Quality of Life and Palliative Care Need in Multiple System Atrophy and Progressive Supranuclear Palsy: A Pilot Study Using Quantitative and Qualitative Methods

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Abstract

Background

Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP) are atypical Parkinsonian disorders which are rapidly progressive. The impact that Parkinsonian disorders has on quality of life (QoL) is increasingly understood, though less work has been done in MSA and PSP compared to Parkinson's disease. The role of Palliative Care in enhancing QoL is beginning to be translated into clinical practice though fewer studies have been done in MSA and PSP compared with Parkinson's disease.

Methods

A cross-sectional study of 23 MSA patients and 24 PSP patients was carried out, assessing aspects of QoL, depression, palliative symptoms and clinical milestones such as dysarthria. Carers for each disease type were assessed in terms of carer strain and QoL. A range of QoL measures including subjective, disease-specific and general QoL scores were taken with the aim of achieving a holistic impression of QoL and symptom burden. A subset of participants were selected for interviews to obtain personal perspectives of living with these conditions. The interviews were evaluated using thematic analysis, to gain a still fuller, richer picture of the implications of these diseases on QoL for patients and carers. The use of both quantitative and qualitative methods was intended to complement each other, with the recognition that QoL is a complex and subjective concept and cannot be encompassed using a single type of assessment.

Results

Using multiple linear regression, QoL was predicted for by depression and palliative need in MSA and PSP, with severity having an influence in PSP only. Carer mental well-being and patient depression influenced different aspects of carer QoL. Issues with legs was the highest-rated symptom in both groups and there was no significant difference in palliative need between MSA and PSP. Subjective QoL using the SEIQoL-DW score produced diverse domains which people felt influenced their QoL. The most commonly nominated were 'family' and 'partner'; some domains in common were discussed in interviews.

The overarching themes in interviews were connection to others, transitions (including adjustment) and seeking support, from peers, palliative care services and sourcing expertise for these rare conditions.

Conclusion

MSA and PSP have a profound effect on QoL, seen using a range of QoL scores. Depression and symptoms frequently managed in palliative care, predict for patient disease-specific QoL, though severity seems to have a greater impact on QoL in PSP compared with MSA. Carer QoL is impacted by patient depression and by carers' own mental well-being. This work emphasises that QoL in progressive neurological disorders is heterogeneous and individual. Patients and their carers would likely benefit from an individualised, palliative approach supporting patients through the course of their disease, maximising QoL to enhance the experience of living with a progressive disease.

Dedication

This thesis is dedicated to the fond memory of Dr Hao Wu, a caring doctor and beloved friend who we miss every day.

Declaration

This project was supervised by Professor David Burn and Dr Katie Brittain with advisory input from Dr Mark Lee. The design of the project was undertaken by myself with guidance from Professor Burn, Dr Brittain and Dr Lee.

Ethical permissions and subsequent amendments for this project were sought by myself as Principal Investigator with Professor Burn as Chief Investigator.

Clinical study visits including consents were all undertaken by myself as was data-checking and analysis. Statistical advice in the form of university one-to-one sessions was provided by Dr Kim Pearce and informally by Dr Rachael Lawson and Dr Brook Galna. Dr Galna assisted in producing an Excel template to enable the calculation of composite scores from one of the questionnaires (RAND-36), the instructions for which were published in the literature.

Qualitative interviewing and analysis was carried out by myself with Dr Brittain reviewing and critiquing the findings as they emerged. Transcription of interviews were carried by a professional transcription service, though the first interviews and those which were difficult to interpret due to speech difficulties, were transcribed by myself.

The production of this thesis has been my own work with feedback from my supervisors and advisor.

The following publications, presentations and lecture have been produced from this thesis.

- **Wiblin, L.,** Lee, M., Burn, D. (2016) Palliative care and its emerging role in Multiple System Atrophy and Progressive Supranuclear Palsy. *Parkinsonism & Related Disorders.* 34, p7-14
- **Wiblin, L.**, Sleeman, I., Burn, D. (2016) Embarking on a research project…or research for the absolute novice. Journal of the Royal College of Physicians (Edinburgh). 46(3): p182-186
- **Wiblin, L**. (2017) Neuropalliative Care-a growing need. *Advances in Clinical Neuroscience and Rehabilitation*. 16(3) p22-23
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Acknowledgements

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Abbreviations

ADL	activities of daily living
AIDS	acquired immunodeficiency syndrome
ANCOVA	analysis of co-variance
ANOVA	analysis of variance
AP	Atypical Parkinsonism
BADLS	Bristol Activities of Daily Living Scale
CARU	Clinical Ageing Research Unit
CBS	Cortico-Basal Syndrome
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CRESTA	Clinics for Research and Service in Themed Assessments
CRF	case report forms
CSF	cerebrospinal fluid
CSI	Caregiver Strain Index
DASS	Depression Anxiety Stress Scale
DASS-21	Depression Anxiety Stress Scale (21 items)
DASS-A	Depression Anxiety Stress Scale anxiety subscore
DASS-D	Depression Anxiety Stress Scale depression subscore
DLB	Dementia with Lewy bodies
EQ-5D	EuroQOL five dimensions questionnaire
(F-18) FP-CIT	(fluorinated N-3-)fluoropropyl-2β-carbomethoxy-3β-(4-iodophenyl) nortropane
FTD	frontotemporal dementia

GP	general practitioner
GT	Grounded Theory
HIV	human immunodeficiency virus
HR-QoL	health-related quality of life
HS	health status
H&Y	Hoehn and Yahr
ICDs	impulse control disorders
iPD	idiopathic Parkinson's disease
IPOS	Integrated Palliative Care Outcome Scale
IQR	interquartile range
KB	Dr Katie Brittain
KS	Kolmogorov–Smirnov
LPA	Lasting Power of Attorney
MCS	mental composite score
MCSI	Modified Carer Strain Index
MD	Doctor of Medicine
MDS	International Parkinson and Movement Disorder Society
MDT	multi-disciplinary team
MND	motor neuron disease
MRI	Magnetic resonance imaging
MSA	Multiple System Atrophy
MSA-C	Multiple System Atrophy - Cerebellar subtype
MSA-P	Multiple System Atrophy - Parkinsonian subtype
MSA-QoL	Multiple System Atrophy Quality of Life Scale
NHS	National Health Service

NICE	The National Institute for Health and Care Excellence
NINDS-SPSP	National Institute of Neurological Disorders and Stroke and the Society for PSP
NIV	Non-invasive ventilation
PBS	point biserial
PC	palliative care
PCS	physical composite score
PD	Parkinson's disease
PDQ-39	Parkinson's Disease Questionnaire 39 items
PEG	percutaneous endoscopic gastrostomy
PET	positron emission topography
PI	principal investigator
POS	Palliative care/Patient Outcome Score
POS-S-PD	Palliative Outcome Scale – Symptoms Parkinson's disease
PQoLc	Parkinsonism Carers Quality of Life Questionnaire
PSP	Progressive Supranuclear Palsy
PSP-P	Progressive Supranuclear Palsy - Parkinsonian-subtype
PSP-PAGF	Progressive Supranuclear Palsy - pure akinesia with gait freezing
PSP-RS	Progressive Supranuclear Palsy - Richardson Syndrome
PSPRS	Progressive Supranuclear Palsy Severity Scale
PSP-QoL	Progressive Supranuclear Palsy Quality of Life Scale
QoL	quality of life
rADC	apparent diffusion coefficient
RAND-36	RAND 36-item Health Survey (SF-36)
REM	rapid eye movement

SD	standard deviation
SEIQoL-DW	Schedule for the Evaluation of Individual Quality of Life - Direct Weighting
SF-36	36-item Short Form Health Survey (RAND-36)
SPC	Specialist Palliative Care
SPSS	Statistical Package for the Social Sciences
SW	Shapiro-Wilk
SWI	susceptibility weighted imaging
TA	thematic analysis
UK	United Kingdom
UMSARS	Unified Multiple System Atrophy Rating Scale
UPDRS	United Parkinson's disease Rating Scale
USA	United States of America
WHO	The World Health Organization
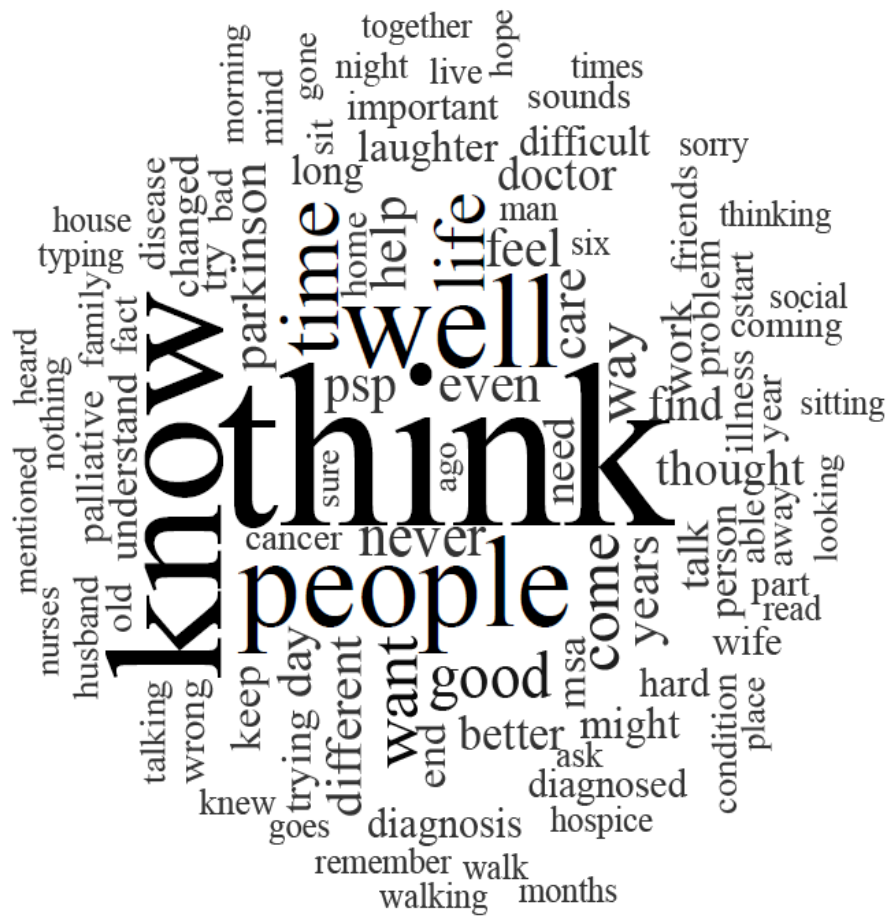
Figure I: Word frequency cloud; size of words proportional to their frequency of use in interviews with patients and carers

Introduction

Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP) are progressive neurodegenerative conditions and belong to a group known as the atypical Parkinsonian disorders. The atypical parkinsonian disorders have some features of Parkinson's disease (PD) but often with poor or transient levodopa response with distinct symptom profiles and more rapid progression and reduced survival (Bukki *et al.*, 2014). They have significant symptom burden (Pillas *et al.*, 2015). The atypical parkinsonian conditions considered in this review will be Multiple System Atrophy and Progressive Supranuclear Palsy.

MSA is a sporadic condition with early and significant disability. It includes key features of Parkinsonism, autonomic failure and cerebellar symptoms (Diem-Zangerl *et al.*, 2009). The subtype MSA-P (Parkinsonian) tends to occur more commonly in the West (Europe and United States of America) whereas the MSA-C (cerebellar) form is the prevalent form in the East, specifically in Korean and Japanese populations (Seo *et al.*, 2010). PSP is characterised by early falling (usually backwards), supranuclear gaze palsy (with vertical gaze typically affected first) and cognitive problems (Williams *et al.*, 2005). PSP-Richardson's Syndrome (PSP-RS) describes the classical constellation of early falls, gaze problems and frontal cognitive dysfunction whereas PSP-Parkinsonism (PSP-P) has more prominent bradykinesia and tremor, is asymmetrical and is often diagnosed as idiopathic Parkinson's disease (iPD) in the early stages (Williams *et al.*, 2005; Jecmenica-Lukic *et al.*, 2014).

Quality of life (QoL) is increasingly recognised as an important outcome measure of patient status, as the significant symptom burden and extended morbidity of these conditions is appreciated. To this end, there has been increasing recognition of the benefit of palliative care (PC) input in patients with neurodegenerative diseases especially those with significant early morbidity, such as the atypical parkinsonian disorders (O'Sullivan *et al.*, 2008; Bukki *et al.*, 2014). Palliative care can be challenging in the context of neurodegenerative disorders. The progression of disease can fluctuate with unforeseen rapid deterioration on a background of inexorable decline. Considerable loss of function and symptom burden can occur relatively early in the disease process resulting in significant periods of time with marked morbidity (Fallon and Foley, 2012). The burden of these conditions is heavy, both for patients and for their carers, and it has been described that patients with atypical Parkinsonism (AP) might benefit from early palliative care (Veronese *et al.*, 2015). The complex combination of

symptoms displayed by this patient group has comparable levels of palliative care need as advanced cancer patients (Higginson *et al.*, 2012).

The aims of this MD project are to explore the demographics of the patients and carers, how important clinical milestones, such as needing a wheelchair, relate to the time of diagnosis and to find how palliative care need (symptom burden) compares between the two disease groups and what patients understand about palliative care as a service. Different aspects of QoL in patients and carers (and strain in the latter) will be analysed using validated measures and statistical analysis will be used to find any differences between them and whether these scores can be predicted for using other participant variables. Finally, individual perspectives will be sought using semi-structured interviewing of a subset of participants, seeking to complement the quantitative analysis with detailed and rich descriptions of living with MSA and PSP, to provide a full and holistic outlook to this work.

