

THE UNIVERSITY OF HULL

Cognitive profile in advanced Duchenne Muscular Dystrophy (DMD)  
and the effects of hypoventilation on cognition

being a Thesis submitted for the Degree of  
Doctorate in Clinical Psychology  
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by

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## Overview

The portfolio has three parts.

Part One is a systematic literature review concerning the nature and severity of the psychological distress experienced by carers (primarily parents) of people with Muscular Dystrophy. Quantitative and qualitative studies investigating distress in these carers have been reviewed and critically evaluated to draw conclusions and implications for clinical practice.

Part Two is an empirical paper aimed at creating a cognitive profile for people suffering from Duchenne Muscular Dystrophy in the advanced stages of the illness. The focus of this cross-sectional study is placed on the investigation of whether hypoventilation, inevitably seen to develop in this population, is related to permanent cognitive deficits in memory and/or executive functioning. The participants who have been identified to suffer from hypoventilation (N=17) are compared on measures of memory and executive functioning to a group of DMD participants of similar age (N=16) who have not yet developed hypoventilation. Other measures are also taken in the form of questionnaires to compare the groups on, including demographics, mood (depression and anxiety), health-related quality of life, sleepiness, and beliefs about sleep.

Part Three comprises the Appendices.

## Contents

*Page No.*

### **Part One: Psychological distress in carers of people with Muscular Dystrophy: A systematic literature review.**

Abstract	8
Background	9
Method	15
Results	20
Discussion	43
Conclusions and Implications	47
References	48

### **Part Two: Cognitive profile in advanced Duchenne Muscular Dystrophy (DMD) and the effects of Non-invasive Positive Pressure Ventilation (NIPPV) on cognition.**

Abstract	59
Introduction	60
Method	65
Results	69
Discussion	74
References	79

### **Part Three: Appendices**

Appendix A – Reflective statement	83
Appendix B – Guidelines for authors for the systematic literature review	87
Appendix C – Guidelines for authors for the empirical paper	90
Appendix D – Search Strategy in PsychINFO for ‘carer’ term	97
Appendix E – Search Strategy in PsychINFO for ‘muscular dystrophy’ term	99
Appendix F – Search Strategy in PsychINFO for ‘psychological distress’ term	100

Appendix G – Standardized Data Extraction Sheet	102
Appendix H – Quality Assurance Checklist: Qualitative studies	104
Appendix I – Quality Assurance Checklist: Quantitative studies	105
Appendix J – Quality Assessment Scores	107
Appendix K – Instructions for recruitment	109
Appendix L – Descriptions of the psychometric measures used	110
Appendix M – Information sheet for main study	113
Appendix N – Consent form	117
Appendix O – Ethical and R&D approval documentation	118

## List of Tables and Figures

*Page No.*

### **Part One: Psychological distress in carers of people with Muscular Dystrophy: A systematic literature review.**

Table 1. Rolland's (1987) conceptualisation of the nature of psychosocial demands present at various stages of a range of chronic illnesses.	13
Table 2. Inclusion criteria and their justification.	16
Table 3. Exclusion criteria and their justification.	17
Table 4. Study design hierarchy (Khan <i>et al.</i> , 2001).	17
Table 5. Main characteristics of the studies included in the review (N=20).	21
Figure 1. A flowchart of the article selection process.	18

### **Part Two: Cognitive profile in advanced Duchenne Muscular Dystrophy (DMD) and the effects of Non-invasive Positive Pressure Ventilation (NIPPV) on cognition.**

Table 1. Psychometric measures used and the corresponding cognitive areas tested	66
Table 2. Demographic information and comparisons of DMDC and DMDV groups	69
Table 3. Mean (SD) score and statistical significance of differences between the DMDC and DMDV groups on ESS, DBAS, HADS, and SF-36.	70
Table 4. Mean (SD) and significance of differences between the DMDC and DMDV groups on the psychometric measures.	71
Table 5. Number of participants in DMDC (N=14) and DMDV (N=17) groups that are on or below the cut-off scores for each measure used.	72

# Psychological distress in carers of people with Muscular Dystrophy: A Systematic Literature Review<sup>1</sup>

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<sup>1</sup> This paper is written in the format ready for submission to the British Journal of Health Psychology. Please see Appendix B for the Guidelines for Authors.

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## **Abstract**

**Purpose** Medical advances have meant people with Muscular Dystrophies are surviving longer and require a high level of care longer-term. Care is increasingly taken up by families, primarily parents, in the home. The question of the impact of providing this care on these individuals has therefore become pertinent. This review aims to determine the degree and nature of distress experienced by carers, and consider service implications.

**Methods** A systematic literature review was conducted of quantitative and qualitative studies investigating distress and people's experiences of caring for a person with Muscular Dystrophy. Data was extracted and analysed using descriptive (non-quantitative) analysis.

**Results** The data suggest that there is a high level of distress amongst carers of people with MD. This distress impacts not only on psychological well-being, but also on social, familial, physical, and financial aspects of life. A positive aspect of caring also emerged, within which carers have felt enriched as they achieved a meaningful and adjusted way of life.

**Conclusions** Distress is present in carers' lives, without necessarily depriving them of hope and enrichment. Services providing medical care for these patients need to include carer distress in their care plans, and provide psychological, as well as practical support and advice, particularly at times of crisis.



## **Background**

Carers of children with Muscular Dystrophy (MD) are part of a wider group of carers, who take on the often life-long task of caring for their chronically-ill child. This review begins with an overview of the literature on carers of chronically-ill children in order to set the context, and is followed by a brief outline of MD along with a summary of the literature involving carers of people with MD, leading onto the aims of this review.

### *Caring for Chronically-Ill Children*

Many studies look at the physical, emotional, and social impact of caring for a chronically-ill child (e.g. McGarth, 2001; Carnevale *et al.*, 2006). Hatzmann *et al.* (2009) noted that “caregiving demands can be extensive, and may lead to adverse psychosocial consequences for parents” (p.2).

Boyer (1986) explains that when parents find out that their child is not healthy they face both practical and emotional turmoil. Financial pressures can arise due to the costs of treatment or the caregiver having to give up their job. Prolonged family stress can lead to physical and emotional symptoms (Burton, 1975), such as distress, anxiety, sleep disturbance, and tensions in family relationships (Colville *et al.*, 1996; Ievers & Drotar, 1997; Wase *et al.*, 1998). The impact on familial relationships often leads to anger, guilt, blame, and denial since caring for the affected child takes time away from other family responsibilities or from the caregivers’ personal time (Boyer, 1986). These tense familial relationships augment the emotional and practical difficulties, which are likely to worsen between transitional stages of the life cycle (Erikson, 1968).

McGrath (2001) found that carers of children with a life-limiting condition request support for practical and emotional issues. However, these parents reported minimal or no support

from extended family, friends, or support groups whilst they were trying to cope with physical, emotional, and social demands from their child's condition.

Carnevale *et al.* (2006) looked at family experiences of caring for a child using ventilator assistance. Their study replicated many of the findings around carer distress including emotional strain, feelings of isolation, and a need for stability and normalisation within the family. Nevertheless, the authors found experiences of distress as well as of enrichment and reward. The emerging overarching theme was that 'the struggle is worthwhile' (p.54) despite the impact on the carer's physical (Patterson *et al.*, 1992) and mental health (Leonard *et al.*, 1993), financial strain, reduced social interactions (Cohen, 1999), a poorer family Quality of Life (QoL) (O'Brien, 2001) and the stress induced by interaction with health professionals (Noyes *et al.*, 1999).

Hatzmann *et al.* (2009) explored the influence of demographic and disease-related factors on parental Health-Related QoL (HRQoL) and found that poor parental HRQoL is explained best by low emotional support, high care dependency, few days on holiday, and being chronically ill as a parent.

### *Muscular Dystrophy (MD)*

MD refers to a group of neuromuscular disorders affecting the muscles or the nerves controlling the muscles. These disorders are generally progressive in nature and often terminal. The body's muscles become progressively weaker, leading to physical disability and often respiratory failure. However, medical advances have resulted in prolonged life expectancy for these individuals (Annane *et al.*, 2007). Moreover, services are now promoting care in the home (Boström *et al.*, 2006). This has consequently resulted in many parents becoming full-time, primary caregivers for a long period of time.

### *Caring for a child with MD*

Many studies focus on the QoL, emotional well-being and social functioning of the children with MD and although carers are recruited, the research focuses primarily on the patient perspective (e.g. Grootenhuis *et al.*, 2007; Kohler *et al.*, 2005). Other researchers have focussed on service provision and service quality for patients and their carers, particularly at the end-stages of the illness, with little focus on the carers' distress over the trajectory of the illness journey (Parker, Maddocks, & Stern, 1999; Dawson & Kirstjanson, 2003). A large number of studies involving carers of people with MD have used participant samples that include other illnesses requiring long-term care and data for MD cannot be extracted (e.g. Brehaut *et al.*, 2009; Dewey & Crawford, 2007).

In one of the original studies looking at caregiver distress specifically in MD, Buchanan *et al.* (1979) using open-ended interviews found that 76% of families expressed psychological distress as a main concern, which in turn led to difficulties in the overall management of the child's illness. They also identified the need for parents to adapt constantly to their child's increasing disability, which led the family to perceive restrictions to their freedom and social activities. However, the prevailing stressor was the anticipation of the future and that of death.

Parker, Maddocks, & Stern (1999) looked into the role of palliative care in MD by interviewing carers and found that there is a communication issue between parents and their ill child, since parents felt uncomfortable to discuss end-of-life issues with their child. Firth *et al.* (1983) suggest parents feel ill-equipped to have this conversation and worry about the negative impact that 'knowing' might have on their child. Lubowe (1989) suggests that family psychotherapy may help promote communication between family members and relieve emotional stress, caused by the loss of the 'perfect' child and the process of life-time mourning.

Polakoff *et al.* (1998) reviewed the literature on psychosocial factors impacting the lives of boys with Duchenne Muscular Dystrophy (DMD) and their families. In line with Lubowe (1989), they report that “...grief has no immediate closure, as exists with a death” (p.121) since during the course of the illness caregivers may experience numerous emotional traumas relating to the illness progression and consequent adjustments that the family is forced to make to its lifestyle. This may result in unresolved grief that lingers for years and continuously consumes coping resources from the caregivers, leaving them exposed to interpersonal and intrapersonal difficulties.

Polakoff *et al.* (1998) also identified the following predictors of psychological distress in carers: the child’s severity in loss of functioning – rather than illness severity as rated by physicians (Canning *et al.*, 1996); lower family income and patient gender (female; Kazak, 1987), and mental health difficulties experienced in the family prior to the child’s illness (Kazak, 1989).

Morrow (2004) also reviewed the literature on DMD and familial distress, basing it on the paradigm that the *family* is the patient. She found that the feelings and thoughts of families thirty years ago still seem to reflect those of families now. Perhaps this is because, although medical advances allow for better illness management, society’s expectations of care have also increased and thus maintain feelings of anxiety and frustration in carers. The emerging themes included guilt towards unaffected siblings, a sense of overprotection, denying the child’s sexuality, developing and adapting coping mechanisms, and the impact on familial relationships with mothers carrying most of the burden of care. Importantly, families seem to perceive that the psychological stress outweighs the daily physical stresses they experience.

Miller (1990), and Street and Soldan (1998) argue that distress is not necessarily an ongoing difficulty in carers of children with MD. Instead, they propose that distress arises at times of crises which closely correspond to the illness progression stages. Miller (1990) explains that

distress is the emotional reaction to a deterioration or change. Denial, shock, grief, anger, guilt is felt and is worked through until a phase of acceptance is reached which is maintained until the next change.

Street and Soldan (1998) argue that the way an illness progresses will define the psychosocial demands placed upon the individual and the family. They present Rolland's (1987) conceptualisation of the five elements across a range of chronic-illness trajectories which group similar psychosocial demands (Table 1).

**Table 1.** Rolland's (1987) conceptualisation of the nature of psychosocial demands present at various stages of a range of chronic illnesses.

<b>Stage</b>	<b>Description</b>	<b>Summary</b>
Onset	Development of illness and symptoms can be sudden or gradual.	Acute versus Gradual
Course	Illness and its symptoms may be constant, progressive, relapsing (stable or progressive), or in episodes of varying intensity.	Constant/Progressive/Relapsing/Episodic
Outcome	Effect on life span lies on a continuum from very little to dramatic (either gradual or sudden).	Prognosis/Morbidity
Incapacitation	Nature and degree of physical, cognitive, and emotional problems can vary.	Impact (and its severity) on physique, cognition, mental health
Uncertainty	Characteristic that overlays all previous attributes. Knowledge about the nature of onset and rate of changes define the degree of predictability.	Predictability, e.g. phases, staged

In line with this, parents of chronically-ill children identify that their psychosocial needs change over time and corresponding support is needed on the basis of the illness progression (McGarth, 2004).

## **Aims of Review**

So far the evidence suggests that parental or carer distress can negatively impact not only the context in which a chronically-ill child is cared for (i.e. through familial relationships), but also the quality of care they receive and consequently their health and adjustment (Friedman *et al.*, 2004). This review therefore aims to address the following questions:

- How does caring for a child with MD impact on carers' psychological well-being, and how do they define the distress they experience?
- In which areas of life is distress felt by carers of children with MD?
- What are the main factors linked to psychological distress in carers of children with MD?
- What are the implications for carers, patients, and services, of psychological distress in carers of children with MD?

## **Method**

### ***Selection of studies for inclusion***

The following electronic databases were searched in December 2009 and updated in June 2010, to identify relevant papers for inclusion in the review: PsycINFO, PsychArticles, Embase, Medline, Scopus, CINAHL, and Web of Knowledge (all 1980 - 2010).

Search terms included ‘carers’, ‘muscular dystrophy’, and ‘psychological distress’. These were all expanded and the resulting search-term strategies used in PsycINFO (as an example) can be seen in Appendices D, E, and F respectively.

The resulting titles were reviewed and relevant ones were selected. An overview of the abstracts further narrowed down the relevant papers, which were then accessed in full for reading and assessment against the inclusion/exclusion criteria. The final selected papers were then evaluated thoroughly. Reference lists from these papers were hand-searched by the author to identify further relevant papers and minimise publication bias (Khan *et al.*, 2001).

### ***Search selection criteria and paper retrieval***

The search strategy produced 1473 papers, 105 of which were selected through the abstracts. Duplicate papers (i.e. papers found in more than one database) were removed (N=27) and a further selection of 26 were removed according to the inclusion and exclusion criteria outlined in Tables 2 and 3.

**Table 2.** Inclusion criteria and their justification.

	<b>Criterion</b>	<b>Justification</b>
1	Subjects diagnosed with any type of neuromuscular disorder <sup>4</sup> as defined by the World Health Organisation	Neuromuscular disorders are all rare and thus populations and studies are limited – specifying a disorder would yield a very small number of papers
2	Study only involves primary carers who cohabit with the subject(s)	Psychological distress will then refer to the emotional strains of full-time, 24-hour care. A wider range of care-profile would limit reliability and validity with which to draw conclusions.
3	Study involves carer self-reports of psychological distress using qualitative and/or quantitative data [NB. <i>Psychological distress includes mood difficulties, anxiety/stress, and any negative emotional impact as defined by the carer</i> ]	Psychological distress is defined as what is <i>felt/experienced</i> by the carer. Criterion also widens the data availability in the literature by including quantitative and qualitative data.
4	Studies published between 1980-2010	Medical advances constantly change the management and prognosis of neuromuscular disorders – going too far back in time may not be representative of present carer distress
5	Study is on levels 1-4 of Khan <i>et al.</i> 's (2001) study design hierarchy	Involves primary data that can be extracted and evaluated
6	Studies available in English language	Resources are not available for translation

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<sup>4</sup> **Neuromuscular disorders include:** Becker muscular dystrophy, Bethlem myopathy, Central core disease, Charcot-Marie-Tooth disease (CMT), Congenital muscular dystrophy (CMD), Congenital myasthenic syndromes, Congenital myotonic dystrophy, Duchenne muscular dystrophy, Emery-Dreifuss muscular dystrophy, Facioscapulohumeral muscular dystrophy (FSH), Fibre-type disproportion, Fibrodysplasia ossificans progressiva (FOP), Inclusion body myositis (IBM), Juvenile dermatomyositis, Limb girdle muscular dystrophies, Manifesting carriers of Duchenne muscular dystrophy, McArdle's disease, Merosin-deficient congenital muscular dystrophy: MDC1A, Metabolic disorders, Minicore (multicore) myopathy, Mitochondrial myopathies, Myasthenia gravis, Myopathy, Myotonias, Myotonic dystrophy, Myotubular (centronuclear) myopathy, Nemaline myopathy, Oculopharyngeal muscular dystrophy (OPMD), Periodic paralyses, Polymyositis, dermatomyositis and sarcoid myopathy, Rigid spine syndrome, Sarcoglycanopathies: LGMD2C, LGMD2D, LGMD2E and LGMD2F, Spinal muscular atrophy (SMA), Ullrich congenital muscular dystrophy.



