by the person living with MND, and primarily influenced by the physical limitations. The reported stress levels were classified as low to medium, and levels of anxiety, depression, pain and fatigue were also noted (Conroy, Velez-Gomez et al., 2023).

Management in MND is challenging due to its multifaceted nature, associated with motor and non-motor symptoms, all of which progress rapidly. The complexity of these symptoms poses significant challenges not only for the person living with MND but also for individuals who assume the role of carer and often find themselves tasked with the care of the person living with MND and confronted with responsibilities and burdens impacting on their lives.

Informal carers of people living with Motor Neurone Disease

Informal caregiving and wellbeing

Providing care for a person living with a terminal illness is a difficult experience affecting carers' daily functioning as it implies a multifaceted role involving psychological, medical and ethical aspects. When the demands of caregiving exceed the resources available to carers, significant challenges may arise for them (Nielsen et al., 2016a). In the UK, informal caregiving is an essential component in addressing the existing demand for care. Over 18% of individuals aged 50 and above are engaged in informal caregiving responsibilities, in contrast to the Organisation for Economic Cooperation and Development (OECD) average of 13.5% (OECD, 2019). Despite the benefits and advantages of informal caregiving, such as serving as a low-cost alternative to formal care, reducing medical expenditures, decreasing the risk of infections and improving the mental wellbeing of the care recipient (Barnay & Juin, 2016; Coe et al., 2019; Van Houtven & Norton, 2008), it can also have negative health effects on carers' physical, psychological and emotional wellbeing (Schulz & Sherwood, 2008).

The concept of physical wellbeing pertains to the state of health, describing the condition of the body and its capacity to perform activities (Capio et al., 2014). Some of the factors linked to carers' physical health include the care recipient's functional abilities, behavioural and cognitive changes, and the hours and duration of care provided (Pinquart & Sörensen, 2007). It has been reported that the physical consequences of caregiving are less intensive than its psychological effects (Schulz & Sherwood, 2008).

Psychological wellbeing is a complex construct, and its conceptualisation and definition remain challenging. It comprises a hedonic approach (i.e., positive emotions and feelings, happiness and satisfaction with life; and avoidance of pain), and an eudaimonic approach (i.e., emphasises purposeful behaviour, including self-acceptance, environmental mastery, positive relationships, personal growth, purpose in life and autonomy), as well as resilience (coping, emotion regulation, healthy problem solving) (Diener, 2000; Ryan & Deci, 2001; Ryff & Keyes, 1995). Conversely, psychological distress has been broadly defined as an undifferentiated group of symptoms ranging from anxiety and depression symptoms to functional impairment, personality traits and behavioural problems (5th ed; DSM-5;

American Psychiatric Association, 2013). Research on carers' psychological distress has been extensively explored over the years across various illnesses and populations. Levels of anxiety, depression, strain, stress and burden are among the most commonly psychological variables investigated in the caregiving context.

Emotional wellbeing has been defined as an umbrella term for concepts such as life satisfaction, life purpose, and positive emotions (Feller et al., 2018). This definition closely aligns with the definition and concept of psychological wellbeing, indicating the lack of conceptual clarity regarding the specific understanding of psychological and emotional wellbeing. Despite the undenied interrelatedness of both concepts, it remains unclear whether psychological wellbeing encompasses emotional wellbeing, if emotional wellbeing is a component of psychological wellbeing, or whether they are two distinct concepts that need further clarification. Consequently, research has interchangeably used either term to refer to individuals' emotions, feelings and thoughts and psychological variables, such as depression and anxiety.

In this thesis, I will refer to emotional wellbeing to describe the feelings and emotions experienced by MND family carers, which contribute to their life satisfaction and quality of life.

Impact of providing informal care in Motor Neurone Disease

In the context of MND, informal carers are family members who predominantly assume the role of primary carers, providing care within the home environment (Connolly et al., 2015). A family carer for a person living with MND faces daily life changes and stress related to the progressive nature of MND as the person living with MND requires increasing levels of assistance. A recent report released by the MND Association (MNDA) in the UK (MNDA, 2022), highlighted that family carers in the UK felt mentally and physically exhausted due to caring responsibilities. Carers dedicated over 75 hours per week to attending the needs of the care recipient, including tasks such as personal care, physical assistance, emotional support, coordination of care services and facilitating social participation. Their caregiving responsibilities leave them with limited time to address their own essential activities and engage in self-care activities, often resulting in neglect of their own wellbeing. Moreover, carers expressed profound worries and fears regarding the future

coupled with feelings of isolation and loneliness due to a perceived lack of support networks.

Findings from this report align with previous literature focusing on MND family carers' wellbeing. The impact that caring has on MND family carers' psychological wellbeing has been well documented along the years. Worldwide research has largely described carers' psychological morbidity reporting high levels of strain (Bruletti et al., 2015), anxiety (Vignola et al., 2008), symptoms of depression and a reduced quality of life (Gauthier et al., 2007), contributing to carer burden (Burke et al., 2017; de Wit et al., 2018; Pagnini et al., 2010). Furthermore, the additional physical exhaustion carers experience during caregiving has been recognised (Baxter et al., 2013; Oyebode et al., 2013).

Adding to the psychological and physical burden that carers of pwMND experience as a consequence of MND, carers often struggle with the emotional impact of the disease. Carers' emotional distress has been associated with the progressive dependence and loss of functions of the person living with MND, worries about managing tasks in the future and the uncertainty of disease progression, changes in relationships and social interactions, limited time for themselves and inefficient care provision and communication with healthcare professionals (HCP) (Holkham & Soundy, 2018; Pinto et al., 2021).

Despite the negative impact and significant challenges associated with caregiving in MND, positive aspects have also emerged for carers of this population. A previous study (Conroy, Kennedy et al., 2023) identified that carers find meaning in life while caring, reflecting on their experiences and reconnecting with the care recipient. This can involve spending quality time together, fostering stronger bonds with the person living with MND, family and friends, and re-evaluating personal values such as love, life purpose and the importance of interpersonal connections. Furthermore, carers expressed personal satisfaction in fulfilling their caregiving duties and feeling healthy and capable of meeting the demands of their role. This sense of fulfillment and accomplishment is particularly rewarding when their efforts are appreciated. This same study revealed how the positive aspects of caregiving changed and adapted throughout the progression of the disease, characterised by experiencing positive aspects linked to finding meaning in life at the beginning and end of the trajectory of the disease, and experiencing personal satisfaction

during the middle phases of MND. Additionally, it suggested that this carer adaptive cycle may coexist with the cycle of anticipatory grief in terminal illnesses (Kübler-Ross & Kessler, 2005).

Anticipatory grief refers to the changes and losses that family members encounter during the progression of an illness, before death, experienced by both the dying person and their loved ones (Simon, 2008) and encompasses progressive losses, past an future (Coelho et al., 2018) . It appears to occur in several stages and evolve over time, including shock, denial and eventual acceptance (Kübler-Ross, 1969). Although there has been a growing body of literature focusing on various aspects related to the experieces of MND caregiving and carers' emotional wellbeing, there still exists a notable gap in relation to how carers transit and grieve the losses and changes during the trajectory of MND.

Anticipatory grief

The definition of anticipatory grief (AG) remains subject to diverse interpretations, leading to persistent uncertainty in its conceptualisation (Coelho & Barbosa, 2017). A previous systematic review revealed the use of more than 18 terms and over 30 distinct definitions to describe this specific form of grief, leading to a lack of uniformity in its terminology. Some of these terms have been categorised as indefinite loss, pre-death grief, pre-loss grief, anticipatory mourning (Singer et al., 2022).

The first definition of AG is attributed to Lindemann (Lindemann, 1994), who characterised it as the emotional process preceding the actual loss of a person and described it as the grief work in anticipation of the impending loss, which may lead them to emotionally detach from the person. Subsequently, the term has been employed to denote the grief experience occurring in advance of the loss of a person. However, since the concept of AG rose, there has been ongoing debate about what constitutes this phenomenon (Evans, 1994). Rando (Rando, 1984, 1986) developed a multidimensional definition and defined AG as the reaction to the impending loss of a terminally ill loved one, as well as the reactions towards past and present losses related to the illness, and all

psychosocial processes stimulated by these losses. For the purpose of this thesis, I will use this definition provided by Rando.

Anticipatory grief in the context of informal caregiving

From the moment a terminal illness is diagnosed, and through the progressive physical, and cognitive decline of a person's advancing illness, family members are confronted with successive losses and changes, leading to experiencing AG emotions. Expressions of AG have been reported as being physical, emotional, cognitive and/or spiritual. These may include sleep changes and headaches, denial/disbelief, anger, guilt, sadness, being disorganised, forgetful and confused, experiencing frustration, ambiguity, irritability, loneliness, shock across multiple life domains (Rando, 1986, 2000; Simon, 2008).

Findings from a systematic review highlighted that grief during caregiving is a risk factor for poor bereavement, including developing prolonged grief disorder (PGD), and does not serve as a protective factor in the adjustment to the loss of the person (Nielsen et al., 2016b). Prolonged grief disorder has been defined as a persistent grief response accompanied by intense emotional responses (e.g., sadness, anger, denial), where disturbances result in significant distress or impairment in important areas of functioning, diagnosed between 6 and 12 months following the loss of a person (American Psychiatric Association, 2022; World Health Organization, 2019).

The overall prevalence of AG in carers of people living with a life-threatening illness is 24.78%, meaning that almost 25 out of 100 carers experience AG emotions (Kustanti et al., 2022). This result shows a higher prevalence of AG compared to PGD in the general population, with a rate of 9.8%, i.e., one out of ten bereaved people is at risk for PGD (Lundorff et al., 2017).

Most of the research in carer AG has been done in relation to terminal and life-threatening illnesses, cancer and dementia. Regarding carers' characteristics, studies have reported that the rates and levels of AG tend to be higher in females and being a spouse carer (Kustanti et al., 2022), are associated with depressive symptoms, carer exhaustion, lack of preparation for death, excessive prognostic information (Nielsen et al., 2017), burden (Coelho et al., 2017) and living with the care recipient (Meichsner et al., 2016). Additionally,

with regards to the patient's disease, AG has been associated to disease severity (Ott et al., 2007) and levels of behavioural symptoms and cognitive impairment (Holley & Mast, 2010).

The impact of caring for someone living with Motor Neurone Disease on anticipatory grief

Over recent decades, research has explored the experiences of carers of pwMND and highlighted the losses and changes encountered by MND carers throughout the progression of the disease. Three relevant reviews have been published, covering published literature from 1994 to 2017, focusing and synthesising findings on carers' experiences during caregiving. Carers have reported they suffer the loss of their social networks, including family and friends, their future retirement years, their former lifestyles and daily routines of self-care, freedom and social activities, and their relationship with the care recipient. They have also related their experience of changes to financial burden due to great expenses on the person living with MND's care, learning to deal with swallowing, eating and ventilation devices and decreased hours of sleep (Aoun et al., 2013; Holkham & Soundy, 2018; Mockford et al., 2006).

It is widely acknowledged that losses and changes during caregiving are directly intertwined with the concept of AG. However, few studies explicitly referred to this term within the context of MND caregiving experiences. For instance, one study mentioned that carers experienced loss and grief across multiple domains of life but did not delve further into the concept of grief (Anderson et al., 2019).

In the context of this population, a notable gap persists in the current literature concerning the identification of risk factors predictive of AG. While considerable attention has been devoted to exploring risk factors associated with various psychological outcomes such as burden (Antoniadi et al., 2020), there is still a paucity of research specifically elucidating factors linked to AG within this demographic.

Coping strategies used by carers of people living with Motor Neurone Disease

Growing research has explored the different coping strategies carers use to face their situation. Coping strategies have been defined as cognitive and behavioural responses individuals employ to manage internal and external circumstances (Lazarus et al., 1984). Findings from one study investigating coping strategies and their relation to psychological distress (anxiety, depression, and burden) within this carer population, have reported that

carers usually adopted a task-oriented coping style, meaning they tried to actively address emerging problems related to caregiving. Moreover, carers adopting an emotion-oriented coping style, i.e., reducing stressful reactions through emotional responses such as expressions of anger, self-blame, resignation and regret, presented with higher levels of psychological distress, evidencing this coping style may not serve as an adaptive strategy (Siciliano et al., 2017). Similarly, another study, using a longitudinal methodology, reported that carers' emotion-oriented coping style was associated with higher levels of psychological distress, though this coping style did not influence the development of distress over time (de Wit et al., 2019). Both of these previous studies found that task-oriented and avoidance-oriented styles, i.e., avoiding stressful situations, feelings and thoughts by distracting oneself by doing other things or not thinking about the current situation, were not related to psychological distress. In addition, further studies have also highlighted coping strategies employed by carers. Some of these have been related to meaning-based coping strategies, such as reappraising difficult circumstances positively or engaging in meaningful activities (Mockford et al., 2006; Oyebode et al., 2013), not planning ahead or thinking about the future and managing time effectively (Gent et al., 2009). A recent study addressing specifically carers' emotional wellbeing, has also reported coping strategies that carers used. For instance, accepting the disease, focusing on the positive aspects of life and the present moment, taking a break from MND and receiving support from others, such as healthcare professionals, friends and family (Pinto et al, 2021).

Despite the convergence of findings across studies exploring coping strategies, whether within an extensive examination of carers' experiences or a specific focus on emotional well-being, there remains a notable absence of research specifically targeting coping strategies in response to the losses and changes experienced. Rather, these coping strategies are often examined as part of a broader context. Moreover, no studies specifically aimed at understanding how carers navigate the losses and changes throughout disease progression and how they grieve these.

Assessment of grief in family carers of people living with Motor Neurone Disease

To date, few assessment tools have been developed to evaluate anticipatory grief, and there is not a gold-standard tool to estimate this phenomenon. The critical problem

within the existing literature on AG is the instrument of AG used, often not capturing specific aspects and the multidimensionality of AG. A cause for this could be the lack of consensus on the conceptualisation and definition of AG. In addition, despite AG measures being used across different demographics, they present limitations as carers may grieve differently in relation to illness trajectories and measures might not be illness sensitive and capture all care-specific aspects of AG.

The importance of assessing AG quantitatively relies on employing a consistent evaluation across different individuals, populations and research studies. By quantifying the extent of grief experienced by individuals, both clinicians and researchers can better understand the impact of AG and tailor interventions accordingly. The most commonly used standardised AG measures in recent years in carers populations have been the Marwit and Meuser Caregiver Grief Inventory (MMCGI; Marwit & Meuser, 2002) and its short form version (MMCGI-SF; Marwit & Meuser, 2005), the Caregiver Grief Scale (CGS; Meichsner et al., 2016) and the Prolonged Grief Disorder Questonnaire-12 (PG-12; Prigerson et al., 2009). However, limitations of these instruments arise as they have been developed for specific populations, such as the MMCGI and CGS in dementia carers, and the PG-12 was modified from the Prolonged Grief Disorder-13 and developed in cancer population.

In this thesis, the MMCGI-SF was selected to assess MND carers' experience of AG across two studies (Chapter 4 and Chapter 5). The decision to utilise this scale was based on several factors. Firstly, the MMCGI-SF is a self-scored measure and maintains the integrity of the original MMCGI scale, which has steadily demonstrated high internal consistency reliability ($\alpha = .96$), and was validated against various instruments including depression, strain, well-being and perceived family support. In addition, it was validated against an existing model of carer grief (Meuser & Marwit, 2001), encompassing female and male spouses and adult-children of individuals living with dementia, also a neurodegenerative and progressive condition like MND. Importantly, the MMCGI-SF (and the MMCGI) presents three sub-scales linked to AG namely Personal Sacrifice Burden, which focuses on the losses and changes experienced by the carer in relation the care provided; Heartfelt Sadness and Longing, which encompasses the emotional reactions the carer experience; and Worry and

Felt Isolation, which relates to the carer's feelings of losing connections and support from others.

To ensure the relevance and appropriateness of the MMCGI-SF assessment for MND carers, I took proactive steps. Specifically, I contacted one of the authors of the MMCGI-SF to obtain permission for its utilisation for research purposes involving MND carers and to discuss potential adaptations tailored to this specific population. Through collaborative dialogue, modifications were made to the item 6 of the MMCGI-SF. Originally formulated as "Dementia is like a double loss…I've lost the closeness with my loved one and connectedness with my family", this item was adapted to "MND is like a double loss…I've lost the closeness with my loved one and connectedness with my family". This adjustment ensured that the assessment instrument resonated accurately with MND carers, thereby enhancing its relevance for research purposes within the MND context.

Thesis aim and research questions

The current literature underscores the need for a comprehensive investigation into the grief experienced by MND carers prior to the death of the care recipient, emphasising the exacerbating effect of caregiving on grief symptomatology.

A notable gap in the literature pertains to the explicit exploration, acknowledgement and validation of AG within the realm of MND carers, reflected by the lack of explicitly mentioning this phenomenon and a limited attention to coping strategies directly addressing the losses and changes experienced by carers.

This thesis aimed to bridge these gaps by identifying the factors affecting anticipatory grief in family carers of people living with MND. By shedding light on the complexity of this phenomenon, this research project seeks to identify crucial aspects that should be considered in future interventions aimed at supporting carers in their grieving process throughout the trajectory of the disease.

The specific research questions were:

- Which are the factors associated with anticipatory grief emotions in family carers of people living with Motor Neurone Disease?
- Which coping strategies do family carers of people living with Motor Neurone Disease use to navigate the emotional impact of the disease?

To this end, four distinct studies were conducted, each contributing valuable insights towards a more comprehensive understanding of AG in the context of MND care.

Chapter 2: Factors associated with grief in informal carers of people living with Motor Neurone Disease

In order to investigate the existing literature on grief among carers of people living with MND, I conducted a systematic review. This approach facilitated a comprehensive and meticulous analysis of the available literature to identify existing gaps in current knowledge about this topic. The aim was to draw robust and well-founded conclusions regarding the known aspects of grief in this population and highlight areas that have yet to be explored.

This chapter is based on the published paper:

Trucco, A.P., Backhouse, T., Kishita, N. & Mioshi, E. (2023). Factors associated with grief in informal carers of people living with Motor Neuron Disease: A mixed methods systematic review. *Death Studies, 48*(2), 103-107. https://doi.org/10.1080/07481187.2023.2191351

Introduction

Informal carers (e.g., family members) of people living with Motor Neurone Disease (MND) are at a high risk of experiencing clinically significant levels of grief. Given the rapid and progressive nature of MND, informal carers are often confronted with a series of loss experiences.

Grief has been defined as "the reaction to the perception of loss with symptoms including yearning, sadness, anger, guilt, regret, anxiety, loneliness, fatigue, shock, numbness, positive feelings and a variety of physical symptoms unique to the individual" (Rando, 1984, p.24). Grieving processes for informal carers of people living with MND (pwMND) can start before the care recipient's death (anticipatory grief) and are linked to the present changes and losses that carers experience during the trajectory of the disease. When distressing grieving experiences remain unresolved following the death of the care recipient (post-death grief), it can lead to prolonged grief disorder (PGD), which involves severe, pervasive, and persistent grief reactions after the death of a person, causing distress

and resulting in functional impairment in daily life (Prigerson et al., 2009). PGD can be diagnosed 6-12 months following the loss of a person according to the International Classification of Disease - 11 (World Health Organization, 2019) and the Diagnostic and Statistical Manual of Mental Disorders (5th ed., text rev., American Psychiatric Association, 2022). The intensity of grief reactions after a loss will gradually decrease in most people and the bereaved person will be able to manage and integrate grief (Lundorff et al., 2017; Szuhany et al., 2021). Nevertheless, a significant minority of bereaved people will develop PGD with a pooled prevalence of 9.8% in the adult bereaved population (Lundorff et al., 2017). Informal carers of pwMND are potentially at a greater risk of grieving more intensely beyond the period typically considered normal (O'Brien et al., 2016) with a prevalence of 49.6% and 8.7% of being at moderate and high risk of developing PGD respectively (Aoun et al., 2020). Moreover, carers of pwMND are suspectible of experiencing poor mental and physical health (Aoun et al., 2013; Bergin & Mockford, 2016; Pagnini, 2013), which are considered to be linked to PGD (Lenger et al., 2020).

Currently, evidence on interventions that can effectively target grief processes among informal carers of pwMND is scarce. Some systematic reviews on interventions for individuals who have experienced the death of a family member with other conditions reported that interventions targeting grief, such as psychotherapy and counselling, have a positive effect on alleviating grief symptoms (Currier et al., 2008; Johannsen et al., 2019; Wilson et al., 2017). Moreover, studies focusing on interventions targeting PGD, such as group psychotherapy (Rosner et al., 2011) and cognitive behavior therapy, have proved to be effective in the general bereaved population (Rosner et al., 2014; Rosner et al., 2015), which may also work for informal carers of pwMND. However, there are no studies reporting if these interventions improve bereavement outcomes in this population and no guidance for how grieving processes should be treated in informal carers pwMND. Understanding factors affecting different grieving processes, specifically in informal carers of pwMND, is critical to inform future research and practice.

There are existing systematic reviews that focused on factors affecting grieving processes in informal carers of other populations (Chan et al., 2013; Crawley et al., 2023; Mason et al., 2020; Sanderson et al., 2022). These reviews were focused on family carers of people living with dementia (Chan et al., 2013; Crawley et al., 2023), patients in intensive

care unit settings (Sanderson et al., 2022) and the bereaved general population (Mason et al., 2020). Findings from these studies reported that poorer carer psychological and physical health, cohabitation with the care recipient prior to institutionalisation (Chan et al., 2013; Crawley et al., 2023) and dysfunctional copying styles (e.g., self-blaming) (Crawley et al., 2023) were associated with increased anticipatory grief symptoms. On the contrary, pre-morbid marriage satisfaction and the provision of more social support decreased anticipatory grief symptoms (Crawley et al., 2023). Greater post-death grief symptoms were related to being a spouse carer and carer pre-death depression (Chan et al., 2013). The strongest predictors of PGD in family carers of non-MND care recipients were found to be being a spouse carer (Chan et al., 2013; Sanderson et al., 2022), living alone following the death of the care recipient (Sanderson et al., 2022), high levels of carer pre-death depression (Chan et al., 2013), how the death occurred (Mason et al., 2020; Sanderson et al., 2022), poor psychological and physical health in carers, negative perceptions of social support and facing multiple deaths (Mason et al., 2020).

Although some of the factors identified in previous reviews may be relevant to informal carers of pwMND, MND carers' experiences can be different from carers of people living with other conditions due to the relative rarity of the disease, the rapid and progressive escalation of symptoms, the increasing personal assistance and care required and a rather short life expectancy. Furthermore, some of the risk factors identified in the previous studies in non-MND carer populations may not be relevant to carers of pwMND such as multiple deaths. Therefore, it is important to bridge this gap in the current literature to inform future interventions aimed at grieving informal carers of pwMND. The aim of this systematic review was to identify factors associated with anticipatory grief, post-death grief and prolonged grief disorder specific to informal carers of people living with MND.

Methods

This systematic review was designed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO registration number: CRD42021292798).

Eligibility Criteria

The Population, Intervention, Comparison, Outcomes and Study (PICOS) model was used as a framework to formulate the eligibility criteria for this mixed-methods systematic review. Due to the nature of our research question, the Intervention and Comparison categories were not considered applicable for this systematic review.

Study Design

Articles published in peer-reviewed journals and in English, Spanish or Portuguese were included. Cross-sectional, longitudinal, and qualitative studies were eligible. For mixed-methods studies, eligibility criteria were applied to the quantitative and qualitative components separately. We excluded dissertations, theses, book chapters, interventional studies and systematic reviews studies.

Population

Studies were eligible if they recruited informal carers of pwMND. Informal carers included both current carers (those currently providing care) and former (bereaved) carers. When a study included both informal and formal carers or included informal carers of people living with other conditions, the findings had to be reported separately for informal carers of pwMND to be eligible.

Outcome

Any type of grief experiences occurring before and after the death of the person living with MND were eligible (anticipatory grief, post-death grief and PGD). Quantitative studies were eligible if they used a standardised measure of grief and explored associations between grief and other variables. Qualitative studies were eligible if they aimed to explore grieving experiences of carers using interviews or an analysis of answers to free-text survey questions. Qualitative studies that aimed to explore MND caregiving experiences in general were also eligible if they included questions explicitly asking about grieving experiences.

Information Sources and Search Strategy

A systematic literature search of published studies was conducted using the electronic databases Scopus, MEDLINE, CINAHL and PsycINFO for English articles and SciELO

and LILACS for Spanish and Portuguese studies. Sources were searched from database inception to 21st November 2021. An additional hand search of reference lists of included studies and relevant published systematic reviews on grief in informal carers was carried out. The search strategy included terms such as grief, informal carers and MND. The complete search strategy for each database is available in the appendices section (Supplementary Table 2.1).

Selection Process

Electronic search results were merged using an Excel sheet. Duplicates were removed by one of the reviewers (APT). The initial screening of the titles and abstracts was conducted by APT. Full-text articles were assessed for eligibility by two reviewers independently (APT and TB). First, three qualitative studies and three quantitative studies were assessed for eligibility by APT and TB separately and compared in order to ensure accurate selection of the eligible studies. Following this, the remaining studies were evaluated for inclusion independently and disagreements were resolved through discussion.

Data Collection Process

A purposely designed electronic data extraction sheet was used to extract the data. The form was first piloted by two reviewers (APT and NK) using two studies selected to represent different research methods. Following this, the data extraction sheet was piloted with another four studies by APT and TB to ensure accurate coding of information. Data were then extracted from all the remaining included studies independently by two reviewers (APT and TB). Discrepancies were resolved by consensus.

Data Items

The following information was extracted from each eligible study: (a) the country where the research was conducted, (b) type of carers (current or former), (c) place of recruitment, (d) sample size, (e) mean and range of carer age, (f) carers' gender, (g) carers' relationship to care recipient, (h) mean and range of duration of care, (i) mean and range of period of bereavement for bereaved carers, and (j) type of grief investigated (anticipatory grief, post-death grief and/or PGD). In addition, results related to factors associated (or not associated) with grief were extracted for quantitative studies. For qualitative studies,

themes identified by original authors and findings related to factors linked with grief, such as quotations and text related to the findings, were extracted. If relevant information was not presented sufficiently, it was recorded as “not reported”. Original authors were not approached for clarification or further information.

Study Risk of Bias Assessment

The methodological quality and risk of bias in included studies were assessed using the Joanna Briggs Institute Critical Appraisal Tools. The Checklist for Analytical Cross-sectional Studies (Moola et al., 2017) was used for quantitative studies. This tool consists of 8 items, which assess different aspects of the methodological quality and reporting quality such as criteria for inclusion, description of subject and setting, identification and management of confounding factors and the validity of measures and statistical analysis used. The Checklist for Qualitative Research (Lockwood et al., 2015) was used for qualitative studies. This tool is composed of 10 items, which assess different aspects of the methodological quality and reporting quality such as the philosophical premises, data collection methods, interpretation of results, influence of the researcher and validity of the conclusion.

Two independent reviewers (APT and TB) assessed and scored each study using the checklists independently. Each checklist was first piloted with two studies to ensure both reviewers had the same understanding of the items. Following this, the reviewers scored all studies independently. Disagreements were resolved through discussion and a third reviewer (NK).

Synthesis Methods

The convergent integrated approach according to the Joanna Briggs Institute guidance on methodology for mixed methods systematic reviews was used to synthesise the findings (Stern et al., 2020). Following the guidance, quantitative data were converted into qualitative data and results from the quantitative studies and findings from the qualitative studies were thematically synthesised. For example, when extracting information regarding the results of statistical analysis conducted in quantitative studies, the relevant text summarising the findings was recorded (e.g., “the factors that increased risk of PGD compared to low risk were having a recent bereavement and being a spouse or partner of

the deceased"). Therefore, extracted information from each study included data in the forms of not only quotations but also text relevant to results and findings within each study (Supplementary Table 2.2 in appendices section). First, APT and TB independently reviewed and created codes for extracted data. Initial codes were compared, discussed and agreed. Codes were then reviewed by three reviewers (APT, TB and NK). Similar codes were grouped into larger categories through discussion, which led to the development of meaningful interpretive themes and sub-themes. Relationships between themes and sub-themes were discussed and each theme and sub-theme were defined through discussion among three reviewers (APT, TB and NK).

Results

Study Selection

Figure 2.1 presents a flow diagram illustrating the study selection process. The search identified 752 studies, of which 85 were excluded as duplicates. The remaining 667 studies were screened based on title and abstract. Thirty-seven studies were deemed potentially relevant and therefore, full texts were obtained and subjected to full eligibility screening. This resulted in nine studies eligible for the review. Two additional studies were identified through a hand search, retrieved, and screened for inclusion, from which only one was eligible. In total, 10 studies were included in this review for analysis.