Chapter 1. Review of Literature

1.1 Multiple System Atrophy and Progressive Supranuclear Palsy

Idiopathic Parkinson's disease is defined as bradykinesia or slowness of movement, akinesia, rest tremor, asymmetrical onset, postural instability and rigidity typically with a good levodopa response (Litvan, 1998; Brooks, 2002). When Parkinsonism is present but has additional or unusual features, this is known as atypical Parkinsonism. Multiple System Atrophy and Progressive Supranuclear Palsy are two sporadic atypical parkinsonian disorders, historically known as the Parkinson's Plus disorders (see figure 1.1).
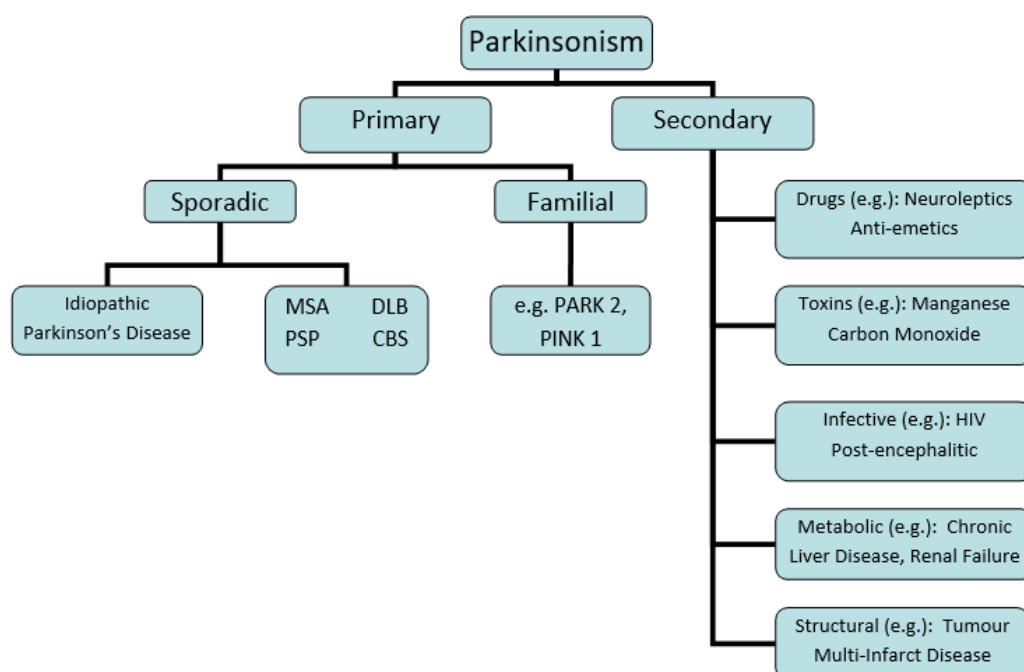
Figure 1.1: Classification of Parkinsonism from (Hughes et al., 2002; Martin, 2011)

1.1.1 Diagnosis and diagnostic criteria

The atypical Parkinsonian disorders tend to progress more rapidly than PD and have a response to levodopa therapy which can be absent or poorly-sustained (Litvan, 1998; Poewe *et al.*, 2015). Distinguishing between PD and the atypical Parkinsonian disorders can be difficult especially in the early stages. Wenning *et al.* (1995) describes 75% of pathologically-confirmed MSA initially being diagnosed with PD.

Hughes *et al.* (2002) emphasises the importance of specialist movement disorder clinics with integrated expertise in the diagnosis of atypical Parkinsonian disorders. In their study, 88.2% of pathologically-proven MSA cases were appropriately diagnosed in this specialist setting and in PSP, 84.2%. Timely, accurate diagnosis is important and it can allow preparation for the more rapid deterioration expected in these disorders, as well as prompt advance care planning and support to be provided.

Diagnostic criteria have been formulated to facilitate accurate diagnosis in MSA and PSP. The NINDS-SPSP criteria only apply to the 'typical' or Richardson's Syndrome subtype (see tables 1.1 and 1.2). It should be noted that in 2017 when this project's data collection had been completed, new diagnostic criteria for PSP were published. However due to the timing of its publication, the new criteria could not be used for this study (Hoglinger *et al.*, 2017).

NINDS-SPSP criteria (applies to PSP-Richardson's syndrome only)	
Possible PSP	Progressive disorder
	Onset 40 years or above
	Vertical supranuclear gaze palsy OR
	Slowing of vertical saccades and falls within first year
	No evidence suggestive of other diseases
Probable PSP	Progressive disorder
	Onset 40 years or above
	Vertical supranuclear gaze palsy AND postural instability with falls in first year of onset
Definite PSP	Possible or probable PSP with autopsy confirmation
Exclusion Criteria	Alien limb syndrome, recent encephalitis, Alzheimer's-type cortical dementia, prominent cerebellar signs, early dysautonomia, asymmetric Parkinsonian signs, relevant radiological abnormality and Whipple's disease

Table 1.1: The NINDS-SPSP (National Institute of Neurological Disorders and Stroke and Society for PSP consensus criteria developed in 1996 (Litvan et al., 1996)

MSA consensus criteria	
Possible MSA	Sporadic and progressive disease
	Onset over 30 years of age
	Features of Parkinsonism (bradykinesia, rigidity, tremor) OR
	A cerebellar syndrome (ataxia, dysarthria, oculomotor features AND
	Features suggestive of autonomic dysfunction
	An additional suggestive feature such as poor levodopa response or stridor
Probable MSA	As above but with defined dysautonomia (drop of 30mmHg systolic/ 15mm Hg diastolic post 3 mins standing, erectile dysfunction or urinary incontinence/voiding difficulty).
Definite MSA	Possible or probable MSA with autopsy confirmation

Table 1.2: The Second Consensus Criteria for MSA (Gilman et al., 2008)

Prompt identification is crucial, not only for appropriate classification, prognostication and communication to patients, but to address patient needs (such as palliative care) which are apparent earlier than in PD. Furthermore, research in AP is growing and accurate diagnosis of disease allows patients the opportunity to participate in research, as has been the case in PD over recent years. Late diagnosis, uncertainty and a lack of information with specialist advice has been reported by patients and carers to be a cause of distress in PSP (Moore and Guttman, 2014). Therefore, key features which may suggest MSA and PSP should be included as part of the diagnostic and review history, especially in the early phase of disease or if progression is unexpectedly rapid for PD. (see tables 1.3 and 1.4)

	Atypical Features	Presence in iPD	Subtypes
MSA	Ataxia	No	**MSA-C** Predominant cerebellar features though Parkinsonism may also be present
	Autonomic dysfunction	Late or treatment-related	
	Cerebellar signs	No	
	Pyramidal signs	No (except hyperreflexia)	
	Stridor and hypoventilation	No	**MSA-P** Predominant Parkinsonism though cerebellar features may also be present
	Poor levodopa response	Good levodopa response	
	Polyminimyoclonus	No	

Table 1.3: Atypical features of MSA (Litvan, 1998; Flabeau et al., 2010)

	Atypical Features	Presence in iPD	Subtypes
PSP	Early falls and instability	Late	**PSP-RS** vertical gaze
	Dysphagia and dysarthria	Late	palsy, axial rigidity,
	Frontal release signs	No	dysarthria and frontal lobe
	Marked axial rigidity	Limb rigidity more prominent	dysfunction
	(Vertical) Supranuclear gaze palsy	No	
	Early wheelchair requirement	Unusual	**PSP-P** asymmetric
	Pyramidal signs	Late	parkinsonism, often a
	Poor levodopa response	Good levodopa response	degree of levodopa
			response

Table 1.4: Atypical features of PSP (Golbe and Ohman-Strickland, 2007; Arena et al., 2015)

1.1.2 Differential Diagnosis

Because of the clinical challenges in making an accurate diagnosis, research has considered several avenues to improve discrimination between PD and AP generally, as well as the more specific diagnosis of MSA or PSP (or indeed other AP forms such as Dementia with Lewy bodies (DLB) or Cortico-Basal Syndrome (CBS)). A full exploration of the search for biomarkers in the differential diagnosis of Parkinsonism is beyond the scope of this thesis, but some considerations will be mentioned.

Autonomic testing: Work by Baschieri *et al.* (2015) using a combination of autonomic tests found that sensitivity to discriminating MSA from PD was 91% with a specificity of 94%. However, participants with comorbid diseases such as diabetes mellitus or cardiovascular disease which could interfere with autonomic testing were excluded; these groups are often those in which diagnostic uncertainty is most problematic. Similarly, pre-motor or early incontinence (as opposed to urinary urgency) or erectile dysfunction can be a helpful discriminator of MSA from PD but prior urological problems can mask this history. Also, the clinical picture is less clear in women, especially if there is a degree of prior stress incontinence (Chandiramani *et al.*, 1997).

Imaging: There is no imaging modality in common clinical use which can currently confidently discriminate AP from PD (or MSA from PSP). Some MRI sequences such as SWI can improve diagnostic certainty of MSA from 25% to 75% in the right clinical context and rADC is also being explored as a readily available MRI sequence which may add to diagnostic certainty (Brooks and Tambasco, 2016). Jin *et al.* (2016) have recently shown in a study with 67 participants with PD, MSA and PSP that early phase PET scanning with FP-CIT may allow discrimination of MSA from PD due to different patterns of cerebral uptake but not PSP.

Biomarkers: CSF and blood biomarkers have been pursued as a means to distinguish AP from PD. Blood biomarkers would be especially valuable as they minimise the need for invasive procedures such as a lumbar puncture. Hansson *et al.* (2017) has shown neurofilament light chains in blood have some promise in distinguishing AP from PD after finding higher levels in AP generally, compared with PD patients and controls.

Other work: Patients with PD perform more poorly than those with MSA or PSP in olfactory testing, so this may have a role as part of diagnostic work-up in the future (Krismer *et al.*, 2016). As speech dysfunction has been recognised as often being more profound in AP, voice analysis has been carried out to seek significant differences between groups, though work thus far has only found non-significant differences in men with MSA compared with PD and other AP patients (Huh *et al.*, 2015).

Diagnosis in AP remains clinical, albeit with a range of tests being further developed in terms of their utility in helping discriminate between PD and AP (and between AP types). A cohort of patients from the UK with AP (including MSA, PSP, CBS and DLB) recently illustrated the issues frequently encountered in trying to achieve a reliable diagnosis. 49% of participants had features considered 'atypical' for that type of AP e.g. severe cognitive dysfunction in MSA or cerebellar signs in PSP. 10% of participants received an alternative diagnosis during the study (Hirschbichler *et al.*, 2016).

In summary, though research is ongoing on many physiological parameters in the hope of improving the clinical accuracy of AP, at present there is often uncertainty and difficulty in the process of diagnosis, especially in early disease. This leads to uncertainty and stress for patients.

1.1.3 Clinical milestones in disease progression and prognosis
MSA and PSP have been observed to fall into distinct phenotypes. To allow better prognostication and advance care planning, studies have been carried out to determine whether the subtype of the AP, or the presence of certain symptoms or signs are associated with a more rapid decline. Dysautonomia and stridor are two such symptoms in MSA.

Comparisons of outcome have been made between MSA-C and MSA-P subtypes. O'Sullivan *et al.* (2008) found that dysautonomia within 2 years, older age at onset and female sex were poor predictors of survival. There was an unexpected survival benefit in nursing home admission; one theory for this was professional catheter care. Japanese studies have also

found poorer outcomes with early dysautonomia (Tada *et al.*, 2007). Stridor is a worrying symptom in MSA with a high degree of uncertainty. Reports of sudden death in connection with it have been made but consensus on the best treatment course is not established. Silber and Levine (2000) reported survival in a cohort as 3 years if stridor was present, 4 years if absent. However, survival was only 0.8 years if stridor occurred in the daytime. Four patients received tracheostomy - two died within the year. NIV did not seem to alter outcome.

Wheelchair dependence occurs between 3.5-5 years (with mean survival at 7-9 years). Watanabe *et al.* (2002) found people with MSA-P deteriorated functionally faster than MSA-C though survival was not statistically different. Other work has suggested MSA-C has better outcomes than MSA-P though the latter may reach more milestones before diagnosis (Schulz *et al.*, 1994; Lee and Koh, 2012). Suggestions for this include the greater difficulty of recognizing MSA-C due to its cerebellar features. An analysis of 20 studies exploring MSA prognosis reported opposing conclusions on whether subtype of MSA, the presence of stridor or the age of onset affected outcome (Glasmacher *et al.*, 2017).

A number of variables have been theorized as being poor predictors of survival in PSP, including subtype, sex, age at onset and development of key symptoms or signs (see table 1.4). PSP-RS has been described as having a worse outcome than PSP-P in a range of studies (O'Sullivan *et al.*, 2008; Williams and Lees, 2009; dell'Aquila *et al.*, 2013). Shorter survival was associated with male sex in a British cohort of pathologically confirmed cases (O'Sullivan *et al.*, 2008) but not in other studies (Nath *et al.*, 2003; Golbe and Ohman-Strickland, 2007). Older age at onset of symptoms has been demonstrated in several studies to lead to reduced survival (Chiu *et al.*, 2010; dell'Aquila *et al.*, 2013). Falls in PSP tend to be the first milestone achieved (O'Sullivan *et al.*, 2008; dell'Aquila *et al.*, 2013) and poorer survival has been associated with shorter periods between symptom-onset and the first clinical milestone (Santacruz *et al.*, 1998). In terms of specific symptoms which might predict a poorer outcome, a meta-analysis of studies observing progression in PSP, earlier dysphagia and cognitive problems had a shorter survival trajectory (Glasmacher *et al.*, 2017).

1.1.4 Comparisons between MSA and PSP

Symptom-burden is significant in MSA and PSP; 93% of patients reach at least one milestone (of seven which the study selected as clinically significant and likely to be well-documented such as falls, wheelchair dependence and dysarthria) in a British cohort (O'Sullivan *et al.*, 2008). The first milestone overall, when all subtypes of MSA and PSP were considered was

frequent falls (Brooks, 2002; Lee and Koh, 2012). PSP patients tended to reach their first milestone earlier (mean 3.9 years) compared with MSA (5.9 years). Work by Jecmenica-Lukic *et al.* (2014) supports the rapid progression to disability and reduced survival of PSP-RS compared to other subtypes, though PSP-P was observed to have a better outcome in terms of survival than MSA-P.

Overall there is evidence that survival is reduced in PSP and MSA overall compared with PD and that significant clinical milestones are reached early in all forms. Symptom-burden is considerable and marked disability is present early in the disease-course, producing extended morbidity as well as increased mortality in these unremittingly progressive conditions. In progressive conditions such as these, the focus of a palliative approach is quality of life.

1.2 Quality of Life

1.2.1 Defining Quality of Life

The World Health Organization (WHO) defines Quality of Life as '*an individual's perception of their position in life in the context of their culture and value systems in which they live and their goals, expectations, culture and concerns*' (World Health Organisation, 1995). Quality of life has been described as a judgement which an individual makes of their life against criteria which that individual has developed for themselves. This is a subjective appraisal of one's life (Pavot, 2009).