**Table 3.** Exclusion criteria and their justification.

	<b>Criterion</b>	<b>Justification</b>
1	Data in study involves a mixed sample of patients with illnesses other than neuromuscular disorders [NB. <i>This does <b>not</b> exclude mixed sample studies – only mixed data</i> ]	Caring for chronically ill individuals may have commonalities with caring for neuromuscular patients, however differences may also exist – therefore specific data of carers for people with neuromuscular disorders must be extractable
2	Study compares carer distress in neuromuscular disorders field with conditions not involving muscle disease	Excluded only if study does not allow for data extraction of each group, i.e. data on neuromuscular disorder carers only

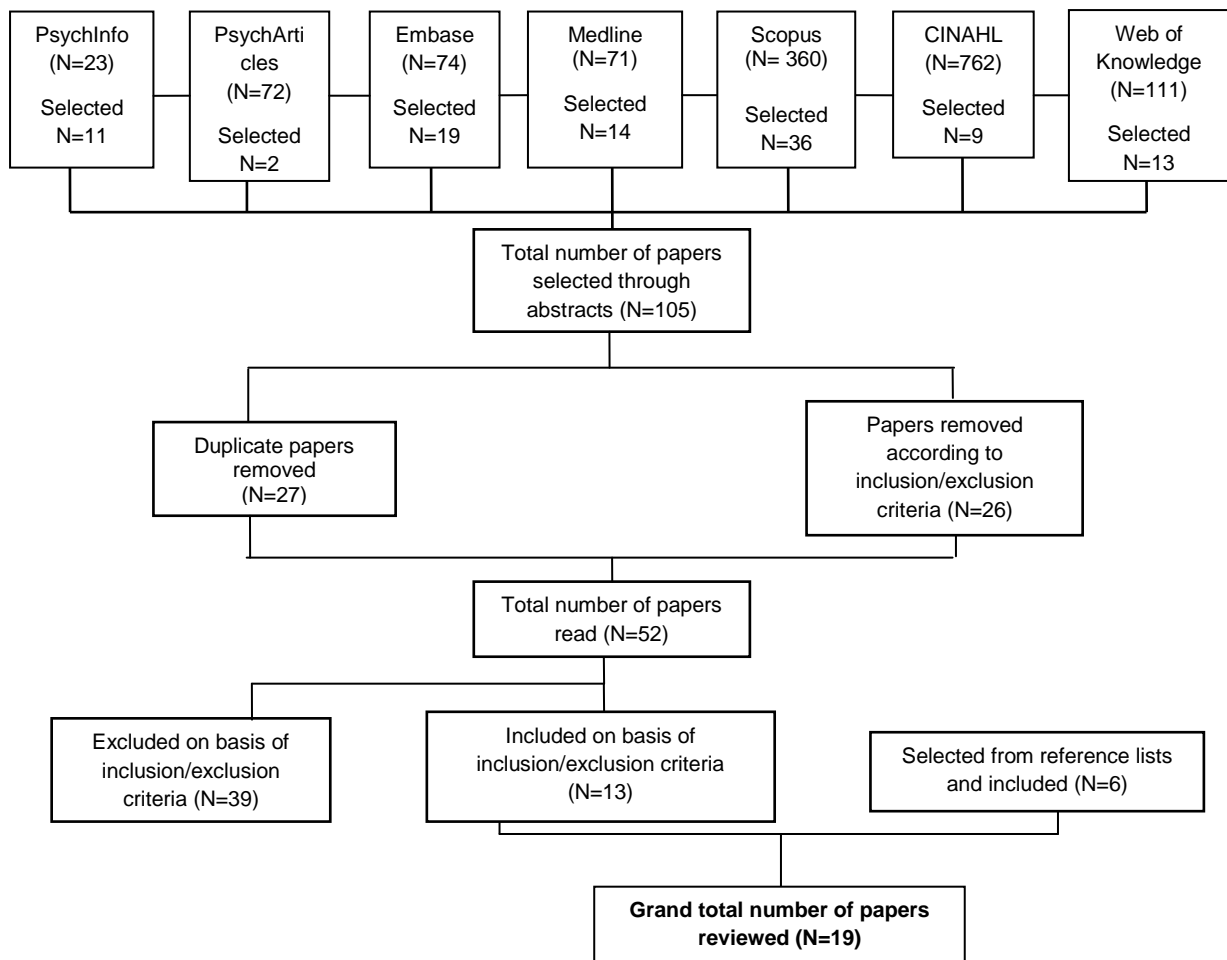
Table 4 outlines Khan *et al.*'s suggested study design hierarchy in decreasing levels of effectiveness. It was decided to include studies falling into the first four levels. Each study design is reported in the synthesis table.

**Table 4.** Study design hierarchy.

<b>Level</b>	<b>Description</b>
1	Experimental studies (e.g. RCT with concealed allocation)
2	Quasi-experimental studies (e.g. experimental study without randomisation)
3	Controlled observational studies
3a	Cohort studies
3b	Case control studies
4	Observational studies without control groups
5	Expert opinion based on pathophysiology, bench research or consensus

Both quantitative and qualitative studies were included due to the limited research in the area.

The remaining 52 papers were obtained and studied and 39 of these were excluded on the basis of the criteria, while the remaining 13 papers were reviewed. Six papers were selected via a hand-search of the reference lists of the 52 papers. Figure 1 illustrates the selection process.



**Figure 1.** A flowchart of the paper selection process.

### ***Data extraction***

A standardized data extraction sheet was piloted with a number of papers, adapted, and used throughout the selection process to ensure unbiased information was drawn from each study (Appendix G).

### ***Data synthesis***

A descriptive (non-quantitative) approach was taken in synthesising the data since both quantitative and qualitative studies were included and the resulting data were too diverse for statistical meta-analysis.

### *Quality assessment*

Quality assessment of the included studies was challenging given the variation in study designs and the scarcity of studies looking at psychological distress in carers of people with MD specifically. There were no randomised controlled trials; in fact many studies did not include matched controls, as most were exploratory in nature perhaps reflecting the limited exploration of this field, despite the fact that studies spanned three decades.

Subsequently, two quality control tools were adapted and used; one for assessing quality of qualitative studies and one for quantitative studies. The National Institute of Health and Clinical Excellence (NICE) published guidelines on checklists used to review clinical evidence. An adapted version of the NICE Guidelines (2009) checklist for assessing qualitative research was used, fitting with the aims of this review (Appendix H). The checklist comprised of several areas for reviewing quality, each of which was assigned either a score of 2 (if the criterion was fully satisfied), 1 (if it was partially satisfied), or 0 (if it was not satisfied). The maximum score obtainable was 28.

Similarly, an adapted version of the Downs and Black (1998) checklist for quantitative studies was also used (Appendix I). Although this checklist was compiled for use with intervention studies, many of the areas for quality review applied well to observational studies. A total of 11 items were excluded from the checklist. The maximum score obtainable was therefore 16.

Each study was given a quality score based on the checklist used, which was reported in the synthesis table. Appendix J outlines the quality scoring assigned to each study. Five papers were randomly selected and assessed on quality using the checklists by an independent reviewer. Inter-rater reliability was assessed and Cohen's Kappa was found to be .64, which is considered 'substantial agreement' by Landis and Koch (1977).

## **Results**

### *Summary of studies*

Table 5 shows a summary of the main characteristics of the studies included in the review and is accompanied by a key to abbreviations used. Study reference numbers have been allocated to assist the presentation and discussion of the results.

Seven of the 19 studies were qualitative and twelve were quantitative. Two studies involved a comparison with a non-MD group. Three studies involved a mixed sample where MD data was extractable. Twelve studies used a DMD population to investigate their research questions, one study used Spinal Muscular Atrophy, and the remaining six used a range of neuromuscular disorders. Five out of twelve quantitative studies did not use a matched control group.

**Table 5.** Main characteristics of the studies included in the review (N=19).

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
1	Webb (2005)  USA	Observational – without control  QL = 21	N=13 (15 families)  Diagnosis – DMD  Age range = 5-23	N=23  NRPP – 1 for N=7 and 2 for N=8  Age range = N/A  RTP = Parents (mothers N=7, fathers N=1, couples N=7)	Semi-structured interviews – lasting 1-2 hours  Grounded theory analysis of interview data (used coding organised in loose-leaf Concept Notebook, then used cut-up-and-put-in-folders method)	Coping themes emerged: Genetics, Diagnosis, Reactions to the Diagnosis, Treatment, Equipment, and School Issues.  Most parents coped realistically and positively. They want to be valued as experts in DMD by professionals and share information with other parents to feel empowered.	Parents face much distress and emotional tension at various stages of illness – yet seem to hold a realistic and positive attitude so although distressed can manage well and keep going.
2	Chen <i>et al.</i> (2002)  China	Observational - Case-control  QN = 15	MD – N=22 Control – N=30  Diagnoses – DMD; children with fever  Ages: MD $\mu=10.9(3.9)$ , Control $\mu=3.6(2.5)$	MD-N=31 (22 families) Control-N=30  NRPP= 1-2  Ages: MD $\mu=37.9(7.5)$ , Control $\mu=32(3.6)$  RTP=Parents	CICI (Foxall & Watson, 1988; Hymovich, 1983), Coping Scale (Felton, Revenson, & Hinrichsen, 1984)  Multivariate analyses using stepwise logistical regression	Control group – higher “stress,” “conflict,” and “help needs.” DMD group – significantly less likely to use emotional expression. Parents' gender was non-significant in influencing variables. “Impact” was influenced by income and religion;	DMD parents indicated 4 times lower stress than controls. DMD parents were less likely to use emotional expression and self-blame for coping, but used wish-fulfilling fantasy more. Mothers of DMD

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
				(fathers N=14, mothers N=17)		and income and mother's age influenced coping strategies (higher income & younger mothers more likely to use them).	showed higher conflict and help needs than the fathers, while fathers needed more information and needed to receive more help from resources. Higher income and no religion showed greater risk for illness impacting on parent.
3	Gravelle (1997)  Canada	Observational – without control  QL = 22	N=8  Diagnoses - DMD, SMA, ML, Retts syndrome, and CP  Age range=2-16	N=11  NRPP= 1-2  Age range = N/A  RTP=mothers (N=5), parental couple (N=6)	Initial unstructured, in-depth interviews lasting 35 minutes - 2 hours, using trigger questions for focus. Second interviews were semi-structured (based on 1 <sup>st</sup> interviews), clarifying information, and validating findings.  Used Giorgi's data analysis & phenomenological analysis. Verified	Main theme of 'facing adversity' through offering care emerged. Parents had to continuously redefine and manage changes (increase in burden of care) resulting from the progressive nature of illness. Normalisation and 'chronic sorrow' are part of theme, as are the challenges of care-giving (particularly of mothers).	Parental distress was reported as highest at times of illness progression (adversity) and through each new stage (as normalisation becomes harder to achieve). Losses (of child's abilities and of caregiver freedom) lead to recurrent grief. Mothers willing and able to share their care-giving role

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
					emerging themes with 3 carers.		reported less stress than those who weren't (i.e. if accepted role due to no other choice then became resentful and frustrated).
4	Abi Daoud <i>et al.</i> (2004)  Canada	Observational - Case-control  QN = 13	MD – N=27 (26 families) Control – N=132  Diagnoses – DMD; general population  Age median=13.5 (11-19)	N=42  NRPP= 1-2  Age range=25-54  RTP= mothers (N=25), fathers (N=14), stepfathers (N=2), foster mother (N=1)	Questionnaire based on (or (for controls) information from) the National Population Health Survey from Statistics Canada (Scales measured: depression, self-esteem, mastery, distress)  Chi-squared analysis and Fisher's exact test, <i>t</i> -tests and nonparametric tests for comparisons between groups	DMD parents showed higher probability of a major depressive episode and significantly lower self-esteem and mastery scores than controls. No variables (age, IQ, and ambulatory status of child, or sex, age, and marital status of parent) predicted any of the scales, with 2 exceptions: single parents had lower scores on the mastery scale; and parents of either males, or older than 13 years were more likely to experience distress.	Psychological distress in DMD parents was more likely than in controls in terms of low mood, poor self-esteem, and low sense of mastery. Single parents were most at risk of low mastery, while parents of males or older than 13yrs were at risk for more distress.

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
5	Boyer <i>et al.</i> (2006)  France	Observational – without control  QN = 12	N=56  Diagnoses - DMD (N=11), BMD (N=14), SM (N=10), FSHM (N=5), C-MD (N=3), LG-MD (N=4), SMA (N=5), U-MD (N=4)  Age $\mu$ =32.7 (range=15-65)	N=56  NRPP=1  Age $\mu$ =48 (range=30-80)  RTP=mothers (N=29), fathers (N=5), spouses (N=17), friends (N=3), half-sister (N=1), grandmother (N=1)	<u>Patients:</u> WIS (Walton <i>et al.</i> , 1994), Modified Barthel Index (Collin <i>et al.</i> , 1988), Katz scale (Katz <i>et al.</i> , 1970), socio-demographic data , SF-36. <u>Carers:</u> ZBI (Bocquet <i>et al.</i> , 1996), SF-36 (McHorney <i>et al.</i> , 1994), GHQ-12 (Goldberg, 1979), HADS (Snaith, 2003), socio-demographic data, no. of care hours provided, no. of external-care hours per week.  Bivariate analyses to determine explicative factors of perceived degree of burden. Multivariate analysis using logistic regression model to find variables explaining care burden and perceived HRQoL.	High burden of care reported (on ZBI). Carer characteristics related to high risk of perceived burden are: self-report of poor social functioning on the SF-36; self report of anxiety on the HADS; and being a carer under 48 years old. Physical dependency, patient characteristics, and level of formal assistance provided were not associated with perceived burden of care.	Carers of people with MD can be at risk of high burden of care (physical and emotional) as defined by the ZBI and of perceived poor HRQoL as measured by the SF-36. (Study also attempted to identify explicative factors of poor HRQoL - namely social functioning, anxiety on HADS, and <48 yrs old; however admit this list is not exhaustive).



Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
6	Bach <i>et al.</i> (2003)  USA	Observational - Case-control  QN = 12	MD-N=47 Control-N=30  Diagnoses – SMA; healthy children  Ages=N/A	MD-N=104 Control-N=30  NRPP=varied- unspecified  Ages=N/A  RTP=mothers (N=44), fathers (N=30), grandparents (N=8), nurses (N=20)	Likert-scales on 6 QoL issues (1. Child's QoL? 2. Your QoL? 3. Effort to care for child? 4. Burden of caring for child? 5. How happy is the child? 6. Child's life worth living?) & choosing 10 polar-adjectives (e.g. hard/easy, miserable/enjoyable)  One-way ANOVA and Mann-Whitney U test used.	Carers indicated high QoL for both children and themselves. Despite higher effort ('harder life') rated by these carers when compared to parents of unaffected children, burden was not rated as higher. However: fathers report less burden of care than mothers; nurses report better personal QoL than both parents; nurses report more effort in caring for child than parents; nurses report more burden of caring for child than parents; grandparents report less burden of caring for child than parents; severity of illness did not play significant role in carer ratings of QoL.	Carers experience good perceived QoL while at the same time recognising that their life is harder than that of a parent of a healthy child. Parental gender (and possibly their responsibilities) may influence perception of burden. Parental relationship may have a positive impact on perception of QoL, burden, and effort.