Study and Participant Characteristics

Participant characteristics

The characteristics of the participants are summarised in Table 2.1. Of the 10 studies included, two studies were quantitative (cross-sectional) studies, which used the same sample (n=393), though reported different outcomes. The remaining eight studies used a qualitative approach. These studies had a relatively small sample size ranging from 4 to 28 except for one study, which qualitatively analysed free-text survey responses collected using the same sample as the two included quantitative studies (n=393). The majority of studies were conducted in Australia (n=6) and most studies recruited participants from MND

Associations (n=6). Most studies recruited former carers or both current and former carers, while only one study solely recruited carers currently supporting the person living with MND. Carer age ranged from 22 to 91 years across seven studies that provided the information. The majority of carers were female spouses of the person living with MND.

Outcome

The two quantitative studies included in the current review focused on post-death grief and PGD as outcomes and used the Prolonged Grief Disorder Diagnostic Tool (PG-13) to measure prolonged grief responses. No quantitative study investigated factors associated with anticipatory grief. Of the eight qualitative studies included, one study solely targeted anticipatory grief by recruiting current carers and three studies focused on post-death grief only. The remaining four qualitative studies targeted experiences over a longer period and investigated both anticipatory and post-death grief or post-death and PGD.

Risk of Bias in Studies

The results of methodological quality rating for the two quantitative studies are presented in the supplementary Table 2.3 in the appendices section. One study presented a high methodological quality meeting all criteria. The other study demonstrated a lower quality due to variables of interest not being measured in a reliable way and confounding factors not being considered during the data analysis. The results of methodological quality rating for the eight qualitative studies are presented in the supplementary Table 2.4 in the appendices section. The quality of included qualitative studies varied, with studies fulfilling between 4 and 9 out of 10 criteria of the tool. The majority of studies did not demonstrate a clear congruence between the philosophical perspective the study was based, and the methodological approach used. None of the studies acknowledged or addressed the influence of the researcher on the research or the research process on the researcher.

Figure 2.1

PRISMA 2020 Flow Diagram for Included Articles

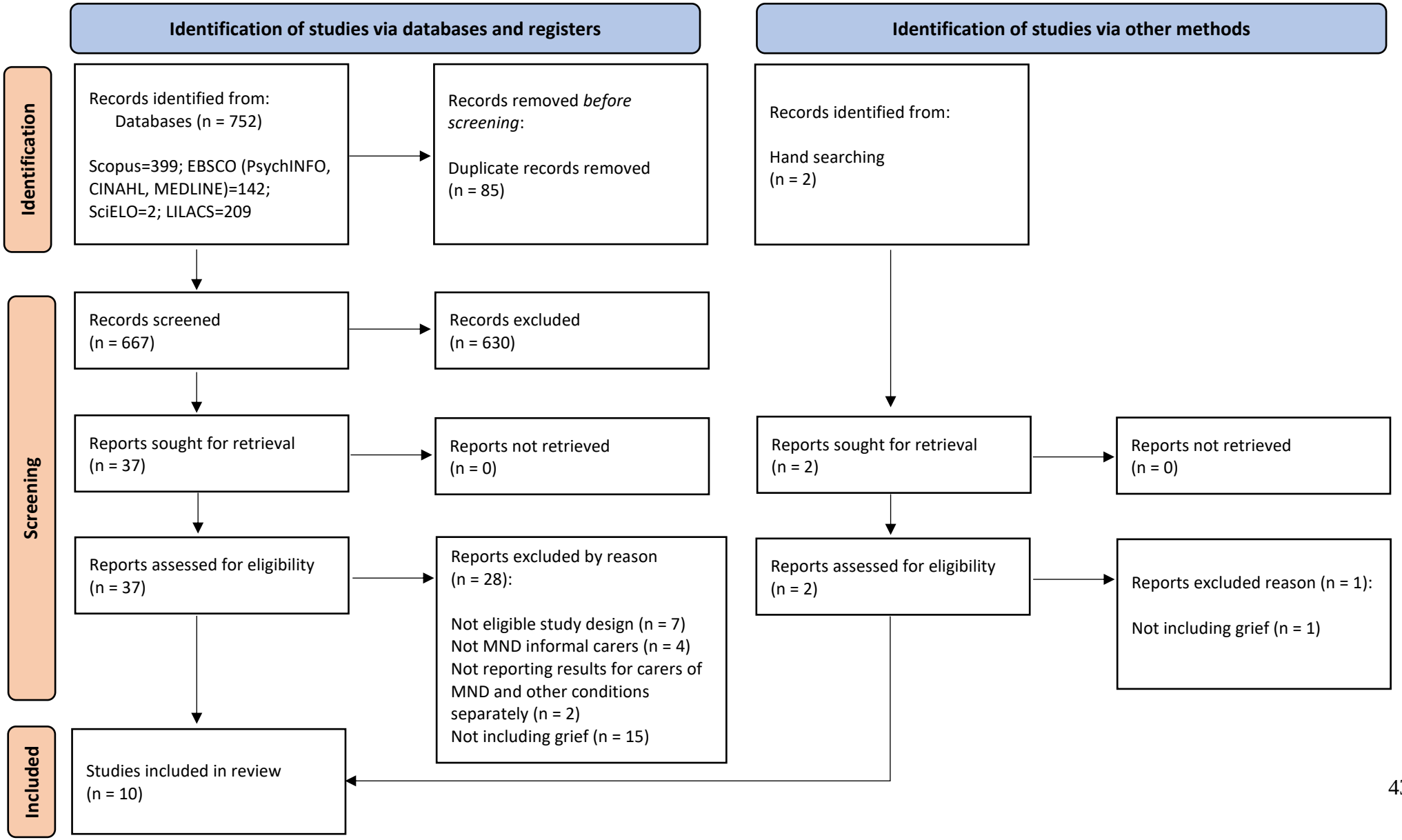


Table 2.1

Characteristics of Included Studies

First author (year)	Country	Carer type Sample size	Place of recruitment	Carer gender (Female %)	Mean age (SD) Age range	Relationship (Spouse %)	Type of grief	Validated measure of grief used
Quantitative (cross-sectional) studies								
Aoun (2021a)	Australia	Former n=393	MND Associations	73.8	63.1 (12.7) 22-91 years	72.2	Post-death Prolonged	PG-13
Aoun (2020)	Australia	Former n=393	MND Associations	73.0	63.5 (12.3) 22-91 year	73.3	Prolonged	PG-13
Qualitative (individual interview) studies								
Aoun (2012)	Australia	Former n = 16	MND Associations	81.3	65.3 (10.3) NR	100.0	Post-death Prolonged	PG-13
Aoun (2021b)	Australia	Former n = 393	MND Associations	73.0	63.5 (12.3) 22-91 years	73.7	Post-death Prolonged	PG-13
Poppe (2022)	Switzerland	Former n = 14	ALS centres	96.0[1]	NR 28-74 years[1]	NR	Post-death	NA
Ray (2007)	Australia	Current n = 24	MND Association	58.3	NR 24-82 years	70.8	Anticipatory	NA
Ray (2014)	UK Australia	Current and former n = 13	MND Associations	NR	NR	92.3	Anticipatory Post-death	NA

Solomon (2015)	US	Former n = 4	Participants known to principal investigator	25.0	NR 52-79 years	25.0	Post-death	NA
Warrier (2019)	India	Former n = 7	National tertiary care centre	71.4	44.6 (9.3) 32-56 years	85.7	Post-death	NA
Whitehead (2012)	UK	Current and former n = 28	MND care and research centre	50.0	NR	NR	Anticipatory Post-death	NA

Note. 1.The study only reported gender distribution and age range for 24 informal carers originally recruited to the study. Of these, only 14 were included in the analysis. Current = carers currently caring for a person living with MND. Former = carers who were caring for a person living with MND in the past. ALS = amyotrophic lateral sclerosis. MND = motor neurone disease. PG-13 = Prolonged Grief Disorder Diagnostic Tool. SD = standard deviations. NA = Not applicable (not used). NR = Not reported. UK = United Kingdom. US = United States.

Results of Syntheses

Five overarching thematic categories were generated to illustrate factors associated with informal MND carers' grief experiences. Figure 2.2 outlines the five key themes and sub-themes and how each sub-theme is associated with the different grieving processes (anticipatory grief, post-death and/or PGD). The five overarching themes were (1) nature of MND, (2) familial and social life, (3) support, (4) carers' emotional reactions and (5) perceptions and experiences of death. A list of illustrative quotations and summary text supporting each sub-theme is provided in the appendices section (Supplementary Table 2.2).

Nature of MND

The findings demonstrated that the nature of MND, such as unclear progression of the condition and high demands of caregiving, was associated with the grieving processes of carers of pwMND. Three sub-themes were identified: (1) knowing about MND, (2) uncertainty and unpredictability and (3) negative experiences of caregiving.

Knowing about MND. Two qualitative studies reported that knowing about the trajectory and progression of MND was linked to experiencing anticipatory grief and post-death grief (Aoun et al., 2012; Ray et al., 2014). For example, knowing the nature of MND in the early stage (incurable like other conditions such as cancer) brought greater feelings of hopelessness, having a negative impact on anticipatory grief (Aoun et al., 2012). Conversely, the findings demonstrated that the carers' prior knowledge about MND can also have a positive impact on anticipatory and post-death grief processes (Ray et al., 2014). The carers' prior knowledge enabled them to construct the death of the person living with MND as a positive release from MND, while carers' lack of knowledge (being unprepared for the symptoms of dying) led to greater loss of hope, negatively affecting anticipatory and post-death grief processes (Ray et al., 2014).

Uncertainty and unpredictability. Three qualitative studies highlighted that the trajectory and progression of MND elicitated feelings of uncertainty and unpredictability in carers of pwMND, impacting negatively on their anticipatory and post-death grief processes (Ray & Street, 2007; Ray et al., 2014; Warrier et al., 2019).

The lack of a set trajectory in MND meant carers faced unforeseen changes, negatively affecting their anticipatory grief (Ray & Street, 2007). Additionally, the way the death of the person living with MND occurred, such as unexpected timing of death (Warrier et al., 2019), or it not following the usual course of MND (Ray et al., 2014), affected carers' anticipatory and post-death grief negatively.

Negative experiences of MND caregiving. Four qualitative studies reported distress related to caregiving and re-experiencing such negative caregiving experiences had negative impacts on the three grieving processes (Aoun et al., 2012; Aoun, Noonan et al., 2021; Poppe et al., 2022; Ray & Street, 2007). For example, carers' exposure to a continual physical and emotional caregiving burden and the physical degeneration of the person living with MND had a negative effect on their anticipatory and post-death grieving processes (Poppe et al., 2022; Ray & Street, 2007). Moreover, symptoms of MND made the disease a difficult illness experience and recalling such experiences after the death of the person living with MND (Aoun, Noonan et al., 2021) and re-experiencing the painful emotions related to death (Aoun et al., 2012) were linked to PGD.

Familial and social life

Findings from the literature suggested that the demographic characteristics of the carer and the person living with MND, and the changes in their intimate relationship and social life impacted carers' grieving processes. Four sub-themes were identified: (1) demographics of the carer and the person living with MND, (2) caught up in loss, (3) relationships and changes in roles and (4) rebuilding life.

Demographics (carer and person living with MND). Only one quantitative study exploring the association between carer- and patient-related demographic factors and PGD was identified (Aoun et al., 2020). Factors associated with a higher risk of PGD as measured by the PG-13 were: being a spouse or partner of the person living with MND, the age of the deceased person living with MND being less than 60 years, longer hours of care provided in the last 3 months prior to the death of the person living with MND, the time of caring being less than one year and a half and the recent death of the person living with MND (bereavement of less or equal to 12 months).

Carers' age, gender, employment status, cultural background and education levels were not associated with higher PG-13 scores (Aoun et al., 2020). One qualitative study also identified that the long hours of care provided negatively impacted carers' post-death grief (Warrier et al., 2019).

Caught up in loss. Six of the eight qualitative studies reported carers' loss of social life and purpose in life, and feelings of loneliness were associated with grieving processes (Aoun et al., 2012; Aoun, Noonan et al., 2021; Poppe et al., 2022; Ray et al., 2014; Ray & Street, 2007; Warrier et al., 2019). The losses carers experienced during the trajectory of the disease, such as feeling deprived of a social life or retirement plans, were related to a negative anticipatory grief process (Ray & Street, 2007), while the loss of purpose in life experienced by carers after the person living with MND's death was associated with post-death grief (Aoun, Noonan et al., 2021). Carers also reported difficulty in mentally moving away from their caregiving role (Ray et al., 2014) and the person living with MND after their death (Aoun, Noonan et al., 2021) which negatively impacted on both anticipatory and post-death grief. Loneliness due to the absence of the person living with MND (Poppe et al., 2022) and difficulties in adjusting to and re-engaging in a new life without the person living with MND (Aoun, Noonan et al., 2021) had a negative impact on post-death grief. Moreover, a constant series of loss experiences leading to feelings of hopelessness were negatively associated with PGD (Aoun et al., 2012).

Relationships and changes in roles. Carers' perceptions of the relationship between them and the person living with MND and the changes in roles in their relationship were found to be important factors affecting carers' grieving processes in four qualitative studies (Aoun et al., 2012; Ray & Street, 2007; Ray et al., 2014; Solomon & Hansen, 2015). For example, feeling uncertain in terms of what it meant to be a partner (Ray & Street, 2007) and experiencing a change in roles from being a spouse to a carer (Aoun et al., 2012) were predominant factors negatively affecting anticipatory grief. Being able to focus on the relationship with the person living with MND in a safe and relaxed context (i.e., home) at the end of life impacted positively on carers' anticipated and post-death grief processes (Solomon & Hansen, 2015). An

open communication style used among family members also created a rich environment towards the end of life and emphasis on family relationships, which was related to a positive post-death grief process (Solomon & Hansen, 2015).

*Rebuilding life***.** Several factors impacting positively on carers' post-death grief were identified in two qualitative studies. These included factors related to how carers re-engaged in a new life and kept active after the person living with MND's death (Aoun, Noonan et al., 2021; Poppe et al., 2022). For example, spending time on self-care, self-reflection and self-improvement helped carers to cope with post-death grief (Aoun, Noonan et al., 2021) Furthermore, doing new things (Aoun, Noonan et al., 2021) keeping busy (Aoun, Noonan et al., 2021; Poppe et al., 2022) and being with others (Poppe et al., 2022) were also important factors in effectively managing their grieving process after the death of the person living with MND.

Support

The quality of support provided to MND informal carers and how it was received by them, during and after the trajectory of the disease, was presented as a fundamental aspect impacting carers' grief. Four sub-themes were identified: (1) negative experiences with healthcare professionals, (2) end of life and bereavement support, (3) psychological support and (4) informal support.

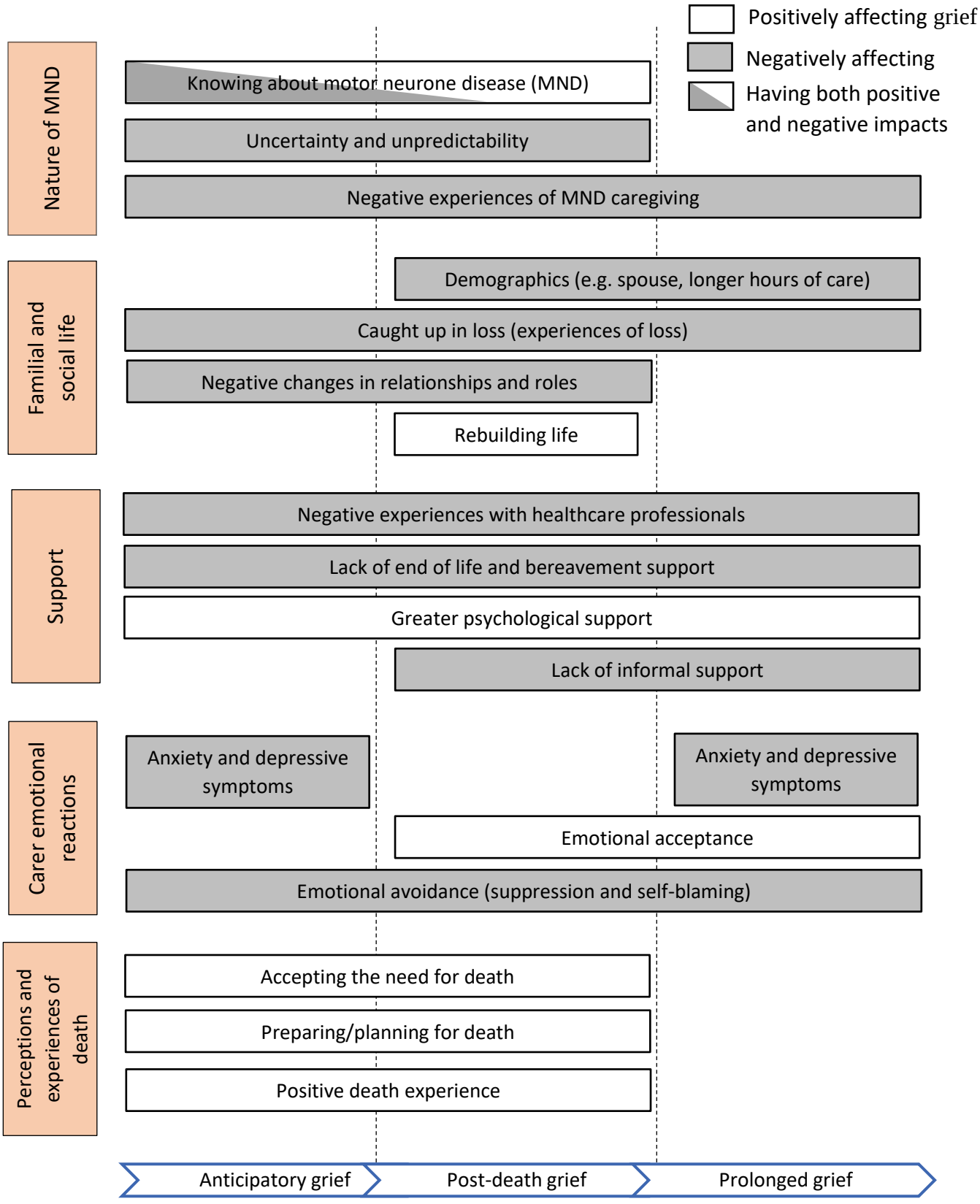
Negative experiences with healthcare professionals. Three qualitative studies found that the undesirable interactions with healthcare professionals experienced by carers negatively affected their grieving processes (Aoun et al., 2012; Aoun, Noonan et al., 2021; Ray et al., 2014). For example, healthcare professionals' unempathetic way of communicating the diagnosis of MND had a negative impact on anticipatory grief (Aoun et al., 2012). Carers' disrespected desires concerning healthcare practices, such as resuscitation decisions, and the lack of choices over the healthcare provided negatively affected carers' anticipatory and post-death grief (Ray et al., 2014). Furthermore, the failure of support from formal services also negatively impacted post-death grief, leaving carers with feelings of anger which was associated with risk of PGD (Aoun, Noonan et al., 2021).

End of life and bereavement support. Four qualitative studies (Aoun et al., 2012; Aoun, Noonan et al., 2021; Ray et al., 2014; Whitehead et al., 2012) and one quantitative study (Aoun et al., 2020) identified that end of life and bereavement support received by carers affected their grieving processes. For example, satisfactory and favorable experiences with hospital staff at the person living with MND's end-of-life (Ray et al., 2014) affected anticipatory and post-death grief processes positively. Bereavement support received after the person living with MND's death also positively affected post-death grief (Whitehead et al., 2012), while not having access to support or receiving unfavorable support in the early post-death days, the withdrawal of services and the end of contact from services negatively affected carers' post-death bereavement (Whitehead et al., 2012) and heightened the risk of PGD (Aoun et al., 2020). The lack of the person living with MND's early access to palliative care services and home-based services were negatively related to carers' PGD (Aoun et al., 2012).

Psychological support. Three qualitative studies (Aoun, Noonan et al., 2021; Poppe et al., 2022; Warrier et al., 2019) and one quantitative study (Aoun, Cafarella et al., 2021) identified that psychological and counselling services received by carers had positive impacts on grieving processes. Counselling received while providing care and after the death of the person living with MND was positively associated with carers' both anticipatory and post-death grief (Aoun, Noonan et al., 2021). Psychological/emotional support was found to have a positive impact on post-death grief in the qualitative studies (Poppe et al., 2022; Warrier et al., 2019), whilst not receiving such support was associated with risk of PGD in the quantitative study (Aoun, Cafarella et al., 2021).

Figure 2.2

Factors Affecting Grieving Processes



Informal support. Two qualitative studies (Aoun, Noonan et al., 2021; Poppe et al., 2022) and two quantitative studies (Aoun et al., 2020; Aoun, Cafarella et al., 2021) identified that informal support received by carers influenced their grieving processes. Receiving support from MND specific support organizations, local MND Associations, friends, community and family members (Aoun, Noonan et al., 2021) as well as support from peers (Poppe et al., 2022) had a positive effect on carers' post-death grief. Lack of support from family and MND-related organizations (Aoun, Cafarella et al., 2021) as well as conflictual family functioning (Aoun et al., 2020) were found to be associated with a higher risk of PGD in quantitative studies (Aoun et al., 2020; Aoun, Cafarella et al., 2021).

Carers' emotional reactions

Carers' psychological symptoms and how carers responded to such psychological challenges were associated with carers' grieving processes. Three sub-themes were identified: (1) anxiety and depressive symptoms, (2) emotional acceptance and (3) emotional avoidance.

Anxiety and depressive symptoms. One qualitative study (Whitehead et al., 2012) and one quantitative study (Aoun et al., 2020) identified that anxiety and depressive symptoms were negatively linked to carers' grieving processes. Worries about the future such as carers worrying about how they would cope as the disease advanced, how death would occur and whether the child/ren of a person living with MND would cope after the loss of a parent were found to be linked to carers' anticipatory grief in the qualitative study (Whitehead et al., 2012). Higher anxiety and depressive symptoms assessed by standardised measures were found to have a strong association with higher PGD risk in the quantitative study (Aoun et al., 2020).

Emotional acceptance. Three qualitative studies identified that carers' ability to accept the illness, the recognition they had provided good care and their capability of embracing the feelings of grief had positive impacts on their grieving processes (Aoun et al., 2012; Aoun, Noonan et al., 2021; Poppe et al., 2022). Accepting the bereavement experience as part of life, expressing and allowing grief as part of adapting to the loss of the person living with MND (Aoun, Noonan et al., 2021) and

viewing grief as a natural process (Poppe et al., 2022) were associated with a positive post-death grieving process. Comments from others reassuring carers that they had done a good caring job, also had positive impacts on their post-death grief (Poppe et al., 2022). Carers' ability to accept the person living with MND's illness as terminal (Aoun et al., 2012), their acknowledgement of not dwelling on the challenges brought by MND and their capability of appreciating the days they had together with the person living with MND (Aoun, Noonan et al., 2021) were associated with a lower risk of developing PGD.

Emotional avoidance. Five qualitative studies identified that carers' tendency to avoid or control thoughts and feelings related to caregiving and their judgmental attitudes, such as self-blaming and self-doubting, had negative impacts on the three grieving processes (Aoun et al., 2012; Aoun, Noonan et al., 2021; Ray and Street, 2007; Warrier et al., 2019; Whitehead et al., 2012). Self-doubting, such as carers questioning themselves regarding their capacity to continue with caregiving demands had a negative impact on their anticipatory grief process (Ray & Street, 2007). Self-criticism and guilt, such as carers thinking that they could have provided better care were associated with carers' post-death grief (Warrier et al., 2019; Whitehead et al., 2012). Trying or pretending to remain strong after the person living with MND died (Aoun, Noonan et al., 2021; Warrier et al., 2019) also had negative impacts on carers' post-death grief. Limiting emotional reactions to the person living with MND's illness and avoiding thinking about the person living with MND's death were linked to a higher risk of PGD (Aoun et al., 2012).

Perceptions and experiences of death

Anticipating and preparing for death and reactions to how the death occurred were associated with carers' grieving processes. Three sub-themes were identified: (1) accepting the inevitability of death, (2) preparing/planning for death, and (3) death experience.

Accepting the inevitability of death. This sub-theme was evidenced by two qualitative studies (Ray et al., 2014; Warrier et al., 2019). Carers' acceptance of the inevitable death as the end of suffering and no further losses for the person living with MND positively affected their anticipatory and post-death grief (Ray et al., 2014).

Additionally, carers experienced a sense of relief when the person living with MND died as the suffering ended, leading to a positive post-death grief process (Warrier et al., 2019).

Preparing/planning for death. Four qualitative studies reported that the carer and the person living with MND planning for death together, such as discussing wishes about how they preferred death to occur, helped carers prepare for their grieving processes before death and during their bereavement (Aoun, Noonan et al., 2021; Poppe et al., 2022; Ray et al., 2014; Solomon & Hansen, 2015). For example, having conversations and making plans on dying and death allowed carers to experience some comfort and these had positive impacts on carers' anticipatory and post-death grief (Ray et al., 2014) and lowered the risk of developing PGD (Aoun, Noonan et al., 2021). Furthermore, supporting the person living with MND in their desire to die at home, created an ideal environment for carers' post-death grieving process and gave carers time to be prepared mentally and emotionally for the person living with MND's death (Solomon & Hansen, 2015).

Death experience. Four qualitative studies identified the importance of carers' experiences on how the death occurred and their reactions towards it and how these affected their grieving processes (Poppe et al., 2022; Ray et al., 2014; Solomon & Hansen, 2015; Whitehead et al., 2012). The person with MND dying at home was found to have a positive effect on anticipatory grief (Solomon & Hansen, 2015) and on post-death grief (Ray et al., 2014; Solomon & Hansen, 2015) as it enabled time to say goodbye to the person living with MND. Most of the factors related to this sub-theme (death experience) impacted positively on post-death grief. These experiences included seeing that death occurred before MND had become too severe (Whitehead et al., 2012), perceiving death as a non-traumatic event (Poppe et al., 2022) carers' feeling that they had closure with the person living with MND (Whitehead et al., 2012), and feeling that the person living with MND had no unaccomplished desires or expectations and was not afraid of dying (Solomon & Hansen, 2015). However, when the death of the person living with MND was felt to be undignified, carers were left

with regrets about how death had occurred, leading to negative grieving processes (Ray et al., 2014).

Discussion

This review aimed to identify factors associated or linked with anticipatory grief, post-death grief and prolonged grief disorder in informal carers of people living with MND. The findings suggested that there may be factors particularly important to target during the early diagnosis of MND as they might affect both anticipatory and post-death grief. These factors included carers' need for greater knowledge about the progression of the disease, coping with changes in the relationship with the care recipient, reduction of anxiety and depressive symptoms of carers, and encouragement of planning for the death of the person living with MND. Findings also highlighted that how carers adjusted and rebuilt life without the person living with MND such as not being alone and engaging in activities, are important factors to consider during their post-grief period. There were factors that were more likely to be relevant to the risk of developing prolonged grief disorder, such as being a spousal carer, formal and informal support received and emotional acceptance. Factors that may affect all three types of grief, including prolonged grief disorder, were also identified, such as negative experiences of caregiving, getting caught in loss experiences, lack of end of life and bereavement support, lack of psychological support and emotional avoidance coping.

Some factors identified in this review were consistent with the findings of previous reviews on factors associated with grief in other populations such as dementia, patients in intensive care units and the general bereaved population (Chan et al., 2013; Crawley et al., 2023; Mason et al., 2020; Sanderson et al., 2022) such as carer depression (Chan et al., 2013; Crawley et al., 2023; Mason et al., 2020), carer anxiety (Mason et al., 2020), lack of social support (Crawley et al., 2023; Mason et al., 2020), being in a spousal relationship (Chan et al., 2013; Crawley et al., 2023; Mason et al., 2020; Sanderson et al., 2022), difficulty in accepting the death (Mason et al., 2020), being unprepared for death (Chan et al., 2013; Crawley et al., 2023; Sanderson et al., 2022) and not accepting the death (Mason et al., 2020). This consistency in factors identified may be due to the fact that, similar to pwMND, people living with other chronic conditions, such as dementia, are often cared by their

spouses (Brodaty & Donkin, 2009; Johansson et al., 2021), and caregiving can affect informal carers' mental health regardless of the condition (Savage & Bailey, 2004; Schulz & Sherwood, 2008). Moreover, it has been reported that 50% of pwMND will present with behavioural changes and 15% will develop frontotemporal dementia (Bäumer et al., 2014; Srong et al., 2017). This overlap between two neurodegenerative diseases, MND and dementia, may explain why carers of both populations face similar grieving experiences.