In medical research, quality of life (QoL), and its measurement, has become increasingly prominent as it is recognized that clinical assessments or disease-rating scales do not encapsulate the patient experience of living with a progressive disease (Rejeski and Mihalko, 2001; Litvan, 2005). This growing appreciation of the importance of QoL, rather than a pure focus upon mortality and disease-measures has led to the development of tools attempting to quantify QoL (Smith, 1999). QoL is a broad concept and difficult to capture in the clinical context. Therefore, the disease-focused 'health-related quality of life' (HR-QoL) has been developed. HR-QoL is restricted to perception of well-being relating to disease, treatment and its impact. HR-QoL is easier to describe but remains a multidimensional concept, dependent on the individual's experience (Den Oudsten *et al.*, 2007a). By contrast, health status (HS) has been thought of as an evaluation of the patient's function, physically, psychologically and socially but not incorporating the individual's judgments. Thus, HS can impact upon HR-QoL but is not equivalent (Murrell, 1999; Zubaran *et al.*, 2008; Martinez-Martin *et al.*, 2011). The

purpose of these measurements is to define outcomes meaningful to the patient. However, HR-QoL and HS are often used interchangeably in literature as 'QoL measures'. It has been suggested that these are in fact complementary and it can be useful to assess both HS and HR-QoL to gain a nuanced impression of the patient's experience (Haave *et al.*, 2006).

1.2.2 QoL in PD

The importance of recognising QoL in progressive neurodegenerative conditions such as PD and AP is increasing. Efforts are being made to maximize patient well-being with the finite societal resources available (Schrag, 2005). QoL research in PD is becoming well-established, as is the understanding of the personal experiences Parkinsonian diseases have on patients.

It has been found that PD patients have lower scores across all well-being dimensions compared with patients with diabetes mellitus and individuals without chronic disease, reporting fatigue, pain and social isolation. Reviews of HR-QoL over four years in PD show a decline though no predictive factors have been identified (Karlsen *et al.*, 1998; Karlsen *et al.*, 2000). Den Oudsten *et al.* (2007a) reviewed studies considering QoL in PD. In 61 studies, all claimed to measure HR-QoL; however only two actually measured HR-QoL, the remainder measured HS. Poorer HS was associated with depression and with sleep disturbance. The authors concluded that use of HR-QoL was sparse and more work needed to be done to appraise well-being using HR-QoL, as the bulk of the literature concentrates on HS alone.

The SEIQoL-DW is a measure that allows patients to define specific issues contributing to their QoL; whereas other HR-QoL instruments tend to impose issues which individuals may not find important (Hickey *et al.*, 1996). A study evaluating PD using the SEIQoL-DW found 87 meaningful domains were created when 123 patients were interviewed, reflecting the subjectivity of QoL and heterogeneity of patient experience. Subjective QoL was predicted by depression (Lee *et al.*, 2006). The presence and severity of depression has been associated with HR-QoL/HS in PD in other studies (Kuopio *et al.*, 2000). Schrag (2006) described depression to have strong associations with HR-QoL in PD. Disease severity had only a moderate effect whereas disease duration had none.

1.2.3 QoL in MSA and PSP

It is recognised that MSA and PSP have marked impact on quality of life and health with a more rapid progression and reduced survival compared with PD (Schrag *et al.*, 2003; Schrag,

2005; Winter *et al.*, 2011). Therefore, as the impact of PD on HR-QoL has become understood, work has begun seeking the impact of MSA and PSP on HR-QoL.

Living with chronic neurological conditions (including MSA and PSP), has been found to have marked impact on HR-QoL (Calvert *et al.*, 2013). Winter *et al.* (2011) found 63% of MSA and PSP patients described serious issues in at least one aspect of their well-being using HR-QoL measures. Predictors of low HR-QoL included female sex, depression and cerebellar symptoms. By contrast, Schrag *et al.* (2003) found no association between gender or age and HR-QoL in individuals with PSP. Generic measures used, like the EQ-5D were reported by patients to lack recognition of their specific concerns in PSP, such as visual disturbance and falling. In PSP patients followed over one year, apathy was the only statistically significant variable found which predicted greater decline in HS (Pekmezovic *et al.*, 2015). Benrud-Larson *et al.* (2005) considered life-satisfaction in MSA patients. Depression was pervasive in the group; 36% had moderate to severe depression (contrasted with 19.6% in PD) and 5% described suicidal ideation. Depression was a significant factor in life-satisfaction though HS was not. However, a European study found that though moderate-severe depression was found in half of an MSA cohort and associated with lower HR-QoL scores; autonomic and motor problems had a stronger association (Schrag *et al.*, 2006a). Therefore, depression is common in MSA and depression does influence QoL, but unlike in PD, it is not thought to be the principal determining factor.

As well as negative factors having an influence on QoL in neurodegenerative disease, it is important to identify whether positive factors exist which might correlate with improved QoL. In Japanese patients with neurological disease, including PD and MSA, improved HR-QoL was associated with having someone to discuss concerns with, hobbies and attending patient-groups. The perception that there were medical facilities that could care for them (should they require it) was also correlated with higher HR-QoL scores (Nishida *et al.*, 2012). QoL is often thought of as being directly related to the severity of the disease of the individual, though this has not been borne out in studies in PD, MSA and PSP as described above. It is often assumed that QoL will fall as disease progresses. The description of the 'response shift' phenomena describes QoL as a more fluid construct, and factors considered to be important to the person can change over time. Re-evaluation of values and how QoL is perceived by the individual is likely influenced not only by changing circumstances of life as disease progresses but how the individual's values adjust (Hickey *et al.*, 1996; Spangers, 1999; Lee *et al.*, 2006). QoL is significantly affected in patients with MSA and PSP. Tools to measure this

have been developed which are disease-specific, but lack comparability between groups (see Chapter 3. Methods). Although disease-specific QoL has begun to be studied in MSA and PSP and objective disease-specific QoL have been developed, there is a paucity of work on the AP disorders in terms of what the individual finds impacts upon their QoL. Neither subjective QoL measures nor qualitative work have been carried out in this diverse group, limiting the data available to the imposed criteria of traditional HR-QoL scores.

Key determinants affecting HR-QoL have been explored in MSA and PSP though no consensus has been reached, unlike in PD where depression is strongly predictive in several studies. As well as the importance of finding and addressing factors which adversely affect QoL, positive factors which may preserve QoL are important as they may allow clinical teams to introduce measures to ameliorate decline in QoL in patient populations. QoL is a changing, subjective construct, and patients may adjust their values and expectations over time. This adjustment of values is more difficult to capture with the predetermined domains of many HR-QoL tools. This lack of a rounded evidence base, without subjective, holistic views of QoL (which by its very nature is a very reflective concept) is lacking in the literature in this patient and carer group.

1.3 Carers

1.3.1 Caregiving and its impact

Caregivers and the importance of their role in the patient experience have been increasingly recognized and discussed as the burden of chronic disease rises. 80% of people with some assistance at home receive this from an informal source, usually their partner or family. Only 10% rely purely on formal services, within the UK (Pickard, 2000). There are around 5 million carers in England and Wales, nearly half over 65 years of age, and 37% provide more than 100 hours of care per week (Health and Social Care Centre, 2010). Carers for people with PD have been shown to have lower QoL compared with non-carers and may suffer an impact upon their mental well-being, social life and ability to earn (McCrone *et al.*, 2007; Hasson *et al.*, 2010; Shin *et al.*, 2012). In MSA and PSP in the UK, unpaid care accounted for 75% and 76% respectively of social costs in 2011 (McCrone *et al.*, 2011).

Older carers in the USA had increased 4-year mortality compared to normal controls of 63% when associated with self-reported strain (Schulz and Beach, 1999). A number of factors influencing caregiver strain have been explored. Strong correlations were found between the length of time carers have spent in the caregiving role, the number of hours caring per day and

strain. The higher the amount of care provided, the greater the caregiver burden (Litzelman *et al.*, 2015).

1.3.2 Factors influencing caregiver strain

Behavioural and psychiatric problems, including depression tend to be associated with greater carer burden in conditions such as Alzheimer's dementia (Jennings *et al.*, 2015). A meta-analysis of 29 studies by Greenwell *et al.* (2015) found that in the context of PD, neuropsychiatric symptoms were associated with poorer caregiver QoL and with caregiver depression. No consistent associations were seen between carer demographic factors, such as gender, and poor QoL in this analysis. Leroi *et al.* (2012) investigated apathy and impulse control disorders (ICDs) and the effect these have on strain experienced by carers. Apathy and the presence of ICDs were statistically significant in increasing caregiver burden.

1.3.3 Adjustment in caregiving

Although some studies have shown increasing patient dependency, disease duration and severity in PD lead to greater caregiver burden, other sources have found positive or stabilising trends in caregiver outlook can take place, with psychological adjustment over time (Martinez-Martin *et al.*, 2005; Au, 2011; Oguh *et al.*, 2013). In a Spanish study, there were correlations between Parkinson's patients and their carers employing 'coping responses' and perceiving positive outcomes from the impact of the disease, such as personal growth and psychological adjustment. This adjustment, in turn led to improved QoL (using the PD HR-QoL tool, PDQ-39) scores in caregivers (Navarta-Sanchez *et al.*, 2016). Suzukamo *et al.* (2006) described the degree of psychological adjustment in PD patients having a greater impact on HR-QoL than the severity of their disease. This is of significance in atypical Parkinsonian disorders, which have more rapid progression and fewer treatment interventions than PD. If interventions to facilitate adjustment can improve HR-QoL in patients and caregivers, this might allow an avenue to improve well-being in a patient group with significant, progressive symptom burden. As associations between patient and caregiver QoL have been found in PD (Martinez-Martin *et al.*, 2005), it seems logical that attempts to improve both patient and carer well-being may be effective in the AP disorders.

1.3.4 Caregiving in MSA and PSP

There is a paucity of evidence for caregiver experiences specifically in the context of PSP and MSA. Uttl *et al.* (1998) investigated caregiver strain in PSP caregivers. It was found that strain increased with disease severity, then plateaued after 18 months. Patient aggression and low mood together with caregiver gender were reported to account for 37% of variance in caregiver strain (with female carers reporting more strain). Of relevance to caregiving in MSA and PSP, a study on caring in PD found correlations with caregiver stress and falling, neuropsychiatric problems and degree of disability. These are all problems which are usually seen earlier, and to a greater extent in AP compared to PD, particularly PSP (Schrag *et al.*, 2006c). From this work, it could be inferred that AP carers would be expected to have more strain than carers of people with PD. Qualitative work with PSP patients and their carers, found caregivers felt a burden of acting as educator, not only to the public about their relative's disease but to medical and community practitioners. The importance of support and information-provision in PSP is in keeping with the findings in caregiving in PD, in which support, even if not accessed ('perceived support'- the belief that help was available, should it be required) acted as a protective buffer against caregiver stress (Edwards and Scheetz, 2002; Martinez-Martin *et al.*, 2014; Greenwell *et al.*, 2015).

The understanding of the impact progressive disease has upon caregivers is established. In the context of PD, the interrelationship between the QoL of patients and their carers has been described, as well as certain factors which can worsen caregiver strain such as patient depression. Informal care provides the bulk of support for patients with a large hidden cost. Efforts to understand the impact of care in MSA and PSP are needed to try and support carers; which, in turn may confer a positive effect on patient QoL. This is one of the aims of this study.

1.4 Palliative Care

1.4.1 Definition of Palliative Care

The 2002 WHO definition of palliative care (PC) is '*Palliative Care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual'* (World Health Organisation, 2002).

The current definition of PC also takes account psychological and spiritual aspects of living with disease, the grieving process, quality of life and crucially, integration of PC to therapies intended to prolong life. There is also understanding of the needs of family and carers and how their needs can be addressed by comprehensive PC. PC should be utilised by existing healthcare systems to provide support throughout the course of illness. There is also the aim that PC should be offered across the health-care spectrum; by generalists as well as specialists and in community settings (Sepulveda *et al.*, 2002).

The current practice of PC arose from the care of patients with malignant disease. It is becoming increasingly apparent that patients with non-malignant, life-limiting conditions can benefit from a 'palliative approach'. Review of evidence outlined this approach as applying PC principles early (the 'upstream approach') and adapting current practice to new populations of patients and practitioners caring for them (Borasio, 2013; Creutzfeld, 2016; Sawatzky *et al.*, 2016). PC as an approach has a growing and important role in enhancing the experiences of patients with neurodegenerative disease and the people who care for them. Some of the characteristics of neurodegenerative diseases which lend themselves to the application of the palliative approach include prolonged morbidity with effect on QoL as well as social impact with issues which PC teams traditionally manage such as pain and nausea (Kristjanson *et al.*, 2003).

1.4.2 Specialist Palliative Care (SPC) versus the Palliative Approach

There is a distinction between clinical professionals who specialise purely in palliative care, whether in hospital, hospice or community settings, known as Specialist Palliative Care (SPC) and practitioners, clinicians or medical-team members who employ the palliative approach. Different authorities have defined SPC in different ways, depending upon tradition, changing times and region but at its heart, SPC is carried out by MDT teams whose purpose is the care of patients and families with palliative needs, chiefly who require this care due to complexity (NICE, 2004).

Interface between general and specialist palliative care

General Palliative Care (Neurology teams):
- Treatment of simple pain
- Treatment of simple depression
- Patient-centred treatment aims
- Discussing prognosis

Overlap:
MDT approach
Joint clinics/referral process
Sharing expertise

Specialist Palliative Care:
- Difficult pain management
- Significant distress from diagnosis
- Hospice services
- Very rapid or unexpected decline
- Mediation when conflict arises around treatment or futility

Figure 1.2: The roles of the palliative approach and SPC and their overlap from Wiblin (2017). General palliative care may be thought of as holistic or multidisciplinary care in the context of other conditions

The palliative approach is a style of care which can be employed by all medical and multidisciplinary practitioners. It considers the needs of the individual with chronic, progressive conditions, incorporating recognition of the whole person (not just medical needs), family needs and support in making decisions for the future. It can also be thought of as 'basic' palliative care, though a palliative approach undertaken by specialists in their own fields (such as renal medicine or neurology) can have profound and positive impacts on patients and families within the structure of a department very familiar with that type of disease (Sepulveda *et al.*, 2002). There are challenges to this, including constraints of time, education and confidence to use a palliative approach on behalf of the clinician and whether the constellation of problems the patient has is especially complicated (Fox *et al.*, 2016). This might prompt those familiar with the palliative approach to involve SPC. The distinction and overlap between the palliative approach and SPC is shown in figure 1.2

In the context of life-limiting illnesses with uncertain trajectories which require advance care planning and complex symptom management, describing the approach of care as 'a palliative approach' is appropriate. Other conditions which may have marked effects on QoL but without reducing life expectancy should have the benefit of a similar strategy with time, rapport and multi-disciplinary care emphasised; but perhaps should be known as a holistic or multi-disciplinary approach.