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
7	Dawson & Kristjanson (2003)  Australia	Observational – without control  QL = 26	N=16  Diagnoses- MD(N=11), MND(N=5)  Ages=N/A	N=16(MD- N=11)  NRPP=1  Ages=N/A  RTP=Familial	Semi-structured interview (1-2 hours) based on literature and clinical experience.  Content analysis and constant comparison techniques used to code interviews and yield the three key themes (and subthemes).	Themes: reactions and responses (grieving every day, fearing each crisis may mean the end, watching life in reverse), health system crossing points (getting lost in the system, living with limits, I want to know who do I ask?), reaching forward (holding on to the big picture, learning from other carers, needing help to plan the future, just getting on with it, don't forget the children)	Many areas of stress for parents revealed - not only related to managing child's illness (constant progressive changes), but also to services available and to adjustment to new life. Complex emotional processes (e.g. grief) noted relating to different areas of impact in parent's life (family, marital, social, leisure/personal).
8	Reid & Renwick (2001)  Canada	Observational – without control  QN = 15	N=32 (36 families)  Diagnoses- DMD  Age $\mu$ =14.9 (1.92)	N=36  NRPP=1  Age $\mu$ =43.05 (5.52)  RTP=parents (N=35), grandmother (N=1)	QRS ( Holroyd, 1987), OSIQ (Offer <i>et al.</i> , 1989), Sociodemographic, disorder-related and other measures via 2 author-developed questionnaires, PPVT-R (Dunn&Dunn, 1981)  Means (SD) calculated for each measure and	Satisfaction with how diagnosis was delivered was almost equally split (47% dissatisfied Vs 44% satisfied). Perception of who found it hardest to cope revealed highest % was fathers (28%), followed by mothers (16%), and both equally affected (16%). QRS showed	Familial/caregiver stress reported is high although not above measure's threshold - however study found that carer stress was high enough to impact negatively on (and predict) child adjustment in the areas of impulse control

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					comparison of scores made to measures' norms using <i>t</i> -tests. Pearson correlations used to examine r/s between familial stress and psychosocial adjustment and function. Stepwise regression analysis conducted to determine variables best predicting level of psychosocial adjustment.	high familial stress (just under clinical cut-off). Familial stress was significantly correlated with adolescent adjustment (OSIQ). Adolescents' scores on OSIQ were significantly predicted by caregivers' scores on QRS alone.	(psychological self), morals (social self), and family relationships (familial self).
9	Mah <i>et al.</i> (2008a)  Canada	Observational – without control  QL = 24	N=15  Diagnoses- DMD (N=3), SMA (N=5), other MD (N=7)  Age range=2-7	N=19  NRPP=1-2  Age range=24-47  RTP=mothers (N=14), fathers (N=5)	Semi-structured interviews (60-90 minutes) based on previous study but adapted to focus on research question. Computer software used to facilitate interpretation within a phenomenological framework.	Main themes: context of mechanical ventilation; caregiving; child's life and QoL; isolation; stress; support, uncertainty; living with loss; expert; changed perspective. Central theme of parents' experience was being the "lifeline" for their child's life and QoL. Experience of recurrent sense of loss and	Distress expressed by parents particularly in view of insufficient support (health-care services) or isolation (social). However, driving force to continue giving care was the overarching experience of being a "lifeline" for child and their child's QoL.

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
						uncertainty, despite expertise in care-giving. Those who perceived insufficient support felt weight of responsibility as sole carers.	
10	Mah <i>et al.</i> (2008b)  Canada	Observational - Case-control  QN = 16	N=109 (ventilated N=19, non-vent. N=90)  Diagnoses- DMD/BMD (N=24), C-MD (N=6), Myotonic dystrophy (N=3), FSHM (N=2), U-MD (N=2), Myopathies (N=19), SMA (N=17), Neuropathies (N=33), O-NMD (N=3)  Age $\mu$ =10.5 (5.2)	N=109  NRPP=1  Age $\mu$ =41 (8)  RTP=mothers (N=87), fathers (N=17), legal guardian (N=5)	PSI (Abidin, 1995) or SIPA (Sheras <i>et al.</i> , 1998), PQoLI (Varni <i>et al.</i> , 2001), a general survey of child's neuromuscular disease and family's socio-demographic characteristics  Bivariate comparisons using Pearson's chi-square or Fisher's exact test on categorical variables. Continuous variables reported as means (SD) or medians (interquartile range) and comparisons using unpaired Student <i>t</i> -tests or one-way ANOVA.	Children on ventilation had significantly lower mean total PQoLI scores than non-ventilated children.  No significant difference in parental stress between ventilated and non-ventilated children.  No significant difference in mean total stress scores found between parents (with or without ventilation) than normative sample.	Distress expressed in both groups of MD parents but no difference in stress levels between parents of ventilated and non-ventilated children; nor was distress above clinical threshold. Added caretaking demands of parents of ventilated children seem to be adjusted to and not identified as creating additional stress.

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11	Nereo <i>et al.</i> (2003)  USA	Observational - Case-control  QN = 14	MD-N=112 Control 1-N=28 Control 2-N=46 Control 3=scale norms  Diagnoses- DMD, CP (N=28), siblings (N=46)  Ages: DMD $\mu=9.43$ (2.81), CP $\mu=6.43$ (0.63), siblings $\mu=10.07$ (3.2)	MD-N=112 CP-N=28 Siblings-N=46  NRPP=1  Ages: DMD $\mu=37.75$ (5.43), CP $\mu=36.75$ (5.61), siblings $\mu=37.90$ (5.30)  RTP=mothers	<u>Mothers:</u> PSI-SF (Abidin, 1995), CBCL (Achenbach, 1991). Longitudinal testing of maternal PSI-SF in DMD (3 time-points). <u>DMD and siblings:</u> PPVT-R; Dunn & Dunn, 1981). <u>CP:</u> PPVT-Third Edition (Dunn & Dunn, 1997).  One-sample <i>t</i> -tests to compare DMD PSI-SF to norms. Linear regression analyses to determine contribution of variables to stress. MANOVA to compare CBCL results between 'stressed' and 'non-stressed' mothers. ANCOVA (CP) or paired <i>t</i> -tests (siblings) used to compare DMD PSI-SF scores. General linear model to compare PSI-SF longitudinally.	Presence of problem child behaviours predicted maternal distress, parent-child interaction problems, and child being perceived as difficult. Stress related to child behaviour was higher in DMD versus normative group. No differences in stress were found between DMD versus CP or versus siblings. Longitudinally, DMD maternal stress reduced with disease progression.	Distress was not higher in DMD mothers than in normative sample. But stress was higher relating to child's problem behaviours, and to social interactions with child. Thus higher stress seems to be related to those factors rather than due to the physical demands of the illness alone (since symptom progression alone could not account for stress levels, suggesting mothers learn to cope with increasing burdens and child social interactions).

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
12	Samson <i>et al.</i> (2009)  Canada	Observational – without control  QL = 26	N=11 (9 families)  Diagnoses- DMD  Age median=15 (range 7.5-17)	N=12  NRPP=1-2  Age median=48 (range 41-60)  RTP=mothers (N=7), fathers (N=5)	Semi-structured interviews – duration $\mu$ = 90 min. Three types of interjections used by interviewers.  Empirical Phenomenological Psychological data analysis method used.	Three major themes indicated ways of perceiving child's illness: (1) a severe loss to face, (2) a call to adapt, and (3) seeing beyond the loss to rediscover child. Each of the 3 cognitive appraisals leads to different ways of hoping. Parents can hope for (1) a cure, (2) the child's well-being, or (3) to see their child becoming a whole person. Hope can help parents absorb the initial crisis, sustain their adaptation, or prepare for the fatal outcome.	Parents seem to move through the 3 cognitive appraisals from diagnosis to the terminal stages, as child grows older. A very positive view of care-giving and working through the distress, so life is enjoyed within the context of evolving (from wishful thinking to more reality-based) hope (an inner supporting resource).

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
13	Bothwell <i>et al.</i> (2002)  Canada	Observational – without control  QN = 12	N=31 families  Diagnoses- DMD  Age $\mu$ =11.4 (4.7)	N=31  NRPP=1  Age range=N/A  RTP=parents	Postal questionnaire developed on basis of DMD literature and clinical practice, rating importance of: services, health issues, & QoL issues, both ‘now’ and ‘in the future’.  Calculated proportion of patients answering ‘very important’ on each item. Compared responses to questions ‘now’ versus in ‘future’ using Wilcoxon signed-rank test. Compared responses between parents whose boys were within 6yrs of diagnosis to those beyond 6yrs using ANOVA to identify changes in importance as disease progressed.	Overall, Psychology/Psychiatry seldom considered important service (now or in future) but parents of older children (diagnosis >6yrs) saw psychiatry as likely to be important in the future. QoL and educational issues were important (now and in the future). Financial concerns, anger, and social isolation for both parent and child were important now and were predicted to increase in future.	Mental health and QoL are important to families. Parents concerned about anger, finance, and social isolation for child and themselves. Felt that depression and anger in their son and family would become more important in future.

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14	Thompson <i>et al.</i> (1992)  USA	Observational – without control  QN = 14	N=35  Diagnoses-DMD  Age range=4-14	N=35  NRPP=1  Age range=N/A  RTP=mothers (N=32), fathers (N=3)	Stress and efficacy ratings (0-100) given on 4 illness-related tasks: Dealing with child's medical prbs, Maintaining child's emotional well-being, Maintaining own emotional well-being, Preparing for an uncertain future. WCQ (Vitaliano <i>et al.</i> , 1985), FES (Moos & Moos, 1981), SCL-90-R (Derogatis, 1977). MCBC (Sines <i>et al.</i> , 1969).  MANOVAS/ANOVA S, Pearson correlations, and hierarchical multiple regression conducted.	57% of parents (primarily mothers) reported poor adjustment, 37% showed clinical distress, 29% depression, and 20% anxiety. Poorly adjusted parents reported higher stress in maintaining own emotional well-being. Palliative coping was used more than adaptive coping. Low levels of family support, and high levels of family conflict. Parental stress, depression, and anxiety accounted for 58% of variance in general distress, 50% in depressive symptoms, and 31% in anxiety symptoms.  89% reported poor child adjustment which was predicted by parental variables.	Poor parental and child adjustment found. High rate of child behavioural problems may reflect parental distress. High levels of parental-perceived stress, palliative coping methods relative to adaptive methods, and high levels of family conflict were associated with parental poor adjustment.



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15	Hatzmann <i>et al.</i> (2008)  Netherlands	Observational – case-control  QN = 14	MD-N=57 Control-N=425  Diagnoses- DMD, healthy children  Ages: MD range=7.6-15.6, Control range=1-19	MD-N=57 Control-N=425  NRPP=1  Ages: MD range=38.4-49.6, Control range=38.2-49.2  RTP:MD-mothers (N=42), fathers (N=15), Control-mothers (N=354), fathers (N=71)	TAAQoL (Bruil <i>et al.</i> , 2004)  Univariate ANOVA carried out for each scale of TAAQoL. Effect sizes ( <i>d</i> ) calculated. Used 25th percentile ranking of healthy population as cut-off between parents 'at risk' and those 'not at risk' for impaired HRQoL.	Four significant areas of difference found between DMD and controls (DMD did worse): social functioning, vitality, positive emotions, and depressive emotions. DMD parents found to be significantly 'at risk' for impaired HRQoL compared to controls on social functioning, vitality, and depressive emotions.	Parental distress was higher in DMD than controls with certain aspects of life under particular stress, i.e. social functioning, vitality, and mood.
16	Firth <i>et al.</i> (1983)  UK	Observational – without control  QL = 21	N=56 (53 families)  Diagnoses- DMD  Age range=4- young adults	N=53 families  NRPP=1-2  Age range=N/A  RTP=parents	Guided interviews – duration= 1-2½ hours. Authors designed interview schedule covering: problems experienced by parents, diagnosis, neonatal screening, effects on marital	15% of reported problems were classed as 'emotional' ('service' - 23%, 'practical' - 62%). Parental emotional difficulties reported by 6%. Isolation and additional problems of mental	Insufficient or inappropriate support when needed is perceived by parents, which adds to their emotional stress. Communication within family around illness is a constant

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					relationship, siblings, effects of DMD on sufferers, and information.  Interview coding developed by authors, as well as verbatim transcriptions of extracts were used.	handicap reported by 4%. Mainly mothers reported fathers found diagnosis harder to accept. Neonatal screening: majority in favour (75%) and 1 of reasons was emotional advantage of more time to adjust. 11 reported negative effect on marital relationship. Siblings: parents felt guilty about neglect or being inappropriately stricter & worried about accepting help versus being a 'burden'. Worried over son's well-being and concerned about what to tell sons about illness.	worry. Worry felt primarily around time of diagnosis, but carries on throughout caring for child and spreads to other areas, such as siblings.
17	Gagliardi (1991)  USA	Observational – without control  QL = 25	N=3  Diagnoses-DMD  Age range=7-9	N=6  NRPP=2  Age range=26-30	Ethnographic logs and memos kept during observations. In-depth interviews conducted twice over 10-week observation period, and third time 1 year	6 themes emerged and were grouped under 3 stages of adapting to disability: Stage 1- Recognition: (1) Disillusionment, (2) Society confirms the	Parental distress evident within family life, social functioning, emotional functioning, marital relationship, through

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				RTP=mothers (N=3), fathers (N=3)	later. Constant comparative method used as context of analysis. Coding used to compare across families.	impossibility of normalcy; Stage 2- Working out: (3) Dynamics of family, (4) A smaller world; Stage 3-Resolution: (5) Letting go or hanging on, (6) Things must change	the themes identified. However, the families rise to the challenge by the end and make the most of their lives, giving a sense that distress is manageable and can be overcome.
18	Holroyd & Guthrie (1986)  USA	Observational – case-control  QN = 12	MD-N=16 Control 1-N=16 Control 2-N=11 Control 3-N=14  Diagnoses-PMD (N=11), SMA (N=3), MO (N=1), O-MD (N=1), CF (N=16), RD (N=11), healthy children (N=14)  Ages: MD $\mu=9.7$ (2), CF $\mu=10.9$ (2.7), RD $\mu=12.5$ (5), controls $\mu=9.9$ (2.9)	MD-N=16 CF-N=16 RD-N=11 Control-N=14  NRPP:1  Age ranges: N/A  RTP: Parents	QRS (Holroyd, 1974), QRS-Short Form (Holroyd & Guthrie, 1986)  MD compared with control group, CF, and RD groups, on 15 QRS scales and 11 'short' scales using <i>t</i> -tests for unrelated means (26 tests).	MD parents reported more stress than CF and RD groups. MD parents scored significantly higher than controls on 11 out of 15 QRS scales (poor health/mood, negative attitude towards ill child, overprotection/dependency, lack of social support, pessimism, financial problems, physical incapacitation of child, lack of activities for child, occupational limitations for child, social obtrusiveness, difficult personality	Higher parental stress experienced in MD group than in healthy controls, CF, or RD populations.

Study ID reference	Reference & Country	Study design (1-4) & Quality score (QN/QL)	N & Patient sample characteristics (diagnoses, ages)	Carer characteristics (N, NRPP, ages, RTP)	Outcome measures & Analyses	Main Findings	Main Findings in relation to psychological distress in carers
						characteristics) & 6 out of 11 of the short-form (cognitive impairment, limits on family opportunities, life span care, terminal illness stress, physical limitations, financial stress).	
19	Im <i>et al.</i> (2010)  South Korea	Observational – without control  QN = 14	N=90  Diagnoses- DMD (N=67), BMD (N=3), myotonic dystrophy (N=5), LG-MD (N=4), C-MD (N=1), U-MD (N=10)  Age $\mu$ =14.5 (7.3)	N=90  NRPP=1  Age $\mu$ =42.9 (8.7)  RTP=mothers (N=81), fathers (N=4), other (N=5)	K-WHOQOL BREF (Min <i>et al.</i> , 2002); K-BDI (Rhee <i>et al.</i> , 1995); K-APGAR (Choi <i>et al.</i> , 2002); emotional status of patients measured by K-BDI and K-CDI (Cho & Lee, 1990) for patients under 18 yrs.  Caregivers divided into 2 groups on basis of DMD, depression, carer gender, employment status, and religious degree. Independent <i>t</i> -tests compared groups in relation with QoL.	Higher family income, high family function and education were associated with higher carer QoL. Depression in carers and children were associated with a lower QoL. Employed carers showed significantly higher QoL. Linear regression analyses showed that emotional and employment status accounted for 15.6% of QoL.	MD parental QoL was linked to their own emotional distress (28.7% of sample had moderate to severe depression) and their child's emotional distress (where high depression linked to low QoL), and their employment status (employed had higher QoL). High income and good family function were also linked to higher QoL.