There are no systematic reviews on factors affecting grief in carers of people living with other rapidly progressing neurodegenerative conditions such as Parkinson's disease, or other neurological conditions such as traumatic brain injury and stroke. Therefore, it is not possible to compare the findings of this systematic review with those of carers of people affected by neurodegenerative conditions of fast progression and poor clinical prognosis. However, there is some emerging evidence. For example, a qualitative study involving five carers of people that had suffered a stroke identified similar factors affecting their grief experiences such as changes in roles and relationships (Hughes & Cummings, 2020). Two further qualitative studies, which involved 16-24 carers of people that had suffered a stroke, identified similar factors such as uncertainty about the future and negative emotions generating emotional distress (Gosman-Hedström & Dahlin-Ivanoff, 2012; McCurley et al., 2019). One quantitative study involving 29 carers of people living with Parkinson's disease found a strong relationship between depression, burden and anticipatory grief (Fox et al., 2020). Due to the limited evidence in other carer populations, it is not possible to conclude whether the factors identified in this systematic review are relevant to wider carer populations.

Nevertheless, it is important to highlight that some of the factors found in the current review may be particularly pertinent for this population such as the knowledge of MND, the uncertainty and unpredictability of the disease and lack of emotional acceptance and presence of emotional avoidance. This might be due to the lack of a set trajectory in MND and the rapid progression of MND symptoms (Bäumer et al., 2014). These findings suggest that tailored carer interventions for this population may be useful to help carers cope with their grieving processes prior to and after the death of the person living with MND and examining these potential interventions is an important next step.

Limitations of evidence

The number of included studies was relatively small (n=10) and were mostly from Australia, and thus the results may not be generalisable to populations from other countries and cultures. Most included studies were qualitative studies with relatively small datasets, meaning the generalisation of the findings might be limited. Furthermore, all factors were not consistently explored across the three grieving processes. For example, demographics were mainly explored in relation to prolonged grief disorder in a single quantitative study. Therefore, the impact of such factor on anticipatory grief is unknown. These suggest that the findings of this review need to be interpreted with caution.

Implications

Clinical implications

A recent systematic review of interventions targeting psychological wellbeing for carers of pwMND (Cafarella et al., 2022), which included a single study that targeted grief among other outcomes, concluded that the majority of studies did not demonstrate significant benefits on outcomes such as carer anxiety and depression. Interventions used in the studies included in the review were mainly single-component interventions (e.g., mindfulness alone, dignity therapy). Considering the findings of the current review, multi-component interventions may be more beneficial for treating grief in this population.

Early educational interventions aimed at providing information about MND symptoms, including how the disease may progress differently across pwMND, and available support resources could be beneficial for coping with both anticipatory and post-death grief. However, these should be provided with psychological support or counselling as increased knowledge could lead to greater negative grieving emotions before it can help carers to cope with post-death grief. Psychological interventions and counselling could also be beneficial to support carers from the point of diagnosis. These could help carers to cope with the emotional impact of the changes in their roles and relationships, reduce anxiety and depressive symptoms and facilitate emotional acceptance rather than emotional avoidance. Designing interventions tailoring end-of-life care for planning for the death could reduce post-death grief symptoms and prolonged grief disorder risk. Additionally, it would

be beneficial to consider educational interventions with healthcare professionals to raise awareness and provide information on how the relationship between healthcare professionals and carers impacts carers' emotional wellbeing.

Research implications

Factors associated with anticipatory grief were less reported and no quantitative study explored factors associated with this grieving process. This might be due to the lack of a standardised measure to assess anticipatory grief in carers of pwMND. Future research should consider designing a validated tool to screen anticipatory grief in this population, which allows researchers to identify factors associated with grieving experiences prior to death. Longitudinal studies assessing the impact of factors affecting anticipatory and post-death grief overtime should be conducted to build on further understanding of the strongest predictors of grief in this population. Moreover, future research should explore the efficacy of interventions targeting the factors identified in this review on the grieving processes in carers of pwMND.

The aforementioned clinical recommendations could potentially be generalisable to other progressive disorders. Future research could explore whether similar risk factors equally contribute to grieving reactions across different carer populations. This would contribute to the general knowledge of how to address grieving experiences in informal carers.

Methodological limitations

There are some methodological limitations, which need to be considered. Searches were limited to studies published in English, Spanish and Portuguese in this review, which may have introduced bias. No studies were excluded on the basis of quality in this review and some of the included qualitative studies demonstrated relatively low quality. Due to identifying limited quantitative studies, both quantitative and qualitative results were incorporated into the same thematic synthesis and the term association was used to demonstrate factors such as situations or conditions that may accompany the grieving processes throughout this review. Since most data for the synthesis was qualitative, we can only suggest factors that the original participants or authors linked to, or mentioned in

relation to grief processes and cannot verify statistically whether these factors are associated with grief.

Conclusion

This review demonstrated that various factors may affect anticipatory grief, post-death grief and prolonged grief disorder in informal carers of people living with MND. Some of these factors may be particularly pertinent to this population, such as the knowledge of MND (as a relative rare condition and its progression), the uncertainty and unpredictability of the progression of the disorder, and emotional acceptance and avoidance. Therefore, tailored interventions targeting specific factors affecting grieving processes in this population should be considered.

This review also highlighted the limited research on anticipatory grief among carers of this population and suggested that early carer interventions targeting anticipatory grief could be beneficial. Addressing anticipatory grief early on might not only support carers during the trajectory of MND and post-death bereavement but also reduce the risk of developing prolonged grief disorder. Future qualitative research explicitly exploring current carers' experiences of changes and losses and quantitative studies utilising large sample sizes with a particular focus on factors associated with anticipatory grief could elucidate the influence of specific personal, clinical and social factors affecting carer anticipatory grief in MND. Such research could enhance support strategies for carers. The following chapters are structured to address this gap in the current literature.

Chapter 3: Experiences of changes and losses of family carers currently supporting people living with Motor Neurone Disease

Building upon the insights elucidated from the preceding chapter, it became evident that factors related to anticipatory grief were less reported when compared to factors linked to post-death grief and prolonged grief disorder. In order to advance our understanding of anticipatory grief in carers of people living with MND, it seems crucial to delve into the experiences of changes and losses carers encounter during the progression of the disease. Additionally, exploring the coping mechanisms employed to navigate daily challenges is essential for a comprehensive understanding of carers' emotions and feelings. By understanding carers' emotional experiences and strategies facilitating emotional coping, we can capture the complexity and depth of the emotional journey carers transit. Qualitative research allows for the exploration of these multifaceted experiences.

This chapter is based on the published paper:

Trucco, A.P., Mioshi, E., Kishita, N., Barry, C., & Backhouse, T. (2023). Navigating an emotional journey: A qualitative study of the emotional experiences of family carers currently supporting people living with Motor Neurone Disease. *Palliative & Supportive Care*. [Advance online publication] https://doi.org/10.1017/S147895152300158X

Introduction

Most people living with MND (pwMND) are cared for at home by a family member (Pagnini, 2013; Peters et al., 2012). Due to the disabling nature of the disease, family carers have a demanding role during caregiving and transit a parallel journey with the person living with MND (Rabkin et al., 2009). Previous systematic reviews (Aoun et al., 2013; Mockford et al., 2006) explored experiences of MND family carers revealing compromised physical and psychological health, diminished quality of life, strained relationships, and challenges in accessing MND information and service provision. Further qualitative research highlighted

the many practical tasks carers had to take care of and learn (Aoun et al. 2012), carers' fears for the future, and feelings of anger and frustration (Oyebode et al., 2013; Whitehead et al., 2012). Qualitative studies have also examined carers' assistance with gastrostomy (Stavroulakis et al., 2016), carers' involvement in decision making (Hogden et al., 2013), non-invasive ventilation's limited influence on carer burden (Baxter et al., 2013) and the need for early palliative care (Flemming et al., 2020). Carer grief has also been explored (Oyebode et al., 2013, Aoun et al., 2012, Whitehead et al., 2012). In addition, a narrative review revealed factors contributing to carer emotional distress, such as the severity of MND symptoms, carers' coping styles, relationship satisfaction, and social support (Gluyas et al., 2017). Emotional wellbeing refers to an individual's positive feelings towards life, including their everyday experiences and reflections about life satisfaction and meaning, and the ability to accomplish goals in life (Park et al., 2022). In this paper, we will refer to emotional wellbeing to describe the emotional experiences of MND family carers, which contribute to their life satisfaction and quality of life.

A review of qualitative literature (Holkham & Soundy, 2018) described diverse experiences impacting MND carers' emotions, such as changes in their lifestyle compromising their personal and social time, and isolation arising from limited communication with healthcare professionals (HCPs), the person living with MND, family members and friends and in their relationships' dynamics. Similarly, a recent systematic review examining factors affecting MND informal carers' grieving processes (Trucco, Backhouse et al., 2023) emphasised how factors such as the uncertainty of the disease, being deprived of a social life, and changes in roles and communication affected carers' emotions during the progression of MND and highlighted the need for emotional support.

Some studies have examined carers' coping strategies to manage their emotional challenges. A qualitative study reported that some coping strategies encompassed carers' attitudes (e.g., having a positive approach, not planning ahead or anticipating problems), problem-solving skills (e.g., negotiating solutions with the person with MND), managing time effectively and socialising with others (Gent et al., 2009). Another qualitative study, found that strategies used were the gradual acceptance of MND, engaging in meaningful

activities, focusing on positive and present aspects of life, spending time without thinking about MND and receiving support from HCPs, friends, and family (Pinto et al., 2021).

The need to better support family carers of this population in the emotional, psychological, practical, informational, and social areas has been documented by review literature (Gluyas et al., 2017; Oh and Kim, 2017). Nevertheless, research focusing specifically on understanding which personal coping strategies family carers use to maintain their emotional wellbeing to be able to manage their own emotions remains sparse. Thus, the aim of this study is to explore the emotional experiences and coping strategies of family carers currently supporting people living with MND. By elucidating carers' emotional journeys, we aim to identify relevant areas of focus for potential interventions to support and meet the needs of carers' emotional wellbeing.

Methods

Design

This was an interpretive descriptive study (Thorne et al., 2004; Thorne, 2016) using semi-structured interviews and a reflexive thematic analysis (Braun & Clarke, 2006, 2021). We used an interpretive descriptive approach as it seeks to uncover and understand recurring themes and patterns within subjective human experience while accounting for participants' and researchers' subjectivity. Beyond the mere description of the phenomenon, it generates credible and relevant experiential knowledge applicable to care practice (Thorne, 2016).

Participants and recruitment

We recruited 14 current family carers from MND carers' support groups via online or face-to-face presentations, MND clinics providing leaflets to family carers, and media releases with study information. Furthermore, participants taking part in an MND questionnaire study, part of a higher degree project, were asked to provide their details if interested in the present study. We contacted potential participants by email or telephone and provided a participant information sheet. To be included in the study, participants had

to be at least 18 years old, have conversational English, have the capacity to consent for themselves and be a partner/spouse currently living with and supporting someone diagnosed with MND. Among 24 interested participants, two were ineligible, two did not join the interview due to unforeseen circumstances, four did not reply to the email sent, one was hospitalised, and one had scheduling constraints. The 14 participants (female=10; male=4), were all co-habiting spouses of a person living with MND and living in different regions of the United Kingdom (UK). All participants signed an informed consent form and completed the interview. No participants were previously known by the researchers.

Data collection

Semi-structured interviews followed a topic guide with broad and open-ended questions specifically designed by APT and TB to examine and understand how carers' experiences of caring affected their emotional wellbeing and how they coped with arising emotions (Supplementary material in appendices section). Questions were developed based on the literature and refined through discussions with two carers of pwMND and one pilot interview. APT (an experienced occupational therapist working with neurological diseases in academic and clinical settings) conducted recruitment and data collection. We assessed sample size during the research process through the constant information power appraisal method. Information power considers the study aim, sample specificity, use of theory, dialogue quality and analysis strategy to evaluate the richness and relevance of the data collected during the research process to ensure it is sufficient to address the research questions. Given our focused aim, specific participants, and the strong dialogue drawing on considerable experience of the researcher with MND carers, we reached information power after 14 interviews. At this point, no new codes and themes were being generated (Braun & Clarke, 2021b; Malterud et al., 2016). To obtain rich and in-depth accounts of participants' experiences, we used probes such as, "How did you cope with these feelings?", "Can you tell me a bit more?". By probing we aimed to generate deeper knowledge without guiding the participant to a specific response. Interviews were audio-recorded if conducted face-to-face (n=6) at a location of the participant's choosing, and video-recorded if conducted online (n=8). We conducted the interviews between August 2022 and February 2023, and they lasted on average 75:33 minutes.

We reassured participants they could withdraw from the study at any stage, not answer questions they did not feel comfortable with and take as many pauses as needed. At the end of the interview, participants were de-briefed, and encouraged to check a wellbeing contact list providing signposting to relevant services if upsetting emotions arose.

Data analysis

Interviews were professionally transcribed verbatim. Subsequently, all identifiable information was anonymised. We decided to not conduct member checking due to the sensitive nature of the study, time and burden implications for carers, and the potential negative impact on participants, since distressing emotions could be triggered when reading their transcripts (Hallet, 2013). APT and TB (an experienced social scientist post-doctoral researcher with a social care background) analysed data inductively with reflexive thematic analysis (Braun & Clarke, 2006, 2021a), which accounts for researchers' subjectivity and perspectives inflected by their position. We independently immersed ourselves in the data during data collection by repeatedly reading the transcripts and began to identify relevant patterns. We met regularly to discuss initial impressions and reflections on the data. We generated codes encompassing both surface (semantic) and underlying (latent) features, with regular discussions to examine analytical observations. Once data collection was complete, APT coded and collated all data. Transcripts were uploaded into NVivo12 Pro to assist in the management of the analysis process. By constantly comparing the codes, collated data, and our interpretations (Clarke & Braun, 2020) and asking big questions of the data such as, "What is happening here?", "What are the dimensions of this?" (Thorne et al., 1997; Thorne, 2016), we proposed initial candidate themes ensuring a coherent pattern between them and participants' experiences. EM (an experienced applied MND researcher and occupational therapist) joined to discuss codes, collated data and potential themes, which were re-checked against coded data, refined, and reviewed further to capture the overall story in the data. The final themes combined both semantic and latent meanings about carers' emotional experiences to account for the reality of their emotions and coping strategies.

Results

Participants' demographics are summarised in Table 3.1. The analysis produced three intersecting themes which reflect the emotional journey current family carers (FC) experienced while caring for a person living with MND.

The analysis examined how changes and losses due to MND impacted on carers' emotions and the coping strategies they identified as useful to face the emotions arising. An overview of the themes is presented in Figure 3.1, and coping strategies most used are summarised in Table 3.2. The three themes were:

1. Destabilisation of diagnosis
2. Adapting to new circumstances and identifying coping strategies
3. Maintaining emotional coping

Destabilisation of diagnosis

The emotional journey started when the first symptoms presented but intensified greatly when the actual diagnosis of MND was conveyed. Diagnosis triggered distress and often left carers not knowing what to do, destabilising their lives.

All participants described the impact of the diagnosis in terms of shock and devastation, characterised by feeling overwhelmed, anxious, and lost.

> *"Just utter shock…disbelief…we'd obviously heard of it, but you just don't think that you and your family are going to be affected…I was just pretty devastated..." (FC3, female)*

These emotions worsened when carers received unclear information about MND. Most participants discussed that when HCPs explained MND symptoms, progression, and prognosis, uncertainty-related emotions, stress, and anxiety reduced. MND nurses, were mentioned by some participants to provide comfort. While some participants self-searched for more information (e.g., internet, books), others preferred not to investigate further. In both cases, knowing more, or not, impacted on carers' emotions by reducing distress.

Table 3.1

Demographics Characteristics of Family Carers and People Living with MND

	Current carer (n = 14)	People living with MND (n = 14)
Age (in years)		
Mean, SD	63.71 (8.55)	67.86 (8.78)
Range	48-80	53-81
Gender (n, %)		
Female	10 (71.43%)	4 (28.57%)
Male	4 (28.57%)	10 (71.43%)
Carer relationship to person with MND (n, %)		
Spouses	14 (100%)	
Time since diagnosis (months)		
Mean, SD		37 (27.28)
Range		7-96
Residence - UK regions (n)		
London	1	
North-East	3	
Yorkshire	3	
East of England	3	
East Midlands	2	
Scotland	1	
Northern Ireland	1	
Subtype of MND (n, %)		
Amyotrophic lateral sclerosis		4 (28.57%)
Progressive bulbar palsy		1 (7.14%)
Primary lateral sclerosis		3 (21.43%)
Do not know		6 (42.86%)

> *"[Name] was given literature about MND and the different impacts…I don't want to know. I will deal with now, there's no point in reading what might happen. Because it might not...For everybody, it's an individual journey." (FC1, female)*

Participants' communication of the diagnosis to others was influenced by the carers and the person living with MND's feelings. While some carers shared the diagnosis

immediately, others delayed as they were concerned about how family members would cope with it, particularly when living far away or experiencing personal stressful situations.

> *"We hadn't told our sons because one of them was in [country] and we wanted to tell them face-to-face…we needed to come to terms with it first…we needed to accept it before…there was also this concern about how much it would affect them mentally and emotionally..." (FC12, female)*

Carers actively worked to cope with and transit the initial shock by adopting personal strategies to gradually temper the early overwhelming emotions. Knowing more about MND, or not, and taking a practical approach by focusing on what the person with MND needed to have comfort were the most common strategies used during this first period.

> *"…the initial diagnosis was difficult for both because you were entering a world of unknown, neither of us knew anything about MND…And I remember us both sitting down and thinking, well crying, and…what could I say to [name] to help him?" (FC5, female)*

Family carers described this first period as causing great destabilisation in their emotions and in their everyday activities and had difficulties embracing this new reality.

Adapting to new circumstances and identifying coping strategies

Following the impact of diagnosis, carers started experiencing everyday changes and losses due to MND and gradually adapted to these by identifying strategies to better face their circumstances.

All participants described changes in their relationship with the person with MND, mainly caused by a shift from being a spouse to a caring role and due to MND symptoms (e.g., communication and physical symptoms).

Carers also expressed having limited family time causing feelings of sadness, particularly when lacking time with children and grandchildren.

> *"One thing that I really do miss…I have a daughter in [city] with three grandchildren. I used to go over once every six weeks…wouldn't leave [name] now, so I miss that." (FC9, female)*

Participants described how losing freedom to perform and engage in personal activities led to frustration, anger, and distress. Self-care time diminished and three carers reported reducing work for caregiving. Most carers also felt deprived of a social life and expressed sadness for the lack of spontaneity to make plans, particularly if these involved holidays.

> *"And it doesn't matter what plans you have made-up until that point…if the plan was today, yesterday…we had plans that were going forward for months or years…that is completely gone out...Your whole life becomes very much more short term." (FC2, male)*

During this period, learning how to do things previously accomplished by the person with MND added to carers' emotional distress. Participants explained how they started performing new household chores, such as fixing things and cleaning, and how this contributed to feelings of anxiety and tiredness.

> *"I was doing everything…learning DIY [Do It Yourself] and how to use saws and screwdrivers and just lots of different things…probably [name] watching me and, you know, I say things and it's tough." (FC3, female)*

Feelings of resignation for not being able to change, fix, or control the present situation arose across all participants.

> *"I suppose the overall feeling is frustration…Frustration that I can't fix her; frustration that I can't make her better; frustration, how did it happen...there is nothing you can do to fix it..." (FC8, male)*

Receiving practical support from HCPs and MND organisations, such as obtaining equipment and having HCPs' appointments reassured carers that the person with MND was well supported. The lack or disorganisation of this support made carers feel anxious, upset, and disappointed.

> *"…I found it totally overwhelming, there were all these different people who were presenting themselves…two people came around, and I thought they were occupational therapists, but they were from Social Services, and we never did understand why they came to see us…" (FC6, female)*

During this period, carers gradually began to accept that their lives had changed. Carers actively found ways for not giving up and continued coping with their emotional journey, represented by sadness, tiredness, anger, frustration, and loneliness, which worsened during the nights as negative thoughts about their reality crept in. Focusing on the present and taking one day at a time were professed as the most useful strategies to help carers emotionally transit this post-diagnosis period.

Maintaining emotional coping

With time, participants identified their own emotional coping strategies. While several emotions still arose, carers were now capable of adapting and accepting continuous changes and losses while maintaining their emotional coping and not destabilising.

At this stage, informal support such as spending time with family and friends, allowed carers to not think about MND, easing negative emotions. Attending MND carers' support groups was helpful for some carers as they felt understood by others facing a similar reality. However, other carers avoided them so as not to encounter MND progression.

One carer had formal carers who came to sit and stay with the care recipient and some carers reported having access to respite care was useful and described it as recharging energy for their continuous caring role.

> *"…my family and my friends are good support…when [name] goes for respite, that's a great support to give me a break…helps me deal with things a little bit better..." (FC14, female)*

How the person living with MND faced their own challenges, changes and losses had an important impact on carers' emotions. When they were positive about the present situation and future, carers felt stronger and happier. When they felt sad, withdrew from social activities, and experienced negative emotions, carers felt distressed. Under these circumstances, carers tried to support the person living with MND by remaining positive but consequently confronted tiredness and burden.

> *"…so, I just felt I needed to support him…I had to carry it for him sort of thing. Be strong for him." (FC9, female)*

Carers' allowance (government payment received for caregiving) made carers feel their role was being recognised. However, carers were disappointed about the amount of allowance and the difficulties accessing it.

Planning for end-of-life care with the person living with MND and having a power of attorney in place made carers experience a sense of relief.

> *"And pre-planning…legal things like with power of attorney and things like that…we got all that sorted and out of the way, so that, at the time we were doing it all, it was very hard but I'm glad that's all sorted." (FC4, female)*

Table 3.2

Overview of Themes and Coping Strategies Family Carers of People Living with MND use

Destabilisation of diagnosis	**Adapting to new circumstances and identifying coping strategies**	**Maintaining emotional coping**
Knowing (or not) about MND Practical approach: focus on person with MND's needs	Practical/formal support Day-to-day approach: focus on the present	Informal support Acceptance Avoidance Respite care Focus on immediate future Being with pets Eating habits

Conversely, some carers preferred not to look into future planning, e.g., discussing preferences on whether death should occur or the possibility of moving home, as it influenced their emotions negatively.

Looking forward to doing things in the immediate future, such as meeting family or friends, or going on holidays were useful strategies most carers identified for coping with their emotions. Some carers also found emotional comfort by changing their eating habits, such as eating chocolate. Pets were also considered a source of emotional support, particularly dogs, with their presence reducing carer stress and anxiety. Furthermore, one

carer reported that having a sense of achievement by completing small tasks, such as tidying the bed, made them cope better as these were things they could control.

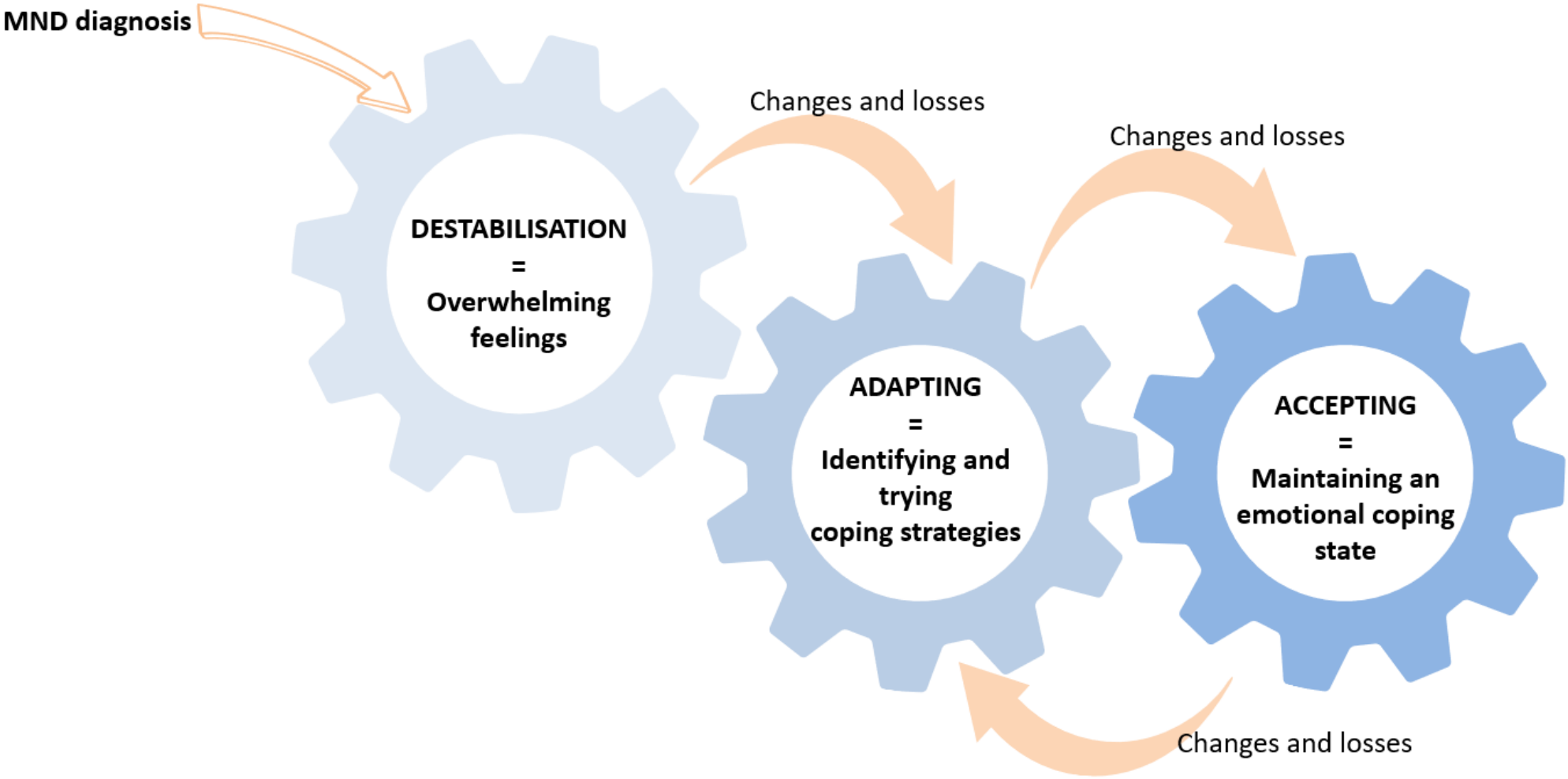
Most carers described that not thinking about what the future could bring and how they would manage with potential changes, was the strategy that best worked for them for managing their emotions.

> *"…it's a day at a time. Try and take a day at a time…just deal with each situation as it arises and try not to worry about what might be and try and live with and not die from." (FC4, female)*

At this time of their emotional journey, while carers still experienced negative emotions with new changes and losses, knowing the strategies that worked for them to maintain their emotional coping made distressing emotions ease quicker.

Figure 3.1

Emotional Journey of Family Carers Currently Supporting People Living with MND



Discussion

This study presented the emotional journey MND family carers experienced while caring for the person living with MND and the strategies they used to maintain their emotional coping when facing continuous changes and losses throughout the progression of MND. Three themes were identified. The first theme revealed the state of shock and devastation carers experienced when receiving the diagnosis and how learning and knowing about MND helped them transit this overwhelming period. The second theme described how carers experienced and gradually adapted to changes and losses happening by identifying coping strategies to manage emotions. The third theme recognised the different coping strategies used by carers, which enabled them to accept and adjust to the constant challenges of changes and losses while maintaining coping.

These findings align with a previous thematic review which identified changes and losses in relationships, future plans, daily activities and feelings of isolation (Holkham & Soundy, 2018). Previous research also identified similar coping strategies, such as focusing on the present moment, receiving support, and not thinking about MND (Pinto et al., 2021). Furthermore, studies have highlighted the importance that support from family, social networks, and formal care have on carers' emotional wellbeing (Aoun et al., 2021; Trucco, Backhouse et al., 2023). Similarly, this study revealed how being close to family, informal support, linking with networks (e.g., MND Associations) and connections with HCPs influenced carers' emotions and caring experiences positively. This study provides an in-depth understanding of carers' emotional journeys and how they adapt and adjust to new circumstances. Our findings show that when conveying the diagnosis, guidance on caring and support options should be provided. Early practical support, particularly from HCPs and MND organisations should be offered as carers' emotions ease when feeling well supported. As disease progresses, addressing isolation such as pursuing family meetings; and targeting acceptance and day to day approaches, could be beneficial. Individual differences in coping mechanisms should be considered, as some carers use avoidance strategies, i.e., not thinking about MND and withdrawing from social activities. In some cases, this avoidant style of coping might have negative effects on advance and end of life care planning, lack of preparedness for deterioration/progression, as well as on emotional wellbeing and grieving

processes after the care recipient's death (Papastavrou et al., 2012; Trucco, Backhouse et al., 2023). Tailoring support to accommodate these individual differences can enhance carers' overall experiences and outcomes.