Increasingly, as the needs of patients with complex diseases are delineated, the requirement to familiarise clinicians with palliative approaches, to educate and create links with SPC teams will grow to maximise patient well-being and quality of care (see figure 1.3). Different geographies and healthcare systems will necessitate different models to embrace this concept. Rural areas may comprise of community teams linking up to a hospital specialist clinic. Very rare conditions could have a super-specialist team who could advise and guide local teams, particularly if the patient becomes too frail to travel to a distant centre. Handing over in a measured way with good communication to a colleague in community neurology or palliative care could maintain good care and connection with housebound patients. In the future, teleconferencing to allow liaising between teams, and possibly as a means for specialist review for patients too infirm to leave their homes, may offer an opportunity to continue a trusted relationship between a specialist and a family without a sense of abandonment when travelling to a clinic is no longer possible.
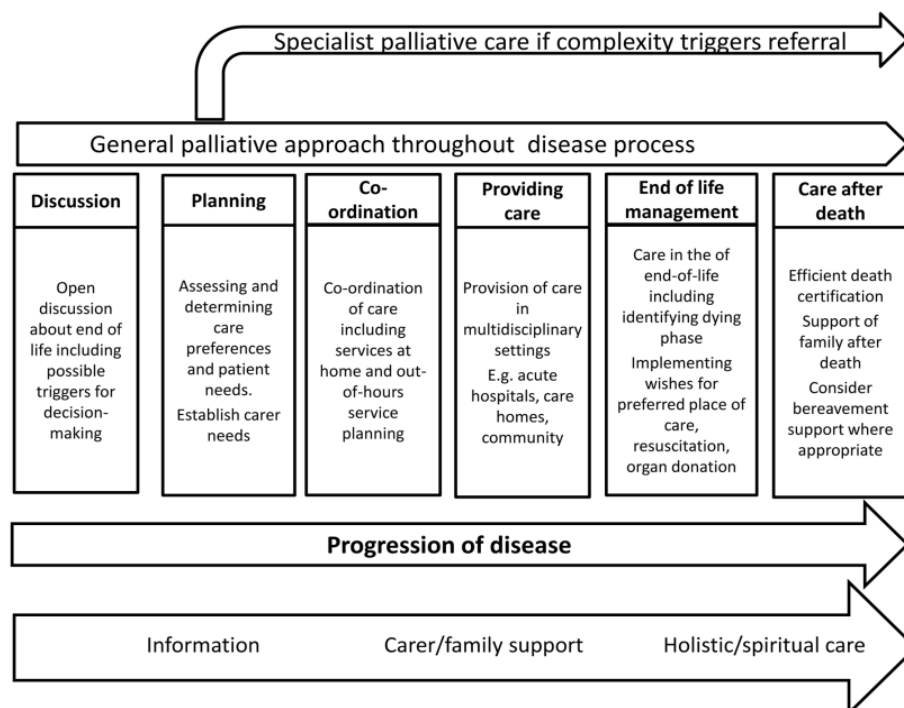
Figure 1.3: A model of the palliative approach as chronic disease progresses from Wiblin (2017)

1.4.3 Trajectories of decline and future planning

Patterns of deterioration in disease have been studied in an effort to allow identification of patients approaching the end of their lives, allowing planning and mobilisation of services such as PC, carer-respite and hospice services. Glaser (1968) described four distinct

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trajectories (though patients with the same disease may demonstrate different or mixed courses):

1. Sudden death (acute illness or accident).
2. Terminal decline, with low disability until a rapid decline is experienced. Classically described in cancer when the disease becomes refractory to life-prolonging treatment.
3. Frailty, portrayed as a steady decline with accumulation of morbidity eventually leading to death.
4. 'Organ failure' trajectory –background deterioration with unpredictable 'crises', leaving the individual with greater disability, should they recover. This gradual decline in a very heterogeneous group with the added strain of uncertainty of a sudden terminal event can be a huge burden for individuals and families, and difficult for clinicians to assess and treat appropriately. The neurodegenerative diseases, encompassing PD, MSA and PSP as well as renal failure and progressive lung problems like chronic obstructive pulmonary disease (COPD) often fall into this last category (Lunney *et al.*, 2002).

A prospective study of older people in nursing homes delineated their course of decline and how these were managed in the community. 'Uncertain dying' took place in 7 of the 23 deaths observed. The hallmark of the uncertain course was a lack of predictability and lack of clarity as to whether patients would survive the worsening of their condition. This led to hospital admissions and in one case, death in hospital, when the nursing home was the preferred place of death. This is very pertinent in neurodegenerative disease, AP in particular. There is early morbidity and a complex symptom load. Exacerbations precipitated by infection have the possibility of being the terminal event. Most patients with AP will be in the community (home or nursing home) when they experience an acute worsening of their condition (Snell *et al.*, 2009). Prior discussion and planning a setting for care may be reassuring for patients, relatives and medical and care practitioners, especially if patients cannot communicate their wishes by the time of the decline. By the very nature of fluctuating and heterogeneous (i.e. 'uncertain') neurological disease, it is difficult to anticipate time-frames and outcomes accurately, but this study suggests that it might be prudent to consider discussion and planning with patients. One trigger to discussion might be residing in a nursing home with a progressive disease. Work has been undertaken to try and understand patterns of change which might predict decline in neurodegenerative disease such as MSA and PSP to allow discussions, and mechanisms to bring in more support, such as physical symptom

control and carer assistance (see table 1.5). Planning and communication of uncertainty in a sensitive way can be thought of as part of the patient management within the palliative approach (Murtagh *et al.*, 2004; Barclay *et al.*, 2014).

Possible indicators of decline in MSA and PSP	
Weight loss	Aspiration pneumonia
Recurrent infection	Dysphagia
Increased frailty	Frequent hospital admissions
Significant cognitive impairment	Increased complexity of symptoms

Table 1.5: Features that may predict deterioration in MSA and PSP. From Wiblin (2017) and the National Council for Palliative care (2009)

Advance care planning (ACP) is a key part of palliative management which can empower patients and relatives by making their wishes known, especially if there is likely to be decline in cognition and/or communication as part of the disease process. ACP has been defined as decisions made by a patient, with the support and input of their medical team, family or friends, about their future care and preferences in the event they do not have the capacity to make decisions or communicate them meaningfully in the future (Detering *et al.*, 2010)Like all PC, this is a process rather than a single statement of intent to be completed, then filed away. Statements of treatment preferences such as whether an individual would want a percutaneous endoscopic gastrostomy (PEG) to permit feeding should swallowing become markedly impaired, should be re-explored where appropriate. This is because people's beliefs and choices can change over time. What may have seemed undesirable at an early stage of disease, such as a PEG, may now seem appropriate to the individual as they recalibrate and adjust to their new circumstances (Sudore and Fried, 2010; Bischoff *et al.*, 2013). Thus, reassurance that decisions are not 'set in stone' must be made. Patients can change their minds and the process should be more like a dialogue with patients, families and clinicians so that ultimately all the information possible is available for clinicians to facilitate informed decisions toward the end of life. This is particularly relevant if patients are no longer competent or able to take part in decisions as their disease advances (Sudore *et al.*, 2014). The other key point is that choosing *not* to consider the future in terms of treatment options and decisions for the future; relinquishing this responsibility to clinicians (aided by family input) is equally as valid a choice, and considers patient wishes. For some, these discussions may be frightening and unwelcome. PC ought to take each person's disease, outlook and evolving

ideas into consideration to improve their lives today and as disease evolves (Scott *et al.*, 2013). This reassurance is equally valid for family members with Lasting Power of Attorney (LPA) for Health, who may feel pressure to make difficult decisions for their family member, which can cause distress. They have the choice to defer their legal right to give a decision on behalf of the patient, should they wish to. Relatives with LPA may not be aware of this, and care should be taken to support them.

There is some evidence that ACP can improve the patient experience at the end-of-life as well as reduce family stress and anxiety after death. A randomised controlled trial comparing formalised ACP with usual practice in elderly patients in Australia found significant differences in wishes of patients being known as observed, improved patient satisfaction and depression scores in relatives after patients in the ACP group had died (Detering *et al.*, 2014). In terms of ACP when capacity is expected to be lost, possibly earlier in the course of disease due to cognitive decline or communication difficulty, it is important to recognise that the time for patients to consider and relate their wishes may be more limited, and patients and families need to be aware of this and supported through this to relay their preferences. Although there may be some interest to discuss these issues, it may be that the MDT needs to revisit and discuss these issues as patients and families may not take the initiative, which can be difficult when capacity could be lost in an uncertain timeframe. Work has shown that in a group of patients with dementia , patients and carers expressed some enthusiasm to make preparations and plans for the future but continued impetus was not maintained, especially if patients and families had to organise further discussions (Lewis *et al.*, 2015).

ACP has some evidence but is a difficult area to research, particularly in the context of cognitive impairment and collecting information at such a sensitive time as at the end-of-life. It has become part of SPC practice and is recommended as part of holistic care for progressive disease in the UK. ACP should be considered early in conditions with impacts on cognition and communication, which can add to the challenge of caring for these patient groups.

1.4.4 Palliative need in Parkinsonian disorders
In the Parkinsonian disorders, there is growing acknowledgement of the benefits for patients and carers in embracing a palliative approach to enhance management. In a study involving 109 patients with PD, symptom burden scores were comparable to that of patients with metastatic cancer (Miyasaki *et al.*, 2012). PSP and MSA patients reach clinical milestones

such as wheelchair-dependence or frequent falls earlier in their disease and can live with these accumulating burdens for some years (O'Sullivan *et al.*, 2008).

A longitudinal study of advanced PD, MSA and PSP over 12 months, measured palliative care need, symptom burden and QoL measures. Two thirds were living with profound symptoms and functional impairment. Most PSP patients had a Hoehn and Yahr score of 5, and nearly half (47%) had this score in MSA. Furthermore, half of the patients deteriorated in symptom burden or level of distress during the study; survival in MSA and PSP was poorer than in the PD sub-cohort. This suggests that the palliative care need in Parkinsonian disorders is present, serious and progresses over time. The observation that many of the symptoms which impact upon patients (such as pain and shortness of breath) are managed routinely and with effective interventions in PC settings for cancer patients, reinforces the appropriateness of a palliative approach in movement disorder services (Higginson *et al.*, 2012). In patients with severe neurodegenerative disease (including MSA and PSP), fast-track palliative care compared with usual care gave significant benefits in HR-QoL as well as pain, sleep-quality and bowel problems. An interesting finding was a decline in psychological well-being. One theory is that this may be due to patients facing the progression of their life-limiting illness. Although not discussed further, the process of adjustment might have been accelerated in this group by psychological interventions. Contrasting psychological well-being between the intervention group and the control arm after a period might have shown whether this was the case (Veronese *et al.*, 2015).

1.4.5 Barriers to Palliative Care

In practice, many practitioners find introducing PC as a concept to patients and relatives to be difficult. Barriers to accessing SPC have been explored in the context of cancer treatment in the USA. Analysis of surveys from practitioners identified inadequate training in the palliative approach and financial constraints to its use, preventing more extensive provision of PC to oncology patients in these centres (Davis *et al.*, 2015; Ramchandran *et al.*, 2015). A Japanese perspective showed a wide range of perceived barriers to PC provision from palliative care practitioners. These included inadequate training in communicating the nature of PC by non-specialists and poor public understanding. End of life care, euthanasia and palliative care were confused with each other (Miyashita *et al.*, 2007).

To explore acceptability and negative associations, the term 'palliative care' and 'supportive care' have been compared. Oncologists were recruited to explore with their patients, their perceptions of the terms 'supportive care' and 'palliative care'. Supportive care was seen more favourably by patients. Palliative care was described by some respondents as care given to people at the end of their lives, whereas the impression of supportive care seemed to be holistic, encompassing psychological support and information. One interesting inclusion in the article was the refusal of one oncologist to participate in the study as they did not want to use the term 'palliative care' with their patients (Maciasz *et al.*, 2013). This suggests that the perception of PC held by some physicians, as well as the public, remains in the end-of-life domain. Whether the 'brand' of palliative care needs to be reviewed by a name-change or by education, the obstacles to incorporating palliative management are multifactorial but perception plays a role. Might differentiating between general palliative care and end-of-life care improve acceptability of an integrated service?

Finally, as well as enhancing QoL it may be that patients who receive prompt PC have better outcomes. In patients with non-small cell lung cancer, early PC did not shorten survival. The early palliative care group actually had longer survival, required a shorter hospice stay at the end-of-life ('less aggressive end-of-life care') and significantly improved QoL and depression (Temel *et al.*, 2010). This suggests that early optimisation of symptom-control and contact with palliative care is of long-term benefit. It has been theorised that better QoL can produce survival benefit, at least in terms of non-small cell lung cancer (Movsas *et al.*, 2009; Irwin *et al.*, 2013). A study looking specifically at palliative care intervention in patients with PSP and CBS, found that after admission to a PC setting for symptom-control, 68% of admissions led to improvement or stabilisation of symptoms. 75% could be discharged home. There was marked burden of symptoms found in this group and the finding that hospice admission helped control these symptoms and in some cases, improve patient status and facilitate discharge, shows PC has a role in managing AP.

There is growing recognition of the benefit of the palliative approach in neurodegenerative conditions. Evidence is emerging showing AP patients would benefit from addressing palliative care need. Further work to explore the palliative need of MSA and PSP patients and QoL in patients and their carers may help develop interventions to improve QoL, especially pertinent with the reduced survival of these disorders.