<b>Study ID reference</b>	<b>Reference &amp; Country</b>	<b>Study design (1-4) &amp; Quality score (QN/QL)</b>	<b>N &amp; Patient sample characteristics (diagnoses, ages)</b>	<b>Carer characteristics (N, NRPP, ages, RTP)</b>	<b>Outcome measures &amp; Analyses</b>	<b>Main Findings</b>	<b>Main Findings in relation to psychological distress in carers</b>
					Linear regression with stepwise variable selection to identify factors associated with QoL.		

QN = Quantitative checklist used (maximum score of 16), QL = Qualitative checklist used (maximum score of 28); Patient/Carer ages are reported in years using the mean(standard deviation), median(interquartile range), or the range, whichever was available; DMD = Duchenne Muscular Dystrophy; MD=Muscular Dystrophy; LM=metachromatic leukodystrophy; BMD=Becker's Muscular Dystrophy; SM=Steinert's myotonia, FSHM=facio-scapular-humeral myopathy, C-MD=congenital MD, LG-MD=limb girdle MD, SMA=spinal muscular atrophy; U-MD=undetermined MD; MND=Motor Neurone Disease; O-NMD=Other neuromuscular disorders; CP=cerbral pulsy; PMD=progressive MD; MO=myositis ossificans; CF=cystic fibrosis; RD=Renal disease; NRPP = number recruited per participant; RTP= relation to participant; N/A = information not available/reported; CICI=Chronic Impact and Coping Instrument; WIS=Walton Impairment Score; SF-36=Short-Form 36 HRQoL; ZBI= Zarit Burden Inventory; GHQ-12=General Health Questionnaire; HADS=Hospital Anxiety and Depression Scale; QRS=Questionnaire on Resources & Stress; OSIQ= Offer Self-Image Questionnaire for Adolescents; PPVT-R= Peabody Picture Vocabulary Test-Revised; PSI= Parenting Stress Index; PSI-SF= Parenting Stress Index-Short Form; SIPA= Stress Index for Parents of Adolescents, PQoLI= Pediatric Quality of Life Inventory; CBCL=Child Behavior Checklist; WCQ=Ways of coping questionnaire; FES=Family Environment Scale; SCL-90-R=Symptom Checklist 90-Revised; MCBC=Missouri Children's Behaviour Checklist; TAAQoL=TNO-AZL Questionnaire for Adult's Health Related Quality of Life; K-WHOQOL BREF=Korean version of World Health Organization Quality of Life Assessment, Life Brief Form, K-BDI=Korean version of Beck Depression Inventory; K-APGAR=Korean version of the family APGAR scale; K-CDI=Korean version of the Children's Depression Inventory

## *Carer distress*

### **Degree and nature of distress**

Most studies suggested the presence of some form and degree of distress in carers of people with MD, although there were a number of studies which indicated that distress in this population may not be as debilitating as hypothesised (1, 2, 6, 11, 12, 17).

Attempts to quantify the level of distress are mostly seen in quantitative studies, where several found clinical levels of distress for the measures they used; including measures of stress, anxiety, depression, self-esteem, adjustment, coping, and QoL (4, 5, 14, 15, 18, 19).

Looking at the *nature* of the distress may be a more meaningful exploration of distress. A major aspect of distress appears to be grief in response to diagnosis and ongoing losses occurring as the illness progresses, and the demand for constant adjustment of carer and family functioning (1, 3, 7, 9, 12, 14, 16, 17). Throughout the illness trajectory carers are repeatedly faced with progressive loss in their child's abilities, and subsequently a progressive increase in the emotional and practical burden of care. In fact, Bothwell *et al.* (2002) found that parents of boys with DMD predicted that their anger and social isolation would increase in the future and that their sons' emotional well-being would deteriorate in the future in terms of anger and depression. Gravelle's (1997) main emerging theme was that of 'facing adversity' by redefining and managing the care parents provided through normalisation and 'chronic sorrow'. Samson *et al.* (2009) explored the experiences of carers for boys with DMD and found that these carers' adjustment to the illness and care demands is progressive and follows the illness and the child's development.

### **Distress in varying aspects of life**

Other studies have presented the psychological, social, interpersonal, physical and financial (9, 16, 18, 19) aspects of life affected by distress. In particular, the impact on QoL has been

investigated with mixed findings. Some studies have found this to be low, or worse in MD carers when compared to controls (5, 15, 19), while Bach *et al.* (2003) found no difference, although they used a small and arguably unrepresentative sample of SMA patients.

Many qualitative studies reveal distress in areas such as social integration resulting in loneliness and a sense of isolation (7, 9, 14, 17, 18). Others highlight interpersonal difficulties within the family (9, 14), i.e. marital conflict (7, 16, 17), or guilt around neglecting or overbearing unaffected siblings (16). Others yet, have found that the carers' relationship with the affected child is tense (18), assimilating mutual feelings of anger, guilt, and worry; particularly parental worry and helplessness around their child's physical and emotional pain, as they watch the gradual deterioration, and are faced with difficult-to-answer questions from the child about the illness and death (7, 16, 17).

### **Socio-demographic predictors of distress in carers**

Several studies suggest that mothers experience higher levels of distress and burden of care than fathers (2, 6). This can partly be attributed to the fact that primary caregivers tend to be mothers (3). Indeed most research samples are significantly skewed towards female carers (1, 3-5, 9-11, 14, 15, 19), with one study (19) comprising of 81 mothers and just four fathers, while another (11) only comprised of mothers. The skewed samples pose a significant limitation to the generalisability of results and limit the reliability of gender as a predictor of distress.

Other studies suggest that fathers find the time of diagnosis harder than mothers (8, 16), however, these conclusions are often drawn from female-skewed samples. Chen *et al.* (2002) found that mothers showed higher stress, conflict, and help needs than fathers, who in turn, had higher needs for information and help from resources.

Bach *et al.* (2003) suggest that a parental relationship to the affected child may lessen the perception of burden and effort in caring (contrary to that of a nurse), but QoL was still perceived to be low. Accordingly, low family support and high family conflict have been linked to higher distress (14).

Other factors linked to distress or high burden of care included being a carer under the age of 48 (5), income level, religious commitment, education and employment (2, 19), whereas other studies (8, 11, 14) found no significant relationship between socio-demographic variables and distress. Overall, there seems to be little consistency in what socio-demographic factors relate to distress in carers and study limitations, such as gender ratios, sample sizes, and absence of optimal controls, pose constraints to interpretation.

### **Psychological predictors of distress in carers**

Several studies have attempted to make links between distress and psychological factors. For example, Im *et al.* (2010) found that depressed carers had significantly lower QoL, while Holroyd and Guthrie (1986) found that expressing negative feelings about the child contributed to parental stress.

Nereo *et al.* (2003) found that child behaviour problems were linked to maternal stress, a 'dysfunctional' parent-child relationship, and perceiving the child as 'difficult'. They also showed that over two years, maternal stress decreased in relation to perceiving the child as 'difficult', suggesting that mothers learned to adjust and cope with their child's worsening symptoms. The study did not investigate additional variables influencing stress, such as support services. However these results suggest that adjustment and coping may be more important factors in predicting stress than illness severity. Nevertheless, this study did not find higher overall stress compared to the normative sample. Similarly, despite significantly



lower physical and psychosocial HRQoL in MD children, parental stress was not found to be significantly higher than a normative sample (10).

Several studies provide evidence in support of adjustment and grief as psychological factors influencing distress (1, 3, 7, 9, 12, 14, 16, 17). Thompson *et al.* (1992) found that 57% of parents fitted criteria for poor adjustment. Poor adjustment correlated significantly with depression, anxiety, stress, and poor coping. Moreover, they found that parental stress, depression, and anxiety accounted for 58% of the variance in general distress, 50% in depressive symptoms, and 31% in anxiety symptoms.

In support of the above findings other studies found that, anxiety (5), poor social functioning (5, 15), poor parental emotional health (18), negative emotions, and lower vitality (15) contributed to higher stress levels as compared to controls. Other contributors were pessimism around long-term outcomes and constant awareness that the illness is terminal, as well as perceiving insufficient support (18).

However, these findings must be interpreted with caution due to design limitations already addressed, such as gender-skewed and small sample sizes, a limited list of variables explored, and the samples often comprising of one MD type, so findings may not necessarily generalise to other MD conditions.

### **Positive aspects of care-giving and coping**

Despite the focus of this review on distress, several studies surfaced the positive aspects of care-giving and adaptive coping (1, 2, 6, 9, 11, 12, 17). For example, although parents of children with SMA reported that life was ‘hard’ significantly more than controls did, their reported QoL was no lower than that of controls (6). Nereo *et al.* (2003) found no significance differences in maternal distress in a DMD group compared to their siblings, a cerebral palsy group, or a normative sample.

Chen *et al.* (2002) found that DMD carers reported four times less stress than parents of a child with fever, and used different coping strategies, including wish-fulfilling fantasy, focusing on the present, normalising, and capitalising on personal strengths.

Some explorative studies found that the emerging themes from carers' experiences are about personal growth, enrichment, and hope (1, 9, 12, 17). Gradual adjustment follows the initial grief reaction, enabling parents to develop positive, realistic, and proactive coping strategies, and fulfil more of their child and family's potential (1). A mutually dependent and nurturing relationship between parent and child inspired the parents to improve family QoL by focusing on positive aspects of life, living in the present, and seeing themselves as the child's 'lifeline' (9).

Two studies (Samson *et al.*, 2009; Gagliardi 1991) have mapped out the carers' journey from loss to enrichment and hope. With the loss of a healthy child comes disillusionment and grief. Carers then move towards achieving a family equilibrium and adapting to challenges over the illness trajectory, to the eventual resolution of a new, meaningful life and the rediscovery of their child's identity. For these families the illness arrives as an external threat alongside hope for a miraculous cure until it becomes a part of the child through the struggles of adjustment, and hope rests in the present successful coping. Eventually, the illness becomes an integral and valued part of the child's identity and hope lies within the child's individuality.

Although the sample sizes in these studies are small, they provide a valuable starting point for further exploration of these aspects of caring.

#### *Qualitative versus Quantitative studies*

As expected, qualitative studies provided 'richer' data than quantitative studies, but are however less generalisable due to smaller sample sizes and limited types of MD in the

samples. However, as illustrated above the main themes from these two types of approaches seem to overlap considerably.

Still, qualitative studies may have presented a more positive view of care-giving than quantitative studies, as they afforded the flexibility of exploring care-giving experiences widely, rather than only looking for specific variables related to distress. This is important to note, as the research in this area seems to still be mapping care-givers' experiences and clearly indicates that they do not solely concern distress or negative experiences but greatly enriching ones as well.

## **Discussion**

This review aimed to address questions relating to the degree and nature of distress experienced by carers of people with MD, the impact on different aspects of life, possible psychosocial factors related to distress, and the implications of distress on the populations and services involved.

While the results do not exhaustively address these questions, they present a rich and meaningful starting point from which further research can begin to pick up and follow the strands comprising the experiences of these carers.

### *Degree and nature of distress*

The review involved a number of qualitative and quantitative studies, using a range of approaches, designs, and measures. As a result, quantifying distress in carers of people with MD poses a challenge. Nevertheless, the studies clearly identify clinical distress levels in this population through the use of various measures (4, 5, 14, 15, 18, 19).

The nature of the distress experienced seems to consist of recurring loss and subsequent unresolved grief. Grief-related emotions usually surface at times of change in the progressive

trajectory of the illness, calling for the carers and families to adjust and manage the increased burden of care (3, 7, 9, 12, 14, 16, 17). The resulting pattern seems to be one of cycles of loss and disarray followed by coping and redefining adversity until the next loss occurs (3).

#### *Affected aspects of life*

The review revealed that the psychological distress experienced affected all areas of life. For instance, Duger *et al.* (2003) found that the higher the child's dependency the higher the severity of maternal back pain. Many studies found that carers feel socially isolated (7, 14, 18) or have self-imposed social boundaries around the family unit which lead to social dysfunction (9, 17). Family conflict and marital problems are also present, as are financial strains (e.g. 9, 16). In fact, several studies found that these carers have significantly lower QoL than controls (5, 15, 19).

#### *Factors linked to distress*

The reviewed studies attempted to identify the factors explaining variability in carer distress scores and these can be grouped into socio-demographic and psychological factors. The evidence emerging is mixed and inconclusive with regards to these factors and study design limitations restrict generalisability.

Nonetheless, the main socio-demographic factors that seem to be related to higher distress are: female carers (2, 6); low family support and high family conflict (14), young carer age (5), lower education, and unemployment (19). Furthermore, the main psychological factors seem to be poor carer emotional well-being in terms of mood, anxiety, and adjustment (5, 14, 15, 18, 19), and child behaviour and socialisation problems (8, 11, 12).

#### *Positive aspects and coping*

Several studies uncovered the issues beyond distress, with carers describing well-adjusted, meaningful lives and an ability to adequately and positively cope with recurring changes (1,

9, 12, 17). These parents map out their personal adjustment and transformation alongside the illness progression. Their hopes and attitudes towards the illness and the child evolve, just as the child evolves and becomes a unique individual. Cohen and Lazarus (1979) support the idea that cognitive appraisal of a source of stress is dynamic and since hope emerges through cognitive appraisal, hope is also dynamic (DuFault & Martocchio, 1985). Carers are clearly able to look 'beyond the loss' and distress to redefine and rediscover their life and their child, using hope as an inner resource (12).

The findings of the review are in line with the wider literature on carers of chronically-ill children, in terms of the nature of distress experienced and the impact on carers' emotional, family, and social worlds (e.g. McGrath, 2001; Carnevale *et al.*, 2006). This review suggests that carers of children with progressive MD will face psychosocial demands throughout the illness, which can however be managed and overcome, as well as at transitional points between stages of progression which are experienced as crises. These findings fit well with Rolland's (1987) conceptualisation of three stages of psychosocial demands: (1) the crisis, (2) the chronic, and (3) the terminal stages. The findings can also be understood in the context of Rolland's (1987) five elements affecting psychosocial demands which relate to the nature of the illness (Table 1). MD disorders are progressive in nature with a high impact on physical, mental, and cognitive health, and despite high predictability of the rate of progression, this comes with a poor prognosis and often a fatal outcome. Unsurprisingly, for the parents who take on a carer role these elements of the disease can be devastating. The literature, however, offers a positive take to these carers' experiences through their reports of hope and enrichment in their lives.

#### *Literature quality and Future Research*

Although the findings are valuable and interesting, several limitations in the studies stand out which may limit their reliability and validity. In line with Polakoff *et al.*'s (1998) findings,

sample sizes in some of the quantitative studies in this area have been small. Although this may be attributed to the rareness of the disorders, the findings need to be replicated with larger samples. Moreover, some studies did not use a control group, or used a non-matched control by comparing to measure norms, which involve non-disabled healthy children and too many variables are perhaps different.

The samples primarily comprised of carers for boys with DMD and further research needs to recruit a range of other MD disorders to allow for greater generalisability of findings. Moreover, the carer samples were skewed towards female carers and the views of male carers were under-represented in many studies and need to be explored in future research.

Furthermore, the majority of studies used a cross-sectional (often retrospective) design, although three studies (3, 11, 17) collected data at multiple time-points. More longitudinal studies are required to add validity to the findings, particularly in relation to how distress and adjustment change throughout the illness journey. Additionally, since any list of factors influencing distress is unlikely to be exhaustive, further research needs to replicate the results of studies identifying predictors and continue to explore further possibilities, with the aim of untangling the influence of socio-demographic and psychological factors influencing distress in carers.

Finally, one must wonder if the nature of qualitative studies brings about issues of social desirability which make it harder for parents to express distress in caring for their child, especially since home-based care is becoming a social expectation. Still, although better controlled quantitative studies can be conducted, the richness in explorative studies may be indicative of research in the area still lying in its early stages. The findings from these studies need to be further explored and understood using a firmer conceptual framework around chronic, genetic illnesses (such as that proposed by Street & Soldan, 1998).