These findings have important implications for professional and support services which highlight the need to provide MND information and offer respite care. Surprisingly, no participants mentioned hospice or generic day services for the person living with MND, and only one participant had formal carers who came to sit and stay with the care recipient. Perhaps these services were not available, the person living with MND was not accessing them, or if they did, it did not impact on carers' wellbeing. However, this type of support could potentially relieve carers from caring responsibilities and should be considered. In addition, psychological interventions, such as Acceptance and Commitment Therapy, could help carers continue engaging in meaningful activities while focusing on the present moment and embracing emotional challenges associated with their present situation (Han et al., 2021). Interventions targeting resilience should also be considered, as they target the negative impact of situations by seeking adaptation by reducing emotional distress caused by the emotional and physical demands of caregiving (Palacio et al., 2020).

This study has limitations that should be considered. We acknowledge that individual caring experiences could have been influenced by economic possibilities to access support and the variation of support received in each UK region (e.g., carers' allowance, availability of MND care coordinators and community neurology nurses), which were beyond the scope of this study and may have affected the findings. Moreover, although the sample size was large enough to provide sufficient information power, we did not collect data from family members other than spouses or on carers' ethnicity which might have captured different emotional experiences. This was a one-time interview study, and we did not recruit according to time of caring and symptoms of MND. Consequently, this might have impacted on the findings, since not all participants were transiting through the same period of the disease. Additionally, since participation was completely voluntary, it is likely that carers who took part were emotionally coping with MND.

We recommend that future studies explore the emotional experiences of family carers of pwMND other than spouses and conduct longitudinal studies to capture their

experiences at different stages of disease progression. Future research could consider focusing on carers' knowledge about support possibilities to assess if this information is correctly disseminated. Exploring coping strategies with a coping scale such as the Brief COPE (Carver, 1997) which assesses similar strategies found in this study, could provide further understanding of mechanisms used in response to different stressors.

Conclusion

This study examined the emotional journeys that family carers of people living with MND experienced since the diagnosis of the disease. Starting with overwhelming feelings of shock and devastation and adapting to the changes ad losses occurring subsequently, carers gradually identified several coping strategies to manage their emotions enabling continued engagement in everyday activities, responsibilities, and caring role.

In order to delve deeper into the emotions of anticipatory grief experienced by carers due to the changes and losses they encounter during the progression of MND, in the next chapter, I will investigate how MND symptoms- and carer-related factors affect anticipatory grief among this population.

Chapter 4: The impact of MND symptomatology on family carers of people living with Motor Neurone Disease anticipatory grief

As highlighted in the previous chapters, the literature indicates a notable gap in investigating factors associated with anticipatory grief in carers of people living with MND, with a distinct absence of quantitative studies exploring this topic. It has also been suggested that future research should consider identifying factors associated with grieving experiences prior to death in this population. By addressing this research gap, I aim to contribute valuable insights and knowledge to enhance our understanding of anticipatory grief in this demographic.

This chapter is based on the manuscript:

Trucco, A. P., Khondoker, M., Kishita, N., Backhouse, T., Copsey, H., & Mioshi, E. (2023) Factors affecting anticipatory grief of family carers currently supporting people living with Motor Neurone Disease: The impact of disease symptomatology. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*. [Advance online publication] https://doi.org/10.1080/21678421.2024.2359559

Introduction

Family carers of people living with MND (pwMND) are continuously experiencing everyday lifestyle changes and losses during the progression of the disease, leading to anticipatory grief (AG) (Evans, 1994; Marwit & Meuser, 2002; Meuser & Marwit, 2001). This phenomenon encompasses grief-related emotions which surface before death, causing emotional destabilisation (Trucco, Mioshi, et al., 2023) and emotional distress (Pinto et al., 2021).

Interest in investigating MND family carers' grieving processes has grown significantly due to the need for a deeper understanding of the factors influencing grief and provide more effective emotional support to carers (Trucco, Backhouse et al., 2023).

However, research revealed that interventions aimed at improving MND carers' wellbeing have not specifically addressed AG to date (Gluyas et al., 2017).

It is likely that AG in MND is influenced by several factors, especially because motor and behavioural symptoms are present. From a motor perspective, studies in Alzheimer's (Meuser & Marwit, 2001) and Parkinson's disease (Carter et al., 2012) revealed that advanced stages of the disease and severe symptoms have greater impact in carer AG. From the behavioural symptomatology perspective, behavioural changes seem to be the best predictive factor of AG in dementia (Holley & Mast, 2010) and a risk factor for higher levels of AG in dementia (Liew et al., 2019) and Parkinson's (Fox et al., 2020). Thus, identifying the role of disease severity and behavioural changes in MND carers' AG seem to be crucial for future interventions. Additionally, current literature in MND suggests that longer hours of care provided to the person living with MND due to MND symptoms impact on carer post-death grief (Warrier et al., 2019), and are associated with carer prolonged grief disorder (Aoun et al., 2020). However, the effect of hours of care provided in carer AG in MND is unclear.

In the exploration of AG among carers, it is also important to delve into carer-related factors, to comprehend the broader context of carer AG. The literature recognises that changes in the carer-person living with MND relationship may negatively contribute to AG emotions (Trucco, Backhouse et al., 2023), but this finding is not universally applicable. Considering the potential role of familism in carer AG is also crucial. Familism is defined as a strong family identification and attachment, characterised by feelings of loyalty and responsibility for care delivery (Sabogal et al., 1987). A previous systematic review revealed that higher familism values were linked to higher anxiety and depressive symptoms in carers of people living with dementia (Tian et al., 2022), and have both positive and negative impacts on emotional distress among this carer population (Losada et al., 2010). Given this association with mental health outcomes, familism values may be related to AG in MND carers.

While awareness of AG emotions among carers has been on the rise, there remains a pressing need for in-depth exploration of this phenomenon to enhance the possibility of effectively addressing it. Based on the present evidence, this exploratory study aims to

examine the predictive effects of different potential factors (disease severity, behavioural changes, relationship closeness, familism and hours of care provided) in current MND family carers' AG.

Methods

This cross-sectional study took place between July 2021 and February 2023. Initially, recruitment commenced in July 2021 in the United Kingdom (UK). To increase participant numbers, the study's information was subsequently disseminated in the United States (US) in October 2022. Recruitment occurred through dissemination of the study information in MND/ALS Associations, carers' support groups and social media (e.g., FactorMND- former Twitter). Additionally, in the UK, two specialist tertiary hospitals (Norfolk and Norwich University Hospitals and Sheffield Teaching Hospitals) disseminated the study information using leaflets, participant information sheets and social media posts.

Participants completed a survey through an online platform or in paper format, in a consistent order by all participants. Online survey data were collected and managed by the Joint Information Systems Committee electronic data. All data were collected anonymously.

Participants

Family carers currently supporting a relative living with MND, who were 18 years or older and unpaid were included in the study. No other inclusion or exclusion criteria were considered.

Instruments

Anticipatory Grief - Carer

The Marwit-Meuser Caregiver Grief Inventory-Short Form (MMCGI-SF; Marwit & Meuser, 2005) was used to measure the grief experience in carers. The measure contains three sub-scales: Personal Sacrifice Burden, identifying individual losses carers experience due to their carer role; Heartfelt Sadness and Longing, identifying intrapersonal emotional reactions related to caregiving; and Worry and Felt Isolation, identifying carers' feelings of losing social connections and support from others. Each of the 18 items is rated on a 5-point

Likert scale ranging from 1=Strongly Disagree to 5=Strongly Agree. Total AG score ranges from 18 to 90. Sub-scores from the sub-scales range from 6 to 30. Scores in the average range are common responses to loss in the caregiving experience, high scores may indicate the need for support and low scores may mean positive coping adaptation or denial. The Cronbach's alpha for total grief score in this study was .94.

For this study, one scale item was adapted to MND carers (with author's permission) as the instrument was originally developed and validated with dementia carers.

MND disease severity

The revised version of the ALS Functional Rating Scale (ALSFRS-R; Cedarbaum et al., 1999) was used to measure the progression of functional disability in the person living with MND. Each of the 12 items is rated on a 4-point Likert scale ranging from 0=no function to 4=normal function (min 0, max 48) with lower scores indicating greater disability.

The ALSFRS-R was completed by carers. Previous research has demonstrated excellent reliability of the ALSFRS-R evaluations conducted by healthcare professionals, carers, and patients (Miano et al., 2004; Montes et al., 2006). Furthermore, the ALSFRS-R included in our study provided clear instructions for scoring, tailored to ensure accessibility to individuals without specialised medical knowledge.

Behavioural changes in MND

The Motor Neurone Disease Behavioural Instrument (MiND-B; Mioshi, Hsieh et al., 2014) was used to establish the presence of apathy, disinhibition, and stereotypical behaviour in the person living with MND. Each of the nine items is rated on a 4-point Likert scale ranging from 1=everyday to 4=no changes from normal behaviour (min 9, max 36). The cut-off score indicating presence of behavioural changes is <34; with lower scores representing greater behavioural changes.

Carer's perception on relationship closeness

The Relationship Closeness Scale (RCS; Noelker, 1996; Whitlatch et al., 2001) was used to detect the current quality of emotional bond between the carer and the person living with MND. Each of the six items is rated on a 4-point Likert scale ranging from

1=Strongly Disagree to 4=Strongly Agree (min 4, max 24). Responses capture carers' degree of agreement about their relationship with the care recipient. Higher scores are indicative of closer dyadic relationships.

Familism - Carer

The Familism Scale (FS; Sabogal et al., 1987) was used to assess the tendency to prioritise one's family over oneself. Each of the 14 items is rated on a 5-point Likert scale ranging from 1=very much in disagreement to 5=very much in agreement (min 14, max 70). Higher scores indicate higher familism values.

While initially designed for Hispanic/Latino populations, the scale demonstrated high familism values among non-Hispanics individuals (Sabogal et al., 1987). Moreover, it has been used in studies involving diverse carer populations and different cultures, including dementia carers, revealing both positive and negative effects of familism values on carers' emotional distress (Losada et al., 2010).

Demographics

Demographic information about the carer and the person living with MND was collected. Information for the carer included age, gender, country of residence, relationship to the person living with MND and hours per week they provided care. Information about the person living with MND included age, MND phenotype, and months since diagnosis.

Statistical Analyses

Descriptive analysis of demographic information was performed to characterise the sample.

To investigate potential factors associated with AG and assess their eligibility for inclusion in a regression model, correlational analyses were conducted with carer AG as dependent variable and potential independent variables (disease severity, behavioural changes, relationship closeness, familism and hours providing care per week). A *p* value threshold of 0.25 was used to screen potential independent variables. Participants' country of residence was included as an adjusting factor to account for any possible difference between responses from the two countries (UK and US).

Subsequently, a multiple linear regression analysis was conducted to examine to what extent different disease- and carer-related factors predicted total score of carer AG. To further understand the relation of AG and predictive factors, three separate multiple regression analyses were conducted with each of the individual sub-scales of the MMCGI-SF as dependent variables and the same independent variables previously mentioned. The overall model fit of each regression analysis was assessed using the *F*-test and the proportion of the explained variation by the model (R^2). A p level < 0.05 was considered statistically significant.

The Tolerance value and variance inflation factor (VIF) were estimated to check multi-collinearity, and the visual examination of the Normal Probability Plot (P-P) and scatterplot of the regression standardised residuals against predicted values were used to check for normality, linearity, and homoscedasticity assumptions.

Data analyses were performed using IBM SPSS statistical software (version 28).

Results

Seventy-nine participants (UK=74; US=5) were recruited for the study. Four respondents partially completed some of the instruments, therefore, they were removed from the data analysis which resulted in a dataset of 75 carers (UK=70; US=5). Post-hoc power calculation for the regression model with the primary outcome (anticipatory grief) shows that our sample size (n=75) is slightly smaller than that required (n=79) to detect the overall effect size (0.19) with adequate statistical power (0.80). However, as the regression coefficients with reasonable size were highly statistically significant, sample size seemed to be adequate for detecting effects of individual predictor variables. This can be considered as a reasonable compromise given the challenging and hard to recruit nature of the targeted population.

The results of each single regression analysis indicated that severity of the disease, behavioural changes, relationship closeness, familism and hours of care provided per week passed the screening step (p<0.25) and were entered to the regression models as independent variables (Supplementary Table 4.1 in the appendices section).

Characteristics of carers and people living with MND

The majority of carers were female (65.3%), their mean age was 63.09 (SD=10.46), they were co-habiting with (94.7%) and looking after a spouse/partner living with MND (89.3%) for an average of 38.64 months. Approximately a quarter of carers provided more than 100 hours of care provided/week (Table 4.1). Carer Relationship Closeness responses (mean=16.61), suggested that, as a group, carers had a relatively close dyadic relationship with the care recipient. Familism responses (mean=42.04) suggested moderate levels of familism values (Table 4.2).

People living with MND were mostly men (60%), mean age was 64.69 (SD=11.74). On average, they had received the formal diagnosis of MND within the previous 45 months (Table 4.1). More than half of them (65.3%) exhibited behavioural symptoms as rated by carers in the MiND-B, highlighting the prevalence of behavioural symptoms within this population. The mean score for the ALSFRS-R was 24.99 (Table 4.2).

Carers' experience of anticipatory grief

Anticipatory grief total scores showed that approximately half of the carers (50.7%) were experiencing common grieving reactions. While 22.6% of carers had more intense grieving reactions and may have been in need of support for better coping, 26.7% of the carers presented a low grief profile, indicating either good coping with emotions or possible denial of emotions (Table 4.2).

Results from each of the sub-scales showed that almost half of the carers (around 50%) were transiting normal grief reactions for each of the three sub-scales, suggesting they were going through expected emotional responses related to their caregiving role. Furthermore, 25.3% of carers were in the high grief categories for Personal Sacrifice Burden, 17.3% for Heartfelt Sadness and Longing, and 24% for Worry and Felt Isolation. The sub-scale Heartfelt Sadness and Longing had the highest percentage of carers in the low grief profile, with 30.7% falling into this group (Table 4.2; Figure 4.1).

Table 4.1

Demographic Characteristics of Family Carers and People Living with MND (n=75)

Family carer	**Frequency (%) or M(SD)**
Age (mean, SD)	63.09 (10.46)
Gender (female)	49 (65.3%)
Relationship to pwMND	
Spouse/Partner	67 (89.3%)
Parent	3 (4%)
Child	4 (5.4%)
Other	1 (1.3%)
Living with pwMND (yes)	71 (94.7%)
Months caring (mean, SD)*	38.64 (44.08)
Country of Residence	
United Kingdom	70 (93.3%)
United States	5 (6.7%)
Hours providing care per week	
<1-8	17 (22.6%)
9-30	19 (25.4%)
31-49	10 (13.3%)
50-99	10 (13.3%)
100 or more	19 (25.4%)
People living with MND	**Frequency (%) or M(SD)**
Age (mean, SD)	64.70 (11.74)
Gender (male)	45 (60%)
Phenotype of MND*	
ALS	37 (49.3%)
Progressive Bulbar Palsy	9 (12%)
Progressive Muscular Atrophy	7 (9.3%)
Primary Lateral Sclerosis	8 (10.7%)
ALS-FTD	2 (2.7%)
Don't know	11 (14.7%)
Months since diagnosis (mean, SD)*	45.08 (47.88)

Note: *Missing data for months caring (n=73/75), phenotype of MND (n=74/75) and months since diagnosis (n=73/75). Phenotypes of MND were reported by carers.

Table 4.2.

Results from Clinical Variables Included in the Multiple Regression Analyses (n=75)

Clinical variables	Frequency (%) or M(SD)
Anticipatory grief (MMCGI-SF)	
Total grief score	
High grief profile	17 (22.6%)
Average grief profile	38 (50.7%)
Low grief profile	20 (26.7%)
Personal Sacrifice Burden	
High grief profile	19 (25.3%)
Average grief profile	38 (50.7%)
Low grief profile	18 (24%)
Heartfelt Sadness and Longing	
High grief profile	13 (17.3%)
Average grief profile	39 (52%)
Low grief profile	23 (30.7%)
Worry and Felt Isolation	
High grief profile	18 (24%)
Average grief profile	42 (56%)
Low grief profile	15 (20%)
Disease severity (ALSFRS-R)	24.99 (9.11)
Behavioural changes (MiND-B)	30.13 (5.86)
Presence of behavioural changes	49 (65.3%)
Relationship closeness (RCS)	16.61 (2.47)
Familism (FS)	42.04 (7.76)

Note. MMCGI-SF (18-90 for total score and 6-30 for each sub-scale) higher scores may indicate the need for support and lower scores may mean positive coping adaptation or denial; ALSFRS-R (0-48) lower scores denote greater disability; MiND-B (9-36; cut-off for presence of behavioural symptoms <34) lower scores represent greater behavioural symptoms; RCS (4-24) higher scores indicate closer dyadic relationships; FS (14-70) higher scores denote higher familism values.

Figure 4.1

Anticipatory Grief Sub-scales based on Carer Self-Report (MMCGI-SF)

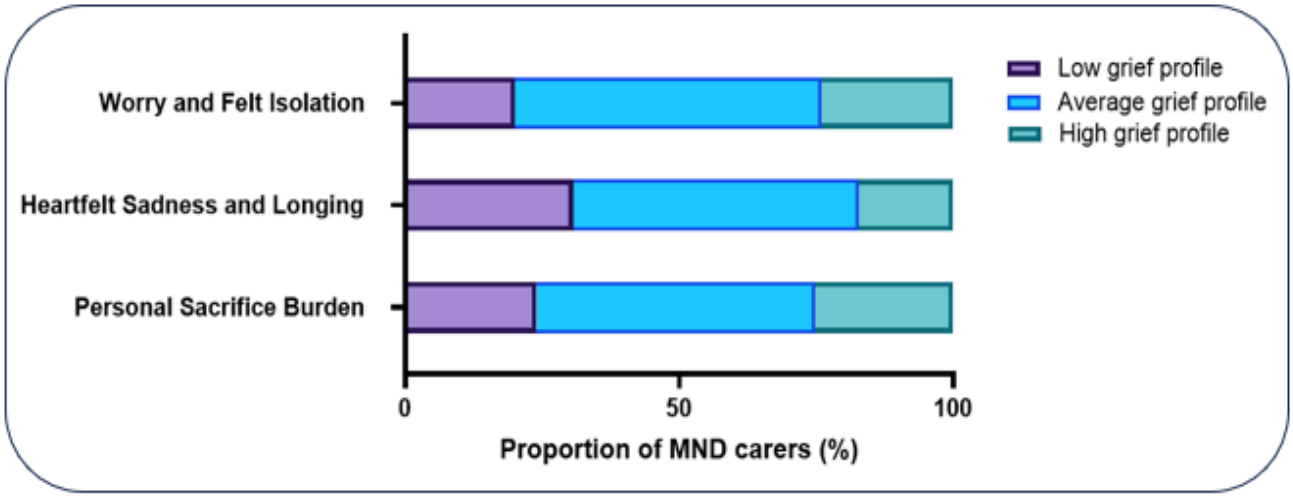


Table 4.3

Pearson's Correlations among Variables when Including MMCGI-SF Total Score as Dependent Variable (n=75)

Variables	1	2	3	4	5	6	7
1. Anticipatory grief (MMCGI-SF)	1.00						
2. Disease severity (ALSFRS-R)	-0.48**	1.00					
3. Behavioural changes(MiND-B)	-0.48**	0.36**	1.00				
4. Relationship Closeness (RCS)	-0.29**	0.18	0.25*	1.00			
5. Familism (FS)	-0.16	0.09	0.14	0.21*	1.00		
6. Hours of care per week	0.28**	-0.48**	-0.19	-0.00	0.03	1.00	
7. Country of residence	-0.12	-0.01	-0.11	0.15	0.18	-0.08	1.00

Note. **p<.01 *p<0.05

Which are the factors that best predict carer AG?

Correlation results for variables included in the regression model with AG total score as dependent variable can be found in Table 4.3.

Disease severity and *behavioural changes* were the only two variables contributing to carer AG, and the model accounted for approximately 38% of the variance (Table 4.4).

The Tolerance (>0.67) and VIF (<1.48) values for total score indicated that there is no obvious concern of multicollinearity for the independent variables. The results of the normal P–P Plot and the scatterplot of the standard residuals showed that the assumption of normality, linearity and homoscedasticity of residuals was met.

Are disease related factors also the best predictors of the different aspects of AG?

When analysing individual sub-scales from the MMCGI-SF separately, results indicated that *disease severity* was the only variable predicting Personal Sacrifice Burden and explained 39% of the variance in this model (Table 4.4). It appears that as MND progresses, carers' grieving emotions related to everyday changes and losses become more pronounced and carers experience increasing levels of grief.

Behavioural changes were the only factor significantly contributing to Heartfelt Sadness and Longing, accounting for 27% of the variance of AG (Table 4.4). This suggests that when behavioural changes are present, carers' intrapersonal grieving reactions, such as sadness, anger, guilt, and feelings of powerlessness are likely to emerge.

Behavioural changes were the only factor predicting Worry and Felt Isolation, accounting for 42% of the variance on carer AG (Table 4.4), suggesting that carers' feelings of losing connections and support from others tend to increase due to the presence of behavioural symptoms.

The Tolerance and VIF values for each sub-scale indicated that multicollinearity is not a significant concern, as all Tolerance values were greater than 0.6, and all VIF values were below 1.49. Additionally, the examination of the Normal P–P Plots and the scatterplots of the standard residuals for each sub-scale suggested no violations of the assumption of normality, linearity and homoscedasticity of residuals.

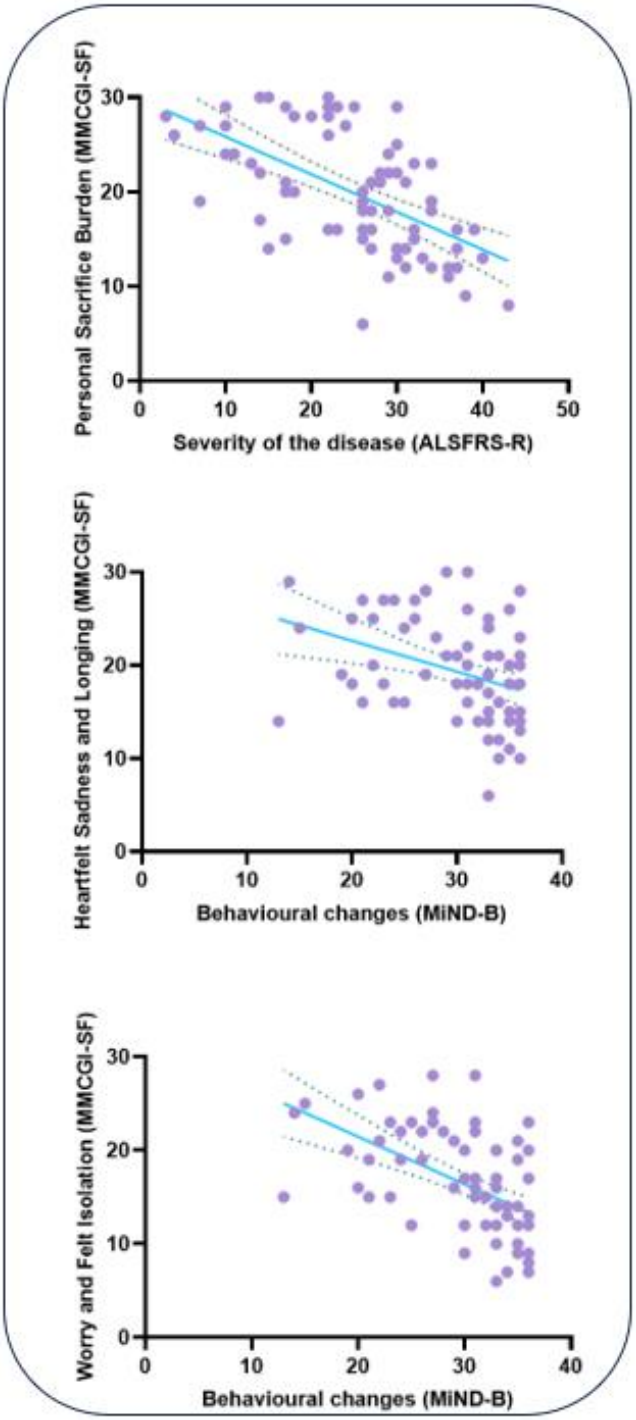
Table 4.4

Factors Explaining the Variance of Carer Anticipatory Grief as Measured by the MMCGI-SF (total score and sub-scales scores) (n=75)

	Anticipatory grief *(Total score)*			95% CI	
Predictors	β	*t*	*p*	Lower	Upper
Disease severity	**-0.31**	**-2.64**	**0.01**	**-0.91**	**-0.13**
Behavioural changes	**-0.34**	**-3.18**	**0.002**	**-1.45**	**-0.33**
Relationship closeness	-0.12	-1.21	0.23	-2.05	0.50
Familism	-0.04	-0.40	0.69	-0.48	0.32
Hours of care provided (weekly)	0.06	0.53	0.60	-0.91	1.58
Country of residence	-0.13	-1.28	0.21	-20.04	4.41
F 7.05 d.f 6 R^2 0.38					
	Personal Sacrifice Burden			95% CI	
Predictors	β	*t*	*p*	Lower	Upper
Disease severity	**-0.39**	**-3.47**	**<0.001**	**-0.42**	**-0.11**
Behavioural changes	-0.20	-1.97	0.053	-0.43	0.003
Relationship closeness	-0.10	-1.00	0.32	-0.75	0.25
Familism	-0.06	-0.62	0.54	-0.20	0.11
Hours of care provided (weekly)	0.20	1.88	0.07	-0.03	0.94
Country of residence	-0.11	-1.10	0.28	-7.42	2.15
F 8.66 d.f 6 R^2 0.43					
	Heartfelt Sadness and Longing			95% CI	
Predictors	β	*t*	*p*	Lower	Upper
Disease severity	-0.24	-1.82	0.07	-0.31	0.01
Behavioural changes	**-0.27**	**-2.27**	**0.03**	**-0.49**	**-0.03**
Relationship closeness	-0.10	-0.82	0.41	-0.74	0.31
Familism	0.01	0.11	0.92	-0.15	0.17
Hours of care provided (weekly)	-0.08	-0.63	0.53	-0.67	0.35
Country of residence	-0.16	-1.44	0.15	-8.65	1.39
F 2.94 d.f 6 R^2 0.21					
	Worry and Felt Isolation			95% CI	
Predictors	β	*t*	*p*	Lower	Upper
Disease severity	-0.17	-1.37	0.18	-0.26	0.05
Behavioural changes	**-0.42**	**-3.81**	**<0.001**	**-0.63**	**-0.20**
Relationship closeness	-0.13	-1.25	0.22	-0.81	0.19
Familism	-0.05	-0.52	0.61	-0.19	0.11
Hours of care provided (weekly)	0.02	0.15	0.88	-0.45	0.52
Country of residence	-0.07	-0.65	0.52	-6.30	3.20
F 5.60 d.f 6 R^2 0.33					

Figure 4.2

Predictive Factors against Each Sub-scale from the MMCGI-SF.



Discussion

This study explored the impact of disease- (i.e., disease severity and behavioural changes) and carer-related factors (i.e., relationship closeness, familism, and hours of care provided) on carer anticipatory grief. Results demonstrate that disease-related factors are significant predictors of AG, but carer-related factors do not appear to have significant impact on AG. Findings suggest that behavioural changes have a strong contribution to carers' intrapersonal feelings of changes, losses, and isolation, over and above other variables.

Behavioural changes, such as disinhibited behaviour, apathy, and stereotypical behaviours, seem to be the primary predictor of AG, including the specific aspects of AG as measured by the MMCGI-SF sub-scale Heartfelt Sadness and Longing, i.e., intrapersonal emotions connected to traditional grief concepts. It appears that feelings of sadness, anger and guilt are strongly linked to changes in the person living with MND's behaviours, which can be related to the emotions of losing the person they knew before behavioural symptoms presented or the difficulties in managing these symptoms. This is consistent with studies involving dementia carers, where behavioural problems were the best predictor of AG (Holley & Mast, 2010), and with carers of people with mild cognitive impairment which reported "missing the person" upon diagnosis (Garand et al., 2012). Additionally, challenging behaviours can strain the carer-person living with MND relationship and impact AG (Trucco, Backhouse et al., 2023). The underlying cause of relationship changes may be the behavioural symptoms. Notably, in this study, relationship closeness did not significantly impact carer AG. This may be because the study measured perceived closeness, not changes in the relationship itself.