1.5 Summary

Quality of life is an important issue to consider in the treatment of MSA and PSP. Given the multidimensional and subjective nature of QoL, one way to facilitate this is through assessment of palliative care requirement and application of a palliative approach. Diagnosis and management of AP is often not straightforward, as they are heterogeneous disorders with uncertain trajectories. This presents challenges for not only patients but also their carers and clinical teams hoping to treat and prepare patients for the future. This work hopes to clarify and discuss some of these issues, from the patient and carer point-of-view, with a mind to the clinician caring for patients with these complex conditions.

Chapter 2. Aims

The aims of this MD project will be explored over three results chapters and then evaluated in a discussion chapter. This project will explore the demographics of the patient and carer study cohort, the onset of important clinical milestones (such as need for a wheelchair) and their relationship to diagnosis. Palliative care need using a validated scale will be compared between the two disease groups and patients' understanding of palliative care services will be assessed. QoL will be compared between groups (patients and carers) using a range of measures such as disease-specific and subjective and factors which might predict for these different aspects of QoL will be analysed. The final results chapter will investigate the personal outlooks of patients and carers, using semi-structured interviewing with a sub-set of participants which will be thematically analysed. This aims to add a fuller, patient-centred dimension to this work.

2.1 Chapter 4 aims

In Chapter 4, the first aim was to determine whether the patient demographics of this cohort were in keeping with previously described literature on MSA and PSP. Following this, the second aim was to describe the onset of ten key clinical milestones and how they related to the time of their diagnosis. Thirdly, patients' symptom burden (palliative care need) in terms of features such as pain or depression were described and a validated scale for palliative care need (POS-PD) was completed by all patients in order to quantify and compare differences in symptom burden between MSA and PSP patients. Finally, perspectives on palliative care and its purpose were examined in the two patient groups.

2.2 Chapter 5 aims

In Chapter 5, QoL was explored in the MSA and PSP patient groups. The first aim was to appraise disease-specific QoL in participants with MSA and PSP and whether demographics or other study variables might predict for these scores using regression analysis. Secondly, subjective QoL using the SEIQoL-DW score was measured in MSA and PSP patients, their scores were compared to each other, and then whether any study variables might predict for these scores, again using regression. Finally, the domains participants nominated in the SEIQoL-DW were evaluated.

2.3 Chapter 6 aims

In Chapter 6, the demographics of the carer participants were assessed, and their level of strain and QoL were investigated using validated questionnaires. Firstly, demographic information was analysed using descriptive statistics. Secondly, caregiver strain was analysed using the MCSI; comparison was made between the two carer groups. Then study variables that might predict for MCSI were evaluated using regression analysis. Thirdly, a specific scale exploring QoL in carers of people with Parkinsonism was used, comparison was made between the two carer groups, and regression analysis was used to see if any study variables predicted for this. Lastly, subjective QoL was assessed using the SEIQoL-DW and regression analysis was used to look for predictors for these scores. Finally, comparisons between the two carer groups (and also the two patient groups) in terms of subjective QoL were made.

2.4 Chapter 7 aims

In Chapter 7, the aim was to explore the concerns and perspectives of a subset of participants (using purposive sampling to achieve a balance of viewpoints in terms of sex, patient and carer as degrees of severity, including communication difficulty) by analysis of semi-structured interviews. The goal in this section was to attain a rich, nuanced description of living with these conditions from a patient or carer perspective, which may provide insight on how clinical systems serve this group and avenues for meaningful research in the future. The semi-structured interviews were designed to give participants an opportunity to describe their experiences in-depth, but the schedule afforded guidance to the interviewer and participant to cover key topics such as the process of diagnosis, living with a chronic, progressive condition and outlooks on services such as palliative care.

Chapter 3. Methods

This chapter will describe the procedures and methods used in the study. Elements specific to particular chapters will be discussed in the respective introductions.

3.1 Methodology

This study used both quantitative and qualitative methods. Each of these distinct methods uses different assumptions and has advantages and disadvantages in their application. I will discuss these two paradigms and the reasons for their use in this study.

3.2 Quantitative methods

Quantitative methods seek to explain observations numerically, usually by the application of statistics or other mathematical modelling. The quantitative paradigm assumes positivism (a fixed reality which is not affected by observer perception), which is reliant on certain assumptions such as empiricism or measurement of observable phenomena, that scientific method is value-free, and that subjective perceptions or beliefs have no bearing on the scientific truth. Positivism was developed in the context of the natural sciences (Green and Thorogood, 2014).

A theory or hypothesis is tested by measuring variables and analysing relationships or making predictions from this. It is assumed that the researcher is objective during this process and their attitudes should not influence what is being studied. To this end, many techniques have been developed to enable this, including randomisation, blinding, and highly structured procedures/protocols to produce standardised responses that are amenable to numerical analysis and to reduce bias. The results generated are therefore considered to be generalisable beyond the sample of the population studied. The quantitative model is deterministic (meaning that actions and events cause or determine further events) (Sale *et al.*, 2002; Yilmaz, 2013).

In order to allow quantitative analysis of trends or perceptions in a population, structured surveys can be used which produce objective and comparable results which can then be generalised from the study population to wider populations (Creswell, 2009b). The quantitative method can be summarised as requiring a hypothesis or theory which the

researcher then seeks to disprove using formal experiment and deduction. Table 3.1 covers some strengths and limitations of the quantitative approach.

Key Features in the Quantitative Approach	
Useful in establishing extent of correlations, associations and predictions	Lacks flexibility
Empirical method reproducible and more objective	Does not permit recognition of human behaviour as unpredictable and varied
Efforts to be objective methods to reduce bias (important in randomised controlled trials)	Large numbers preferable to provide sufficient statistical power
Generalisable	Experiences must be "fitted" into fixed responses e.g. closed response questionnaires
Results can be summarised succinctly (numerically)	Statistical analysis may produce a simplification or misleading view of phenomena

Table 3.1: Features of the quantitative paradigm in research. From Green and Thorogood (2014), Baum (1995) Yilmaz (2013) Klassen et al. (2012)

3.3 Qualitative methods; considerations, thematic analysis

Qualitative methods cannot be defined by their methods of data-collection, nor by the type of data collected; though qualitative methods do tend to use language-based data rather than numerical and use certain techniques such as interviews (though quantitative methods may explore linguistic data or use interviews in some cases) (Green and Thorogood, 2014).

Whereas the quantitative method tests a theory via measurement and statistical analysis of the relationship between variables, the qualitative method attempts to describe the 'how' and 'why' of phenomena. The aim is to understand more about subjective perceptions of a subject rather than seek to measure variables on the subject (Pope and Mays, 1995). The overarching qualitative method (which comprises of many theoretical and epistemological schools) is defined by Gay and Airasian as *'the collection, analysis and interpretation of comprehensive narrative and non-numerical data to gain insights into a particular phenomenon of interest… qualitative researchers do not necessarily accept the view of a coherent and stable world.'* (Gay, 2013). Although there are many differences in qualitative methods and theoretical stand-points in this diverse approach, some commonalities can be seen in qualitative work, which I have discussed below. Figure 3.1 shows the hierarchy of standpoints in research, from the overall theory of knowledge, down to methods or techniques used.
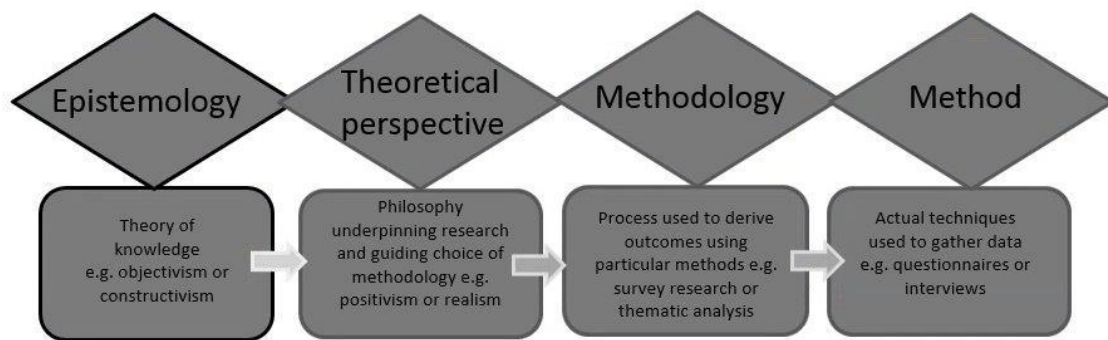
Figure 3.1: Hierarchy of understanding in research theory and positions. From Gray (2014) and Crotty (1998)

Interpretivist: In contrast to the positivist philosophy espoused in quantitative work, many qualitative methods are based within interpretivism. This describes the differences between the natural reality which can be explained by laws of science (for example, gravitation) and the social reality of how individuals perceive events and therefore how their behaviour is affected. Consequently, the methods used to attempt to understand and explain human behaviour must be distinct from the empirical methods of natural science, trying to take this individual reality into account. This is important in the context of health and social sciences, where human factors and the interplay with disease require an understanding of why people behave how they do, to understand how to better manage healthcare (Gray, 2014; Green and Thorogood, 2014). There are 'intermediate' standpoints. The standpoint of realism has some features in common with positivism in that it states that there is a reality that can be understood. Critical realism tries to integrate natural sciences and the social sciences. A researcher can use analysis and generate theory in order to better understand the social reality they are studying, in order to try and produce change or improvements (this is a commonly subscribed theory in economics and the social sciences) but the researcher's concept of reality is not the *only* reality (as positivism would have it) (Fletcher, 2017).

Naturalistic: Bearing in mind the contextual importance in human behaviour, qualitative methods recognise the importance of research in as-natural an environment as possible to try and capture a more realistic view of the subject. In-depth interviewing is one approach to this. It must be kept in mind however, that the setting of an interview is still fairly artificial, though may allow a more natural response than techniques used in quantitative work (Bryman, 2008b). Table 3.2 discusses some of the strengths and limitations of the qualitative approach.

Flexibility: a process of ongoing reflection and refinement of methods, allowing modification of the research method and question as analysis is carried out (Braun and Clarke, 2006).

Key Features in the Qualitative Approach	
Produces rich, detailed accounts exploring the 'why' of phenomena	Lacks reproducibility and generalisability
Small samples can be used; useful for rare conditions	Methods to ensure transparency and rigor less defined
Flexibility of approach	More difficult to succinctly represent results
Allows contextual understanding of different viewpoints	Researchers must account for their own beliefs in their analysis (reflexivity)

Table 3.2: Features of the qualitative paradigm in research. (Bryman, 1984) (Sale et al., 2002; Bryman, 2008b; Yilmaz, 2013; Green and Thorogood, 2014)

A plethora of methods exist within the qualitative armoury, such as observational ethnography, focus groups, in-depth interviews and analysis of written documents. This project has used a combination of quantitative methods, namely validated questionnaires and structured clinical examination, together with semi-structured participant interviews. These methods were selected pragmatically to achieve meaningful results allowing comparison, correlation and some prediction between conditions as well as exploring perspectives on living with these rare conditions, and their impact upon the individual.

3.3.1 Thematic analysis

Thematic analysis (TA) is increasingly seen as a key method in qualitative analysis, one reason being that learning to generate themes is held in common throughout many techniques used in the qualitative approach. Although some qualitative researchers regard thematic analysis as a technique learned within different qualitative disciplines, Braun and Clarke (2006) argue that thematic analysis is a practical method in itself which can be carried out in a systematic way, yet with the advantage of flexibility. This flexibility is borne of thematic analysis' freedom from theoretical constraints and assumptions which other techniques such as Grounded Theory (producing a theory from the data 'grounded' within it) are subject to (Charmaz, 2006). This can be understood by TA being a method or technique rather than a theory-embedded methodology that can be employed within many theoretical models as appropriate (Braun and Clarke, 2013).

TA of in-depth interviews was selected as the analytical method for this research project due to its versatility and the key feature of producing themes to give nuanced views of data, themes being a common feature of many types of qualitative methods. Although many studies which use TA as a method claim to adhere to Grounded Theory (GT), they may not fully conform to the true methodology, as GT requires the ground-up production of theories from data collected, without preconceptions from previous literature. The defined research aim (crucial in most research proposals in terms of ethical and funding applications) are also not true to GT which requires the question to be generated as the data is collected and analysed (Bryman, 2008b; Creswell, 2009b).

The suitability of TA to this study is its power to allow detailed description of heterogeneous subjects (participants with differing conditions at varying stages of severity, carers of differing ages, and sex) and explore similarities or differences. The flexibility of TA is helpful considering the theoretical stance of the project; a compromise between an inductive approach to the data, making conclusions from ongoing analysis but conceding that some deductive (theory-driven) element exists, in that a prior literature review took place and a research aim was in place from the beginning, albeit a broad one (Boyatzis, 1998; Frith and Gleeson, 2004).

3.3.2 Assumptions and standpoints at outset

It is important to define viewpoints and the position of the interviewer at the outset of a qualitative project, as reactions to different individuals may vary (for example, participants may respond differently to men and women interviewing). These declarations are important in terms of transparency and trustworthiness in qualitative work (Golafshani, 2003). I have laid out these statements below.

As the interviewer carrying out the interviews, I was also a clinician with prior doctor-patient relationship with many of the participants. This may have affected the power dynamic of the interviews and the discussion of disease and perspectives on clinical input by the participant. In some cases, it was difficult to widen the focus of interviews, at least initially, as participants (particularly patient-participants) seemed to treat the interview as a clinical consultation and described their symptoms, though all were able to give wide and varied accounts; the semi-structured design of the interviews was helpful with this.

The approach taken to analysis was mainly an inductive or data-driven one, rather than imposing pre-conceived theory upon the data. However, a literature review was carried out in preparation of the project as well as conceiving the research aim prior to beginning data collection. Therefore, some theoretical context was known before data collection in relation to the research question.

The theory of knowledge held when the project was designed was a realist one, assuming that that individual's perceptions and motivations have a straightforward relationship with language used. The contrast to this is constructivism, which considers the psychosocial frameworks that bring about individual's responses rather than the meanings of individual responses themselves. Realism looks for meaning in the individual's descriptions whereas constructivists are concerned with contexts and interactions and how these might shape individual accounts (Braun and Clarke, 2006; Creswell, 2009b; Gray, 2014). Throughout the project, my standpoint did not alter and I feel the epistemology remained realist throughout data-collection and analysis.