### *Conclusions and Implications*

It is clear that caring for a person with MD can be a distressing and challenging experience. This is particularly the case if the carer has a familial relationship with the person, since the caring context becomes the entire family. This inevitably broadens the experience and impact of caring onto the family unit. Despite the undeniably strenuous (emotionally, physically, and socially) experience for carers, patients and their families, caring nevertheless also offers opportunities for growth and enrichment.

The distress experienced by carers impacts on their ability to provide care and subsequently impacts on patient QoL, their experiences, and personal growth. As care for people with chronic conditions moves largely to the home environment (Boström *et al.*, 2006) support for the carers will directly influence the quality of care for the patient (e.g. Im *et al.*, 2010). It is clear that services need to consider carers and their families' emotional well being in care plans and offer psychological support at points of crisis, as well as practical help and advice. Carers need to be brought together to enable a sense of belonging, understanding, and support. Through mutual advice-sharing these carers can feel empowered and in control as has been repeatedly reported by carers joining support groups (1, 9, 12, 17).

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Cognitive profile in advanced Duchenne Muscular Dystrophy (DMD) and the effects of hypoventilation on cognition.<sup>5</sup>

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<sup>5</sup> This paper is written in the format ready for submission to the Journal of Neurology, Neurosurgery, and Psychiatry. Please see Appendix C for the Guidelines for Authors.

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## **ABSTRACT**

*Objectives:* DMD is a life-limiting condition affecting the muscles. Cognitive deficits in areas of memory have been consistently found in children with DMD. Their life expectancy has been extended by Non-invasive Positive Pressure Ventilation (NIPPV) which is administered when hypoventilation develops. However, little is known about the cognitive profile of this older DMD population and the effects of hypoventilation and NIPPV on cognition.

*Method:* Two groups with advanced DMD were recruited. The boys in the Duchenne Muscular Dystrophy Ventilated (DMDV) group (N=17) were on NIPPV while the boys in the Duchenne Muscular Dystrophy Control (DMDC) group (N=16) did not need NIPPV. Both groups were tested on memory, executive function, mood, quality of life (QoL), and beliefs about sleep. *Results:* The groups were compared on performance on each measure. No significant differences were found on any of the measures. The performance of the whole sample revealed differences between verbal and visual memory, as well as between list recall and story recall. *Conclusions:* Hypoventilation does not seem to lead to permanent cognitive deficits in advanced DMD subjects. Moreover, verbal capacity span may remain limited in this population as was found in studies of younger samples. Implications and suggestions for future research are discussed.

## **INTRODUCTION**

### **Duchenne Muscular Dystrophy (DMD)**

DMD is an inherited, progressive muscular disorder, predominantly affecting boys. It is caused by a gene mutation where the defective gene hampers the production of dystrophin, a crucial protein for the muscle fibres and the central nervous system. [1, 2] Lack of this protein leads to a progressive weakening and degeneration of the muscles which results in a significantly reduced life expectancy. [3]

DMD is rare, with prevalence in the general population of about one in every 3,500 male births [4], yet it is one of the most severe and common forms of progressive muscular disorder.

### **Cognition in DMD**

Based on a meta-analysis, general intellectual functioning was found to be normatively distributed but shifted downwards by approximately 1 standard deviation, (mean Full Scale IQ = 80.2 (SD = 19.3)) [5]. Other studies [3,6,7] however, have found general intellect to be within the normal range and support the presence of a specific deficit in verbal working memory, affecting verbal span capacity but not recall [2]. For example, Wicksell *et al.* [7] used the Ravens Matrices, instead of the Wechsler Intelligence Scales which require the use of short-term memory already established to be impaired in this population [3, 6], and found intellect is in the normal range. Hinton *et al.* [2] maintain that lower IQ scores found in past studies may reflect the fact that “missing dystrophin...may make it harder to process large verbal loads” (p.127), for instance the structured administration guidelines which do not allow the repetition of instructions.

Hinton *et al.* [2, 3, 6, 8] have completed a series of studies which support the presence of a specific cognitive profile in the DMD population characterised by lower verbal IQ, poor

attention to complex auditory material and specific deficits in immediate verbal memory and verbal processing. The authors hypothesise that immediate verbal working memory may become taxed more readily in boys with DMD, and refer to Baddeley *et al.*'s [9] "phonological loop", responsible for acquiring, rehearsing and consolidating information. They suggest that this loop is limited in children with DMD and thus less information can be processed once heard than that normally expected.

The literature appears to generally agree on the presenting deficits around verbal working memory (i.e. limited verbal span) which may have potential implications in academic achievement and social integration (Hinton *et al.*, 2007). [2] However, a recent study by Donders and Taneja ([10]; p.302) argues for '...neurobehavioral impairments, affecting verbal and nonverbal cognitive domains, as well as some aspects of psychosocial and meta-cognitive abilities'. It is therefore clear that a definitive cognitive profile for children with DMD is still a matter of debate and further research. [10]

Cotton *et al.* argue that, while most studies focus on verbal and language development in children with DMD, non-verbal intelligence remains largely unstudied. [5] This is particularly true for studies of executive function. [10]

### **Hypoventilation in DMD**

Respiratory problems are almost inevitable as the weakening of the muscles around the breathing apparatus causes them to fail. Problems first become evident during sleep and eventually lead to hypoventilation and hypoxic episodes. [11] In DMD lack of dystrophin has been shown to render specific neuronal populations susceptible to hypoxic insults, particularly the hippocampus [12] and cerebellum [13], which could potentially contribute to the development of cognitive deficits.

Hypoventilation can also cause daytime sleepiness, reduced quality of life (QoL) and social functioning, and impaired cognitive performance. [14] The effects of hypoventilation on cognition have been studied in conditions such as amyotrophic lateral sclerosis [15] but not in DMD. These studies have shown that sleep-disordered breathing can lead to specific cognitive deficits, such as memory and executive functioning difficulties. [12]

### **Treatment with nocturnal ventilation**

It has been shown in different medical conditions that many of the effects of hypoventilation can be effectively reversed with Non-Invasive Positive Pressure Ventilation (NIPPV) – a generally nocturnal supply of oxygen which treats hypoventilation. [14-16] Specifically quality of sleep, QoL, and cognitive performance have been shown to improve while daytime sleepiness reduces. [14]

Moreover, research has shown that NIPPV significantly extends the life expectancy of DMD sufferers as hypoxic episodes are reduced or even eliminated for an extended period of time. [4, 17] The increase in life expectancy has given rise to an emerging and unforeseen population of late-stage DMD sufferers well into their twenties. [18]

There is no definite evidence on how the cognitive profile of this population changes over the years, i.e. whether cognitive deficits seen in the younger population remain the same, worsen, or improve, and whether any further cognitive deficits develop. Studies have suggested a cumulative deterioration of academic achievement and social functioning, as the deficits impair development [7] while others present evidence that deficits reduce with age. [5, 19] Moreover, even less is known around the effects of hypoventilation on cognition in advanced DMD and the effects of nocturnal ventilation on cognition.

### **Attitudes and beliefs about sleep**

Smith *et al.* found a high prevalence of insomnia in people with hypoventilation, and also found that these individuals express dysfunctional beliefs about sleep. [20] It has been found that dysfunctional beliefs about sleep, such as ‘there is little one can do about poor sleep’, may underlie and perpetuate anxiety about, and difficulties with sleep in people with sleep problems. [21-23]

In a study of primary insomniacs, Edinger *et al.* found that ‘CBT is effective for reducing dysfunctional beliefs about sleep’ as compared to controls who received treatment as usual. [24]

It is therefore, important to consider whether dysfunctional beliefs about sleep can be observed in the DMD population similar to those found in other populations with sleep difficulties, and if so then DMD sufferers may also benefit from CBT focusing on sleep.

### **Gaps in literature and rationale for study**

As Rahbek *et al.* note ‘knowledge of adult life with DMD is sparse’ (p.17). [18] The cognitive profile of advanced DMD remains speculative based on that of the younger population. Moreover, the effects of hypoventilation on cognition and the extent of their reversibility with ventilation treatment in this population remain unknown. Additionally, the attitudes about sleep held by DMD patients with hypoventilation, who suffer from poor quality and quantity of sleep, are unknown.

### **Research Questions**

1. What is the cognitive profile of advanced DMD (specifically visual/verbal memory and executive functioning)?
2. Do hypoxic episodes result in specific cognitive deficits which are not reversible by NIPPV (specifically visual/verbal memory and executive functioning)?

3. Do QoL, mood (depression and anxiety), daytime sleepiness and beliefs about sleep differ between ventilated and non-ventilated DMD sufferers (and do they improve following ventilation treatment)?

### **Methodology**

Two DMD groups were used; Duchenne Muscular Dystrophy – Ventilated (DMDV) comprised of boys with hypoventilation on NIPPV treatment, and Duchenne Muscular Dystrophy – Control (DMDC) comprised of boys who had not yet developed such difficulties. Both groups underwent neuropsychological testing and completed measures of sleepiness, mood, beliefs about sleep, and QoL.



## **METHOD**

Ethical approval was obtained from the South Humber Ethics Committee before the commencement of the study (Appendix O).

### **Design**

This cross-sectional study investigates differences in cognitive abilities, mood, sleepiness, QoL, and beliefs about sleep of boys with DMD at two time-points of the illness; before hypoventilation (DMDC, N=16) and during treatment for hypoventilation (DMDV, N=17).

### **Participants**

Participants were English native speakers with a diagnosis of DMD, over the age of 16. Due to the limited research in the advanced DMD population, power calculations were conducted on the basis of previous literature with other relatively rare neurodegenerative disorders. Specifically, Newsom-Davis *et al.* (2001) investigated the effects of NIPPV on cognition in people with Amyotrophic Lateral Sclerosis and used nine participants for the experimental group and ten for the control group. [15] Given the cross-sectional design an approximate doubling of those figures was aimed for recruitment.

Participants were identified by their healthcare teams using inclusion/exclusion criteria (Appendix K) during routine procedures or via their medical files. Routine medical practice involves an assessment of DMD patients in relation to signs of hypoventilation every 6 months. Forced lung capacity measurements are taken to determine if NIPPV is needed. Participants in the DMDV group were identified by healthcare staff as those already on NIPPV treatment. Participants in the DMDC group were identified either during their routine assessment or via their notes as patients not anticipated requiring NIPPV in the next 6 months.

Recruitment was carried out from three national centres for neuromuscular disorders, namely; The Newcastle Muscle Centre, the Neurology department at Leeds General Infirmary, and Treloar College in Surrey.

### Measures

Psychometric measures for verbal and visual memory were selected since most deficits reported in DMD literature involve memory skills, as well as tests to measure executive function skills since these have not been previously well studied. The tests and the cognitive areas they target are listed in Table 1 and detailed information can be found in Appendix L.

**Table 1.** Psychometric measures used and the corresponding cognitive areas tested.

Test	Subtest	Cognitive area tested
Adult Memory & Information Processing Battery (AMIPB) [25]	List learning Story recall	Verbal recall (without and with context)
Digit Span (DS)	Researcher-created based on the Wechsler Adult Intelligence Scale-III	Working Memory
Doors and People [26]	Doors test Names test	Visual recognition Verbal recognition
Delis and Kaplan Executive Function System (D-KEFS) [27]	Colour-Word Interference test Sorting test (Recognition) Twenty Questions test	Executive function: Problem solving, cognitive set shifting, attention, categorising, organizing
Ravens Standard Progressive Matrices [28]	-	Logical reasoning and current intellectual functioning

## *Questionnaires*

The Epworth Sleepiness Scale [29] and the Short-Form 36 health survey [30], widely used in hypoventilation literature, were administered. Moreover, the Hospital Anxiety and Depression Scale [31] was selected as an established, standardized measure of mood. Previous studies using the HADS with physically disabled individuals have omitted the item '*I feel as if I have slowed down*' [15] so as to avoid an artificial rise in scores. This was not done in this study as the aim was to consider differences between groups, and not scores relating to the generic measure norms. Finally, the abbreviated version of the Dysfunctional Beliefs and Attitudes about Sleep (DBAS) scale [32] was used as a validated measure of beliefs about sleep.

## **Procedure**

Candidates identified by the healthcare team were given the information sheet and consent form (Appendices M & N) and were asked to consent for their contact number to be provided to the researcher. The researcher then contacted the participants by phone to discuss the research in detail and formal consent was obtained.

An appointment was arranged and all the questionnaires were sent out by post to be completed prior to the appointment. The psychometric measures were administered during the appointment over an average of one hour and thirty minutes.

All the participants were seen at their residence due to the complexities of transportation.

*Hypotheses*(a) There will be no significant differences between the DMDV and DMDC groups on measures of sleepiness, mood, beliefs about sleep, or QoL.

(b) There will be no differences in general intellectual ability between the two groups.

(c) The DMDV group will perform worse on measures of executive function and memory than the DMDC group due to irreversible cognitive deficits caused by hypoxic episodes prior to NIPPV commencement.

## RESULTS

### *Participants*

All patients meeting the inclusion criteria were invited to take part in the study. Sixteen participants consented from Leeds, eleven from Newcastle, and six from Treloar College. Table 2 shows the groups' main characteristics. Comparisons between groups on demographic variables using Pearson Chi-squared tests (and Mann-Whitney for the age variable) revealed that the DMDV group was significantly older and had higher education, with most participants stating 'unemployed', whereas in the DMDC group most participants were still in education.

**Table 2.** Demographic information and comparisons of DMDC and DMDV groups

<b>Demographic variable</b>	<b>DMDC (N=16)</b>	<b>DMDV (N=17)</b>	<b>Statistical differences (<i>p</i> value)</b>
<i>Age</i>	18.81 (2.74)	22.24 (4.01)	.01*
<i>Education (highest level completed)</i>			.012*
Primary school	0	1	
Secondary School	13	6	
College	3	5	
University	0	5	
<i>Living arrangements</i>			
Living with 2 parents	13	12	} .840
Living with 1 parent	2	2	
Living alone	1	3	
Living with 1 sibling	7	3	} .198
Living with >1 sibling	2	6	
Not living with siblings	7	8	
<i>Occupation</i>			.011*
Employed	0	1	
Unemployed	3	10	
In education	13	5	
Other	0	1	

Age is reported as mean (standard deviation). Remaining variables are reported as frequencies.

\*  $p < 0.05$

## Analyses

### Questionnaires

Table 3 gives a summary of the mean (standard deviation) on each questionnaire administered for each group, and the  $p$  value of statistical differences between groups. No significant differences were found. ESS approached significance in the expected direction of DMDC scoring higher.

**Table 3.** Mean (SD) score and statistical significance of differences between the DMDC and DMDV groups on ESS, DBAS, HADS, and SF-36.

Questionnaire	DMDC (N=16)	DMDV (N=17)	Statistical differences ( $p$ value)
ESS	3.38 (.87)	1.82 (.58)	.072
DBAS	3.45 (.40)	3.40 (.41)	.866
HADS – Depression	5.00 (.65)	3.71 (.47)	.139
HADS – Anxiety	3.06 (.39)	2.76 (.53)	.462
<i>SF-36</i>			
Physical functioning	16.63 (3.73)	15.44 (.70)	.488
Role of physical functioning	51.38 (6.70)	47.92 (10.07)	.402
Bodily pain	54.32 (5.47)	52.90 (8.26)	.557
General health	44.48 (6.38)	41.31 (9.08)	.557
Vitality	56.15 (6.81)	55.18 (9.32)	.901
Social functioning	51.37 (7.54)	51.71 (8.58)	.845
Role of emotional functioning	50.73 (8.57)	52.24 (8.94)	.581
Mental health	50.44 (7.64)	50.18 (10.22)	.736
Physical Component Score	36.26 (3.21)	33.03 (5.70)	.127
Mental Component Score	59.52 (7.26)	60.80 (9.16)	.444

\*  $p < 0.05$

### Psychometric tests

One participant from the control group did not complete the psychometric testing, while another completed only the digit span and Doors and People tests.

All the psychometric measures were compared between groups using exact Mann-Whitney tests. Effect sizes, if present, were not expected to be large given the small sample sizes, therefore no correction for multiple statistical tests was applied.