Similarly, behavioural changes were the sole factor significantly affecting Worry and Felt Isolation sub-scale, which encompasses carers' feelings of isolation and lack of support. Previous research has linked these feelings to progressive caregiving duties and a lack of communication with healthcare professionals, family, friends and the person living with MND (Holkham & Soundy, 2018). Building upon the literature, this study identified their impact on AG. It is likely that carers experience increased isolation as difficulties arise when socialising. For example, the person living with MND may exhibit disinhibited behaviour

towards others, and carers may reduce social contact to avoid potential embarrassment from these behaviours. Moreover, carers may not feel well supported as assessment and guidance on behavioural symptoms do not feature in most MND services (Crockford et al., 2017; Francis et al., 2023). As such, these symptoms sometimes occur without acknowledgement that they are part of MND and carers may not articulate or understand the changes they observe and are not offered specialist support to manage behavioural symptoms (Francis et al., 2023).

While existing evidence has highlighted the impact of the carer-person living with MND relationship, and hours of care provided on post-death and PGD in MND carers (Trucco, Backhouse et al., 2023), this study finds that when modelled alongside disease-related factors, they do not significantly explain carer AG. Furthermore, no association was discovered between familism and AG in this study. A possible explanation for these findings may be that grieving emotions may be primarily linked to the anticipated loss of the person with MND, reflected on the progressive deterioration of the person, rather than being influenced by their previous relationship or familism values as measured by scales used, or the hours providing care. These factors may act as contextual variables that influence the intensity of grieving reactions by either exacerbating or alleviating emotions and coping, albeit not being directly linked to AG. Another possible reason might be the lack of diversity in the closeness of dyadic relationship and familism within the sample.

The present study identified disease severity as the strongest predictor of Personal Sacrifice Burden items in the MMCGI-SF, i.e., of the losses and changes carers experience due to their carer role. A systematic review revealed that some changes and losses result from carers' lack of personal time due to increasing hours of care provided (Holkham & Soundy, 2018). Interestingly, our study suggests that AG might not be influenced by additional strain caused by hours providing care, implying that other factors play a more substantial role in the perception of loss. It is plausible that AG responses are triggered as disability progresses, leading the family to mourn the person they once knew and anticipate future losses and changes. This aligns with findings in other neurodegenerative diseases, such as dementia and Parkinson's, where grieving emotions intensify as the disease advances (Meuser & Marwit, 2001; Carter et. al, 2012).

The low R^2 scores of the analyses conducted, implied the presence of additional variables influencing AG. For example, certain factors considered to be protective for carer wellbeing, such as social support (Taylor, 2011) and coping strategies have not been included in this study and should be explored in future studies. Previous research with MND carers (Aoun et al., 2021; Pinto et al., 2021) highlighted the vulnerability and loneliness that carers experience, as well as the insufficient emotional and practical support services available to address their needs. Consequently, it is not surprising that in this study carers reported higher scores in the Personal Sacrifice Burden and Worry and Felt Isolation domains on the MMCGI-SF. Furthermore, research has identified coping mechanisms, such as adopting a proactive approach to daily changes, focusing on positive aspects of life, and compartmentalising negative thoughts, as effective strategies for managing everyday changes and losses due to MND, and merit further investigation (Pinto et al., 2021; Trucco, Mioshi et al., 2023).

This study has some limitations. The MMCGI-SF was used to assess carer AG, where low scores might mean that carers are in denial and not necessarily coping well and adaptively; thus, these findings need to be interpreted with caution. Moreover, carers from this study presented a close dyadic relationship, which could have influenced the findings. It is important to note that while it has been well established the impact of caregiving on carer psychological health, this study did not include any psychological variable, such as anxiety and depression, as confounding factors, which might have impacted carers rating on the scales. Cognition in the person with MND was not assessed in this study. Considering the prevalence of changes in cognition in this population, future studies should include and assess how cognitive symptoms may affect carer AG. Furthermore, the vast majority of carers in this study were spouses/partners of the person living with MND. Future research should consider examining the AG experience of other family carers not living in the same residence, or carers who may have a different relationship with the person living with MND, such as adult-children; as well as investigating AG emotions between genders.

This study enhances our understanding of factors influencing AG. Addressing disease severity and behavioural changes in the person living with MND poses a significant challenge in supporting carers' experiences of losses and changes. The behavioural

responses observed in the person living with MND may occur directly from the neurological effects of the disease, i.e., manifesting as neurological or organic symptoms. However, emotional responses to the experience of living with MND or as a result of the interaction between the impairment caused by living with MND and the environment can also occur and can be confused with behavioural symptoms. For instance, emotional responses (e.g., frustration) due to difficulties in performing daily activities or relating to others are common. Notably, reactive behaviours or those that indicate behavioural distress may be modifiable and this should be considered accordingly. The findings underscore the need for targeted interventions to help carers cope with AG emotions. Additionally, this study emphasises the importance of addressing and managing behavioural symptoms in MND. Providing HCPs with training and offering carers strategies to handle behaviours they find challenging could have a positive impact on AG emotions. The MiNDToolkit, a novel psychoeducational online intervention for carers (Radakovic et al., 2020), may be a potential route to support MND carers managing behavioural symptoms in MND.

Conclusion

This study deepens our understanding of carer AG and highlights the significance of MND symptoms, particularly disease severity and behavioural symptoms. Interventions targeting support as MND progresses and education on behavioural management could alleviate grieving symptomatology and enhance MND carers' wellbeing. In addition, exploring factors that could potentially alleviate the impact of MND symptoms in carer AG is recommended.

In the next chapter, I will explore if carer psychological inflexibility (i.e., difficulty in being present in the moment and engaging in value-based actions due to rigid patterns and avoidance strategies) is a moderating factor between the relationship of disease severity and behavioural changes and carer AG. Psychological inflexibility is a modifiable factor as it can be improved by targeted interventions. These interventions may help individuals recognise and accept their thoughts and feelings, fostering adaptive coping strategies which can lead to alleviating AG emotions.

Chapter 5: The role of psychological inflexibility in the relationship between Motor Neurone Disease symptomatology and carer anticipatory grief

In the last chapter, it was identified that factors related to MND symptomatology (i.e., disease severity and behavioural symptoms), emerge as the primary predictors of AG experienced by MND carers. In light of this, it becomes imperative to explore avenues for better ways to support carers in relation to AG emotions. This study seeks to investigate the role of carer psychological inflexibility as a moderator factor between MND symptomatology and carer AG. The focus of psychological inflexibility is driven by its potential for intervention.

This chapter is based on the manuscript:

Trucco, A.P., Khondoker, M., Kishita, N., Backhouse, T., & Mioshi, E. (2023). Does carer psychological inflexibility moderate the relationship between Motor Neurone Disease symptomatology and carer anticipatory grief emotions? *(Under preparation).*

Introduction

Research has revealed that providing care for someone living with MND can significantly impact the emotional wellbeing of the primary carer, usually a close relative or family member (Pinto et al., 2021; Trucco, Mioshi, et al., 2023). Carers face a series of changes and losses throughout the trajectory of this disease, often experiencing anticipatory grief (AG). AG is a normal grief response motivated by the perception of past and present losses and changes, and expectations of future losses culminating in death (Rando, 1984, 1986), and a complex experience that carers face involving the relationship with the care recipient, the changes resulting from the losses and the carers coping with this new reality (Nielsen et al., 2016a). It has been suggested that various illness trajectories may influence carers' AG experience differently (Coelho & Barbosa, 2017). Due to the rapid progression and uncertainty that accompanies MND, it is important to delve into the experience of AG in

carers of people living with MND (pwMND), as their support needs are likely distinct from other populations.

A previous systematic review (Trucco, Backhouse, et al., 2023) revealed that factors associated with AG in carers of pwMND include the uncertainty of the disease, carer anxiety and depressive symptoms, changes in carer-care recipient relationship, and a diminished social life. This review highlighted that the majority of existing studies in this area appear more focused on post-death grief and prolonged grief disorder (PGD) than present AG symptoms. A recent study indicated that MND disease-related factors (i.e., disease severity and behavioural changes) are more significant predictors of AG emotions, rather than carer-related factors (Trucco, Khondoker et al., 2024). This presents a challenge for this carer population due to the challenges encountered due to the progression and dependency caused by these disease-related factors.

It is crucial to better understand how MND carers regulate and process their feelings and emotions in response to changes and losses encountered; as grief during caregiving has been found to be a risk factor for poor bereavement outcomes (Nielsen et al., 2016a) and when not processed adaptively, there is high risk of developing PGD (Aoun et al., 2015). AG is often no different in intensity or quality from post-death grief (Meuser & Marwit, 2001). Importantly, the prevalence of AG among family carers of persons living with a life-threatening illness, such as MND, was found to be higher than post-death grief in the general adult population (Kustanti et al., 2022). Consequently, investigating potential modifiable factors that could moderate the relationship between MND symptomatology and carer AG grief emotions seems essential for providing better support to carers and informing future clinical non-pharmacological interventions.

Psychological inflexibility may have a critical role in explaining the impact of MND symptoms on carer AG emotions. Psychological inflexibility refers to the attempt to decrease internal private experiences, such as thoughts and feelings, even when doing so is inconsistent with personal values (Hayes et al., 2006). When MND carers are faced with symptoms of MND, these can act as stressors and could lead to increased levels of negative thoughts and feelings. When a carer is presenting with higher levels of psychological inflexibility, they tend to devote a lot of effort and energy to controlling and suppressing

such negative thoughts and feelings (e.g., denial) rather than embracing them, which in turn, could lead to worse mental health outcomes (e.g., anxiety). The construct of psychological inflexibility is composed of a set of core sub-processes which include experiential avoidance, in which individuals seek to alter the form, frequency or intensity of private experiences such as thoughts and feelings, even when doing so is costly, ineffective or unnecessary (Hayes et al., 2013). Research has suggested that when grief emotions are avoided or denied, these cannot be processed, and as a consequence they remain high, leading to distress (Coelho et al., 2018). In addition, a previous study reported that MND carers who are more willing to accept and adjust to their reality are able to cope better with challenges MND may bring to affected families. (Trucco, Mioshi, et al., 2023).

A recent systematic review (Han et al., 2021) that explored the effectiveness of Acceptance and Commitment Therapy (ACT), an intervention which directly targets psychological inflexibility on mental health outcomes in family carers, demonstrated that reducing psychological inflexibility through ACT is effective in reducing anxiety and depressive symptoms and stress among the carer population. However, studies targeting AG are scarce. For example, a recent systematic review (Jones et al., 2022) that explored the effectiveness of ACT for managing grief only identified two eligible studies, and targeted bereaved family carers of patients in palliative care but not specifically AG. Thus, no studies have specifically examined the impact of psychological inflexibility in AG in MND carers, a true gap in the available scientific literature.

Consequently, to address this research gap, this cross-sectional study explored the role of psychological inflexibility as a moderator variable capable of explaining the relationship between MND symptoms and carer AG emotions.

Methods

Participants and procedure

The participant sample used in the present study is the same as that utilised in the previous study – Chapter 4. As such, the same sample of 79 family carers currently supporting pwMND who were 18 years or older and provided unpaid care were included.

Recruitment was conducted from July 2021 to February 2023, commencing in the United Kingdom (UK) and subsequently expanding to include United States (US). The process involved disseminating study information through MND/ALS Associations, carers' support groups and various social media platforms such as Twitter (@FactorMND). In the UK, two tertiary hospitals, namely Norfolk and Norwich University Hospitals and Sheffield Teaching Hospitals, also facilitated recruitment by distributing the study information via leaflets, participant information sheets and social media posts.

Participants had the option to complete a survey either through an online platform or in paper format. Online survey data were collected and managed by the Joint Information Systems Committee electronic data system, ensuring anonymity for all participants.

Instruments

Carer Anticipatory Grief

The Marwit-Meuser Caregiver Grief Inventory-Short Form (MMCGI-SF; Marwit & Meuser, 2005) was employed to assess grief experience among carers. Each of the 18 items is rated on a 5-point Likert scale ranging from 1=Strongly Disagree to 5=Strongly Agree, with a score range from 18-90. Scores in the average range represent common responses to loss and change in the carer experience, high scores (i.e., 1+ SD above the mean) may indicate the need for support and low scores (i.e., 1+ SD below the mean) may mean positive coping adaptation or denial. The Cronbach's alpha for the current study was .94.

It is important to note that for the purpose of this study, one item from the scale was modified with the author's permission (TM) to better suit MND carers, as the original wording was tailored for dementia carers.

Carer Psychological Inflexibility

The Acceptance and Action Questionnaire-II (AAQ-II; Bond et al., 2011) was used to assess the degree of carer psychological inflexibility. Each of the 7 items is rated on a 7-point Likert scale ranging from 1=never true to 7=always true. The items of the AAQ-II include the following statements "My painful experiences and memories make it difficult for me to live a life that I would value", "I'm afraid of my feelings", "I worry about not being able to control my worries and feelings", "My painful memories prevent me from having a fulfilling

life", "Emotions cause problems in my life", "It seems like most people are handling their lives better than I am" and "Worries get in the way of my success". With a normative mean of approximately 25 or above, the maximum score is 49, where higher sum scores indicate greater psychological inflexibility. The Cronbach's alpha for the current study was .93.

MND disease severity in the person living with MND

Disease severity was assessed by the revised version of the ALS Functional Rating Scale (ALSFRS-R; Cedarbaum et al., 1999). This measure comprises four domains including bulbar function, fine motor function, gross motor function and respiratory function and reflects motor impairment and disability progression. Each of the 12 items is rated on a 4-point Likert scale ranging from 0=no function to 4=normal. Maximum score is 48; lower scores denote greater disability. The Cronbach's alpha for the current study was .86.

Carers were responsible for evaluating the ALSFRS-R. While this measure has initially been developed to be scored by healthcare professionals, past studies (Miano et al., 2004; Montes et al., 2006) have shown high reliability in ALSFRS-R assessments conducted by healthcare professionals, carers and pwMND themselves. Moreover, the ALSFRS-R utilised in our research offered explicit scoring instructions to be comprehensible to lay-individuals, thus ensuring accessibility.

Behavioural changes in the person living with MND

Changes in behaviour were measured by the Motor Neurone Disease Behavioural Instrument (MiND-B; Mioshi, Hsieh et al., 2014), completed by the carer. The instrument comprises three sub-scales: disinhibition, apathy, and stereotypical behaviour. Each of the nine items is rated on a 4-point Likert scale ranging from 1=everyday to 4=no changes from normal behaviour. The cut-off score indicating presence of behavioural changes is <34; with lower scores representing greater behavioural symptoms. The Cronbach's alpha for the current study was .87.

Demographic Information

In conjunction with the utilisation of standardised assessment tools, demographic data pertaining to both the carer and the person living with MND were systematically collected. For carers, information included age, gender, length of time providing care,

country of residence and relationship to the care recipient. Regarding the person living with MND, data collection provided by the carer encompassed age, MND phenotype, and months since their initial diagnosis.

Statistical analysis

Of the 79 participants recruited (UK=74; US=5), four participants partially completed the measures for this study. This resulted in a dataset of 75 family carers (UK=70; US=5).

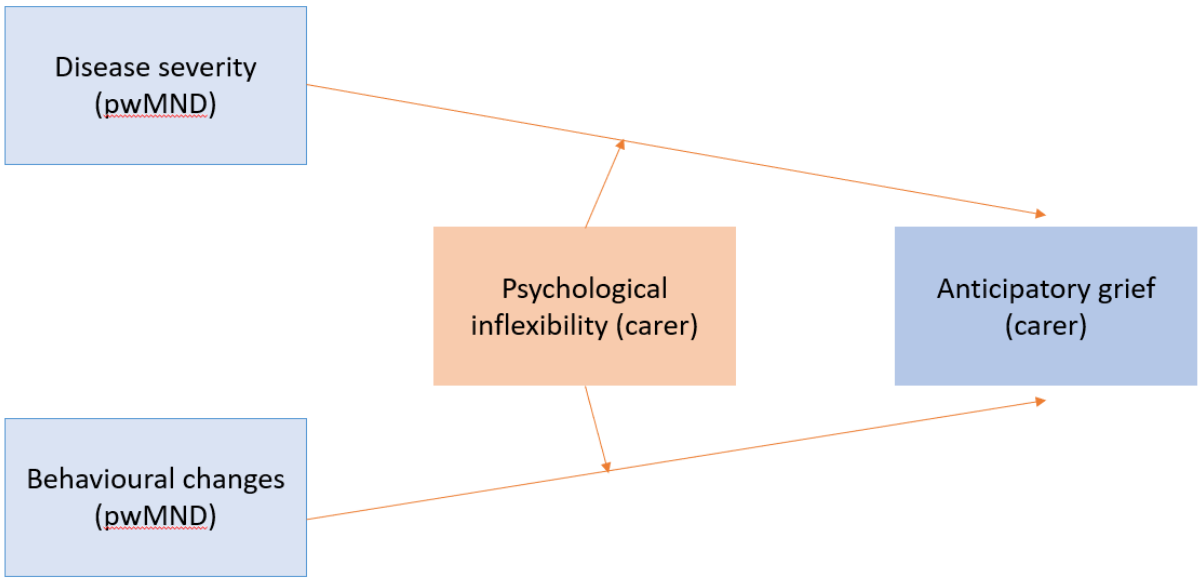
Descriptive analysis of demographic information was performed to characterise the sample of carers and pwMND. Pearson's *r* correlations were conducted between potential covariates (carer age and length of care) and the independent (ALSFRS-R; MiND-B), moderator (AAQ-II) and dependent (MMCGI-SF) variables to account for possible issues of multicollinearity. The presence of multicollinearity between variables was checked against a correlation coefficient of >0.70 among two or more variables (Shrestha, 2020). Control, independent and moderator variables that demonstrated significant correlations with AG at a *p* level of <0.05 were included in the moderation analyses.

To investigate the moderating role of psychological inflexibility on the association between MND symptoms and carer AG, two separate moderation analyses were conducted with severity of the disease and behavioural changes as independent variables, psychological inflexibility as moderator and carer AG as outcome variable (Figure 5.1). The moderation effect of psychological inflexibility was assessed via statistical significance of the two interaction effects: "psychological inflexibility x severity of the disease" and "psychological inflexibility x behavioural changes" respectively. The PROCESS computation macro (Model 1; Hayes, 2013) was used to perform the analyses. Demographic variables significantly correlated with AG emotions were included in the analyses as covariates to account for their potential confounding effects. All continuous variables included in the analyses were mean centred.

The analyses were performed using SPSS statistical software (Version 28).

Figure 5.1

Conceptual Framework of Moderation Analyses



Results

Participants

Descriptive statistics are reported in Table 5.1. The majority of participants were female carers (65.3%), spouses of the person living with MND (89.3%) and lived with the carer recipient (94.7%).

The results derived from the MMCGI-SF revealed that approximately half of carers (50.7%) fell within the average grief profile, indicating they were experiencing common grieving emotions. In addition, 22.6% carers presented heightened and intense grieving emotions. Conversely, the remaining 26.7% were categorised within the low grief profile, indicative of adaptive coping mechanisms or potential denial of emotions. Total AAQ-II group mean score was 18.99/49 (SD 8.20), indicative of average and healthy levels of psychological flexibility (Table 5.1).

Table 5.1

Demographic Characteristics and Clinical Variables of Family Carers and People Living with MND (n=75)

Family carer	**M(SD), % or frequency**
Age (mean, SD)	63.09 (10.46)
Gender (female %)	65.3
Relationship to pwMND (%)	
Spouse/Partner	89.3%
Parent	4%
Child	5.4%
Other	1.3%
Living with pwMND (yes %)	94.7%
Months caring (mean, SD) *	38.64 (44.08)
Country of Residence (frequency)	
United Kingdom	70
United States	5
Anticipatory grief (MMCGI-SF, %)	
High grief profile	22.6%
Average grief profile	50.7%
Low grief profile	26.7%
Psychological inflexibility (AAQ-II)	18.99 (8.20)
People living with MND	**Percentage or M (SD)**
Age (mean, SD)	64.70 (11.74)
Gender (male %)	60%
Phenotype of MND (%) *	
ALS	49.3%
Progressive Bulbar Palsy	12%
Progressive Muscular Atrophy	9.3%
Primary Lateral Sclerosis	10.7%
ALS-FTD	2.7%
Don't know	14.7%
Months since diagnosis (mean, SD)	45.08 (47.88)
Disease severity (ALS-FRS)	24.99 (9.11)
Behavioural symptoms (MiND-B)	30.13 (5.86)
Presence of behavioural symptoms	65.3%

Note: *Missing data for months caring (n=73/75), phenotype of MND (n=74/75) and months since diagnosis (n=73/75). MMCGI-SF (max 90) higher scores may indicate the need for support and lower scores may mean positive coping adaptation or denial; ALSFRS-R (max 48) lower scores denote greater disability; MiND-B (max 36) lower scores represent greater behavioural symptoms; AAQ-II (max 49) higher scores indicate higher level of psychological inflexibility.

The majority of pwMND in the study were male (60%) and, on average, the formal diagnosis of MND was conveyed within the previous 45 months. Behavioural symptoms were identified in nearly two thirds of the pwMND (65.3%) and the mean for severity of the disease was 24.99 (SD 9.11) (Table 5.1).

Correlations

Pearson's correlations among demographic variables showed that carer age was negatively associated with AG emotions, which meant that being younger was associated with higher levels of grief. Therefore, carer age was controlled in the moderation analyses.

No correlation between the control (carer anticipatory grief), independent (disease severity and behavioural changes) and moderator (psychological inflexibility) variables exceeded the recommended threshold of 0.70, resulting in no identified multicollinearity issues (Table 5.2).

Table 5.2

Pearson's Correlations among Variables (n=75)

Variables	1	2	3	4	5	6
1. Carer age	1.00					
2. Length of care (months)	0.07	1.00				
3. PwMND disease severity	0.15	-0.08	1.00			
4. PwMND behavioural symptoms	0.35**	0.17	0.36**	1.00		
5. Carer psychological inflexibility	-0.31**	0.06	-0.19	-0.37**	1.00	
6. Carer anticipatory grief	-0.25*	0.05	-0.48**	-0.48**	0.50**	1.00

**Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed).

Does carer psychological inflexibility moderate the relationship between MND symptoms and carer AG?

In two separate interaction analyses, we investigated whether psychological inflexibility was a significant moderator variable between disease severity and behavioural changes and carer AG. In other words, might high or low carer psychological inflexibility differentially influence (moderate) carer grief responses?

Disease severity. Results showed that the main effect of severity of the disease on carer AG emotions was significant (*b*=-0.70, p<0.00, 95%CI -1.01 to -0.39) and the main effect of psychological inflexibility on carer AG was also significant (*b*=0.76, p<0.00, 95%CI 0.40 to 1.12). However, the interaction effect between severity of the disease and AG was found to be non-significant (*b*=0.03, *p*=0.13, 95%CI -0.01 to 0.08), meaning no moderation effect of psychological inflexibility. The full model with severity of the disease and psychological inflexibility as independent variables, explained 43% of the variance of carer AG (Table 5.3).

Behavioural changes. Results showed that the main effect of behavioural changes (*b*=-0.88, *p*<0.00, 95%CI -1.45 to -0.31) and psychological inflexibility (*b*=0.70, *p*<0.00, 95%CI 0.30 to 1.10) on carer AG were both significant. The interaction effect for this model was also non-significant (*b*=-0.01, *p*=0.81, 95%CI -0.08 to 0.07). The final model, including behavioural symptoms and psychological inflexibility as predictors, and carer AG as dependent variable, explained 35% of the variance of carer AG (Table 5.4).

In practical terms, these results suggest that levels of carer psychological inflexibility independently affect their AG emotions arising from MND symptoms (i.e., higher or lower levels of carer psychological inflexibility may ease or exacerbate carer AG but psychological inflexibility does not moderate the relationships between MND disease severity and behavioural changes with carer AG).

Table 5.3

Results of Moderation Analysis – Disease Severity

	b	SE	t	LLCI	ULCI	*p*
Intercept	58.34	9.24	6.32	39.91	76.76	0.000
ALSFRS-R_centered (X)	-0.70	0.16	-4.44	-1.01	-0.39	**0.000**
AAQ-II_centered (W)	0.76	0.18	4.18	0.40	1.12	**0.000**
ALSFRS-II x AAQ-II (X x W)	0.03	0.02	1.55	-0.01	0.08	0.127
Age (C)	-0.04	0.15	-0.26	-0.33	0.25	0.796

R^2=0.43
MSE=143.41
F(70,4)=13.21
p<0.001

Note. ALSFRS-R, assessment of person living with MND disease severity; AAQ-II, assessment of carer psychological inflexibility; LLCI, Lower level of 95% confident interval; ULCI, Upper level of 95% confidence interval.

Table 5.4

Results of Moderation Analysis – Behavioural Changes

	b	SE	t	LLCI	ULCI	*p*
Intercept	57.37	9.94	5.77	37.54	77.19	0.000
MiND-B_centered (X)	-0.88	0.29	-3.06	-1.45	-0.31	**0.003**
AAQ-II_centered (W)	0.70	0.20	3.52	0.30	1.10	**0.001**
ALSFRS-II x AAQ-II (X x W)	-0.01	0.04	-0.24	-0.08	0.07	0.812
Age (C)	-0.03	0.16	-0.21	-0.35	0.28	0.838

R^2=0.35
MSE=162.75
F(70,4)=9.56
p<0.001

Note. MiND-B, assessment of person living with MND behavioural symptoms; AAQ-II, assessment of carer psychological inflexibility; LLCI, Lower level of 95% confident interval; ULCI, Upper level of 95% confidence interval

Discussion

The present study explored two moderation models examining the role played by carer psychological inflexibility in explaining the relationship between MND symptomatology (i.e., motor and behavioural symptoms) and carer AG emotions. Results suggested that while MND symptoms and carer psychological inflexibility are associated with carer AG, psychological inflexibility as measured by the AAQ-II is not a significant moderator between MND symptoms and carer AG. This suggests that MND symptoms and psychological inflexibility, independently affect carer AG.

The association of disease severity and behavioural symptoms on carer AG is consistent with previous literature, underscoring these two factors as the most significant predictors of heightened levels of AG (Trucco, Khondoker et al., 2024). Considering that there is no treatment available to revert MND symptomatology (McDermott & Shaw, 2008), it becomes imperative to explore alternative routes for alleviating the emotional distress experienced by carers in response to the progression of MND. A previous systematic review emphasised that the lack of, or insufficient information on MND progression negatively impacts carer AG (Trucco, Backhouse, et al., 2023). Therefore, providing carers with information on how MND might evolve in terms of motor and behavioural symptoms, might be a proactive approach with positive impact in carers' emotional experiences throughout the trajectory of MND. Additionally, offering carers strategies on how to address motor and behavioural symptoms might be beneficial. The MiNDToolkit, a psychoeducational intervention for the management of behavioural symptoms in MND could offer valuable support (Mioshi, Grant et al., 2024; Radakovic et al., 2020). Recommending respite care services to family carers for regular breaks from caregiving could also enhance self-care and alleviate emotional distress (Trucco, Mioshi, et al., 2023).

No previous research has investigated the relationship between psychological inflexibility and carer AG in MND. Findings from this study build upon current knowledge by illustrating the impact of carer psychological inflexibility on carer AG. While the results did not support the potential moderating role of psychological inflexibility, the present study demonstrated that psychological inflexibility still directly affects carer AG. A previous study demonstrated that carers may employ emotional avoidance as a means of adjusting for

lifestyle changes while refraining from disrupting feelings of AG (Trucco, Mioshi, et al., 2023). In the context of psychological inflexibility, emotional avoidance is related to the concept of experiential avoidance (a sub-core process of psychological inflexibility). This would suggest that emotional avoidance may act as an effective coping mechanism carers use to navigate their circumstances in the short term. However, existing research has reported that avoiding or supressing feelings and emotions, while an adaptive response to loss during acute grief responses, may, if persistent, prolong the grieving period and contribute to complicated grief (Baker et al., 2016; Eisma & Stroebe, 2021) and prolonged grief disorder (Nanni et al., 2014; Thomas et al., 2014).

The potential adverse long-term impact of emotional avoidance concerning AG emotions emphasise the importance of a comprehensive approach to undermine psychological inflexibility. Psychological interventions such as ACT can enhance psychological flexibility, which is the opposite of psychological inflexibility. ACT aims to improve one's psychological flexibility through three sets of skills: stepping back from restricting thoughts and approaching or allowing painful emotions; focusing on the present, connecting with what is happening in the moment; and clarifying and acting on what is most important to do and building larger patterns of effective values-based actions (Hayes et al., 2013).