3.3.3 Sampling for qualitative phase

Sampling from the quantitative arm of the study for the interviews was conducted using purposive sampling rather than random selection from those who consented to being included in the interview arm. This was to achieve good representation of different groups for example, patients and carers, MSA or PSP carers, male and female and different stages of severity/communication ability. Some special sampling was used to include participants with marked communication problems as their contribution was seen to be especially valuable, as previous research has not included participants with these difficulties. By necessity, pragmatism had to be used as many of these patients have advanced, complex disease so participants who interviewed were selected purposively in the main, but were those who were physically well enough during the data-collection period and were enthusiastic to take part. This is a limitation to be aware of, though efforts were made to interview as diverse and representative a range of individuals as possible (Pope and Mays, 1995; Plano Clark, 2008).

3.3.4 Process of Thematic Analysis

Practitioners of TA, like GT have sought rigour in terms of the process of analysis. Braun and Clarke (2006) have described guidelines to this process. It is an essential part of the

qualitative approach to remember that throughout data collection, transcription and analysis, a cyclical process should be followed rather than a linear one. The data, codes and themes should be revisited and re-explored as the project advances and is analysed (Bryman, 2008b). See figure 3.2.
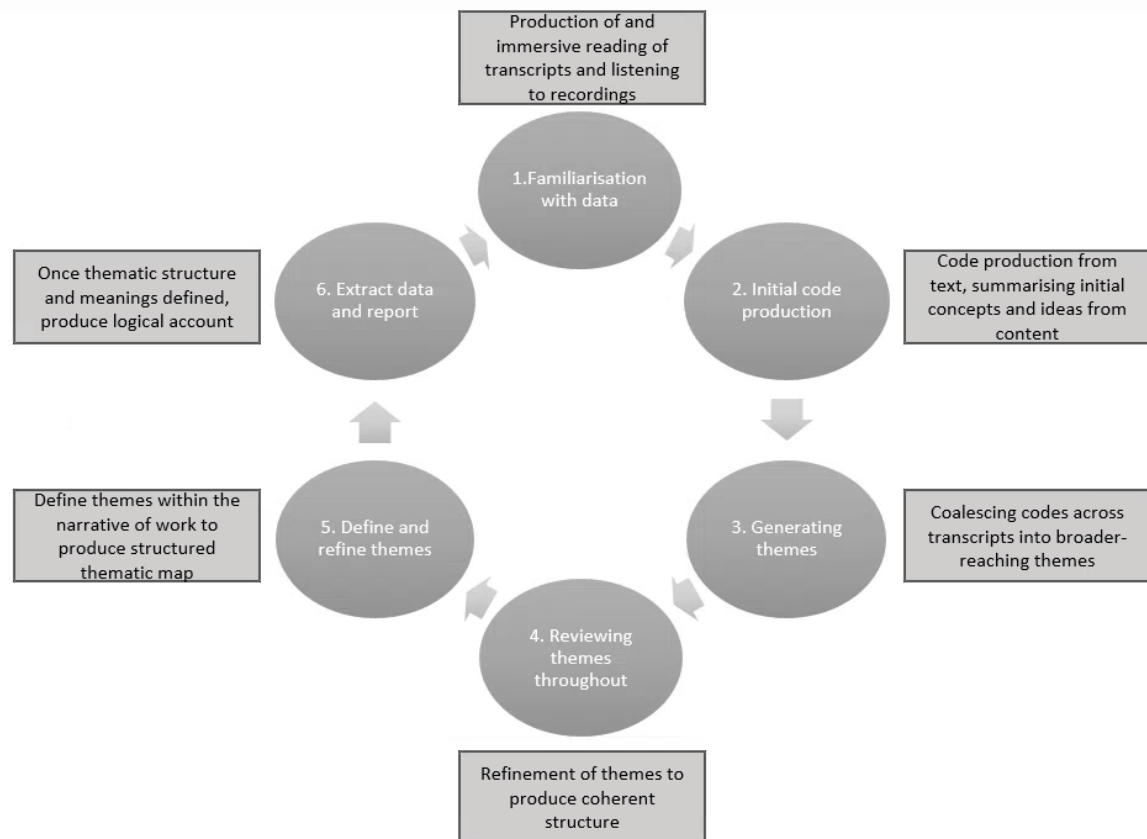
Figure 3.2: Stages of Thematic Analysis from Braun and Clark 2006

The data produced from interviewing of participants is extensive. Some of the interviews were transcribed by the primary researcher, namely the first two to allow familiarization of the process and appreciation of the process of verbatim transcription, as well as interviews which were challenging to transcribe due to speech difficulties or semantic problems of the participants. Others were transcribed by a reliable transcription service which has been used by Newcastle University and local NHS services in the past.

When transcription was completed into a Word file, repeated reading and note-taking began, coupled with listening to the original recorded interviews to ensure context and meaning were not lost, including non-verbal responses, pauses and intonation affecting meaning (especially

if the transcript was produced by the transcription service). Field notes were also considered during analysis. Codes were then produced. Coding gives a name to a section of data in an effort to sort and understand it (Charmaz, 2006). In this report, codes are distinct from themes, the latter being a more refined, and overarching product of analysis of constituent codes produced from the data. Coding was data-driven (derived from the data available rather than codes produced looking specifically in response to research questions and then data 'fitted' into it, though as the interviews were semi-structured, some *a priori* theoretical 'scaffold' does exist.

As codes were produced from interviews, themes began to coalesce from the many codes generated. Themes are patterns within the data, seen by the process of encoding it and permits explanation or interpretation of an aspect of the data (Boyatzis, 1998). At this point, reviewing literature against these themes and reviewing the coding as well as thematic structure began. Themes were then defined and labelled and the report was constructed using meaningful extracts from the data to support the analysis (Braun and Clarke, 2006; Braun and Clarke, 2013). Interviews were ongoing throughout these stages and ended when no more important patterns were recognised during analysis. Nineteen interviews were carried out in total, above the initial estimate (of ten), as saturation was not felt to occur until that point. Theoretical saturation, originally defined in the context of GT, describes the point at which no new insights are being added by further data collection (Bryman, 2008b).

3.4 The Mixed Methods approach

Quantitative and qualitative methods, as discussed above, have different strengths and limitations. To try and embrace this, a combination of methods, the concept of 'mixed methods research' integrates these paradigms together to gain a more comprehensive view. The aim of mixed methods work is to offset the perceived failings of one outlook by using techniques from the other. There are varying definitions and approaches to mixed methods research and there does not need to be equal weighting of the two disciplines; a study may have a majority of quantitative method yet still conform to a mixed method model for example (Bryman, 2008a)

There are some proponents that claim mixed methods as a concept is not feasible as the quantitative positivism and qualitative intrepretivism are at odds. Therefore, how can they be combined? Pragmatism tries to reconcile these viewpoints by seeking to adhere to a position of compromise. It states that an ideology is of no use if its paradigm acts to constrain the

acquisition of knowledge and a more 'realistic' view of the world. Therefore, a research outlook should be based on an intermediate standpoint, taking into account elements of positivism and interpretivism, provided this stance allows the acquisition of knowledge which will bring benefit to learning and/or society. In some ways, pragmatism *requires* the combination of quantitative and qualitative techniques, else there cannot be truly nuanced understanding of complex subjects where there is a combination of numeric and human factors, such as those found in medicine and economics (Feilzer, 2010)

There are a number of ways that methods can be mixed. There are also a number of terms to describe how the combining of methods can be achieved and what form of mixed methods project will be produced. One type of mixed method construct is sequential design. Either a quantitative portion can precede a qualitative portion (explanatory sequential - the qualitative work is guided by the typically greater weighting of the quantitative work) or initial qualitative data informs what quantitative data is gathered (exploratory sequential). Other techniques may be embedded, collecting quantitative and qualitative information simultaneously. Data is often transformed so that it can be integrated together meaningfully for analysis. This is often described as 'triangulation' in which multiple data types collected by differing methods are analysed together to seek validity and consistency of findings. There are arguments that qualitative data cannot be 'numericised' or made to fit in with quantitative work in a way that retains its content, though matrices, sometimes using computer software are available (Bryman, 2008a; Bryman, 2008c; Creswell, 2009a).

Mixed method studies cannot be assumed to negate the inherent problems in quantitative and qualitative research but a well-designed project may produce a richer and more considered perspective on complex research questions.

Is this project a mixed methods study? I would argue that, despite the advantages of claiming it as mixed methods, it is not truly so. It could be posited that the study takes the form of a sequential mixed methods project with a degree of results-combination at the point of analysis. However, I would argue that mixed methods studies require integration; either at the data collection or analysis stage (or both). This study evolved from a purely quantitative study mainly concerned with exploring QoL. The importance of subjective QoL became clear during the planning and literature review stage and this then led naturally to the utility of qualitative interview work as a means to gain detailed, personal accounts from participants using qualitative analysis. There was separate analysis and then results were described in a complementary but not integrated way. Therefore, this study could be described as using

quantitative and qualitative methods to achieve fuller, richer conclusions rather than sequential mixed methods work.

3.5 Quantitative and qualitative summary

Quantitative and qualitative methods have differing approaches and outlooks. Pragmatically, these approaches can explore different problems or issues in different but often complementary ways. For example, a positivist, deductive outlook using a quantitative approach in drug trials to reduce bias, allows comparison and summarises results parsimoniously, which is important when judging the safety and efficacy of a drug. An aspect of the drug trial which requires a more subjective view, is exploring the reasons people have for taking part in a drug trial. This would suit a qualitative approach, perhaps using interviews or focus groups and a range of qualitative methodologies such as grounded theory or thematic analysis. Some research seeks to use the strengths of these approaches together, employing 'mixed methods', overcoming conflict between the two paradigms. This can be done in different ways but all combine quantitative and qualitative methods to look at the same data, known as triangulation (Plano Clark, 2008).

This project is not a true mixed methods study according to this definition, as it uses the quantitative approach for some of its aims and a qualitative approach to others without trying to integrate the results. It uses these paradigms in a complementary fashion, seeking a more holistic view of the overall conditions being investigated. However, this project does use some mixed methods, especially when interviews' overarching themes are compared with their SEIQoL-DW nominated areas (which were gathered in the quantitative portion of the study). This was an effort to understand if the more concise SEIQoL-DW can act to capture some of the concerns voiced by participants in their interviews (which are shown in Appendix C).

3.6 Evaluating research validity

In quantitative, cross-sectional research, quality is measured by replicability, reliability, and validity. In this study, efforts were made to ensure:

Replicability by using a defined protocol of questionnaires and examination instruments for each participant group e.g. MSA patient, PSP patient, MSA carer or PSP carer. This could be

carried out by a research practitioner (with training in the use of the instruments employed) if they had access to the protocol.

Reliability or consistency of a measurement. All questionnaires used in the study have been deemed reliable in multiple studies looking at Parkinsonism or care-giving.

Validity or whether an instrument intended to measure something actually does so. There are different ways to consider this. Face validity, at the most basic, shows whether an instrument seems to assess what is under study e.g. QoL. This is usually appraised by an expert or body of experts. Other forms of validity include content validity (whether important points on the topic are included) and construct validity (whether the tool can give information which cannot be derived by direct observation) (Golafshani; Bryman, 2008b; Dowrick *et al.*, 2015).

All questionnaires used in this study have been found to be reliable in patient and carer groups and have been validated in Parkinsonism or caregiving. Any non-validated information, e.g. disease duration, was recorded in identical fashion using standardised pro-forma.

In qualitative research, the quality of analysis is described as reliability or validity. Although these terms are interpreted in different in different ways by various practitioners, trustworthiness and credibility are frequently used to encompass the need for quality and rigor in interpretivist work (Golafshani, 2003; Bryman, 2008b). Criticism of validity and reliability, as applied to qualitative research, are that many of the underlying principles have parallels with quantitative analysis, indeed they were developed from that paradigm. For example, validity as whether 'you are observing, identifying or "measuring" what you say you are' (Mason, 1996). Methods like using inter-user reliability (another researcher to 'test' codes produced) are not helpful if there is an assumption that there is a subjective reality of both the researcher and the subjects involved.

By contrast, Yardley (2000) suggests four alternative criteria which they nominate as being more appropriate for the qualitative approach:

1. **Sensitivity to context**: the context including potential ethical, psychosocial and theoretical issues

2. **Commitment and rigor**: having the appropriate expertise, wish to engage with the topic under review and methical process of collecting and analysing data

3. **Transparency and coherence**: definition of methods used and declaration of researcher assumptions, belief and motivations (reflexivity)

4. **Impact and importance**: will the work have implications for academic theory, the group under study (and in clinical or applied humanities work) will it influence policy or practice?

Published qualitative work often uses the COREQ (Consolidated Criteria for Reporting Qualitative Research) guidelines as a means to evaluate how the research was carried out, standpoints of the researchers, and a check for quality without imposing positivist ideals on the work. The COREQ is divided into three domains; research team and reflexivity, methods and analysis, and findings. The COREQ covers the similar points as Yardley, but in a more structured way, which can be reassuring for those seeking rigour in qualitative work using different methods and viewpoints (Tong *et al.*, 2007). A COREQ checklist is included in Appendix E.

There are many different criteria to try and appraise the quality of qualitative work. As opposed to quantitative studies which can summarise method, methodologies and results succinctly, the subjective and diverse nature of qualitative approaches make this more complex. However, maintaining as much of an understanding of prior assumptions and how this may affect the process of data collection and analysis is imperative to having rigorous and reflexive practice.

3.7 Procedures

3.7.1 Ethics

Ethical permission for this study was sought from and granted by Yorkshire & The Humber – Bradford-Leeds Research Ethics Committee via proportionate review. Newcastle upon Tyne Hospitals Joint Research Office sponsored the study. St Benedict's Hospice, Ryhope and James Cook University Hospital, Middlesbrough acted as Participant Identification Centres with permissions obtained from their local research and development departments. Participation in this study was voluntary and required informed consent.