Table 4 shows the mean (standard deviation) of each group on each measure and the *p* values obtained. No significant differences were found between the control and experimental group in any of the tests.

**Table 4.** Mean (SD) and significance of differences between the DMDC and DMDV groups on the psychometric measures.

<b>Measure</b>	<b>DMDC (N=14)</b>	<b>DMDV (N=17)</b>	<b>Statistical differences (<i>p</i> value)</b>
<i>Ravens Standard Progressive Matrices</i>	38.07 (9.24)	38.18 (7.22)	.953
<i>Digit Span</i>	7.93 (1.44) <sup>a</sup>	9 (2.60)	.455
<i>Doors and People</i>			
Doors test	16.93 (3.45) <sup>a</sup>	15.82 (3.73)	.502
Names test	19.73 (2.52) <sup>a</sup>	21.18 (1.51)	.114
<i>AMIPB</i>			
List Learning			
<i>List A1-A5</i>	45.93 (7.04)	46.06 (10.61)	.953
<i>List A6</i>	9.43 (3.78)	10.71 (2.89)	.468
Story Recall			
<i>Immediate Recall</i>	22.00 (12.61)	20.18 (8.89)	.769
<i>Delayed Recall</i>	19.36 (12.21)	17.59 (9.29)	.830
<i>D-KEFS</i>			
Colour-Word Interference			
<i>Condition 1</i>	39.36 (8.57)	39.47 (8.75)	.468
<i>Condition 2</i>	28.29 (7.47)	27.71 (4.41)	1.00
<i>Condition 3</i>	71.43 (21.11)	76.18 (31.25)	.769
<i>Condition 4</i>	74.43 (23.91)	76.76 (21.37)	.653
Sorting (Recognition)	21.93 (10.77)	22.35 (10.61)	.860
Twenty Questions			
<i>Initial Abstraction</i>	28.79 (4.84)	26.81 (9.48)	.951
<i>No. of questions</i>	27.07 (7.36)	30.71 (12.16)	.681
<i>Weighted Achievement</i>	15.36 (3.63)	14.18 (3.50)	.597

\* *p* < 0.05

<sup>a</sup> N=15 for DMDC group

### Overall sample performance

An investigation of each group's performance in relation to the measure cut-off points for deficits (i.e. how many participants in each group scored below the 2% cut-off for impairment on the measure based upon data from the normative sample) was carried out to determine how many subjects scored at the cut-off, providing thus a generic cognitive profile for this population (Table 5). The results suggest that both groups had relatively high numbers scoring on or below cut-off. Moreover, the number of subjects below cut-off seems to be higher overall in the DMDV group, particularly on List Learning (A1-A5), Story Recall, and Conditions 1 and 3 of the Colour-Word Interference test. Nevertheless, the mean scores for each test obtained by each group were all above the clinical cut-offs, with the exception of the Ravens matrices where both groups scored below the 5<sup>th</sup> percentile.

**Table 5.** Number of participants in DMDC (N=14) and DMDV (N=17) groups that are on or below the cut-off scores for each measure used.

Measure	Number in DMDC on or below cut-off (N=14)	Number in DMDV on or below cut-off (N=17)
<b>Digit Span</b>	10*	10
<b>Doors &amp; People</b>		
Doors Test	2*	5
Names Test	1*	0
<b>AMIPB</b>		
List Learning (A1-A5)	3	7
List Learning (A6)	3	5
Story Recall (Immediate)	4	7
Story Recall (Delayed)	5	7
<b>DKEFS</b>		
Colour-Word Interference		
<i>Condition 1</i>	5	8
<i>Condition 2</i>	3	6
<i>Condition 3</i>	7	8
<i>Condition 4</i>	5	5
Sorting		
<i>Card Sets 1 &amp; 2</i>	2	4



<i>Card Sets 3 &amp; 4</i>	1	4
Twenty Questions		
<i>Initial Abstraction Score</i>	0	0
<i>Total no. of questions asked</i>	1	3
<i>Weighted Achievement Score</i>	2	1

\* N=15

The data from each group was combined (N=34) given the absence of significant differences on measures between the groups to further explore a likely cognitive profile for advanced DMD.

A paired-samples *t*-test was used to compare the group's performance on visual and verbal recognition memory (Doors Vs Names test). The difference was statistically significant ( $t = -5.25, p < .000$ ), indicating a higher performance in verbal rather than visual memory.

Scores were converted to percentages and comparisons were also made between recall conditions (AMIPB) and digit span. No notable differences between immediate and delayed recall (Story Recall) were found. However, performance on digit span and List Learning were higher than in Story Recall.

## **DISCUSSION**

This study aimed to provide a cognitive profile of advanced DMD and identify any permanent cognitive deficits following hypoventilation in individuals receiving NIPPV treatment. The subjects recruited were considerably older as compared to most studies of DMD investigating cognitive abilities. [2, 3, 6-8, 10] Previous studies typically involved DMD subjects aged between 6-16 years old, whereas the current study involved subjects aged 16 years and over. Measures of memory, executive function, and overall intellectual ability were taken, along with measures of sleepiness, beliefs about sleep, mood, and QoL.

The results of the study indicate no permanent cognitive deficits resulting from hypoventilation, since no differences were found on any of the measures between the ventilated and the control group. This is contrary to literature warning that lack of dystrophin leaves hippocampal and cerebellar neuronal populations vulnerable to hypoxic damage. [12, 13]

However, it remains a possibility that during hypoventilation cognitive deficits do develop and are later reversed by NIPPV treatment, as has been found in other conditions. [14, 15]

### **Demographics and Questionnaires**

Despite some variability in family composition ranging from single parents to couples and living independently, and from no siblings, to one or more siblings, it appears that most DMD boys in the advanced stages live with two parents, as there were no differences between the groups. This suggests that family units are maintained even during this difficult stage, contrary to literature on family breakdown in other childhood terminal illnesses. [33]

The only questionnaire approaching significance was the ESS, where controls tended to score higher than ventilated boys. This is to be expected as the ventilated group are receiving

treatment that has been shown to reduce sleeplessness in other conditions and the controls are possibly beginning to move towards hypoventilation.

Despite possible issues with using the HADS in a population with physical disabilities [15] both groups scored well below the measure's cut-off for depression and anxiety.

DMD boys seem not to hold dysfunctional beliefs about sleep, contrary to the literature that suggests sleeplessness is a central issue in the illness journey. [20-22] Moreover, in line with other literature QoL seems not be affected by the use of NIPPV since the groups reported comparable QoL on the SF-36. [34] This is further supported by the comparable, and indeed low scores in anxiety and depression.

### **Psychometrics**

The literature on cognitive abilities and DMD has largely focussed on people under 16 years old. It is thus unknown whether these individuals maintain the abilities outlined by the literature throughout their life, or if these change. Evidence around this issue is mixed, with some suggesting a further deterioration [7], while others point to an improvement in deficits. [5, 19]

The data was considered in relation to clinical cut-off scores for each measure. Notably the experimental group showed a higher number of participants below cut-off for most of the measures, but both groups' means were above clinical cut-offs. The Ravens matrices was used as a measure of general intellectual ability and although this is a validated alternative to IQ tests it must be used with caution. The sample scored below clinical cut-off on this test. This result was taken as possibly indicative of a specific developed deficit in visuospatial ability, as opposed to a deficit in intellectual ability, since the sample's performance on all the other tests was above clinical cut-off.

Given the absence of significant differences between the groups, the data was merged to create a larger sample of advanced DMD patients from which a preliminary cognitive profile could be drawn. Performance between different measures was considered, indicating that verbal recognition was stronger than visual recognition. This was a surprising result given the extensive literature supporting verbal memory deficits. [2, 3, 6, 8]

However, when considering verbal recall it appears that the participants scored higher on list learning than story recall, which is in support of literature positing a specific verbal deficit affecting verbal capacity span in DMD children. [6] It is possible the story ‘overloaded’ the auditory processing capabilities of the participants’ ‘phonologic loop’, contrary to the less complex and repeated exposure of the list learning. [9] Performance on Story Recall also seemed poorer to digit span performance, indicating perhaps a slower processing speed of the story information than of the numbers, possibly due to a limited phonologic loop capacity. Nevertheless, design limitations in this study require that these observations are explored further in studies with larger samples to determine the effect sizes of any replicated results.

### **Limitations and future research**

The study applied a cross-sectional design which limits the conclusions that can be drawn on the basis of causality. Furthermore, sample sizes for the two groups were relatively small, limiting thus the statistical analyses possible as well as the power of the study. These limitations are typical of studies in DMD and call for larger longitudinal studies. [35]

Moreover, demographic comparisons revealed significant differences between the groups on age, education, and occupation. Although all the subjects were over the age of 16, the control group was significantly younger, and thus still in education. However, an older ventilated group is reasonable since hypoventilation becomes more likely with age, and although differences in age may influence cognitive performance the measures used either

encompassed the whole age range within the same group for scaled scores, or the scaled scores were identical or overlapping between age groups.

Future studies should further investigate the abilities tested by the Ravens matrices in older DMD populations to determine why the sample scored selectively low on this test in relation to the other measures and investigate the possibility of a developing specific deficit.

A more informative study could involve larger samples of controls and boys who are about to start on NIPPV, tested on cognitive functioning and retested following a period of NIPPV treatment in the experimental group (and treatment as usual for the control group). Such a design would address the question of not only whether cognitive abilities decline during hypoventilation, but also how far those deficits are reversible by NIPPV. This will in turn provide further evidence on the role of dystrophin in the brain, but more importantly will allow services to proactively support families in how to incorporate the presence of cognitive deficits in the care they provide (during or after hypoventilation).

## **Conclusions**

This study suggests that hypoventilation during advanced DMD does not result in any permanent cognitive deficits. This may be attributed to well-designed services that monitor and efficiently respond to the changing needs of DMD patients, establishing NIPPV treatment soon after hypoventilation develops, thereby limiting the occurrence of hypoxic episodes.

However, the possibility of reversible cognitive deficits during hypoventilation remains an open question which needs to be addressed by further investigation. Hypoventilation is a very difficult transitional stage in the illness trajectory for both patients and carers, as it signifies a marked deterioration in health and significant changes in illness management. Therefore, any

behavioural and emotional changes attributable to cognitive decline need to be identified to enable an optimal management of this phase by everyone involved.

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## **Appendix A**

### **Reflective Statement**

Embarking on a research journey has been an enriching experience throughout, from the initial stages of planning the research and deciding on how to answer the research questions, to organising logistical and practical aspects prior to recruitment such as getting forms, engaging services, and going through ethical approval, through to carrying out the testing and working through the data, until finally write-up and contemplating on the implications of the work I produced.

*From theory to practice: letting go of 'the dream'*

Designing a well-thought out study can be difficult, but it is only when you achieve this that the real challenge is revealed. Materialising a study design is always dictated by the resources available to you. I was faced with this reality at all the different stages of my research journey, and I soon had to become more realistic about numbers (recruitment), resources (time, money, people, motivation), and subsequently the aims of my study.

Resource limitations are too many to outline, however time is primarily significant particularly with regards to initiating and completing the recruitment phase. I felt I was in a constant race against time to coordinate all my recruitment centres, complete the logistical aspects and motivate the staff I relied upon to recruit my participants, and throughout the recruitment stage to maintain that motivation and push for as many participants as possible in order to meet my planned numbers. As I watched time run out I was forced to make difficult decisions regarding my design, which I then needed to push forward with all the recruitment centres, even adding another centre to meet the demands of my new plan.

Another major resource constraint was the budget. The available money dictated and forced changes to my study design, for instance on how far and often I could travel to participants,

but particularly around the psychometric tests I was able to choose when planning the study. The challenge was to minimise spending while also minimising limitations to the research design by ensuring the chosen tests were adequate to answer the research questions.

While my design adapted to the available resources, be it time or money, stress was building up at the thought of my ‘flawed study’, until I was able to reflect on a philosophical view of research: i.e. is there a perfect study? I remembered that in any study there are always areas for improvement, and someone will always be able to come up with a better plan or idea, however, the bottom line is one can only always work within the limits of their resources and abilities. When I felt satisfied with my philosophical exploration I was able to see beyond the limitations of the study and acknowledge the importance of what I was exploring as something no one had looked at before (irrespective of how ‘un-perfect’ my way of looking at it was).

#### *Measure selection*

Selecting measures did not simply involve considering what the research questions were and how to answer them. Beyond the money measures would cost I also had to consider my population and the abilities, limitations, and confounders that may arise with a DMD population. And although sharing thoughts, ideas, and plans with colleagues was invaluable in guiding my decisions, I discovered that everyone has an opinion! Sometimes, too many heads put together can lead to chaos while clarity can be found in isolation.

#### *Collaborators*

From the start it was clear that finding the right people to engage would be crucial to recruitment and subsequently the entire project. However, it soon became apparent that finding the people was only the first step. Beyond keeping everyone up to date with constant changes and ensuring they are clear about their role, there were challenges in getting every

site ready in time. More crucially, I found myself constantly having to remind and motivate collaborators to keep the project in mind and help me recruit throughout. Having to relinquish so much control was difficult and stressful to say the least. I literally depended and relied upon them for recruitment and the future of the whole project.

### *Becoming a chameleon*

A constant demand throughout testing was flexibility and adaptability, not just in terms of managing travelling time and cost and trying to organise appointments in as much an efficient manner as possible, but also during the testing session itself. Due to the varying physical limitations which go hand in hand with DMD participants who can be at different levels of agility and mobility, I was faced with a range of testing conditions. Some boys were able to sit upright in wheelchairs (with some having an adequate attached table for laying out testing material, and others not having a table at all), while others were lying in bed. Being creative in order to carry tests through while maintaining standardised testing procedures was a challenge.

To add to this challenge the concerned or simply curious parents sometimes joined in the session, pending the participant's permission, and I found myself having to maintain a humanistic approach to their comments in-between tests while maintaining objectivity and standardisation at the same time. Moreover, other challenges of testing people at home included noise and disruptions from people coming in and out of the house or even the room.

### *What have I learnt then?*

The experiences throughout this journey have been challenging but ultimately rewarding as they were overcome and I crossed the finish line. I have learnt valuable lessons which will undoubtedly serve me in the future.

A key conclusion is that planning and organisation must be at the heart of any research endeavour. However, one must also keep in mind that things almost never go exactly as planned no matter how well organised you are. It is thus important not to just plan but to also have back-up plans and be prepared to adapt to changing circumstances. Change seems to be inevitable as too many factors are at play when conducting research that are out of one's control, including collaborating with people perhaps less motivated to carry the project through.

In terms of research within the field of Muscular Dystrophy (MD), it has become clear that longitudinal (and other) research is needed to explore new areas which have opened up following progressions in the medical field. However, research with such rare populations (even within a DMD population which is the most common of all MD) requires a long recruitment period to get satisfactory numbers. Time is of the essence, and even though I knew and tried to account for this in my research I was still over-optimistic and underestimated how my inclusion/exclusion criteria would narrow even further the small recruitment pool I had. Nevertheless, the hurdles I faced have not discouraged me from conducting research in this area, instead the challenges have only made me feel more passionate about promoting research in this field.

My experience of conducting a research project was coloured by good and bad moments and has left me with an overall drive to do more and do it better in the future.

## Appendix B

### Author Guidelines for the British Journal of Health Psychology

#### Notes for Contributors

The aim of the **British Journal of Health Psychology** is to provide a forum for high quality research relating to health and illness. The scope of the journal includes all areas of health psychology across the life span, ranging from experimental and clinical research on aetiology and the management of acute and chronic illness, responses to ill-health, screening and medical procedures, to research on health behaviour and psychological aspects of prevention. Research carried out at the individual, group and community levels is welcome, and submissions concerning clinical applications and interventions are particularly encouraged.

The types of paper invited are:

- papers reporting original empirical investigations;
- theoretical papers which may be analyses or commentaries on established theories in health psychology, or presentations of theoretical innovations;
- **review papers, which should aim to provide systematic overviews, evaluations and interpretations of research in a given field of health psychology; and**
- methodological papers dealing with methodological issues of particular relevance to health psychology.

#### 1. Circulation

The circulation of the Journal is worldwide. Papers are invited and encouraged from authors throughout the world.