A recent feasibility study of ACT for pwMND demonstrated possible signals of efficacy, in particular to psychological quality of life in patients (Gould et al., 2023). In addition, a recent systematic review (Han et al., 2021) that explored the effectiveness of ACT on mental health outcomes in family carers demonstrated that ACT is effective in reducing anxiety and depressive symptoms among the carer population, which are two psychological outcomes contributing negatively to MND carers AG (Trucco, Backhouse, et al., 2023). Offering psychotherapy to MND carers is not routinely part of standard care within MND serviced in the UK despite the National Institute for Health and Care Excellence guidelines recommending support for this population during the progression of the disease (NICE, 2016). Considering ACT as a potential intervention for MND carers for better emotional coping is promising.

While these findings are important in light of the need of providing emotional support to carers during the trajectory of MND, certain limitations should be acknowledged. Firstly, the 7-item AAQ-II was used to assess carer psychological inflexibility. Although this measure has been widely used in research as a generic measure of psychological inflexibility, questionable internal consistency has been raised and concerns about measuring global distress rather than psychological inflexibility have been reported due to its simplicity (Wolgast, 2014). Future studies should consider the inclusion of a more population-specific measure of psychological inflexibility, such as the Experiential Avoidance in Caregiving Questionnaire (EACQ; Losada et al., 2014), or a recently developed more comprehensive measure of psychological inflexibility, which covers the broader aspects of psychological inflexibility, such as the 23-item Comprehensive assessment of Acceptance and Commitment Therapy processes (CompACT; Francis et al., 2016).

Additionally, most carers from this study presented average levels of psychological inflexibility. Future studies involving participants with diverse levels of psychological inflexibility and from different cultural backgrounds should be conducted to enhance the generalisability of the findings. Moreover, it is important to explore additional moderating factors between MND symptomatology and carer AG. For instance, emotional exhaustion, characterised by feelings of overload and emotional depletion when confronted the demands of caregiving and the needs of the care recipient, presents itself as a potential moderator factor (Gerain & Zech, 2019). Furthermore, conducting longitudinal studies to account for disability progression and how this might affect AG should be considered.

Notwithstanding the limitations outlined above, the findings of this study are remarkably novel. To our knowledge, there is a lack of research exploring the moderating effect of psychological inflexibility on AG, thereby contributing significantly to the existing body of literature in this field.

Conclusion

This study suggested that carer psychological inflexibility does not moderate the relationship between MND disease severity and behavioural symptoms, and carer AG. Nevertheless, it is noteworthy that all three factors – disease severity, behavioural

symptoms and carer psychological inflexibility – are individually associated with carer AG. These findings suggest ACT could be a potential intervention for addressing and enhancing psychological flexibility and better support carers emotionally.

In the next chapter I will integrate the findings reported by the four studies encompassing this thesis. I will provide a summary of findings and discuss their implications and future research directions.

Chapter 6: General Discussion

This thesis aimed to identify distinct factors that may affect anticipatory grief emotions in family carers of people living with MND and understand their emotional experiences of changes and losses during the trajectory of the disease. By unravelling and taking into consideration critical facets of this phenomenon in this population, future interventions targeting carers' emotional wellbeing can be more effectively developed and tailored to address their needs.

First, I provide a concise overview of the key findings from the four studies conducted within this thesis. Subsequently, I introduce the theoretical and clinical implications of the results. Finally, I present a comprehensive conclusion summarising my research project.

Summary of key findings

The first study in this thesis, Chapter 2, synthesised the existing literature on factors affecting grieving processes (anticipatory grief, post-death grief and prolonged grief disorder) of informal carers of people living with MND. This chapter highlighted significant factors that have been related to AG in this population: knowledge of MND, uncertainty and unpredictability linked with the disease, experiences while providing care, losses encountered throughout the progression of MND, changes in relationships and roles, carer anxiety and depressive symptoms, interactions with HCP, absence of end-of-life support, emotional avoidance and acceptance, and pre-death experiences. This systematic review also demonstrated that most of the present research within this field and population has primarily focused on post-death grief and prolonged grief disorder, and limited studies had targeted AG.

To strengthen the findings from the previous chapter, Chapter 3 qualitatively explored the experiences of changes and losses experienced by carers, with a specific focus on delving into their feelings. An adaptive cycle comprising destabilisation, adaptation and eventual acceptance of changes and losses emerged. Carers reported feelings of

resignation, sadness, tiredness, anger, loneliness and frustration through the course of the disease. Furthermore, this chapter explored the different coping strategies employed by carers to face their emotions associated with AG. As such, the following coping strategies were found: knowing about MND, taking a practical approach to address the needs of the care recipient, receiving practical, formal and informal support, focusing on the present and accepting the circumstances or avoiding thinking about them.

Chapter 4 investigated how distinct MND symptoms-related factors (i.e., severity of the disease and behavioural changes) and carer-related factors (relationship closeness, familism, hours of care provided) contributed to levels of carer AG. Incorporating both MND symptoms- and carer- related factors was a novel approach in MND quantitative studies. Four multiple regression analyses were conducted and showed that MND symptoms-related factors (i.e., disease severity and behavioural changes) were the only factors predicting carer AG, as measured by the MMCGI-SF. Due to the progressivenature of these factors, these findings presented challenges for carers themselves, potential interventions to support carers and areas of research, such as exploring modifiable factors that could serve as moderators to alleviate carers' negative emotions related to AG.

Based on the findings from the previous chapter, Chapter 5 investigated the role of psychological inflexibility as a moderator factor in the relationship between disease severity and behavioural changes and carer AG. This chapter demonstrated that while psychological inflexibility predicted AG, it did not serve as a moderator factor between MND-symptoms and carer AG. Moreover, it emphasised the potential role of interventions aimed at improving psychological flexibility, such as ACT, in enhancing the emotional wellbeing of carers.

Theoretical and clinical implications

The findings of the studies I conducted as part of this thesis have revealed several implications relating to how various factors contribute to carer AG, coping strategies carers use to manage daily changes and losses, and potential interventions that could be beneficial for this population. How these translate into theory and practice is discussed next.

Theoretical implications

This thesis provides valuable insights about the multifaceted nature of anticipatory grief. Findings from the multiple regression analyses conducted in Chapter 4 revealed that disease severity and behavioural changes emerged as the primary factors predicting AG-related emotions, surpassing carer-related factors such as, familism, relationship closeness and hours of care provided. However, single correlation analyses indicated that relationship closeness and hours of care provided were also associated with carer AG. Additionally, Chapter 5 demonstrated that psychological inflexibility, a carer-related factor, did not act as a moderator factor between MND symptoms and carer AG, although it was also associated with carer AG. These novel results prompt a critical inquiry: are carer-related factors identified in this thesis (such as those reported in Chapter 2, Chapter 4 and Chapter 5) direct contributors to carer AG, or do they serve as contextual influences on the levels of AG emotions and reactions and the ramifications of the primary factors, i.e., MND symptoms, associated with MND? This question highlights the complex interplay between various factors affecting carer AG.

Upon analysis of the MMCGI-SF results, both disease severity and behavioural changes consistently emerged as the most influential factors for the total AG score and scores from each sub-scale—addressing losses experienced during the caregiving role, interpersonal emotional reactions and feelings of loneliness. This highlights the prominence of MND symptoms as the primary predictors across various facets of AG. Consequently, there is a compelling case for the reconsideration of the factors influencing AG. It is important to consider a distinct delineation between factors deemed to *impact directly* on carer AG, such as MND symptoms, and those that may *influence* the intensity of grief experiences, for example carers' perception of relationship closeness and the care provided.

The severity of the disease and behavioural changes present on the person living with MND may act as initial triggers for and direct contributors to carer AG emotions, signaling the impending loss of the care recipient. Additionally, losses and changes carers experience as a consequence of MND, such as changes in the relationship with the care recipient, the loss of personal freedom, and alterations in personal time and social life might also directly contribute to AG. Given that AG in the context of providing care refers to the

changes and losses experienced by individuals throughout the course of the disease, including the anticipation of the future loss of the person, findings from this thesis can suggest that both MND symptoms and changes and losses experienced by carers may be the causal factors of AG. Other factors associated with AG in this thesis (reported in Chapter 2, Chapter 4 and Chapter 5), such as the knowledge of the disease, anxiety and depression symptoms, familism, hours of care provided, closeness in the relationship and psychological inflexibility may not directly cause AG but can influence its *intensity* by either *mitigating or exacerbating* AG emotions. For instance, anxiety symptoms might influence how changes in relationship are perceived by carers, while knowledge (or lack thereof) of the disease might alleviate AG emotions by reducing uncertainty and enabling better preparation for potential loss of freedom and personal time. In line with these thoughts, some factors, as discussed in Chapter 4, might warrant their own category as factors affecting how carers perceive changes and losses and the intensity of emotions linked to the changes and losses experienced, which are the underlying reasons to grieve. It is important to note that results from Chapter 5, that found that psychological inflexibility did not moderate the relationship between MND symptoms and carer AG, did not discourage or contradict these implications. Rather, it prompts a deeper examination of the complexity of carers' emotional responses and suggests that multiple factors, beyond psychological inflexibility alone, may influence carer AG.

Factors influencing carer AG may be divided into those directly related to carer AG emotions and those that may influence carers' experiences and perceptions of changes and losses. Causal factors directly linked to AG may include *MND symptoms-related factors*, reflecting the potential loss of the person (i.e., behavioural changes and disease severity), and *illness experience-related factors,* encompassing the changes and losses experienced due to the carer role. Additionally, MND symptoms-related factors may contribute to changes and losses experienced, i.e., illness-related factors. Factors that may affect how carers experience and perceive losses and changes may be divided into *carer-related factors* (pertained to the emotional, psychological and physical health of the carer) and *contextual factors* (such as support received, hours of care provided, access to respite care). Expanding on this, carer-related factors and contextual factors may influence each other. For example, a carer's avoidant coping style (carer-related factor) may impact on the hours of care

provided (contextual factor), which in turn have an impact on changes in the relationship (illness-related factor). It is important to note in this case that, the changes in the relationship, are likely to make the carer grieve.

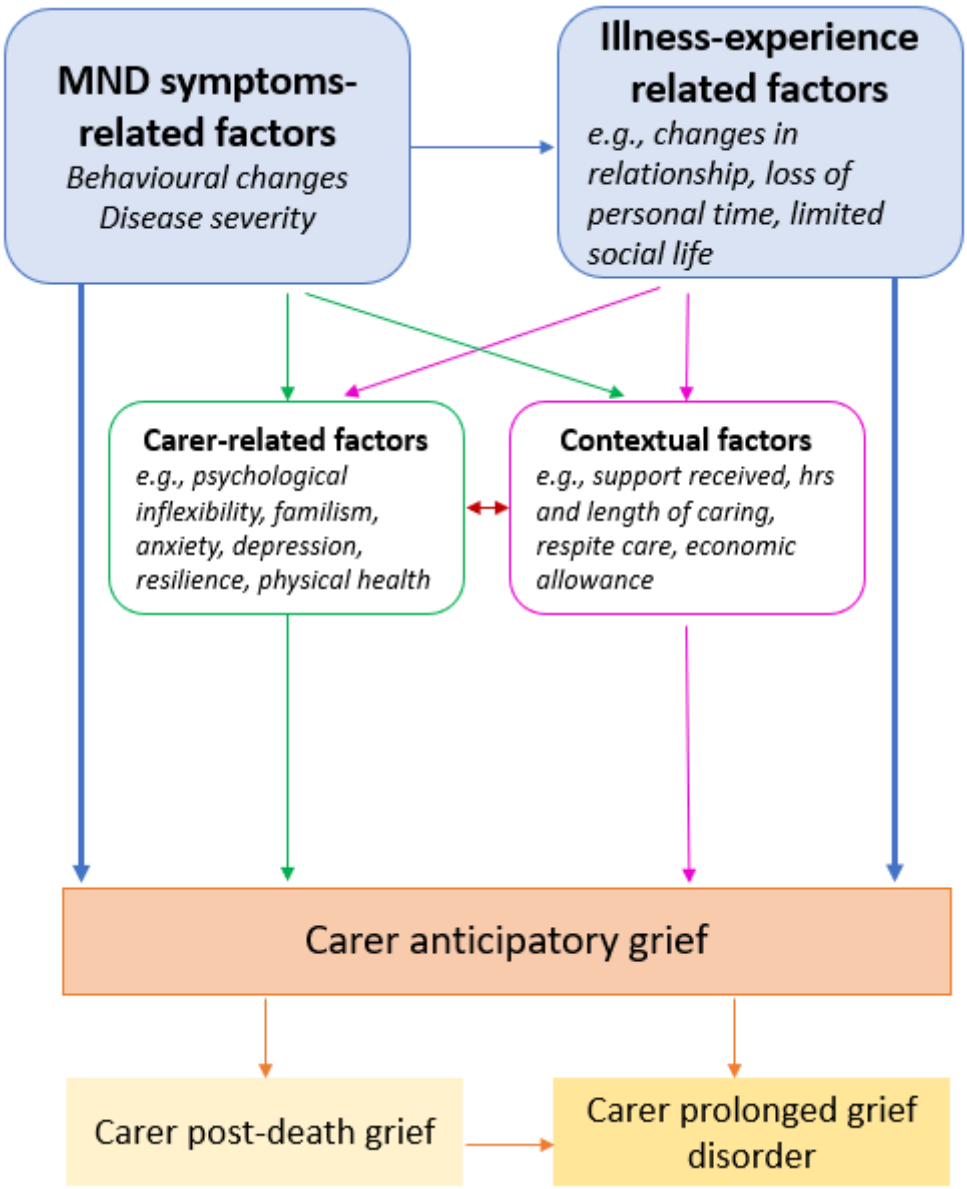
Building upon the aforementioned propositions, the findings of factors affecting AG in Chapter 2 and carers' coping strategies in Chapter 3 may require further elucidation. Factors such as knowledge of the disease, support received (including respite care) and carer avoidance have been considered factors affecting carer AG in Chapter 2 and coping strategies carers use to manage their emotional state in Chapter 3. Either way, these factors and/or coping strategies demonstrate the interplay between internal and external variables that shape carers' emotional experiences. It is pertinent to consider how coping strategies may intersect with the factors influencing AG and how they influence on how carers perceive and react to AG emotions. For instance, coping strategies such as avoidance, acceptance and focusing on the present entail psychological processes initiated by the carer themselves, thereby constituting carer- related factors. Conversely, coping strategies such as seeking formal and informal support and accessing respite care are contingent upon external factors and support systems, thus falling under the category of contextual factors. This nuanced perspective demonstrates the dynamic interplay between internal coping mechanisms and external support structures in the caregiving journey.

This section has described how the findings of this thesis support the categorisation of factors affecting anticipatory grief in family carers of people living with MND and the consideration of a potential model is proposed (Figure 6.1). Understanding the factors that influence AG in this population could contribute to theories of grief and bereavement by highlighting the multifaceted nature of AG and its interplay with various individual, interpersonal and contextual factors. For instance, it can aid in the development of predictive models of grief and the integration of carer-related and contextual factors into existing grief models. Additionally, theoretical frameworks can be refined by considering factors that contribute to AG. For example, the transactional model of stress and coping (Folkman, 1984) can be enriched by considering factors influencing AG as it emphasises how individuals appraise and cope with stressors, including those related to providing care and

impending loss. Moreover, findings can assist in the development of potential measures to assess carer AG and clinical interventions.

Figure 6.1

Causal Factors Affecting MND Carer Anticipatory Grief and their Interconnectedness with Carer-related and Contextual Factors



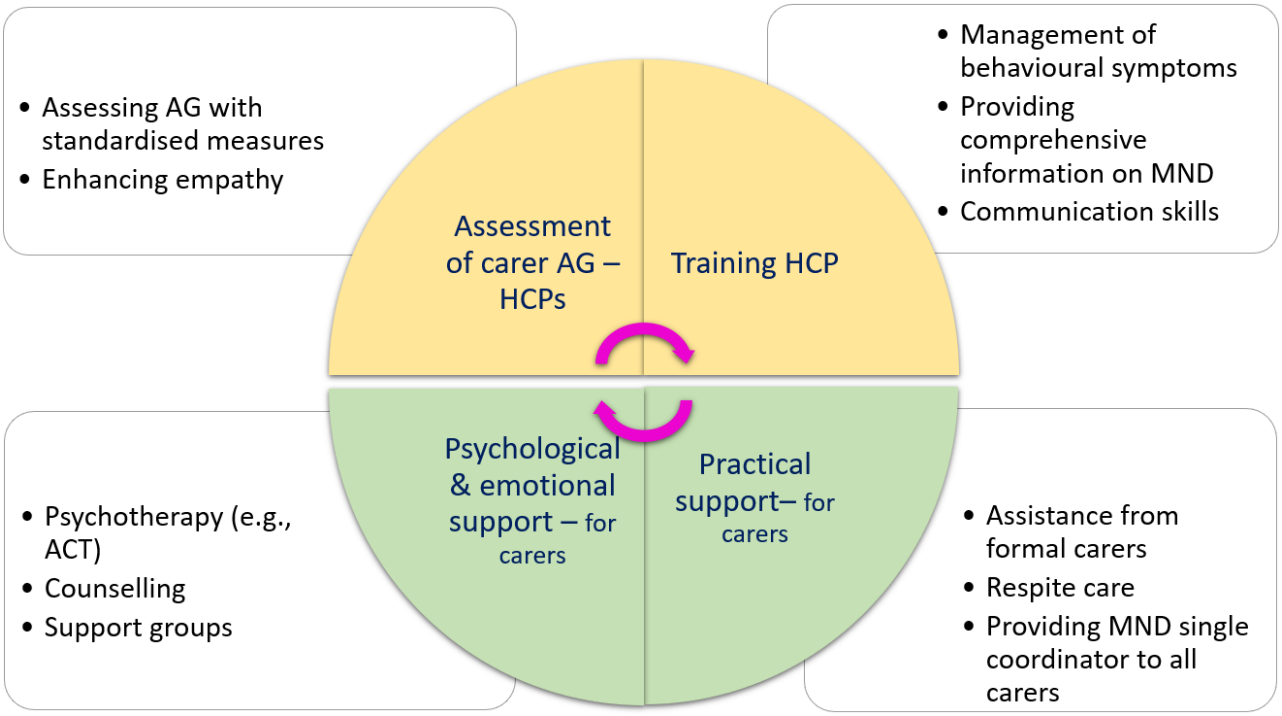
Clinical implications

This thesis offers meaningful contributions for the development of future interventions to address carer AG. Due to the current progressive nature of primary factors predicting AG emotions (i.e., behavioural changes and disease severity), challenges arise, encouraging a concerted effort to explore and implement the most effective strategies to support carers in their emotional journey.

Figure 6.2 summarises recommended key components to consider for future interventions. As discussed in the previous section, the dynamic relations and inter-connectedness of factors influencing AG in this carer population, underscore the necessity of multicomponent (i.e., multiple active strategies), multimodal (i.e., multiple modes and methods), and integrated (i.e., intersectoral collaboration) interventions combining multiple approaches to assist carers.

Figure 6.2

Recommended Components for Future Interventions to Address Anticipatory Grief in Carers of People Living with MND



Assessment of carer anticipatory grief

Assessing AG in the MND carer population is crucial as it would enable HCPs to identify carers who may be experiencing heightened levels of grief and emotional distress and may help identify the emotional, psychological and practical needs of carers. Recognising levels of AG would allow for the development of personalised support plans aimed at alleviating AG symptoms and improving carers' wellbeing, as well as more efficient resource allocation – while enhancing HCP empathy

As discussed in the Introduction section, there is a lack of a specific measure to address AG in this population. However, existing measures, such as the MMCGI-SF, might still be useful in obtaining a general understanding of carers' AG symptoms. Training HCPs in the use of AG measures (e.g., MMCGI-SF) to assess this phenomenon should be considered for two main reasons. Firstly, AG symptoms have been related to changes in sleep patterns, appetite, fatigue, fear, helplessness and anxiety (Simon, 2008). These symptoms can overlap with those of clinical depression. A careful distinction between AG and clinical depression should be examined as psychotropic medication dispensed to someone undergoing the natural process of AG may not be indicated (Worden, 2018). Secondly, symptoms such as forgetfulness, limited attention, difficulty in concentrating and making decisions have also been linked to AG (Simon, 2008). As mentioned in the interviews conducted in Chapter 3, during the MND journey, carers often need to take important decisions, such as end-of-life care planning, power of attorney arrangements and financial plans. These decisions can be laden with intense emotions, and carers may face the tension and stress which comes with HCPs demands for answers in a moment where carers' clarity and lucidity might be compromised (Fowler et al., 2013). Assessing and acknowledging the impact of AG on carers could enhance HCPs' empathy and understanding towards carers' emotions, leading to collaborative conversations to assist carers in decision making. In addition, the regular assessment of AG may facilitate ongoing monitoring of carers' emotional wellbeing and the effectiveness of interventions over time.

Recommended components for future interventions to address MND symptoms management

Training healthcare professionals on behavioural symptoms management

Findings from Chapter 4 highlighted that particularly behavioural changes (such as disinhibition, apathy and stereotypical behaviour) are linked to carer AG feelings including sadness, anger and guilt. Often these behavioural changes go under recognised in the person living with MND, and when they are, there is limited information on symptom management (Francis et al., 2023). Research has identified a notable lack of awareness, assessment and identification of behavioural symptoms in the MND care system, so limited information regarding this aspect is often delivered to carers (Francis et al., 2023; Mioshi, Heal & Katangwe-Chigamba, 2024). Training HCPs on the identification, assessment and management of behavioural symptoms could effectively bridge this gap. In addition, providing carers with information and skills for behavioural symptoms management could also prove beneficial. For instance, the MiNDToolkit, is an innovative psychoeducational online intervention designed for both HCPs and carers for the management of behavioural symptoms and has shown to be feasible as an intervention, warranting a future trial (Mioshi, Grant et al, 2024). HCPs have revealed that the MiNDToolkit is an invaluable educational resource for practitioners and provided them with skills and knowledge to identify and better address behavioural symptoms (Katangwe-Chigamba et al., 2024). Moreover, carers expressed they were able to accept behavioural changes when understanding distressing symptoms and gaining strategies to address them (Mioshi, Heal & Katangwe-Chigamba, 2024).

Enhancing healthcare professionals' communication skills and coordination

There are additional considerations I would like to emphasise concerning MND symptoms and the healthcare system. The interviews conducted in Chapter 3 highlighted the essential role of HCPs in delivering MND information during the trajectory of the disease. The importance of providing carers with clear and comprehensive information about disease symptoms, could potentially alleviate their emotions related to the diagnosis and uncertainty surrounding MND. This aligns with previous studies, which have also found the significance of carers' knowledge about disease symptoms (Aoun et al., 2013).

Furthermore, Chapter 3 revealed varying preferences among carers regarding the extent of information they desired post-diagnosis. A possible way to address this could involve training HCPs to recognise the individual emotional needs of carers and tailor the delivery of information accordingly during consultations and appointments. For instance, a simple inquiry about the carer's emotional state and preferences for discussion topics could be a straightforward strategy to provide personalised support.

Providing practical support for carers

This thesis also revealed disease severity as the most significant predictor of the losses and changes carers experience, as measured by the MMCGI-SF (Chapter 4). Items from the MMCGI-SF pertaining to these losses and changes included sacrificing personal pursuits and time to fulfil caregiving duties, a sense of losing freedom and uncertainty about the future. Interestingly, though not surprisingly, these same losses and changes were highlighted by carers interviewed as part of this thesis (Chapter 3), as well as by the systematic review (Chapter 2). The progressive nature of the disease, combined with the inability to reverse symptoms, underscore the necessity to explore alternative methods to support carers. Moreover, Chapter 4 revealed that an increase in the number of hours dedicated to providing care to the person living with MND was positively associated with AG, indicating that more hours devoted to the care recipient, were related to heightened negative emotions. A previous review identified the importance of practical support in this population (Harris et al., 2018). As suggested in Chapter 3, accessing respite care and formal support through the care system, such as providing formal carers, might be effective strategies to assist carers. Aiding carers with dedicated time for themselves could help in alleviating negative grief symptomatology related to the changes and losses experienced due to disease severity, thereby enhancing their wellbeing.

Chapter 3 also remarked the frustration experienced by carers when faced with calls and visits from different and multiple HCPs without identification of their roles. This finding is consistent with previous research, which highlighted the challenges posed by the high volumes of involved HCPs without clarity about each of their roles and without a key member to contact (O'Brien et al., 2011). Establishing a designated point of contact for carers to access care services for the person living with MND, particularly within community

healthcare settings, is advisable. This designated coordinator could facilitate communication by informing carers about upcoming home appointments with HCPs and providing details about the professionals' names and roles. This approach aligns with research indicating that carers value having a single point of contact, such as MND nurses through whom the care needs were synchronised (O'Brien et al., 2012). Moreover, the Motor Neurone Disease Association, UK, advocates for the establishment of MND clinics staffed by multidisciplinary teams working cohesively and co-ordinately (MNDA, 2021).

It is important to note that while the grief stemming from the behavioural changes and disease severity may persist, a deeper understanding of behavioural changes and its management, and tackling care and support services addressing disease progression could alleviate carers' negative feelings and emotions. Related to this, it is interesting to note that a literature review aimed at identifying factors relevant to intervention development and testing in carers of people living with MND (Gluyas et al., 2017) highlighted that behavioural changes and disease severity were both linked to carer burden. Consequently, these MND symptoms-related factors reflect worse psychological and emotional outcomes for carers. Addressing AG carer-related and contextual factors could mean not only improving carers' emotional state but addressing psychological outcomes as well.

Recommended components for psychotherapeutic interventions

Chapter 3 shed light on the changes in roles that family carers experience, particularly the transition from being a spouse to assuming the role of a carer. Although relationship closeness was not identified as a significant predictor of carer AG in Chapter 4, it was nevertheless associated with it. This reflects the importance of the emotional dynamics within the relationship and its potential impact on carer AG. Previous literature has highlighted the difficulties for carers in recognising their own needs (Ewing et al., 2020; MNDA, 2022), potentially influenced by their evolving role impacting on the relationship with the care recipient and feelings of familism. Offering support to carers to help them identify their own needs in this transitional period may be a critical component to consider in future interventions. Consistent with previous research, (Gluyas et al., 2017), counselling sessions involving both carer and care recipient might be beneficial, as well as assisting carers in the recognition of their new carer role, while also acknowledging their own needs.

Another important finding in this thesis was the positive correlation of carer psychological inflexibility and carer AG in Chapter 5, indicating that higher carer psychological inflexibility may contribute to increased levels of carer AG. Psychological inflexibility encompasses various processes, one of which is experiential avoidance — the unwillingness to remain in contact with aversive circumstances and take action to alter them (Hayes et al., 2013) and has been associated with negative outcomes such as greater disfunction and increased distress including prolonged grief (Baker et al., 2016). Chapter 3 showed that some carers employ an avoidant coping style to maintain their emotional wellbeing. However, this avoidant inner control may result in excessive efforts and energy devoted to suppressing negative emotions and avoiding pursuing valued goals and being in contact with the present moment (Hayes et al., 2006). While avoidance may offer short-term relief, addressing it is imperative as it does not provide sustainable coping mechanisms (Karekla & Panayiotou, 2011; Ottenbreit & Dobson, 2004). As discussed in Chapter 5, interventions aiming to improve carers psychological flexibility, such as Acceptance and Commitment Therapy (ACT), may have a strong potential in alleviating negative carer AG feelings and emotions. This behavioural therapy does not aim to change uncomfortable feelings and thoughts as it states that human suffering is inevitable in life but aims to embrace them as they are and help individuals to connect to what is genuinely important and meaningful to them and use that knowledge to enhance goal-directed behaviours (Hayes et al., 2012; Harris et al., 2019). In addition, ACT promotes acceptance, which aligns with some carers' coping strategies identified in Chapter 3. Moreover, acceptance – recognising the reality and circumstances of a diagnosis, is one of the stages of AG (Kübler-Ross, 1969) and has been correlated with AG emotions (Davis et al., 2017). As such, given the potential benefits in both avoidance and acceptance coping styles, ACT seems very promising within this population.

In Chapter 3, it was found that attending MND carers' support groups was beneficial for some carers as they could connect with peers facing similar challenge, which made them feel understood. Previous research has identified that attending to support groups, if timely, could be helpful as they offer opportunities to learn from other carers and gain social support (Gluyas et al 2017; Mockford et al., 2006). Interventions involving support groups are recommended, however, considerations should be taken into account regarding carers'

needs and preferences. As also stated in Chapter 3, some carers may be reluctant to attend these groups as they confront the progression of the disease.

As a final remark of this section, I would like to highlight the ongoing need for tailored interventions aimed at supporting carers of people living with MND. Numerous reviews dating back to 2006 (Aoun et al., 2013; Gluyas et al., 2017; Mockford et al., 2006; Pagnini et al., 2013), including the systematic review conducted within this thesis in Chapter 2 (Trucco, Backhouse et al., 2023), have consistently highlighted this gap in interventions. Despite the passage of a decade, the findings from this thesis regarding anticipatory grief echo these earlier observations, suggesting that effective support for carers remains elusive. This underscores the persistent need for targeted interventions to enhance family carers of people living with MND wellbeing and quality of life.