3.7.2 Protocols and visit plan

The study was a pilot observational, cross-sectional design. Potential participants had a known diagnosis of Multiple System Atrophy or Progressive Supranuclear Palsy and an informal (not paid) carer. Participants were identified via the Newcastle upon Tyne Hospitals NHS Foundation Trust movement disorder service, South Tees Hospitals NHS Foundation Trust Neurosciences movement disorder service or St Benedict's Palliative Neurology-themed clinic. Potential participants were given Participant Information Sheets at clinic with contact details of the PI should they have any questions. The PI would discuss the information with them (if present in the clinic) or would contact after a week, should the potential participant have completed a 'permission to be contacted' form. If participants were willing to take part, after time to consider and opportunity to ask questions, a research visit at CRESTA clinic, Newcastle Hospitals, St Benedict's Hospice, or a home visit was arranged at a time suitable for the participants. The clinical (questionnaire-based) portion of the study was completed in the majority of cases within a single visit. The tasks that required a researcher to assist were prioritised so should the participant become fatigued the remainder could be completed in their own time and posted with a postage-paid envelope left for this purpose. Telephone support to complete these questionnaires was offered, though was never required. Different QoL measures were recorded on the same day wherever possible, so that direct comparisons could be made, although participant fatigue was considered and visits were split if required. Table 3.3 shows the protocol for patient-participants in both groups. Table 3.4 shows the protocol for carer-participants of both groups.

PSP patient-participants	MSA patient-participants
Consent process	Consent process
Demographic information	Demographic information
Hoehn and Yahr staging	Hoehn and Yahr staging
Progressive Supranuclear Palsy Severity Scale (PSPRS)	Unified Multiple System Atrophy Rating Scale (UMSARS)
Progressive Supranuclear Palsy Quality of Life Scale (PSP-QoL)	Multiple System Atrophy Quality of Life Scale (MSA-QoL)
Short Form/RAND 36 (participant-reported measure of health status)	Short Form/RAND 36 (participant-reported measure of health status)
Bristol Activities of Daily Living Score (BADLS)	Bristol Activities of Daily Living Score (BADLS)
Palliative care/Patient Outcome Score (POS-S-PD)	Palliative care/Patient Outcome Score (POS-S-PD)
Depression Anxiety Stress Scale (DASS-21)	Depression Anxiety Stress Scale (DASS-21)
Schedule for Evaluation of Individual Quality of Life - Direct Weighting (SEIQoL-DW)	Schedule for Evaluation of Individual Quality of Life - Direct Weighting (SEIQoL-DW)
If purposively selected and consented to do so, semi-structured interview	

Table 3.3: Protocol of questionnaires for MSA and PSP patient-participants

PSP carer-participants	MSA carer-participants
Consent process	Consent process
Demographic information	Demographic information
Modified Carer Strain Index (MCSI)	Modified Carer Strain Index (MCSI)
Parkinsonism Carers Quality of Life questionnaire (PQoLc)	Parkinsonism Carers Quality of Life questionnaire (PQoLc)
Short Form/RAND 36 (participant-reported measure of health status)	Short Form/RAND 36 (participant-reported measure of health status)
Schedule for Evaluation of Individual Quality of Life - Direct Weighting (SEIQoL-DW)	Schedule for Evaluation of Individual Quality of Life - Direct Weighting (SEIQoL-DW)
If purposively selected and consented to do so, semi-structured interview	

Table 3.4: Protocol of questionnaires for MSA and PSP carer-participants

If participants gave their consent for a semi-structured interview and were purposively selected, the participant was contacted to arrange a further research visit in CRESTA, St Benedict's clinic or a home visit as chosen by the participant. Interviews were carried out after consent was re-discussed and confirmed. A digital recording device was used to capture interview content. All participants interviewed consented to a recording being made. A semi-structured sequence of questions was used to guide the interview if required for both patient-participants and carer-participants. The style of interview was, in part, a traditional social science interview with set open-ended questions (responding to answers with follow-up exploratory responses to elicit a more thorough reply) and a pragmatic interview, seeking input on problems and issues which could be developed into possible solutions or approaches. An interview guide or schematic was drawn up with the assistance of Dr Katie Brittain (KB) who has expertise in interviewing practice and with reference to literature (see Appendix B). The advantage of such a framework is that it allows flexibility but within a structure which ensures key points or questions are relayed to the interviewee. The framework is especially helpful in keeping 'on topic' when there is limited time or participants may be at risk of fatigue, so the crucial research areas are explored with the interviewee (Patton, 2015). The question structure appeared to allow participants to discuss their experiences according to their personal perspectives, whilst addressing the research questions. No changes to the semi-structured interview format were made throughout the qualitative portion of the study consequently, and to maintain consistency.

3.7.3 Sampling

The study aimed to recruit a minimum of 20 patients with MSA and 20 patients with PSP with their carer, totalling 40 patients with atypical Parkinsonism and 40 carer-participants.

There was no upper limit of recruitment and recruitment was scheduled to end in December 2016 to allow sufficient time for data processing and analysis. All patients and carers underwent the questionnaire portion of the study. These numbers were selected as a feasible number for the clinical sites involved in the study, the time the study would be conducted over and estimates that pilot work should generally aim to have 10-40 participants per group to try and establish some significant findings within the confines of preliminary work. This range of 10-40 per group is often described for rare conditions or difficult-to-reach populations, as in this study (Hertzog, 2008). No upper limits were selected to maximise the significance of statistical analysis in the quantitative arm and to allow for saturation in the qualitative arm (discussed in the Qualitative methods section). Sampling and statistical analysis methods were reviewed by a statistician at intervals throughout the project.

A subgroup of patient and carer-participants was selected for semi-structured interviews using purposive sampling to explore experiences and concerns around living with atypical Parkinsonism, the process of diagnosis and perceptions of palliative care. 37 of the 47 patient-participants and 40 of the 46 carer-participants consented to being considered for the interview arm. 14 participants (six patient-carer pairs, one individual patient-participant and one individual carer-participant) were approached to interview but this did not take place due to illness and difficulties scheduling interviews with their other commitments such as respite, appointments and holidays. As well as the interviews, QoL questionnaires, depression questionnaires and carer-strain questionnaires were carried out privately to avoid bias or pressure on the participant when discussing personal or emotive issues.

3.7.4 Data entry
Hard copies of participant clinical research data (case report forms, CRF) were held within a secure document storage facility within the Clinical Ageing Research Unit (CARU), accessible by the PI and relevant regulatory individuals (sponsor, auditing and quality team). Research data from patients, including transcripts were stored on a university computer with a password protected login. The data was anonymised so not to permit identification of the participant without the demographic data (which was held in the Master Site file, in the secure document storage facility within the CARU). Data was entered onto a purpose-built Excel template designed by the PI and re-checked prior to analysis. Transfer of data from Excel was carried out using the import function of statistics package IBM SPSS Statistics for Windows, Version 22.0. (Armonk, NY: IBM Corp).

3.7.5 Clinical issues

In the event of concerns being elicited during the research visit, the PI (an experienced neurology clinical practitioner) was able to assess whether urgent intervention was required in the context of the patient-participants' neurological disease. Any routine observations which came to light from a neurological point-of-view were communicated by letter to the patient's Neurology consultant and/or Parkinson's disease Specialist Nurse. Notice of patient-participants' involvement in the study was routinely communicated by letter to their General Practitioner (GP); the GP was contacted by telephone and/or letter should any observations be made that might require medical input or review. Carer-participants' GPs were not routinely informed of their involvement within the study but the protocol and consent forms discussed that any issues that might arise from a clinical research visit would be discussed with the appropriate GP or practitioner if there was concern for the participant from a physical or mental health perspective. This did not arise during the study.

3.8 Inclusion and exclusion criteria

3.8.1 Inclusion criteria

1. Diagnosis of PSP or MSA according to clinical coding and inclusion on specialist clinic lists and clinical database. During the study process, patients were reviewed against the consensus statement diagnostic criteria for MSA or NINDS-SPSP for PSP.

2. Patient has regular carer who provides majority of care (not a paid employee).

3. Valid, written, informed consent given by patient and carer to take part.

4. Ability for carer and patient to give interviews in English, which can be recorded and transcribed.

5. Ability to travel to CRESTA/St Benedict's clinic for interviews and to use telephone for surveys or receive home visit by PI

3.8.2 Exclusion criteria

1. Diagnostic uncertainty

2. Difficulty of communication at primary interview stage

3. Irregular or paid carers

4. Inability to consent to inclusion in the study

3.8.3 Duration of participant participation

Participation in the study ranged from one day to four weeks, depending upon whether they consented to and were selected for interviewing after the quantitative battery of questionnaires. There were never more than three contact visits for any participants, this being on the rare occasions that a 'split' visit was required to allow participants to complete the questionnaires and then took part in interview.

3.9 Questionnaires

A number of questionnaires and scales were used in this study. I will briefly describe each measure and the rationale for its use below. Several scales such as severity scales (PSPRS and UMSARS), HR-QoL scales (MSA-QoL and PSP-QoL) and POS-S-PD are the only widely-known and validated scales in AP. All questionnaires can be found in Appendix A.

3.9.1 PSPRS (Progressive Supranuclear Palsy Rating Scale)

A dedicated rating scale for PSP, developed by Golbe and Ohman-Strickland in 2007 and called the Progressive Supranuclear Palsy Rating Scale (PSPRS). Prior to this, severity was assessed by PD-specific rating scales such as the UPDRS (United Parkinson's Disease Rating Scale) but such scales do not capture symptoms or signs which might be expected in PSP (Cubo *et al.*, 2000). This score was developed longitudinally with a cohort of 162 patients with PSP of varying severities and subtypes. The overall score for the PSPRS is between 0-100 and has 6 sub-categories (history, behaviour, bulbar, ocular, motor and gait). The scale has good inter-rater reliability. The PSPRS is frequently used in clinical research studies as a specific measure of severity in PSP (Schrag *et al.*, 2003; Boxer *et al.*, 2014; Bang *et al.*, 2016).

3.9.2 UMSARS (United Multiple System Atrophy Rating Scale)

The Unified Multiple System Atrophy Rating Scale or UMSARS is a disease-specific scale which was developed by Wenning *et al.* (2004). Originally developed with 40 MSA patients of both subtypes, diagnosed according to the (first) consensus criteria. It is reliable and valid for assessing severity of MSA. The scale is divided into four parts; history, motor system examination, autonomic and disability rating. The UMSARS uses a 1-5 Likert scale for the history and motor sections comprising of a 12-question symptom review and a 14-point examination. The autonomic section measures their lying and standing blood pressure and heart rate. The UMSARS is owned and recommended by the MDS and has been used extensively in clinical research studies (Novak *et al.*, 2012; Low *et al.*, 2015; Ahn *et al.*, 2016).

3.9.3 RAND-36

The RAND-36 or Short Form (SF)-36 was selected as a generic health status score (though described by the authors as a health-related QoL score) (Ware and Sherbourne, 1992). The SF-36 was developed with a cohort of over 2000 Americans with chronic diseases ranging from hypertension to depression (Tarlov *et al.*, 1989). The SF-36 (the RAND-36 being the version in the public domain) has been used extremely widely in many groups including PSP, MSA and Parkinson's disease patients (Den Oudsten *et al.*, 2007b; Pekmezovic *et al.*, 2015; Kubo *et al.*, 2016) as well as in carers of individuals with serious health conditions including Parkinsonism to allow comparisons between patient and carer (Schrag *et al.*, 2006c; Greenwell *et al.*, 2015; Corallo *et al.*, 2016). The RAND-36 comprises eight sub-scores evaluating different dimensions of well-being such as physical functioning, role limitation due to physical problems, role limitations due to emotional problems and energy/fatigue. Two overall scores; physical and mental composite scores (PCS and MCS) can also be derived from the eight sub-scores. It is straightforward to complete and takes between 10 to 20 minutes to administer (Ware and Sherbourne, 1992). The SF-36 is recommended as a possible tool for assessing well-being in Parkinson's disease by the Movement Disorder Society and has been used in clinical trials to assess well-being in AP (Apetauerova *et al.*, 2016; MDS, 2017). It has the advantages of being used for many years as a general measure in Parkinsonism and having mental and physical well-being summary scores. In this thesis, I will use the abbreviation RAND-36 to mean the public domain version of SF-36.

3.9.4 MSA-QoL (Multiple System Atrophy Quality of life)

MSA-QoL was developed to address specific symptoms which affect patients with MSA affecting HR-QoL. Prior to its development, generic QoL scores such as SF-36 and scores designed for PD were used. It was developed with the input of MSA patients regarding their disease-related concerns and was tested on MSA patients of both subtypes. MSA-QoL has good reliability, is specific and correlates well with established QoL scales used in Parkinsonism (specifically PD) such as PDQ-39 (Schrag *et al.*, 2006a). MSA-QoL has been assessed with other scales such as the UMSARS to verify sensitivity to clinical change. UMSARS is more sensitive to change, possibly as QoL constructs are distinct to severity (Meissner *et al.*, 2012; Matsushima *et al.*, 2016).

3.9.5 PSP-QoL (Progressive Supranuclear Palsy Quality of life)

Like the MSA-QoL, the PSP-QoL was designed with the intention of being able to capture the problems individuals tend to experience in PSP. Like the MSA-QoL, patients with PSP were interviewed to ascertain issues of import to them in its design. However, it was not clear whether original testing involved PSP-RS and PSP-P though it has been used in both groups subsequently.   The PSP-QoL is a disease-specific measure with the advantage of addressing disease-specific features. The scale has good validity and reliability and correlates with the PDQ-39 amongst other measures (Schrag *et al.*, 2006c).

3.9.6 DASS (Depression, Anxiety and Stress scale)

DASS has been used in PD as well as many different adult populations in clinical and research settings. It has good internal consistency and validity (Simpson *et al.*, 2013). There is a longer DASS scale and the briefer DASS-21, both of which have been used in the context of research in PD (Bucks *et al.*, 2011; Landau *et al.*, 2016). The scale is quick and has the advantage of giving three measures of altered mental well-being; depression, anxiety and stress (Troeung *et al.*, 2014). The score is not a measure of suicidality risk and must be assessed separately from the DASS. Suicidality was not explored in this project. The depression and stress subscales have been found to have good reliability in the context of PD, however the anxiety subscale may have some overlap with the physiological symptoms of PD (e.g. presence of tremor) so may be less reliable for Parkinsonian individuals than the depression or stress results (Johnson *et al.*, 2016). The instrument will be referred to as DASS-21. Subscores will be specified as in terms such as "DASS-D" or "DASS-depression"

for the depression domain of the tool. The instrument was decided upon as it gave degrees of severity and several subscales, though depression was the key outcome it was used for. During the planning of this study, no evidence was found for particular depression scales being more suitable in the context of frontal cognitive issues (Sheehan, 2012).