#### 2. Length

Papers should normally be no more than 5000 words (excluding the abstract, reference list, tables and figures), although the Editor retains discretion to publish papers beyond this length in cases where the clear and concise expression of the scientific content requires greater length.

#### 3. Editorial policy

The Journal receives a large volume of papers to review each year, and in order to make the process as efficient as possible for authors and editors alike, all papers are initially examined by the Editors to ascertain whether the article is suitable for full peer review. In order to qualify for full review, papers must meet the following criteria:

- the content of the paper falls within the scope of the Journal
- the methods and/or sample size are appropriate for the questions being addressed
- research with student populations is appropriately justified
- the word count is within the stated limit for the Journal (i.e. 5000 words)

#### 4. Submission and reviewing

All manuscripts must be submitted via our online peer review system. The Journal operates a policy of anonymous peer review. **Authors must suggest three reviewers when submitting their manuscript, who may or may not be approached by the Associate Editor dealing with the paper.**

#### 5. Manuscript requirement

- Contributions must be typed in double spacing with wide margins. All sheets must be numbered.
- Tables should be typed in double spacing, each on a separate page with a self-explanatory title. Tables should be comprehensible without reference to the text. They should be placed at the end of the manuscript with their approximate locations indicated in the text.
- Figures can be included at the end of the document or attached as separate files, carefully labelled in initial capital/lower case lettering with symbols in a form consistent with text use. Unnecessary background patterns, lines and shading should be avoided. Captions should be listed on a separate sheet. The resolution of digital images must be at least 300 dpi.
- For articles containing original scientific research, a structured abstract of up to 250 words should be included with the headings: Objectives, Design, Methods, Results, Conclusions. Review articles should use these headings: Purpose, Methods, Results, Conclusions. Please see the document below for further details:

 British Journal of Health Psychology - Structured Abstracts Information


- For reference citations, please use APA style. Particular care should be taken to ensure that references are accurate and complete. Give all journal titles in full.
- SI units must be used for all measurements, rounded off to practical values if appropriate, with the imperial equivalent in parentheses.
- In normal circumstances, effect size should be incorporated.
- Authors are requested to avoid the use of sexist language.
- Authors are responsible for acquiring written permission to publish lengthy quotations, illustrations, etc. for which they do not own copyright.

For guidelines on editorial style, please consult the APA Publication Manual published by the American Psychological Association.

#### 6. Publication ethics

All submissions should follow the ethical submission guidelines outlined in the documents below:

 Ethical Publishing Principles – A Guideline for Authors

 Code of Ethics and Conduct (2006)



## **7. Supplementary data**

Supplementary data too extensive for publication may be deposited with the British Library Document Supply Centre. Such material includes numerical data, computer programs, fuller details of case studies and experimental techniques. The material should be submitted to the Editor together with the article, for simultaneous refereeing.

## **8. Copyright**

On acceptance of a paper submitted to a journal, authors will be requested to sign an appropriate assignment of copyright form. To find out more, please see our Copyright Information for Authors.

## Appendix C

### Author Guidelines for Journal of Neurology, Neurosurgery, and Psychiatry

#### Papers

Full papers must present important and substantial new material. Articles should be of direct relevance to clinical practise. Thus we do not generally publish research based on animal experiments nor studies of normal nervous system function.

Word count: 3500 words maximum.

Abstract: 250 words.

Tables/Illustrations: should not normally exceed 8.

References: 40.

#### Manuscript format (BMJ Group)

**All manuscripts must be submitted via Bench>Press.**

All material submitted is assumed to be submitted exclusively to the journal unless the contrary is stated. Submissions may be returned to the author for amendment if presented in the incorrect format.

If you are submitting a randomised controlled trial, please send with your manuscript the following:

The registration number of the trial and the name of the trial registry - in the last line of the paper's structured abstract. Trials that begin enrolment of patients after 1 July 2005 must register in a public trials registry at or before the onset of enrolment to be considered for publication. Trials that began patient enrolment on or before 1 July 2005 must register before 13 September 2005 to be considered for publication. Please see the Statement from the International Committee of Medical Journal Editors.

#### Cover letter

Your cover letter should inform the Editor of any special considerations regarding your submission, including but not limited to:

1. Details of related papers published or submitted for publication.
  - Copies of related papers should be submitted as supplementary data to help the Editor decide how to handle the matter.
2. Details of previous reviews of the submitted article.
  - The previous Editor's and reviewers' comments should be submitted as supplementary data along with your responses to those comments. Editors encourage authors to submit these previous communications and doing so may expedite the review process.

Whether any of the material could be published as data supplements rather than in the print version of the article.

## Title page

The title page **must** contain the following information:

1. The title.
2. The name, postal address, e-mail, telephone and fax numbers of the corresponding author.
3. The full names, institutions, city and country of all co-authors.
4. Up to five keywords or phrases suitable for use in an index (it is recommended to use MeSH terms).
5. Word count - excluding title page, abstract, references, figures and tables.

## Manuscript format

The manuscript format must be presented in the following order:

1. Title page
2. Abstract (or summary for case reports)
3. Main text (tables should be in the same format as your article and embedded into the document where the table should be cited; images must be uploaded as separate files)
4. Acknowledgments, Competing interests, Funding
5. Copyright licence statement
6. References
7. Appendices

Do not use the automatic formatting features of your word processor such as endnotes, footnotes, headers, footers, boxes etc.

Provide appropriate headings and subheadings as in the journal. We use the following hierarchy: **BOLD CAPS**, **bold lower case**, Plain Text, *Italics*.

Cite illustrations in numerical order (fig 1, fig 2 etc) as they are first mentioned in the text.

Tables should be in the same format as your article and embedded into the document where the table should be cited.

Images **must not** be embedded in the text file but submitted as individual files (view further details in File Formats.)

## File naming convention

Where possible, please name your manuscript and image files as shown below. (Please note: the manuscript ID # appears at the top of each submission page as soon as you start your submission; author refers to the corresponding author's last name.)

1. Your manuscript file should be named as: **yr\_manuscript id number\_author**  
(for example: 2005\_001234\_clark)
2. Your image file should be named as: **yr\_manuscript id number\_F#**  
(for example: 2005\_001234\_F1)

## Statistics

Statistical analyses must explain the methods used.

## Style

Abbreviations and symbols must be standard and SI units used throughout except for blood pressure values which are reported in mm Hg.

Whenever possible, drugs should be given their approved generic name. Where a proprietary (brand) name is used, it should begin with a capital letter.

Acronyms should be used sparingly and fully explained when first used.

## Figures/illustrations

**Black and white** images should be saved and supplied as **GIF, TIFF, EPS or JPEG** files, at a **minimum resolution of 300 dpi** and an image size of 9 cm across for single column format and 18.5 cm for double column format.

**Colour** images should be saved and supplied as **GIF, TIFF, EPS or JPEG** files, to a **minimum resolution of 600 dpi** at an image size of 9 cm across for single column format and 18.5 cm for double column format.

Images should be mentioned in the text and figure legends should be listed at the end of the manuscript.

During submission, when you upload the figure files please label them as Figure 1, Figure 2, etc. The file label will not appear in the pdf but the order in which the figures uploaded should be sufficient to link them to the correct figure legend for identification.

We can accept multi-page Powerpoint files. Alternatively, Powerpoint files can be saved as JPEG files and submitted as a standard image file.

Histograms should be presented in a simple, two-dimensional format, with no background grid.

**Please note:** Do not submit colour figures unless you are willing to pay the cost of publishing your figures in colour. If you do not wish to pay the colour charges please submit your figures in black and white.

The journal charges authors for the cost of reproducing colour images on all unsolicited articles. This charge is heavily subsidised by the journal and covers origination costs only. If an image is supplied as a **composite figure** that contains numerous parts (for example, fig 1A-D), the image will be considered as a single image, provided that all the parts are supplied within a single file that prints out at an overall size no larger than A4 (210 mm x 297 mm).

The charge for **colour** processing will be **£100 + VAT** for the figure. Multi-part colour images supplied as **separate files will be charged at £100 + VAT for each file**. The charge only applies to images accepted for print publication and not online only or data supplement

files.

Care should be taken in planning composites because combining different images with widely varying colours can lead to contamination or loss of colour and poor quality results. When submitting your manuscript, please ensure to include a name and address where the invoice should be sent for the colour reproduction costs. If an address is not included, the invoice will be sent to the corresponding author.

### **Unacceptable file formats**

Any file using OLE (Object Linking and Embedding) technology to display information or embed files, Bitmap (.bmp), PICT (.pict), Photoshop (.psd), Canvas (.cnv), CoreIDRAW (.cdr); Excel (.xls); and locked or encrypted PDFs are not acceptable.

### **Tables**

Tables should be submitted in the same format as your article and embedded into the document where the table should be cited. Please note: Bench>Press **cannot** accept Excel files. If your table(s) are in Excel, copy and paste them into the manuscript file. In extreme circumstances, Excel files can be uploaded as supplementary files; however, we advise against this as they will not be acceptable if your article is accepted for publication.

Tables should be self-explanatory and the data they contain must not be duplicated in the text or figures.

### **References**

Authors are responsible for the accuracy of references cited: these should be checked against the original documents before the paper is submitted. It is vital that the references are styled correctly so that they may be hyperlinked.

#### **In the text**

References must be numbered sequentially as they appear in the text. References cited in figures or tables (or in their legends and footnotes) should be numbered according to the place in the text where that table or figure is first cited. Reference numbers in the text must be given in square brackets immediately after punctuation (with no word spacing) - for example, [6] not [6].

Where more than one reference is cited, separate by a comma - for example, [1, 4, 39]. For sequences of consecutive numbers, give the first and last number of the sequence separated by a hyphen - for example, [22-25]. References provided in this format are translated during the production process to superscript type, which act as hyperlinks from the text to the quoted references in electronic forms of the article.

#### **In the reference list**

References must be double spaced (numbered consecutively in the order in which they are mentioned in the text) in the [slightly modified] Vancouver style. Only papers published or in press should be included in the reference list. (Personal communications or unpublished data must be cited in parentheses in the text with the name(s) of the source(s) and the year. Authors should get permission from the source to cite unpublished data.)

**Punctuation of references must follow the [slightly modified] Vancouver style:**

12 Surname AB, Surname CD. Article title. Journal abbreviation. Year;Vol:Start page-End page.

Use one space only between words up to the year and then no spaces. The journal title should be in italic and abbreviated according to the style of Medline. If the journal is not listed in Medline then it should be written out in full.

List the names and initials of all authors if there are 3 or fewer; otherwise list the first 3 and add et al.

Example references:

### **Journal**

13 Koziol-Mclain J, Brand D, Morgan D, et al. Measuring injury risk factors: question reliability in a statewide sample. *Inj Prev* 2000;6:148-50.

### **Chapter in book**

14 Nagin D. General deterrence: a review of the empirical evidence. In: Blumstein A, Cohen J, Nagin D, eds. *Deterrence and incapacitation: estimating the effects of criminal sanctions on crime rates*. Washington, DC: National Academy of Sciences 1978:95-139.

### **Book**

(personal author or authors) (all book references should have specific page numbers)

15 Howland J. Social norms and drunk driving countermeasures. In Graham JD, ed. *Preventing automobile injury: new findings from evaluative research*. Dover, MA: Auburn House Publishing Company 1988:163-96.

### **Abstract/supplement**

16 Roxburgh J, Cooke RA, Deverall P, et al. Haemodynamic function of the carbomedics bileaflet prosthesis [abstract]. *Br Heart J* 1995;73 (suppl 2):P37.

### **Electronic citations**

Basically, websites are referenced with their URL and access date, and as much other information is given as is available. Access date is important as websites can be updated and URLs change. The "date accessed" can be later than the acceptance date of the paper, and it can be just the month accessed. See the 9th edition of the AMA Manual of Style for further examples.

electronic journal articles:

Morse SS. Factors in the emergency of infectious diseases. *Emerg Infect Dis* 1995 Jan-Mar;1(1). [www.cdc.gov/nciod/EID/vol1no1/morse.htm](http://www.cdc.gov/nciod/EID/vol1no1/morse.htm) (accessed 5 Jun 1998).

Use as much information as the author gives. The volume/number information in the URL will take the user to the start of the individual document; ask the author to supply or confirm. Also ask authors to supply the date they accessed the file.

### **Online First**

Each Online First article has a unique Digital Object Identifier (DOI). This should be included in all citations.

**BEFORE** the article has appeared in an issue

Use the citation format:

Sabin MA, Ford AL, Holly JMP, Hunt LP, Crowne EC, Shield JPH. Characterisation of morbidity in a UK, hospital based, obesity clinic. Arch Dis Child. Published Online First: 24 October 2005. doi:10.1136/adc.2005.083485

**AFTER** the article has appeared in an issue

Use the citation format:

Sabin MA, Ford AL, Holly JMP, Hunt LP, Crowne EC, Shield JPH. Characterisation of morbidity in a UK, hospital based, obesity clinic. Arch Dis Child 2006; 91:126-130 doi:10.1136/adc.2005.083485 [published Online First: 24 October 2005].

### **Electronic Letters**

Author. Title of letter. Journal name Online [eLetter] Date of publication. url

eg: Krishnamoorthy KM, Dash PK. Novel approach to transseptal puncture. Heart Online [eLetter] 18 September 2001. <http://heart.bmj.com/cgi/eletters/86/5/e11#EL1>

### **Digital Object Identifiers (DOIs)**

DOIs are a unique string created to identify a piece of intellectual property in an online environment, particularly useful for articles which have been published online before appearing in print (therefore the article has not yet been assigned the traditional volume, issue and page number reference).

The DOI is a permanent identifier of all versions of an article, whether raw manuscript or edited proof, online or in print. Thus the DOI should ideally be included in the citation even if you want to cite a print version of an article.

### **How to cite articles before they have appeared in print**

To cite an electronic article that has not yet appeared in print please use the following citation format:

1. Alwick K, Vronken M, de Mos T, et al. Cardiac risk factors: prospective cohort study. Ann Rheum Dis. Published Online First: 5 February 2004. doi:10.1136/ard.2003.001234

### **How to cite articles once they have appeared in print**

Once the article has been printed the citation should also include the traditional year, volume and page numbers, as well as the DOI and original date of publication.

1. Vole P, Smith H, Brown N, et al. Treatments for malaria: randomised controlled trial. Ann Rheum Dis 2003;327:765-8 doi:10.1136/ard.2003.001234 [published Online First: 5 February 2004].

**PLEASE NOTE: RESPONSIBILITY FOR THE ACCURACY AND COMPLETENESS OF REFERENCES RESTS ENTIRELY WITH THE AUTHORS.**

### **Supplementary files**

You may submit supplementary material which may support the submission and review of your article. This could include papers in press elsewhere, published articles, appendices, video clips, etc.

**Online only material**

Additional figures and tables, methodology, references, video clips, raw data, etc may be published online only to supplement the printed article. If your paper exceeds the word count you should consider if any of the article could be published online only as a "data supplement". These files will not be copyedited or typeset.

**Bench>Press**

All supplementary data files should be uploaded to Bench>Press using the supplementary file section. These files are not converted to PDF but will be provided to reviewers and editors in the format in which you supply them.