Strengths, limitations and future research

This thesis represents a significant advancement in the study of MND carer anticipatory grief emotions. With limited prior research in this area, it fills a crucial gap in the literature by providing novel insights into the AG emotional experiences of MND carers.

A key strength of this thesis is its pioneering comprehensive approach towards understanding and addressing AG in this population. The utilisation of a mixed methods approach integrating qualitative and quantitative methodologies, in addition to a systematic review synthesising existing research within the field of investigation contribute to the robustness of my research project and strengthens the validity of the findings. In addition, the consideration of a potential model of factors affecting MND carer anticipatory grief stemming from the findings of this thesis hold significant promise, as it could serve as a valuable tool to guide future research, inform clinical practice and enhance support services.

Each individual chapter (Chapter 2, Chapter 3, Chapter 4 and Chapter 5) addressed the specific limitations related to each of the studies. However, I would like to synthesise them in this section, in addition to presenting general limitations of my thesis and the potential areas of research that arise from the findings and should be considered in future studies.

It is important to address the potential selection bias present in the participant sample of Chapter 4 and Chapter 5 due to the recruitment strategies employed. In the studies detailed in Chapter 4 and Chapter 5, both studies used the same sample. Participants were recruited through various avenues (e.g., carers' support groups, MND clinics, dissemination of the study in MND organisation websites and media platforms such as Twitter) and chose to take part. The recruitment strategies did not include prior screening for eligibility criteria. Consequently, the sampling method and number of participants were not controlled in terms of relationship to the person living with MND, ethnicity, carers' age, length of care and MND diagnosis, which could have ensured greater diversity. As a result, the sample was predominantly composed of spouses of people living with MND, mainly women and mostly were white British. This led to the underrepresentation of other family carers and ethnic groups who may present different emotional experiences. The selection bias impacts the generalisability of my findings. The results and conclusions drawn from these studies may not be applicable to the broader MND carer population, as the sample does not adequately reflect the diversity of experiences and backgrounds within this group. Recognising this limitation is crucial for interpreting the studies' outcomes and for guiding future research towards more inclusive and representative sampling strategies. It is recommended in future to implement stratified sampling techniques to ensure a more diverse participant pool, and the previous screening of participants for eligibility criteria, such as screen for demographic factors.

While this thesis is titled "Factors affecting anticipatory grief in family carers of people living with Motor Neurone Disease: The role of MND symptomatology" it is essential to note that the focus was primarily on behavioural symptoms and overall disease severity. Although disease severity is related to motor symptoms, there was no particular analysis of specific motor symptoms. For instance, certain symptoms, such as bulbar symptoms were not explicitly explored. Bulbar symptoms, which affect speech and swallowing, can be particularly distressing for both carers and pwMND due to their impact on communication and daily care activities and might heighten the emotional reactions and burden on carers, potentially intensifying AG. Similarly, other motor symptoms, such as weakness in the upper and/or lower limbs, may cause significant limitation in mobility and increased dependency of the person living with MND, which can also affect carers' emotions. In relation to

behavioural symptoms, the measure to assess behavioural changes (MiND-B) included apathy, disinhibition and stereotyped behaviour. Research has shown that the breadth of behavioural symptoms in the person living with MND is much more extensive, also including loss of sympathy and empathy, hyperorality, psychotic symptoms and loss of insight (Trucco, Backhouse & Mioshi, 2024). A more detailed exploration of each behavioural change, including those not investigated in this thesis, would provide a more comprehensive understanding. Additionally, it would have been important to understand the impact of cognitive changes in the person living with MND in carer AG in Chapter 4 and Chapter 5, as more than 50% of pwMND might present with cognitive symptoms (Strong et al., 2017). Exploring the impact of this potential factor would have led to a deeper understanding on how MND symptoms might affect this population. Future research should consider investigating these areas to enhance our understanding of the complex dynamics between MND symptomatology and carer AG. By exploring the differential and detailed impact of various MND symptoms, including specific behavioural, motor and cognitive symptoms, more targeted support interventions for family carers could be developed, ultimately improving their emotional wellbeing and coping mechanisms.

In addition, it would have been important to consider and include potential confounding factors, such as depression, anxiety and burden in Chapter 4. Particularly depression and anxiety have been linked to carers AG (Chapter 2). In addition, burden has been associated with carer AG in other populations (Li et al., 2022), and contribute to emotional exhaustion – feelings of overload and being emotionally drained when providing care (Gerain & Zech, 2019). Indeed, these variables could have impacted the rating on the measures, including the MMCGI-SF.

Another limitation relies on the use of the MMCGI-SF, that despite having been updated for studies in Chapter 4 and Chapter 5, was not developed in the MND carer population. Although the Cronbach's alpha of this measure in the studies from this thesis was high (=.94), having assessed carers with a specific AG MND measure would have provided more detailed findings. It would be important that future research developed a validated measure to assess AG in this population considering the potential factors identified in this thesis. This may lead to carer interventions to manage MND symptoms, to

address changes in their relationships, to stay connected with the present and do things that matter to them.

In relation to demographics, most carers included in this thesis were white British and spouses of the person living with MND. It would be interesting to replicate studies in Chapter 3, Chapter 4 and Chapter 5 in other ethnic groups and other family members, such as adult-children to further validate findings and promote their generalisation.

It would also be recommended in the future to explore how contextual (e.g., respite care) and carer-related factors (e.g., avoidance) may serve as moderators or mediators between MND symptoms-related factors and carer AG.

Concluding remarks

Anticipatory grief in carers of people living with MND had been underexplored in previous literature. This thesis sheds light to the understanding of this phenomenon by identifying key factors that affect AG in this population and enhances our comprehension of how the interplay of various factors contribute to carers' emotional experiences. Notably, MND symptoms (i.e., behavioural changes and severity of the disease) emerged as the most significant predictors of AG. Given the progressive nature of MND and the absence of a cure to date, interventions targeting both carer-related and contextual factors provide potential avenues to address carer AG. By addressing these factors, non-pharmacological interventions could effectively support carers in navigating their emotional journey throughout the trajectory of the disease.

It is noteworthy that findings from the four studies of this thesis concluded that there is a critical need for a more holistic support system for carers of people living with MND and the adoption of a proactive approach to addressing their diverse needs. This may include the regular assessment of carer's needs, including AG, the development of tailored interventions to manage MND symptoms, provision of psychotherapy, offering practical support like respite care and formal carers, and the provision of support services to all those affected by MND, such as a MND coordinator. Consequently, carers may receive the necessary resources, tools and assistance required to navigate the multifaceted losses and

changes experienced during the progression of MND, feel better supported in their essential role and ultimately improve their emotional wellbeing.

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Appendices

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Ethical Approvals

Factor-MND Approval

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

Prof Eneida Mioshi
Professor of Dementia Care
University of East Anglia
Queens Building
Norwich
NR4 7TJ

29 July 2020

Dear Prof Mioshi

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Factors Affecting Family Carers in Motor Neuron Disease**
IRAS project ID:	**281943**
Protocol number:	**V1**
REC reference:	**20/WM/0185**
Sponsor	**University of East Anglia**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **281943**. Please quote this on all correspondence.

Yours sincerely,
Helen Penistone
Approvals Specialist

Email: approvals@hra.nhs.uk

Copy to: *Tracy Moulton*

Amendment 1 – substantial amendment

Health Research Authority

West Midlands - Black Country Research Ethics Committee

The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

08 June 2021

Prof Eneida Mioshi
Professor of Dementia Care
University of East Anglia
University of East Anglia
Queens Building
Norwich
NR4 7TJ

Dear Prof Mioshi

Study title:	**Factors Affecting Family Carers in Motor Neuron Disease**
REC reference:	**20/WM/0185**
Protocol number:	**V1**
Amendment number:	**Substantial Amendment 1**
Amendment date:	**17 May 2021**
IRAS project ID:	**281943**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [Amendment tool]	1	17 May 2021
Copies of materials calling attention of potential participants to the research [Factor_MND Participant leaflet_V2_10.05.2021]	2	10 May 2021
Covering letter on headed paper [Cover Letter]	1	11 May 2021
Other [Factor-MND_CRF_V2_tracked changes]	2.0	10 May 2021
Other [Factor-MND Participant leaflet_V2_highlighted changes]	2.0	10 May 2021

Participant information sheet (PIS) [Factor_MND_PIS_V2_10.05.2021]	2	10 May 2021
Participant information sheet (PIS) [Factor-MND_PIS_V2_tracked changes]	2.0	10 May 2021
Research protocol or project proposal [Factor-MND_Protocol V2_tracked changes]	2.0	10 May 2021
Research protocol or project proposal [Factor_MND_Protocol V2_10.05.2021]	2	10 May 2021
Validated questionnaire [Factor-MND_Questionnaires]	2	10 May 2021

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 281943:	**Please quote this number on all correspondence**

Yours sincerely

pp.

Dr Hilary Paniagua
Chair

E-mail: blackcountry.rec@hra.nhs.uk

Amendment 2 – substantial amendment

Health Research Authority

West Midlands - Black Country Research Ethics Committee

The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

14 March 2022

Tracy Moulton
Queens Building
University of East Anglia
Norwich
NR4 7TJ

Dear Tracy Moulton

Study title:	**Factors Affecting Family Carers in Motor Neuron Disease**
REC reference:	**20/WM/0185**
Protocol number:	**V1**
Amendment number:	**Substantial Amendment 2**
Amendment date:	**24 February 2022**
IRAS project ID:	**281943**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Recommendation

The members of the Committee recommended including links to support services within the interview participant information sheet.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [Amendment tool]	v1.6	24 February 2022
Copies of materials calling attention of potential participants to the research [Factor-MND_leaflet_v3_16.02.2022]	3	16 February 2022
Copies of materials calling attention of potential participants to the research [Factor-MND_Interview Participant leaflet_v1]	1	16 February 2022
Covering letter on headed paper [Cover Letter for Substantial Amendment 2]	1	25 February 2022

Interview schedules or topic guides for participants [Factor-MND_Interview Topic Guide_v1]	1	16 February 2022
Letters of invitation to participant [Factor-MND_Invitation Letter Interview_v1]	1	16 February 2022
Other [Factor-MND_Interview Helplines_v1]	1	16 February 2022
Other [Factor-MND_Study Protocol_v3_16.02.2022]	3	16 February 2022
Other [Factor-MND_Protocol_v3_track changes]	3	16 February 2022
Participant consent form [Factor-MND_Interview Consent Form_v1]	1	16 February 2022
Participant information sheet (PIS) [Factor-MND_PIS_track changes]	3	16 February 2022
Participant information sheet (PIS) [Factor-MND_PIS_v3_16.02.2022]	3	16 February 2022
Participant information sheet (PIS) [Factor-MND_PIS Interview_v1]	1	16 February 2022

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 281943:	**Please quote this number on all correspondence**

Yours sincerely
pp

Miss Nicola Brooks
Chair

E-mail: blackcountry.rec@hra.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: Prof Eneida Mioshi, *University of East Anglia*

West Midlands - Black Country Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 15 March 2022 via correspondence

Committee Members:

Name	*Profession*	*Present*	*Notes*
Miss Nicola Brooks (Chair)	Solicitor	Yes	
Miss Suzy Wignall	Clinical Governance Advisor	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Mia Crispin	Approvals Administrator

Amendment 3 – substantial amendment

Health Research Authority

West Midlands - Black Country Research Ethics Committee

The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

23 August 2022

Prof Eneida Mioshi
Professor of Dementia Care
University of East Anglia
University of East Anglia
Queens Building
Norwich
NR4 7TJ

Dear Prof Mioshi

Study title:	**Factors Affecting Family Carers in Motor Neuron Disease**
REC reference:	**20/WM/0185**
Protocol number:	**V1**
Amendment number:	**Substantial Amendment 3**
Amendment date:	**04 August 2022**
IRAS project ID:	**281943**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [Amendment tool_3]	v1.6	04 August 2022
Participant information sheet (PIS) [Interview Participant Information Sheet]	v.2	29 July 2022
Participant information sheet (PIS) [Interview Participant Information Sheet_tracked changes]	v.2	29 July 2022
Research protocol or project proposal [Study Protocol]	v.4	29 July 2022

Research protocol or project proposal [Study Protocol_tracked changes]	v.4	29 July 2022
Validated questionnaire [Factor-MND_CRF]	v.3	29 July 2022
Validated questionnaire [Factor-MND_CRF_tracked changes]	v.3	29 July 2022

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 281943:	**Please quote this number on all correspondence**

Yours sincerely
pp

Miss Nicola Brooks
Chair

E-mail: blackcountry.rec@hra.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Tracy Moulton; University of East Anglia*

West Midlands - Black Country Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 16 August 2022 via correspondence

Committee Members:

Name	*Profession*	*Present*	*Notes*
Miss Nicola Brooks (Chair)	Solicitor	Yes	
Miss Dorabella Moskovic-Thomas	Student	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Mia Crispin	Approvals Administrator

Amendment 4 – non substantial amendment

IRAS 281943. Amendment

NI New IRAS Dev <no-reply-iras@hra.nhs.uk>
To Ana Paula Trucco (HSC - Staff) 30/09/2022

You forwarded this message on 03/10/2022 11:31.

Warning: This email is from outside the UEA system. Do not click on links or attachments unless you expect them from the sender and know the content is safe.

IRAS Project ID: 281943
Sponsor amendment reference: Substantial Amendment 4

Thank you for submitting your study amendment. In accordance with the outcome of your completed amendment tool, this amendment requires no further regulatory review. Please now share this amendment with your UK research sites, in accordance with the instructions in your completed amendment tool.

For studies with more than one UK research site, your amendment will now be automatically shared with the R&D offices of any NHS/HSC research sites in Scotland and Northern Ireland, but you should share the amendment by email directly with those Research team/s.

For all NHS research sites in England and Wales, please now share this amendment by email directly with those sites, including both the R&D offices and research teams.

Do not reply to this email as this is an unmonitored address and replies to this email cannot be responded to or read.

This message may contain confidential information. If you are not the intended recipient please inform the sender that you have received the message in error before deleting it. Please do not disclose, copy or distribute information in this e-mail or take any action in relation to its contents. To do so is strictly prohibited and may be unlawful. Thank you for your co-operation..

The summary of the amendment tool states :
This amendment aims to clarify that only participants who are residents in the United Kingdom will be invited to participate in the qualitative interview study if they wish to leave their details at the end on the survey. Wellbeing contact numbers for participants living in United States and Australia have also been included at the end of the survey (CRF). The participant information sheet for the quantitative survey has also been updated with the addition of the reference number which corresponds to the dissemination of the study internationally (approved by the correct organisation), minor edits to fit the information for participants in the UK and living overseas and correct contact details.

Factor-MND International approval

University of East Anglia
Norwich Research Park
Norwich. NR4 7TJ

Email: ethicsapproval@uea.ac.uk
Web: www.uea.ac.uk

Study title: Factors affecting family carers' wellbeing in Motor Neurone Disease

Application ID: ETH2223-0204

Dear Ana Paula,

Your application was considered on 14th October 2022 by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee).

The decision is: **approved**.

You are therefore able to start your project subject to any other necessary approvals being given.

If your study involves NHS staff and facilities, you will require Health Research Authority (HRA) governance approval before you can start this project (even though you did not require NHS-REC ethics approval). Please consult the HRA webpage about the application required, which is submitted through the IRAS system.

This approval will expire on **31st December 2023**.

Please note that your project is granted ethics approval only for the length of time identified above. Any extension to a project must obtain ethics approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) before continuing.

It is a requirement of this ethics approval that you should report any adverse events which occur during your project to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) as soon as possible. An adverse event is one which was not anticipated in the research design, and which could potentially cause risk or harm to the participants or the researcher, or which reveals potential risks in the treatment under evaluation. For research involving animals, it may be the unintended death of an animal after trapping or carrying out a procedure.

Any amendments to your submitted project in terms of design, sample, data collection, focus etc. should be notified to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) in advance to ensure ethical compliance. If the amendments are substantial a new application may be required.

Approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) should not be taken as evidence that your study is compliant with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018. If you need guidance on how to make your study UK GDPR compliant, please contact the UEA Data Protection Officer (dataprotection@uea.ac.uk).

Please can you send your report once your project is completed to the FMH S-REC (fmh.ethics@uea.ac.uk).

I would like to wish you every success with your project.

On behalf of the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee)

Yours sincerely,

Paul Linsley

Who is invited to participate in this study?

People that have a relative who has been diagnosed with Motor Neurone Disease (MND) are invited to participate in this study. Participation in this study is entirely voluntary.

All data is anonymous in this study. No personal data will be taken.

All information and data collected from you as part of this study is confidential and kept in compliance with the Data Protection Act (2018).

The information we collect will enable us to understand the challenges that might occur for carers of people with motor neurone disease

For more information and any questions please contact:

Email: mnd.research@uea.ac.uk

Phone: 07825 863389

Sponsored by the University of East Anglia

Neurodegeneration Network
Queen's Building
Norwich Research Park
Norwich
Norfolk
NR4 7TJ

nnet neurodegeneration network

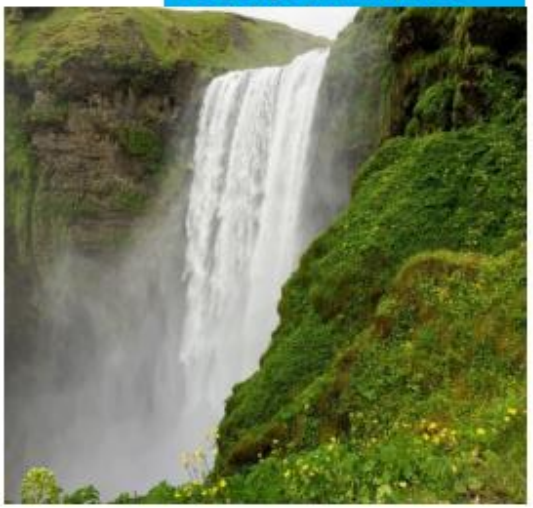
IRAS No: 281943
Version 3, 16 February 2022

University of East Anglia

Factor-MND

Factors Affecting Family Carer's Wellbeing in Motor Neurone Disease - survey study

Leaflet for participants



What is this study for?

We are interested in understanding what certain family factors may contribute to the carer's wellbeing, such as family values and personal relationships, psychological flexibility, and potential changes in behaviour of the person with MND.

This research aims to help us learn how to better support family carers of people with MND.

What would I have to do?

As a carer of someone with Motor Neurone Disease, we are asking you to complete some questionnaires about your personal wellbeing, family, relationships, and your family member's diagnosis of MND. There are 82 questions in total and they are mostly multiple choice, with some background questions. It is estimated this will take you 30 minutes. These can be completed online (via a web link) or via paper and pen format.

How do I join the study?

Either:

- Complete the online survey at:

https://uea.onlinesurveys.ac.uk/factor-mnd

- Give us a call on 07825 863389
- Email us: mnd.research@uea.ac.uk
- Fill out the attached slip and mail back to receive survey packet.

If you would prefer a pen and paper packet mailed to you, please complete the slip.

Your name: .....

Your address: .....

Phone: .....

Email: .....

Return to:
Eneida Mioshi, Queen's Building, School of Health Sciences, University of East Anglia Norwich NR4 7TJ

This study is being led by Prof Eneida Mioshi from the Faculty of Medicine and Health Sciences at the University of East Anglia in the United Kingdom.

The information we collect will enable us to understand the challenges that might occur for carers of people with motor neurone disease and how carers manage emotionally the changes that might occur in their daily life.

For more information and any questions about the studies please contact:

Email:
mnd.research@uea.ac.uk

Phone: (+44) 7825 863389

Sponsored by the University of East Anglia, Norwich, UK

Neurodegeneration Network
Queen's Building
Norwich Research Park
Norwich
Norfolk
NR4 7TJ
UK

Version 1, 13 September 2022

nnet network

University of East Anglia

Factor-MND

Factors Affecting Family Carer's Wellbeing in Motor Neurone Disease/Amyotrophic Lateral Sclerosis

Leaflet for International participants

Who is invited to participate in this study?

People that have a relative who has been diagnosed with Motor Neurone Disease (MND)/Amyotrophic Lateral Sclerosis (ALS) are invited to participate in this project. Participation in this project is entirely voluntary.

All data is anonymous in this study. No personal data will be collected.

All information and data collected from you as part of this study is confidential and kept in compliance with the Data Protection Act (2018).

What is this project for?

We aim to understand better what certain factors and how experiences of being a family carer for someone living with MND/ALS may contribute to carer's wellbeing
We are particularly interested in how family carers emotionally manage the changes that MND/ALS might bring to everyday life

This research aims to help us learn how to better support family carers of people with MND/ALS.

What would I have to do?

As a carer of someone with Motor Neurone Disease, we are asking you to complete some questionnaires about your personal wellbeing, family, relationships, and your family member's diagnosis of MND. There are 82 questions in total, and they are mostly multiple choice, with some background questions. It is estimated this will take you 30 minutes.

How do I join the study?

Complete the online survey at:

https://uea.onlinesurveys.ac.uk/factor-mnd

Participant information sheet – survey study

IRAS No: 281943 UEA FMH REC ETH2223-0204

University of East Anglia

Factors Affecting Family Carer's Wellbeing in Motor Neurone Disease

Participant Information Sheet

You are invited to take part in a research study. In order to help you decide to participate, we would like to share with you why the research is being done and what it will involve.

Why have I been invited?
You have been invited because you have a relative who has been diagnosed with Motor Neurone Disease (MND)/Amyotrophic Lateral Sclerosis (ALS). Participation in this study is entirely voluntary.

What is this study about?
We are looking to understand better how being a family carer for someone living with MND impacts the carer's wellbeing. This research aims to help us learn how to better support family carers of people with MND.

Who is organising this study?
This study is being led by Professor Eneida Mioshi from the Faculty of Medicine and Health Sciences at the University of East Anglia in the United Kingdom.

What will happen to me if I take part?
As a carer of someone with MND/ALS, we are asking you to complete eight questionnaires about your personal wellbeing, family, relationships, and your family member's diagnosis of MND/ALS. There are 82 questions in total which are mostly multiple choice, and some background questions. It is estimated this will take you approximately 30 minutes, however you can take longer if you require any breaks in between questionnaires. We kindly ask that you complete all questionnaires within the same week if possible. These can be completed online (via a web link) at https://uea.onlinesurveys.ac.uk/factor-mnd

How will we use information about you?
We will need to use information from your questionnaires for this research project. This information will include your anonymized data. People will use this information to do the research or to check your records to make sure that the research is being done properly. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. Since all individuals are participating anonymously no-one will be able to work out that you took part in the study.

Anonymized research data may be shared between other members of the department, and UEA collaborators, and with researchers undertaking other ethically approved research including national and international collaborations, who all adhere to relevant data protection legislation and confidentiality.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

Will this study benefit me?
We cannot guarantee that the study will be of direct benefit to you, although you may experience some indirect positive effects, such as knowing that you are helping researchers learn more about everyday experiences of carers, which may improve the wellbeing of others, now or in the future.

Some of the questions may be of sensitive nature and it is possible that these questions may bring up upsetting or distressing emotions. If any questions do this for you, we ask that you please contact your GP for support. If you are feeling distress while completing the questionnaires, you can stop taking part in the study at any time and contact your GP.

Who will be able to access or see my data?
All results and documents associated with this research are strictly confidential and stored securely in compliance with the Data Protection Act (2018) and the General Data Protection Regulation (GDPR). All data will remain anonymous.

What if I have a complaint, or if something goes wrong?
In the unlikely event of anything problematic happening, you may complain directly to the Dean of the School of Health Sciences: Sally Hardy, S.Hardy@uea.ac.uk

Where can you find out more about how your information is used?
You can find out more about how we use your information

- At www.hra.nhs.uk/information-about-patients/
- Our leaflet available from University of East Anglia
- By asking one of the research team (see emails below)

Tick the box to consent you have read participant information sheet and consent to participate in the study: ☐

If you would like more information, or need to contact our research team after taking part, please contact us at:

Ana Paula Trucco (PhD Student)
Queens Building
School of Health Sciences
University of East Anglia
Norwich NR4 7TJ
Phone: +44 (0)7825863389
Email: mnd.research@uea.ac.uk

Prof Eneida Mioshi (Chief Investigator)
Queens Building
School of Health Sciences
University of East Anglia
Norwich NR4 7TJ

Email: mnd.research@uea.ac.uk

What happens next?

1. We will contact you (by phone or email) to answer any questions you may have and to make sure that you are happy to take part.

2. If you decide to participate in the study, we will ask you to sign a consent form.

3. We will arrange a time to have the interview, either face-to-face or online.

4. We will store your information on a secure database.

All information and data collected from you as part of this study is strictly confidential and kept in compliance with the Data Protection Act (2018).

The information we collect will enable us to understand how carers of people living with MND manage emotionally the changes that might occur in daily life when caring for the person with MND.

If you would like to take part in this study, or have questions or concerns, please contact the researcher at any time:
Email: mnd.research@uea.ac.uk
Phone: +44 (0) 7825 863389

If you decide to take part in the interview, but change you mind later, you can withdraw at any time without having to give a reason. Or if you don't want to join right now, you can also decide to participate at a later stage.

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Neurodegeneration Network
Queen's Building
Norwich Research Park
Norwich
Norfolk
NR4 7TJ

IRAS No: 281943
Leaflet v.1, 16 February 2022

University of East Anglia

Factor-MND

Factors Affecting Family Carers' Wellbeing in Motor Neurone Disease – interview study

Leaflet for potential participants

What is this study for?

People that support a relative who has been diagnosed with Motor Neurone Disease (MND) are invited to participate in this study.

We aim to understand better how the experiences of being a family carer for someone living with MND impact the carer's wellbeing. We are particularly interested in how family carers emotionally manage the changes that MND might bring to everyday life.

This research aims to help us learn how to better support family carers of people with MND.

What would I have to do?

If you decide to take part in the study, we will invite you to participate in an interview about your experiences of caring for the person you support and how you are coping with changes in the person you care for and in your daily routine.

The interview will be held either face-to-face or online, for example using a platform like zoom, and will take approximately 30-90 minutes.

How do I join the study?

Either:

- Complete the slip attached to this leaflet and return it by post.
- Give us a call on 07825863389.
- Email mnd.research@uea.ac.uk

What will happen if I don't want to join the study?

You do not have to take part. Whether you take part or not, your medical care or participation in other studies will not be affected at all. Participation in this study is for research purposes and is entirely voluntary.

If you would like more information or would like to take part, please fill the following slip

Your name: .....

Your address: .....

Phone: .....

Email: .....

Return to:
Eneida Mioshi, Queen's Building, School of Health Sciences, University of East Anglia Norwich NR4 7TJ

Participant information sheet – interview study

IRAS No.281943

University of East Anglia

Factors Affecting Family Carer's Wellbeing in Motor Neurone Disease – interview study

Participant Information Sheet

You are invited to take part in a research study. In order to help you decide whether to participate, we would like to share with you why the research is being done and what it will involve. Participation in this study is entirely voluntary.

Why have I been invited?

You have been invited because you have a relative who has been diagnosed with Motor Neurone Disease (MND).

What is this study about?

We are looking to understand better how the experiences of being a family carer for someone living with MND impacts the carer's wellbeing. We are particularly interested in how family carers manage emotionally the changes that MND might bring in your everyday life. This research aims to help us learn how to better support family carers of people with MND.

Who is organising this study?

This study is being led by Professor Eneida Mioshi from the Faculty of Medicine and Health Sciences, University of East Anglia.

What will the study involve?

As a carer of someone with Motor Neurone Disease, we are inviting you to participate in an interview about your experiences of caring for your loved one and how you are coping with changes in the person you care for and in your daily routine. If you agree to take part, you will be asked to sign a consent form, either in paper format or online. The interview will be held either face-to-face or online, depending on your preference and the possibility of travelling. If it is held face-to-face, the interview can take place at a place of your choosing: at your home, in our research clinic at the University of East Anglia or any other appropriate place you would feel comfortable. Travel expenses will be paid. With your permission, the interview will be audio-recorded if held face-to face or video-recorded if held online. You will be able to switch off the camera if you wish to do so. It is estimated it will take 60-90 minutes. The interview can be split over several sessions as needed and can be conducted during evenings and weekends if easier for you. The researcher will ask you questions about your experiences, you do not have to answer any question that you do not want to. You can stop or pause the interview at any point.

Who will be able to access or see my data?

All information associated with this research is strictly confidential and stored securely in compliance with the General Data Protection Regulation and the Data Protection Act 2018.