## **Appendix D**

### **Search Strategy in PsychINFO for 'carer' term**

DE "Caregiver Burden" or DE "Caregivers"

caregiv\* OR carer\* OR "care giv\*"

caretaker\* OR "care tak\*" OR children N2 caring OR families N2 caring

sons N2 care

sons N2 caring

daughters N2 care

daughters N2 caring

friends N2 care

friends N2 caring

grandparen\* N2 care

grandparen\* N2 caring

grandparen\* N2 support

grandparen\* N2 supporting

grandchil\* N2 support

grandchil\* N2 supporting

neighbor\* N2 care

neighbor\* N2 caring

neighbor\* N2 support

neighbor\* N2 supporting

neighbour\* N2 care

neighbour\* N2 caring

neighbour\* N2 support

neighbour\* N2 supporting

relatives N2 care

relatives N2 caring

relatives N2 support

relatives N2 supporting

parent N2 caring

parents N2 caring

mother N2 caring

mothers N2 caring

father N2 caring

fathers N2 caring

families N2 support\*

TX (S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14  
or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27  
or S28 or S29 or S30 or S31 or S32 or S33 or S34)

## **Appendix E**

### **Search Strategy in PsychINFO for ‘muscular dystrophy’ term**

TX muscular dystroph\*

TX “neuromuscular conditions”

TX “neuromuscular condition”

TX neuromuscular

TX "neuromuscular disorders"

TX "neuromuscular disorder"

TX muscle N3 disease

S37 or S38 or S39 or S40 or S41 or S42 or S43

S36 and S44 [combined ‘carer’ combination and ‘MD’ combination]

## **Appendix F**

### **Search Strategy in PsychINFO for 'psychological distress' term**

distress

stress

pressure

emotion\* N2 pressure

psychol\* N2 pressure

worry

strain

psychol\* N2 strain

emotion\* N2 strain

difficult\*

psychol\* N2 difficult\*

emotion\* N2 difficult\*

burden

psychol\* N2 burden

emotion\* N2 burden

mood

anxiety

anxiousness

depress\*

psychol\* N2 stress

psychol\* N2 distress

psychol\* N2 tension

emotion\* N2 stress

emotion\* N2 distress

emotion\* N2 tension

coping

psychol\* N2 coping

emotion\* N2 coping

angst

psychol\* N2 angst

emotion\* N2 angst

anguish

psychol\* N2 anguish

emotion\* N2 anguish

psychol\* N2 reactions

emotion\* N2 reactions

psychol\* N2 responses

emotion\* N2 responses

## **Appendix G – Standardized Data Extraction Sheet**

Study title

Authors

Year of publication

Journal title and reference

Study Design

Type of data (Qualitative/Quantitative)

Quality Score

Number of participants

Gender ratio (male:female)

Participant diagnoses

Age of participants (mean, standard deviation, range)

Number of carers interviewed per participant

Total number of carers interviewed

Does carer live with the participant (Y/N)

Carer's relationship with the participant

Age of carers (mean, standard deviation, range)

Details of data collected (what was measured, interview schedules, which questionnaires)

Duration of study

Number of times data collected

Summary of Method

Theoretical perspective

Participant recruitment

Procedure

Analyses

Statistical tests

Software used

Summary of Results (main findings and statistical significance)

Summary of discussion/conclusions

    Main findings

    Interpretation of findings – links to literature

    Implications of findings

    Study limitations

Where/How paper was obtained

Notes

## Appendix H

### Quality Assurance Checklist: Qualitative studies

(Based on the NICE Guidelines (2009) for assessing qualitative research quality)

Criteria	Score		
	2	1	0
<i>Section 1: theoretical approach</i>			
Is a qualitative approach appropriate?	Appropriate	Not optimally appropriate	Inappropriate
Is the study clear in what it seeks to do?	Clear	Mixed	Unclear
<i>Section 2: study design</i>			
How defensible/rigorous is the research design/methodology?	Defensible	Partially defensible	Not defensible
<i>Section 3: data collection</i>			
How well was the data collection carried out?	Appropriate	Partially appropriate	Inappropriate
<i>Section 4: validity</i>			
Is the role of the researcher clearly described?	Clear	Partially clear	Unclear/Not described
Is the context clearly described?	Clear	Partially clear	Unclear/Not described
Were the methods reliable?	Reliable	Partially reliable	Unreliable
<i>Section 5: analysis</i>			
Is the data analysis sufficiently rigorous?	Rigorous	Mixed	Not rigorous/not reported
Are the data 'rich'?	Rich	Partially rich	Poor
Is the analysis reliable?	Reliable	Partially reliable	Unreliable
Are the findings convincing?	Convincing	Partially convincing	Not convincing
Are the findings relevant to the aims of the study?	Relevant	Partially relevant	Irrelevant
Are the conclusions adequate?	Adequate	Partially adequate	Inadequate
<i>Section 6: ethics</i>			
How clear and coherent is the reporting of ethical considerations?	Clear	Partially clear	Not clear
<b>Totals</b>			
<b>Total quality score (max. = 28)</b>			



## Appendix I

### Quality Assurance Checklist: Quantitative studies – based on Downs & Black (1998)

<i>Quality Criterion</i>	<i>Scoring</i>		
	<i>Yes (1)</i>	<i>No (0)</i>	<i>N/A (1)</i>
<b>Reporting</b>			
1. Is the hypothesis/aim/objective of the study clearly described?			
2. Are the main outcomes to be measured clearly described in the Introduction or Methods section?			
3. Are the characteristics of the patients included in the study clearly described?			
4. Are the main findings of the study clearly described?			
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?			
6. Does the study provide estimates of the random variability in the data for the main outcomes?			
7. Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?			
<b>External validity (<i>generalisability</i>)</b>			
8. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?			
9. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?			
<b>Internal validity – bias</b>			
10. If any of the results of the study were based on “data dredging”, was this made clear?			
11. Were the statistical tests used to assess the main outcomes			

appropriate?			
12. Were the main outcome measures used accurate (valid and reliable)?			
<b>Internal validity - confounding (selection bias)</b>			
13. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?			
14. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?			
15. Were study subjects randomised to intervention groups?			
<b>Power</b>			
16. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?			
<b>Totals</b>			
<b>Total Score (max = 16)</b>			



Study Name and Checklist used (Quantitative – QN, Qualitative – QV)	Quality Checklist Item Number																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total
Mah <i>et al.</i> (2008b)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	<b>16</b>
Nereo <i>et al.</i> (2003)	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	<b>14</b>
Reid & Renwick (2001)	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	<b>15</b>
Thompson <i>et al.</i> (1992)	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	<b>14</b>

## **Appendix K – Instructions for recruitment**

### **Research Project**

Cognitive profile in advanced Duchenne Muscular Dystrophy (DMD) and the effects of hypoventilation on cognition

#### **Instructions to clinical health care team members recruiting participants**

##### **Inclusion Criteria for Experimental Group**

- Person has a pure DMD diagnosis
- Person is 16 years or older.
- Person is a native English speaker.
- Person is on NIPPV treatment.

##### **Inclusion Criteria for Control Group**

- Person has a pure DMD diagnosis
- Person is 16 years or older.
- Person is a native English speaker.
- Person is a **not** candidate for NIPPV treatment anytime within the next 6 months, i.e. reports no sleep-related difficulties and experiences no (or very minor) hypoventilation problems.

##### **What do I do when I identify someone suitable?**

1. Introduce the prospect of participation in research.
2. Give out the Information Sheet and Consent form and briefly explain what the research is about.
3. Ask for the **patient's** consent for you to pass on their telephone number to Georgia Papadopoulou (Researcher), and ask for the best day and time for her to call the patient to discuss the project and obtain formal consent if they decide to take part.
4. If the patient consents, email (G.Papadopoulou@2007.hull.ac.uk) or call Georgia (078XXXXXXXX) to pass on the patient's details.

Thank you!

*For any questions, comments, or issues please contact Georgia on either her email or phone.*

## Appendix L

### Description of the psychometric measures used

#### **Adult Memory & Information Processing Battery (AMIPB)**

- **List Learning:** The aim of this subtest is to look at verbal recall performance. It involves the verbal presentation of a list of 15 unrelated words to the subject, who then is required to recall as many of the words as he/she can, without a time constraint and in any order they want. This procedure is repeated five times, providing an opportunity for a learning slope. One point is awarded for each correctly recalled word and all the points are summed up at the end. A different list is then read out for distraction, and the subject is required to recall as many of those words as he/she can. Following this, the subject is then required to recall as many words for the original list as possible without the list being read to him/her again.
- **Story Recall:** The aim of this subtest is to look at immediate and delayed verbal recall performance within a contextual frame of a storyline, presenting a higher load for auditory processing. The subject is read a short story about a woman being burgled and is asked to reproduce the story at the end of the reading with as much the same words as possible. Points awarded range from 0-2 depending on the accuracy of recollection of each section of the story. The subject is then asked to remember the story for later re-testing. The story is requested from the subject following a series of other irrelevant subtests to investigate longer-term memory and retention of information.

#### **Digit Span**

This researcher-created subtest is based on the Wechsler Adult Intelligence Scale (WAIS) digit span subtest. It aims to test working memory by verbally presenting the subject with strings of random numbers ranging from 1 to 10 which the subject is required to repeat back immediately following presentation. The test begins with low demands on working memory

by presenting the subject with a string of only 2 numbers. Following successful reproduction of at least one of two trials of the string of numbers an additional number is added to the string, increasing recall demands. The final string comprises of nine numbers. The subject is awarded 1 point for each correct recall with a maximum score of 16.

### **Doors and People**

- **Doors Test:** This subtest measures visual recognition memory. It involves 12 target doors presented consecutively for 3 seconds each. The subject is then asked to recognise the target doors among three distracters without a time limit. One point is awarded for each correct answer. A second set of 12 doors is then presented and the participant is warned that this is the harder set to recognise. An identical procedure is followed, giving a maximum possible score of 24 points.
- **Names Test:** This subtest measures verbal recognition memory. It involves 12 female names presented and read out by the participant (to assist encoding and storage via rehearsal). The subject is then asked to recognise the target names among three distracters with no time limit. One point is awarded for each correct answer. A second set of 12 male and harder names is then presented and an identical procedure is followed yielding a maximum possible score of 24 points.

### **Delis-Kaplan Executive Function System (D-KEFS)**

- **Colour-Word Interference Test:** The subtest explores cognitive flexibility and simultaneous processing, and involves four conditions: Naming, Reading, Inhibition, and Switching. In the first condition the subject is presented with a page filled with patches of the colours red, green, and blue, and he/she is asked to name the colours as quickly as possible. In Condition 2 the subject is presented with a page with the words 'red', 'blue', and 'yellow' written on it, and is asked to read the words as quickly as possible. In Condition 3 the words

are written in a different colour ink to what they actually say and the subject must inhibit reading the words and has to name the ink colour instead. Finally, in Condition 4 the subject is asked to name the ink colours again but to also switch to reading the word if a word is enclosed in a box. Therefore cognitive flexibility is tested both in terms of inhibition as well as switching cognitive sets. Response times are recorded and converted to scaled scores.

- **Sorting Test (Recognition):** This subtest looks at problem solving and concept formation abilities, as well as initiation and cognitive flexibility. The test involves the presentation of six different cards that can be grouped into two groups of three cards in each group. The examiner groups the cards in different ways and the subject is given 45 seconds to describe the rules used to group the cards. Responses receive scores ranging from 0-2 and total scores are converted to scaled scores.
- **Twenty Questions Test:** This subtest measures logical thinking, hypothesis testing, and deduction, as well as category formation. The subject is presented with 30 familiar objects and is asked to guess which one the examiner has picked by asking Yes/No questions. The subject is asked to try and guess with the fewest number of questions. The number of questions and a weighted achievement score are converted to scaled scores, as is the initial abstraction score (representing the minimum number of items eliminated by the first question asked).

### **Ravens Standard Progressive Matrices**

This test of abstract reasoning was used as a measure of general intellectual ability. It requires subjects to identify the missing item that completes a pattern, out of six or eight multiple choices. The test comprises of five sets of twelve items which become progressively harder. A total score is computed from the number of correct responses out of a maximum of sixty.



## **Appendix M**

### **Patient Information Sheet**

Cognitive profile in advanced Duchenne Muscular Dystrophy (DMD) and the effects of hypoventilation on cognition

#### **Part 1**

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish.

Part 1 tells you the purpose of this study and what will happen if you take part.

Part 2 gives you more detailed information about the study.

Ask us if there is anything that is not clear, or if you would like more information.

#### **What is the purpose of the study?**

The study is looking at patients with DMD over the age of 16 years. We are using some questionnaires and tests to look at the ‘thinking’ or ‘cognitive’ abilities of this group of patients. Examples of cognitive abilities would be your memory and problem solving. This will help us understand if these abilities change as you grow up.

We are also looking at how breathing difficulties during sleep affect your mood, quality of life and thinking, and whether treatment for breathing difficulties (called non-invasive positive pressure ventilation or NIPPV) helps to improve these areas.

#### **Why have I been invited?**

Your nurse, physiotherapist, or doctor has referred you for this research because you have a diagnosis for DMD and you meet the age criteria to take part. You may also be on a ventilation machine to help you with your breathing overnight.

We are inviting around 40 more patients with DMD over the age of 16 years some of which are on a ventilation machine and some of which are not.

#### **What is ventilation treatment or NIPPV?**

NIPPV is a machine that helps maintain oxygen levels in your body through use of a simple face mask covering your mouth and nose. This is usually used during sleep when breathing difficulties occur.

Patients with DMD often require this treatment, but not everyone will need to start using it at the same age or using it to the same extent. This is the reason you may not be aware of the treatment at the moment.

### **Do I have to take part in the study?**

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. If you would like to take part we will ask you to sign a consent form, to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

### **What will happen to me if I take part?**

- Once you agree to take part we will arrange a face-to-face appointment. This can take place at your home or hospital whichever is most convenient for you. Before this appointment some brief questionnaires will be sent to you by post. They should not take you more than 20 minutes to complete. We will ask you to bring these with you to your first appointment.
- The appointment itself will last no longer than 1 ½ hours. During this appointment we will be doing some brief tests looking at how well some of your different thinking abilities work, for example your memory for seeing things, your memory for hearing things, etc.

Therefore, your involvement with the study will be completing a set of questionnaires and having a single appointment.

### **What will I have to do?**

All you will need to do is fill out the questionnaires when they are sent to you, and attend the arranged appointment (which may be at your home). If you cannot attend please let the researcher know. You will not have to do anything else over and above your normal treatment.

### **What are the possible disadvantages and risks of taking part?**

There are no health risks in taking part in this study. The appointment takes place either at your home or at the hospital, whichever you prefer.

We appreciate that everyone's time is precious, so the tests we use are generally brief and we take regular breaks if and when necessary during the testing to ensure you do not feel tired or in discomfort.

**What are the possible benefits of taking part?**

We cannot promise the study will help you personally, but the information we get from this study will help improve our understanding of cognitive abilities in people with DMD. This will help improve our understanding of DMD and the care we can give to people.

**What happens when the research study stops?**

Your treatment will continue as usual when the study ends. If you have started using ventilation treatment this will continue for as long as it is helpful to you, and this decision is to be made with your healthcare team. If you were not using ventilation treatment during the study and your healthcare team feel this is necessary at any point in the future, treatment will be offered as usual.

**What if there is a problem?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

**Will my taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

*If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.*

**Part 2**

**What will happen if I don't want to carry on with the study?**

You can withdraw from the study at any point. If you withdraw from the study we will destroy all the data we collected from you.

**What if there is a problem?**

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (01482 464164). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure (or Private Institution). Details can be obtained from the hospital.

**Will my taking part in this study be kept confidential?**

All information which is collected about you during the course of the research will be kept strictly confidential, and any information about you which leaves the hospital/surgery will have your name and address removed so that you cannot be recognised. We will keep all information in a safe, locked place and destroy it at the end of the study. All data use is in line with the Data Protection Act and the rules of the NHS.

**What will happen to the results of the research study?**

The findings of the study will be submitted for publication. If you wish to gain access to the final report of the results please let us know and we will ensure you receive a copy. No participants will be identified in any report/publication.

**Who is organizing and funding the research?**

This research is part of a doctoral degree at the University of Hull. The Humber Mental Health Teaching NHS Trust is the sponsor and funder of the research.

**Who has reviewed the study?**

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion the South Humber Local Research Ethics Committee.

**Who should I contact if I have any questions or concerns after reading this document or during the study?** - You can contact the researcher (Georgia Papadopoulou) for any questions or concerns at 01482 464164.

## Appendix N

Centre Number: 1 / 2 / 3

Patient Identification Number:

### CONSENT FORM

Title of Project: Cognitive profile in advanced Duchenne Muscular Dystrophy (DMD) and the effects of non-invasive positive pressure ventilation (NIPPV) on cognition

Name of Researcher: Georgia Papadopoulou

Please initial  
box

1. I confirm that I have read and understand the information sheet dated December 2008 (version 1.5) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by researchers from Hull University, regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I agree to take part in the above study.

\_\_\_\_\_  
Name of Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of Person  
taking consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

When completed, 1 copy for patient; 1 for researcher site file; 1 (original) to be kept in medical notes

## **Appendix O**

The documentation relevant to Ethical and R&D approval follows.