Hard copy data will be stored under secure conditions within the School of Health Sciences at the University of East Anglia; electronic data will be stored on secure servers and managed using databases encrypted with industry standard methods and protected by passwords. Only the research team will have access to the personal data. Only you and the research team will know that you are participating in the study. Please note that in some circumstances it may be necessary to breach confidentiality should concerns arise about safeguarding issues with regard to yourself or the person you support.

The interview will remain anonymous, as participants' names will be replaced with a numerical code. When interviews are typed up, any identifying features will be removed. Anonymised research data will be stored for a minimum of 10 years and destroyed thereafter. Anonymized research data may be shared between other members of the department, and UEA collaborators, and with researchers undertaking other ethically approved research including national and international collaborations, who all adhere to relevant data protection legislation and confidentiality.

Can we withdraw from the study?

You can withdraw from the interview at any point, without giving a reason. Once the interview is concluded, you will have the possibility of withdrawing your data from the study for 24hours by telephoning or emailing Ana Paula Trucco (contact details at the end of this information sheet).

Will this study benefit me?

We cannot guarantee that the study will be of direct benefit to you, although you may experience some indirect positive effects, such as knowing that you are helping researchers learn more about everyday experiences of carers, which may improve the wellbeing of others, now or in the future.

What are the risks of taking part?

Some of the questions may be of sensitive nature and it is possible that these questions may bring up upsetting or distressing emotions. The researcher is an occupational therapist who is experienced in supporting people during conversations like this and will do everything possible to make you feel more comfortable.

Consent form – interview study

IRAS No.281943

University of East Anglia

Factors affecting Family Carer's Wellbeing in Motor Neurone Disease – interview study

Consent form

Chief Investigator: Professor Eneida Mioshi **Participant ID: .....**

Please initial box

1. I confirm that I have read, have understood and accept the conditions contained in the Participant Information Sheet for this study (v.1, dated 16 February 2022), and that I have had the opportunity to ask questions and any questions have been answered to my satisfaction. ☐

2. I confirm that the procedures required for the interview and the time involved have been explained to me, including any possible risks and benefits. ☐

3. I understand that my participation is voluntary. I am free to withdraw during the interview without giving any reason and if I choose, I have 24hours to contact the research team to withdraw my data after the interview; without my medical care or legal rights being affected now or in the future. ☐

4. I understand that my interview will be audio-recorded or video-recorded and following this it will be typed up. Identifiable information will be removed while typing up the interview and only anonymous data will be used for analysis. ☐

5. I understand that anonymised typed up interviews may be accessed by researchers working in, or in collaboration with, the University of East Anglia School of Health Sciences in similar ethically approved studies. This may include studies running outside the UK. The data may also be used in the development of novel interventions, which may be licensed. ☐

6. I understand that my involvement is strictly confidential. I understand that any research data gathered from the results of the study may be published, however no information about me will be used in any way that is identifiable. ☐

7. I agree to be contacted by the study team about further research opportunities which may arise in future. This is optional, please initial the box if you wish to be informed about future studies. ☐

.....	.....	.....
Name of Participant *(Please print)*	Date	Signature
.....	.....	.....
Name of Research Team Member *(Please print)*	Date	Signature

A copy of this signed declaration will be provided to you for your records. An additional copy of the signed declaration will also be retained by the study team.

For more information about the study, contact the study team:

Ana Paula Trucco
School of Health Sciences
University of East Anglia
Norwich NR4 7TJ
Phone: +44 (0) 07825863389
Email: mnd.research@uea.ac.uk

Prof. Eneida Mioshi
School of Health Sciences
University of East Anglia
Norwich NR4 7TJ
Phone: +44 (0) 1603593300
Email: mnd.research@uea.ac.uk

To make a complaint, contact the Dean of School of Health Sciences, University of East Anglia:

Sally Hardy
School of Health Sciences
University of East Anglia
Norwich NR4 7TJ
Phone: +44 (0)1603 593940 | +44 (0)7585 887 996
Email: s.hardy@uea.ac.uk

Interview topic guide

IRAS No.281943

Factor MND Interview topic guide

*Note that this topic guide is meant to serve as a starting point which may be adjusted when piloting the interview with current MND family carers.

Participant: Current family carer of people living with MND

Aim: ***To explore current MND family carers' experiences of anticipatory grief during the progression of the disease through qualitative interviews.***

1. **Introduction**

Thanks. Introduce self. Re-state purpose of the interview and use of audio-recording if face-to-face, or videorecording if online. Remind participant they can take a break, pause or stop at any time and do not have to answer any questions they do not want to.

If the participant agrees, commence the recording.

1. **Background**

I am first going to ask you a little bit about yourself and the person you support. Could you please tell me:

Demographics	
Carer's age	
Carer's age	
Relationship to the person	
For how long you have been together (if spouses/partners)	
Length of time you have been supporting the person	
Time since diagnosis	
Subtype on MND if known	
pwMND's age	
pwMND's gender	
Employment status	

2. **Experiences**

Q1. Could you describe how you felt when receiving the diagnosis of MND?

Probes (to be used as needed)

- How did you cope with these feelings?
- What, if anything, do you think helped you manage these feelings?

- What, if anything, made it harder for you to manage these feelings?

Q2. Could you tell me how MND has impacted your everyday routine?

Probes (to be used as needed)

- How did these changes affect you emotionally?
- What change has been hardest for you? Why?
- Has anything made these changes easier to cope with?

Q3. Could you tell me how MND symptoms have impacted on how you interact with the person with MND?

Probes (to be used as needed)

- Physical symptoms (limbs)
- Respiratory symptoms
- Swallowing symptoms
- Behavioural symptoms

Q4. Could you tell me if you have had to stop doing anything due to your present situation?

Probes (to be used as needed)

- How are you coping with these changes?
- What, if anything, has helped you cope?
- What, if anything, has made it more difficult for you to cope?

Q5. Is there any aspect of the things you used to do that you miss the most?

- How does this make you feel?
- Is there anything that makes you feel better able to cope with this feeling?

Q6. Could you tell me what things, if any, you have had to start doing or learnt due to the current situation?

Probes (to be used as needed)

- How did these new changes make you feel?
- What, if anything, has helped you adapt?
- What, if anything, has made it more difficult for you to adapt?

Q7. How has your emotional relationship with the person you support changed due to the present situation?

Probes (to be used as needed)

- If changed: why do you think this relationship has changed?
- How do you feel about these changes?
- Has anything helped you cope with these changes?
- Has anything made it more difficult to cope with these changes?

Q8. Can you tell me about any experiences since the diagnosis that have been particularly useful to help you manage emotionally?

Q.9 What about experiences that have been particularly difficult for you emotionally throughout the progression of the disease?

Q10. What are your sources of support?

Probes (to be used as needed)

- Do these supports make you feel better about the changes we were talking about before?
- Do you have any support from other family members?

Q11. Is there something that you think might be beneficial to support you emotionally?

Q12. Are there any other things we have not talked about that have made it harder for you emotionally during your caring journey?

Q13. Are there any other things we have not talked about that have helped you emotionally during your caring journey?

Q14. What advice would you give to a family carer that has just been informed that they have a relative with MND to help them cope emotionally with the changes they might experience?

3. **Other comments**

Any other issues that the participant would like to raise
Thank them for their time.
Debrief

Recruitment strategies

PPIE meetings

22/02/2021: meeting with Research lead MND Scotland.

25/08/2021: meeting with Head of Regional Care Partnerships – Central and West; MND Association.

15/09/2021: meeting with Head of Regional Care Partnerships – Central and West; MND Association.

07/10/2021: PPIE meeting with HCP from Sheffield Teaching Hospitals.

21/10/2021: meeting with potential collaborator from US.

08/11/2021: meeting with Head of Regional Care Partnerships – Central and West; MND Association.

11/11/2021: meeting with MND Scotland.

16/12/2021: meeting with potential collaborator from US.

14/02/2022: meeting with Head of Regional Care Partnerships – Central and West; MND Association.

01/03/2022: meeting with Wales MND care coordinators.

23/05/2022: meeting with MND Scotland.

08/06/2022: meeting with potential collaborator from Australia.

27/07/2022: meeting with potential collaborator from US.

04/08/2022: meeting with MND Scotland.

13/10/2022: meeting with Head of Regional Care Partnerships – Central and West; MND Association.

Presentation at carers' support groups and meetings with coordinators

07/10/2021: carer's support group - MND Association

12/10/2021: carer's support group - Hertfordshire

27/10/2021: carer's support group - London and Essex

07/11/2021: Wortwell get together event - Norfolk, Norwich & Waveney branch of MND Association.

15/12/2021: carer's support group - Gloucestershire

08/03/2022: carer's support group - Cornwell and Devon

08/03/2022: carer's support group - Cleveland, York, Hambleton & Rochmondshire, Scaraborough & Bridington, Hull & East Yorkshire

09/06/2022: carer's support group - Nottingham

30/06/2022: meeting with MND Association volunteers - Nottinghamshire

27/07/2022: meeting with MND Association volunteers - Nottinghamshire

17/08/2022: carer's support group - East Midlands

18/08/2022: carer's support group - Brisbane

07/11/2022: carer's support group - North West Wales

15/11/2022: meeting with MND Association volunteers - Wales

22/02/2023: MND Coffee morning - Fritton

Extending beyond the aforementioned efforts, all branches, affiliates, and groups associated with the MND Association (UK) were contacted to facilitate the dissemination of the study. Additionally, MND Care centres (UK) across various regions were contacted for collaboration.

Supplementary material Chapter 2

Supplementary Table 2.1

Systematic Review Search Strategy Terms

Database	Search terms	Search filter
PsycINFO, CINAHL, MEDLINE	(carer* OR caregiver* OR spous* OR partner* OR child* OR parent* OR famil*) AND (“amyotrophic lateral sclerosis” OR “motor neuron disease” OR “motor neurone disease” OR “Lou Gehrig's disease” OR “MND” OR “ALS” OR “neurodegenerative disease” OR “neurodegenerative disorder”) AND (grief OR bereavement OR bereaved OR mourning OR griev*) AND NOT (“systematic review”)	
SCOPUS	(carer* OR caregiver* OR spous* OR partner* OR child* OR parent* OR famil*) AND (“amyotrophic lateral sclerosis” OR “motor neuron disease” OR “motor neurone disease” OR “Lou Gehrig's disease” OR “MND” OR “ALS” OR “neurodegenerative disease” OR “neurodegenerative disorder”) AND (grief OR bereavement OR bereaved OR mourning OR griev*) AND NOT (“systematic review”)	
LILACS	(cuidador OR pareja OR espos* OR hij* OR madre* OR padre* OR pai* OR mae* OR familia* OR casal OR filhos OR pat* OR mat* OR marido) AND ("esclerosis lateral amiotrofica" OR "enfermedad de la motoneurona" OR "enfermedad de la neurona motora" OR "enfermedad de Lou Gehrig" OR "ELA" OR "enfermedad neurodegenerativa" OR "desorden neurodegenerativo" OR	

	“esclerose lateral amiotrofica” OR “doença do motoneuronio” OR “doença do neuronio motor” OR “doença neuro degenerativa” OR “desordem neuro degenerativa”) AND (duel* OR perdida OR afliccion OR luto OR perda OR afliçao) AND NOT (“revisão sistemática” OR “estudio sistematico)
SciELO	cuidador OR pareja OR espos* OR hij* OR madre* OR padre* OR pai* OR mae* OR familia* OR casal OR filhos OR pat* OR mat* OR marido) AND ("esclerosis lateral amiotrofica" OR "enfermedad de la motoneurona" OR "enfermedad de la neurona motora" OR "enfermedad de Lou Gehrig" OR "ELA" OR "enfermedad neurodegenerativa" OR "desorden neurodegenerativo" OR “esclerose lateral amiotrofica” OR “doença do motoneuronio” OR “doença do neuronio motor” OR “doença neuro degenerativa” OR “desordem neuro degenerativa”) AND (duel* OR perdida OR afliccion OR luto OR perda OR afliçao) AND NOT (“revisão sistemática” OR “estudio sistematico)

Supplementary Table 2.2

Illustrative Quotations

Theme and sub-theme	Illustrative quotations (examples) from qualitative studies and key findings from quantitative studies	Record reporting sub-theme
Nature of MND		
Knowing about MND	Feelings of hopelessness were reported by 11 carers, including all who met the criteria for prolonged grief. The hopelessness was described by one participant as 'the most defeating thing'. The sense of hopelessness that participants felt seemed to be compounded further when they contrasted MND to cancer. For example, one stated, "With cancer there is hope; with MND, there is nothing". (Aoun et al., 2012) Although in one case, finding the person dead was a surprise, the trajectory to date and the caregiver's knowledge of MND enabled her to construct death as a positive event. "I just went into [name] room and there he was...the expression on his face indicated to me that he was peaceful, he stayed at home with us for 24 hours". (Ray et al., 2014)	Aoun et al., 2012; Ray et al. 2014.
Uncertainty and unpredictability	People living with MND reported living in a constant state of uncertainty as they confronted the ongoing losses. They expressed frustration that, unlike cancer, this disease had no set trajectory and that they must manage constant changes without knowing exactly what these changes might be: "With a disease like this no-one can give you its parameters or where it's going or how long it's going…This is so undetermined you just don't know it from one moment to the other". (Ray & Street, 2007) The unexpected nature of [x] partner's death, while in hospital, was contrary to her understanding of the illness trajectory (she imagined him becoming bedbound and needing increasing care) and deprived her of being at his side in	Ray & Street, 2007; Ray et al., 2014; Warrier et al., 2019.

	the death event. “I wasn’t there with him, he died alone, the end was quick, unexpected, it shocked me, I was unprepared. He wasn’t going to die; it wasn’t part of the plan”. (Ray et al., 2014)	
Negative experiences of MND caregiving	Participants in every risk [of complicated grief] category reported experiencing a range of emotions such as anger, depression, regret, guilt, sadness, and shock as part of their grief…Caregivers at moderate risk [of complicated grief] were more often distressed by remembering the MND symptoms: “I find it very difficult to put the images of my husband’s body wasting away before my eyes out of my head” and “I couldn’t bear having anything that reminded me of MND”. (Aoun et al., 2021b) Several caregivers expressed that they felt severe burden or grief after bereavement. They noted how bereavement after death from ALS was different due to the extensive nature of caregiving provided to the person with ALS. A widower who had cared for his wife with ALS at home succinctly described the bereavement as different from other deaths in light of the exhausting and long caregiving needed for his wife. “It is not like that/I have already experienced several deaths: parents, brothers and everything else … That was much less burdening, but if you have it in a way where you are still exhausted, where the reserves decrease and then comes the case X. …[ehm] I was amazed how much energy you get when you need it. Because I don’t know where you get it from”. (Poppe et al., 2022)	Aoun et al., 2012; Aoun et al., 2021b; Poppe et al., 2022; Ray & Street, 2007.
Familial and social life		
Demographics (person living with MND and carer)	A quantitative study demonstrated that marital status, education level, relationship to the deceased, the period of bereavement, length of care, type of involvement in caring, and intensity of caring in hours significantly differed between the three risk groups (high, moderate, and low risks of PGD) (all $p <$ 0.05). After adjusting for confounding variables, the factors that increased risk	Aoun et al., 2020; Warrier et al., 2019.

	of PGD compared to low risk were having a recent bereavement and being a spouse or partner of the deceased. (Aoun et al., 2020) A quantitative study demonstrated that age, gender, employment status, and cultural background of the bereaved did not differ significantly between the three risk groups (all $p > 0.05$). (Aoun et al., 2020)	
Caught up in loss	[One] caregiver talked about wrestling with the images of what might have been, especially the retirement that they had planned "You just keep in grieving for the life you have lost, for the life you were going to have, the life you are not going to have (cries) and for all he has lost. It's awful". (Ray & Street, 2007) Being alone and struggling with loneliness was a common experience for people in the moderate and high [grief risk] categories. Caregivers reported "it being difficult suddenly living alone" and a feeling of "loss of purpose...nothing prepares you for being alone". (Aoun et al., 2021b)	Aoun et al., 2012; Aoun et al., 2021b; Poppe et al., 2022; Ray & Street, 2007; Ray et al., 2014; Warrier et al., 2019.
Relationships and changes in roles	Most participants described the loss of what is means to be a partner and loss of what the patient gave in their relationship…Commitment to her relationship with her partner was providing some sustenance for one caregiver; however, the impact of the physical and emotional responsibility and the loss of a reciprocal relationship increased caregiver strain and substantially changed the relationship: "I don't feel like I have a better half, I feel like I've got a baby. So, yeah, but I mean, I still love him to death and I'd do anything for him, but, you've sort of been left with the whole burden on you, to carry. I feel like I've got a baby, I haven't got a husband". (Ray & Street, 2007) "She didn't express any fear of dying. She gave me plenty of time to be prepared mentally and emotionally. And she and I were able to talk, to experience each other. And I was able to experience my love for her. So I didn't have any unfulfilled desires that interfered with or contaminated my bereavement. There was complete closure. I was ready when she was ready". (Solomon & Hansen, 2015)	Aoun et al., 2012; Ray & Street, 2007; Ray et al., 2014; Solomon & Hansen, 2015.

Rebuilding life	"Doing new things" and "keeping busy" were the most common ways family caregivers coped with their loss in the low- and moderate-risk [grief] categories. Caregivers described actively needing to re-engage with their life. "I re-joined the bowling club"; "I just did an amazing overseas trip" and "I went on a three day walk, and it was better than any drugs the doctors gave me". (Aoun et al., 2021b) The next important finding in positive bereavement experiences is related to self-reflection and self-improvement. Once again, caregivers who were in the low-risk category are most represented in this section. Caregivers expressed feelings of gratitude, empowerment and positive emotions: "Gratitude for my life and what I have/ Yes I now realise more than ever the shortness of life and need to live for now, in the present be more mindful and patient and understanding of others and self. I feel more able to make my own decisions – empowered and feel I am now on a reflective learning journey. It's the quality of the journey NOT the end result". (Aoun et al., 2021b)	Aoun et al., 2021b; Poppe et al., 2022.
Support		
Negative experiences with healthcare professionals	The lack of empathy from medical professionals left the participants feeling shocked, bewildered, angry and devastated. One participant recalled: "The neurologist told us that he knew someone with MND and that they shot themselves right away. Hearing that was just terrible "cause here I am thinking we will beat this. Nah, we didn't go to that neurologist again". (Aoun et al., 2012) Breaches of the patient wishes and minimal support from health-care workers were reported…The "not for resuscitation" order and the family caregiver's wishes were ignored. The family caregiver felt powerless to change the situation. The ensuing chaos left the caregiver with regrets about the undignified nature of his wife's death. "I couldn't [make them stop], stop it, don't give her artificial resuscitation but…"; "Well she'd already started, you	Aoun et al., 2012; Aoun et al., 2021b; Ray et al., 2014.

	know, but those carers were in a hell of state and hysterical, well one of them was hysterical … a green no resuscitation and that ought to be in big letters and told to all the carers. That's the one disappointment; I would have loved her to go peacefully". (Ray et al., 2014)	
End of life and bereavement support	Not being provided with support in the early days following her husband's death was exceptionally distressing for one bereaved carer. She stressed the importance of a sense of closure following the death, particularly because the withdrawal of services and ending of contacts came across as a stark administrative process "When (patient) died (Specialist nurse) never got in touch with me [. . .] I was absolutely devastated about that, I couldn't get over it, couldn't get over it. . .You are just cut off then [after the death], it goes in a drawer, the notes go in a drawer". (Whitehead et al., 2012) Three of the five participants who demonstrated prolonged grief had accessed palliative care services less than one month before the death of their spouse. In addition, four out of the five participants who had prolonged grief and had used palliative care services reported gaining access to homebased services later than they would have liked. (Aoun et al., 2012)	Aoun et al., 2012; Aoun et al., 2020; Aoun et al., 2021a; Aoun et al., 2021b; Poppe et al., 2022; Whitehead et al., 2012; Ray et al., 2014.
Psychological support	Those people at moderate and high [grief] risk were more likely to recommend professional support "Get as much counselling throughout the caring period and after for at least six months". (Aoun et al., 2021b) In general, family caregivers mentioned support needs for bereaved children as "the children themselves grieved, each in their own way". A few participants also stated that support for children came mostly from the family or schools. These family caregivers mentioned that psychological support for children would have been helpful but was not available. Participating caregivers also mentioned psychological growth on their and their children's part. (Poppe et al., 2022)	Aoun et al., 2021a; Aoun et al., 2021b; Poppe et al., 2022; Warrier et al., 2019.

Informal support	The strong theme across all the [grief risk] categories was that social and family support was essential. Caregivers in the low-risk category frequently provided statements such as: "One gets on with life and keeps in touch with family, friends and hobbies" and "I was very fortunate to have the friend and family I have. They have been with me whenever I needed support, distraction or someone to reflect with". (Aoun et al., 2021b) A quantitative study revealed that after adjusting for confounding variables, the factor that increased risk of PGD compared to low risk was poor family function (low involvement or conflictual family function) ($p < 0.05$). (Aoun et al., 2020)	Aoun et al., 2020; Aoun et al., 2021a; Aoun et al., 2021b; Poppe et al., 2022.
Carer emotional reactions		
Anxiety and depressive symptoms	"I mean I know there has been a vast deterioration in the last three months and I keep thinking what's it going to be like in the next three months and the three months after that, I don't know how I will cope, I will cope but I don't know how I will cope, and I am worried". (Whitehead et al., 2012) A quantitative study demonstrated prolonged grief was significantly associated with anxiety and depression. After adjusting for confounding variables, when comparing high-risk PGD group vs low-grief PGD group, anxiety ($p = 0.015$) and depression ($p < 0.001$) were found to be factors that increased risk of PGD. Depression was found to increase the risk of PGD when comparing high-risk group vs moderate-risk group ($p = 0.008$) and moderate-risk group vs low-risk group ($p = 0.011$). (Aoun et al., 2020)	Aoun et al., 2020; Whitehead et al., 2012.
Emotional acceptance	Those participants who did not meet the criteria for prolonged grief generally indicated in their interviews that they accepted the notion of their partner dying, right from their diagnosis. For instance, one stated, "From the start, definitely, yes. Had no problem with that in the sense of accepting, you know, we'd had a really good life, we were both in our sixties". (Aoun et al., 2012)	Aoun et al., 2012; Aoun et al., 2021b; Poppe et al. 2022.

	It was common for caregivers in the low-risk category to view expressing and allowing grief as a critical part of adapting, suggesting "The grieving process to wash its way through. Don't ignore it. Don't rush it and have tools/people on hand for when it gets too much" and "Stay open. Allow yourself to grieve. Recognise that not all days are going to be bad". (Aoun et al., 2021b)	
Emotional avoidance	The participants who met the criteria for prolonged grief minimised their emotional reactions to their partner's illness by 'switching off' their emotions in order to manage the day-to-day responsibilities of care. One participant described becoming "robotic and mechanical", while another described trying to "keep busy, not think about it, avoid any discussion, avoid any acknowledgment [and] just keep going". (Aoun et al., 2012) Four of the six participants who met the criteria for prolonged grief avoided thinking about and re-experiencing the painful emotions associated with the death of their partner. For instance, one described having "a complete shutdown" and another stated, "There are things I've left undone because I haven't been able to face them". (Aoun et al, 2012)	Aoun et al., 2012; Aoun et al., 2021b; Ray & Street, 2007; Warrier et al., 2019; Whitehead et al., 2012
Perceptions and experiences of death		
Accepting the inevitability for death	Caregivers were able to construct death as the final part of the MND disease process. Despite having a variety of experiences of the dying process, caregivers reflected that while their loss of their partner was extremely significant; "there is a huge space there that [person] occupied"; they did not want them to continue to suffer with MND or go on facing the continual losses. "I wouldn't have liked her to get any worse…the body was not worth having, I wouldn't have wished that [MND] on anyone". (Ray et al., 2014) Many caregivers expressed the relief that the suffering for the individual has come to an end. "For eighteen days after discharge, we really struggled… But not more than that, and I am happy about that". (Warrier et al., 2019)	Ray et al., 2014; Warrier et al., 2019.

Preparing/planning for death	"She gave me plenty of time to be prepared mentally and emotionally. And she and I were able to talk, to experience each other. And I was able to experience my love for her. So, I didn't have any unfulfilled desires that interfered with or contaminated my bereavement. There was complete closure. I was ready when she was ready". (Solomon & Hansen, 2015) In cases where conversations about dying and death had occurred, positive experiences were reported. Plans had been made, and caregivers were able to achieve some sense of comfort. "He told us everything he wanted; he always had done from the end of last year. He said you know I want this, I don't want that". (Ray et al., 2014)	Aoun et al., 2021b; Poppe et al., 2022; Ray et al., 2014; Solomon & Hansen, 2015.
Death experience	All three of the patient's adult children, and the patient's spouse, spoke eloquently about how being situated at home, supporting the patient in her wish to die there, allowed a safe and relaxed context to focus on relationships. They suggested this not only helped the patient feel her life was fulfilled, but also offered an ideal environment for their own anticipatory loss and bereavement: "Because she was comfortable and because we were doing everything she wanted, it made it so much easier for us. I don't think we have regrets. I don't think we feel guilty about needless procedures that traumatized her or us". (Solomon & Hansen, 2015) Generally, pointing to the normality of grief for most caregivers, one daughter of a person with ALS described not needing to access psychological support due to the non-traumatic nature of death from ALS in her case: "Neither of us did. But I think simply because it/it was somehow good and it wasn't a traumatic experience for us actually/it was bad, sure, but it wasn't [ehm]/I imagined it worse". (Poppe et al., 2022)	Poppe et al., 2021; Ray et al., 2014; Solomon & Hansen, 2015.

Note. MND = motor neurone disease. ALS = amyotrophic lateral sclerosis. PGD = Prolonged Grief Disorder.

Supplementary Table 2.3

Quality Rating of Quantitative Studies Included in the Review (Joanna Briggs Institute Appraisal Checklist for Analytical Cross-sectional studies)

First author (year)	Item 1 Criteria for inclusion	Item 2 Description of subject/setting	Item 3 Measurement of the exposure	Item 4 Measurement of the condition	Item 5 Identification of confounding factors	Item 6 Management of confounding factors	Item 7 Validity of measures	Item 8 Statistical analysis used
Aoun (2021a)	Yes	Yes	No	NA	No	NA	Yes	Yes
Aoun (2020)	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes

Note. Item 1 = Were the criteria for inclusion in the sample clearly defined? Item 2 = Were the study subjects and the setting described in detail? Item 3 = Was the exposure measured in a valid and reliable way? Item 4 = Were objective, standard criteria used for measurement of the condition? Item 5 = Were confounding factors identified? Item 6 = Were strategies to deal with confounding factors stated? Item 7 = Were the outcomes measured in a valid and reliable way? Item 8 = Was appropriate statistical analysis used? NA = Not applicable.

Supplementary Table 2.4

Quality Rating of Qualitative Studies Included in the Review (Joanna Briggs Institute Appraisal Checklist for Qualitative Research)

First author (year)	Item 1 Philosophical premises	Item 2 Objectives and study methodology	Item 3 Data collection method	Item 4 Data analysis	Item 5 Interpretation of results	Item 6 Researchers' orientation	Item 7 Influence of the researcher	Item 8 Representation of participants	Item 9 Evidence of ethics	Item 10 Conclusions
Aoun (2012)	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Aoun (2021b)	No	No	Yes	No	No	No	No	Yes	Yes	Yes
Poppe (2022)	Unclear	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Ray (2007)	No	Yes	Unclear	Yes	Yes	Yes	No	Yes	Yes	Yes
Ray (2014)	No	Yes	Unclear	Unclear	Yes	No	No	Yes	Yes	Yes
Solomon (2015)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Warrier (2019)	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes

Whitehead (2021)	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes

Note. Item 1 = Is there congruity between the stated philosophical perspective and the research methodology? Item 2 = Is there congruity between the research methodology and the research question or objectives? Item 3= Is there congruity between the research methodology and the methods used to collect data? Item 4 = Is there congruity between the research methodology and the representation and analysis of data? Item 5 = Is there congruity between the research methodology and the interpretation on results? Item 6 = Is there a statement locating the researcher culturally or theoretically? Item 7 = Is the influence of the researcher on the research, and vice-versa, addressed? Item 8 = Are participants, and their voices, adequately represented? Item 9 = Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body? Item 10 = Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data? Unclear = Not enough information provided to make the decision.

Supplementary material Chapter 4

Supplementary Table 4.1

Potential Independent Variables to be Included in the Linear Regression Analysis with MMCGI-SF Total Score as Dependent Variable (n=75)

Potential independent variables	*p* value
Disease severity (ALSFRS-R)	<0.001
Behavioural changes (Mind-B)	<0.001
Relationship closeness (RC Scale)	0.011
Familism (Familism Scale)	0.158
Hours of care provided per week	0.015