3.9.7 BADLS (The Bristol Activities of Daily Living Scale)

The Bristol Activities of Daily Living Scale (BADLS) was developed in 1996 by Bucks *et al.* (1996) as a simple-to-complete questionnaire to assess functional abilities of patients living in the community with mild cognitive impairment. The scale was designed for caregivers to contribute their impression of the ability of the person to carry out their regular activities. It is sensitive to change, is reliable and sensitive (Bucks and Haworth, 2002). The advantage of this scale is that it acknowledges cognitive impairment in functional ability and is intended for caregivers' input, whereas many similar scales are not. This is important in MSA and PSP where cognitive impairment is present (in MSA, variable and often underestimated). It has been used in AP and PD (Allan *et al.*, 2006; McKeith *et al.*, 2006) as well as other neurological conditions (Stephens *et al.*, 2005). The BADLS is brief and was used as a functional surrogate of severity (disability) in this study when comparing the two disease groups. The BADLS was selected ahead of the Schwab and England score (also commonly used in research with patients with Parkinsonism) as it has a continuous scoring and is designed with carer input in mind.

3.9.8 POS-S-PD (Palliative Outcome Scale-Symptoms Parkinson's disease)

The palliative outcome scale (POS) is widely used clinically and in research studies for assessing palliative requirements in patients with a range of conditions including malignancy, renal disease and neurological conditions (Hearn and Higginson, 1999). The POS is a generic measure and this and further developments like the IPOS (Integrated Palliative Care Outcome Scale) are often used to assess change in patient status and response to intervention in palliative settings. The POS-S-PD asks about symptoms in Parkinsonism, yielding a score that reflects palliative need (Saleem *et al.*, 2013). It was designed from work with 82 patients with Parkinsonism (48 PD, 18 MSA and 16 PSP), considered to have advanced symptoms. Therefore, the tool from its conception did consider AP, though most patients who have been assessed with it from the literature had PD.

3.9.9 The Modified Caregiver Strain Scale (MCSI)

The MCSI was developed from the Caregiver Strain Index (CSI) produced in 1983. The authors discriminate between the concepts of stress, strain and burden for clarity which are often used as substitutable terms in the literature. It has good internal and retest reliability and compared to the CSI, the change from dichotomous yes/no scoring to an ordinal scale including a 'sometimes' option was introduced after feedback from pilot testing. The MCSI has slightly better internal reliability than the CSI (Thornton and Travis, 2003). The MCSI and CSI have been used in studies of caregiver strain in Parkinson's disease, cognitive impairment and palliative care, which was why it was selected for this study (Greenwell *et al.*, 2015; Hoefman *et al.*, 2015; Jennings *et al.*, 2015).

3.9.10 PQoLc (Parkinsonism carers Quality of Life)

The Parkinsonism Carers QoL is a purposively designed instrument which specifically assesses the impact upon QoL of carers looking after individuals with atypical Parkinsonism. The instrument was designed via pilot testing with patients with both MSA and PSP and was found to be reliable and consistent. The advantage of this scale is its specificity in assessing QoL of carers for people with MSA and PSP (Pillas *et al.*, 2015).

3.9.11 SEIQoL-DW (The Schedule for the Evaluation of Individual Quality of Life – Direct Weighting)

The Schedule for the Evaluation of Individual Quality of Life (SEIQoL) was developed in 1993 in response to the recognition of the need to assess individuals' quality of life and well-being in the context of disease. One concern in appraising HR-QoL was that most instruments used for the purpose impose external values and ideas, failing to allow issues important to the person to be explored (Hickey *et al.*, 1996). The SEIQoL-DW was developed to be quicker to apply from the original SEIQoL. The SEIQoL-DW is interview-based and asks the interviewee to volunteer five areas of import to them as individuals; then line-drawing and adjustment of coloured interlocking disks are used to assign functioning and relative importance to the life areas. A continuous score out of 100 (higher values having a higher QoL) can then be generated out of a series of subscores. The output is complex and can be analysed in a range of ways. The SEIQoL-DW has been used in diverse conditions such as HIV/AIDS, malignancy, MND and Parkinsonism, including MSA and PSP, though it has never been used to exclusively assess MSA and PSP patients and has not to our knowledge

been used to assess MSA and PSP carers (Neudert *et al.*, 2004; Lee *et al.*, 2006; Saleem *et al.*, 2013).

3.10 Statistical methods

Statistical analysis was carried out using the IBM SPSS version 23 software package. Graphs were produced using either SPSS or Microsoft Excel where appropriate. Data was tested for normality using visual inspection of histograms and the Shapiro-Wilk (SW) test as this has greater power to detect differences in smaller samples (therefore is often used when smaller samples of below 50 are used) (Ghasemi and Zahediasl, 2012). To find differences between means, independent t-tests were carried out. If there was a non-normal distribution found, a non-parametric alternative to the independent t-test was used, the Mann Whitney U-test. As a non-parametric test, rather than detect the differences in means between the samples, the Mann-Whitney U detects differences in ranked scores. If differences were being investigated between three or more non-normally distributed continuous scores, the Kruskall-Wallis-H test was used to see if the ranked scores were significantly different. If there were differences, post-hoc pairwise comparisons were run to see between which of the categories the differences lay. Dunn's comparison was used as the standard post-hoc test after Kruskall-Wallis-H in SPSS (Howitt and Cramer, 2014).

If differences between two groups were being explored and the variables were categorical or nominal, a test of two proportions or chi-square test for homogeneity was carried out. This was used in descriptive analysis, for example whether proportions of males and females were statistically different between the two disease groups.

Relationships between variables were explored using Pearson's Correlation Coefficient if normally distributed. If there was a non-normal distribution, Spearman's Rho which ranks the data to account for non-normality, was used. If correlations between discrete dichotomous variables (male or female, yes or no), and a continuous dependent variable were being investigated, point biserial (PBS) correlation was used (Pallant, 2007; Field, 2014). The strength of association was described using Cohen's guideline which is summarised in table 3.5 (Cohen, 1988).

Correlation Coefficient (r)	Strength of Association
<0.1	Trivial
0.10 – 0.29	Small
0.30 – 0.49	Medium
0.50 – 1.0	Large

Table 3.5: Descriptions of strength of associations from Pallant (2007) and Cohen (1988)

Regression analysis was used to look for predictive power of variables, if correlation analysis suggested a relationship. Simple linear univariate analysis was used initially to see if the variable could significantly predict a proportion of the dependent variable. Multiple linear regression was then used if more than one predictor was being considered together. As an exploratory study, stepwise regression was used (with backward elimination). This placed all variables being tested into the model initially; testing for any loss of significance as each independent variable is removed. This method is frequently used in medical and health research. Stepwise regression has been suggested as more suitable to producing models for exploratory or pilot work with hierarchical regression a more suitable method for model validation (Thayer, 2002; Jacobs *et al.*, 2006; Hanna and Cronin-Golomb, 2012). Unless specifically stated otherwise, all variables used in regression analysis in this study were continuous and quantitative.

The assumptions and tests used for linear regression were:

- All independent variables considered were tested for multicollinearity. Multicollinearity would mean independent variables correlate too strongly with each other, producing problems with producing the regression model. If this was present, this was discussed and adjustments made (such as removing the variable with the lesser correlation coefficient).

- Each dependent variable was tested for the presence of a linear relationship with the dependent variable, required in multiple linear regression.

- Homoscedasticity or similarity of variances of the dependent variables against predicted regression values. This was judged by plotting standardized residuals against standardized predicted values. A random, evenly spaced set of points would suggest homoscedasticity.

- Any outliers found in a regression model were assessed for their influence on the overall model using Leverage values and Cook's distances. This was discussed in the text if the situation arose (Pallant, 2007; Field, 2014).

In terms of the number of subjects per dependent variable to carry out regression analysis, there are varying opinions of how many are required. This ranges from 200 overall subjects in any regression analysis to 2 per dependent variable. Green has suggested between 10 and 20 subjects per dependent variable ideally, but recommends a minimum of 5 per subject variable (Green, 1991; Austin and Steyerberg, 2015). In the exploratory regression analyses performed, the minimum subjects per dependent variable was between 5-10. To check the validity of the regressions produced, all model residuals were tested in terms of SW normality tests and visual inspection of histograms.

Generalized linear models comparing variance using a covariate (ANCOVA) have been used to detect differences between disease groups whilst accounting for a covariate. The comparison then can compare the two adjusted groups with the influence of the covariate removed. The assumptions are that the dependent variable and covariate are continuous, the independent variable is categorical and that the observations are independent from another.

Other assumptions were tested before carrying out this test.

- These were the presence of a linear relationship between the covariate and the independent variables being testing (using scatter plots).
- Another assumption which must be considered before carrying out this test is homogeneity of regression slopes which looks for interactions between the covariate and the independent variable. This is tested by carrying out a Shapiro-Wilk (SW) normality test on the combined term of the covariate and the test variable. If the SW test is not statistically significant, there is not interaction between covariate and the dependent variable which might interfere in the test.
- Homoscedasticity is a requirement of ANCOVA; this is defined as the size of the errors that exist in the relationship between the independent and the dependent variable being uniform. Homoscedasticity can be shown by plotting the standardised residuals against the predicted values. If the error terms are equal, an even spread of points and no pattern will be generated.
- Levene's test was used to test whether the variance of the residuals was the same between the two testing groups, as significant differences can produce problems in the

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analysis; the assumption was not violated if there was no statistically significant result ($p < 0.05$).

- Testing for the influence of outliers was carried out and is assumed not be present if standardized residual values were approximately below ±3SD. Normality testing of residuals within the groups was tested by visual inspection of histogram and SW testing of standardised residuals in each group.

Other specific statistical tests are described in the methods sections of individual chapters.

3.11 Interviewing and interview analysis

Unlike the quantitative portions of this study, the demographics of the participants in the qualitative arm will be included in the methods chapter. See table 3.6.

All interviews were transcribed verbatim from recordings. Interviews were either transcribed by the investigator or by a specialist transcription service, then reviewed to ensure accuracy. The semi-structured interview plan was designed in the context of known literature regarding AP and PD and with input from KB, who is an expert in interviewing methods and the qualitative methodology. Sampling was purposive and pragmatic. Open coding was used to generate initial codes which were then refined into overarching themes as data collection and ongoing thematic analysis continued.

QSR International NVIVO version 11 was used as an aid to analysis and data retrieval in thematic analysis. Interviewing ceased when saturation took place i.e. when no more meaningful codes were being generated.

All quotations used from the qualitative arm to illustrate description are indented and italic. Punctuation has been used pragmatically (commas for short pauses and full stops for natural breaks in speech). Ellipses (…) were used to show omissions and square brackets to show a change to the quote (replacing true names for pseudonyms for example). Sounds considered superfluous have been removed to aid flow and readability e.g. "um". Speech marks are used to show the interviewee is quoting another.

Two participants used speech aids; a tablet computer with a 'speech' function and a light writer. Their typed responses, 'spoken' by the device are shown in bold. The reason for this is partly to distinguish from the spoken word but also to emphasise that their voice has been missing from research and therefore I wished to make their contribution more prominent.

Noises that illustrate their difficulty in speaking have been included in these participants, as they sometimes made efforts to produce intelligible speech that is integral to the content and meaning of their interviews.

Pseudonym	Sex	Condition	Role	Age	Profession	Marital status
Matthew	Male	MSA	Patient	64	Retired lawyer	Married to Sally
Emma	Female	MSA	Carer	61	Retired charity worker	Married to Matthew
Sally	Female	PSP	Carer	70	Retired dental nurse	Married
Bryce	Male	PSP	Patient	76	Retired technician	Single
Doris	Female	MSA	Patient	59	Retired librarian	Married to Bill
Bill	Male	MSA	Carer	57	Director	Married to Doris
Rose	Female	MSA	Patient	71	Retired teacher	Married to Jackie
Jackie	Male	MSA	Carer	73	Retired head teacher	Married to Rose
Julia	Female	MSA	Patient	62	Retired hotelier	Married to Tiberius
Tiberius	Male	MSA	Carer	66	Retired hotelier	Married to Julia
Sarah*	Female	PSP	Patient	67	Retired teacher	Married to Tom
Tom	Male	PSP	Carer	70	Retired oil chemist	Married to Sarah
Helen	Female	PSP	Patient	68	Retired newsagent	Married to Earl
Earl	Male	PSP	Carer	70	Retired accountant	Married to Helen
Mary*	Female	PSP	Patient	69	Retired newsagent	Married to Bob
Bob	Male	PSP	Carer	69	Retired newsagent	Married to Mary
Gary	Male	PSP	Patient	58	Retired project manager	Married to Pat
Pat	Female	PSP	Carer	62	Analyst	Married to Gary
Jack	Male	PSP	Patient	71	Retired HGV manager	Married

*Table 3.6: Summary and demographic information of patients and carers who gave interviews. All names are pseudonyms. * = used communication device due to speech difficulty.*

Chapter 4. Symptoms and Palliative Care Need

4.1 Introduction

MSA and PSP are known to have a range of symptoms, physical, cognitive, as well as emotional, that exert marked burden upon sufferers for an extended period.

A study combining patients with advanced PD, MSA, and PSP (Hoehn and Yahr 3-5) found that Parkinsonism in this patient group overall, had moderate palliative needs with symptoms which are routinely and effectively treated by palliative care teams, such as pain, constipation and drooling (Saleem *et al.*, 2013).

Palliative care is now beginning to be integrated into the medical model of Parkinson's disease management, particularly in the advanced stages, when symptoms are especially complex or when the condition becomes refractory to, or the patient is not a candidate for further treatment, such as deep brain stimulation (Lokk and Delbari, 2012). It must be noted however, that patients who have received complex therapy like deep brain stimulation should not be excluded from palliative care as their disease will continue to progress.

MSA and PSP, as discussed in more detail in Chapter 1, have earlier complications such as wheelchair requirement and falls, relentless and accelerated progression compared to PD and an extended palliative phase often without good symptomatic treatment response characterised by the 'honeymoon period' of PD. There is a lack of work that specifically characterises particular symptom burdens in subtypes of AP that this chapter aims to address in part.

4.2 Aims

This chapter will discuss the demographics of the patient-participants involved in this study. It explores the specific symptom profiles of MSA and PSP, time scales of symptoms and their onset. It also explores the similarities and differences of symptoms, the prevalence of palliative care input amongst the cohort, and perceptions of palliative care amongst the patient-participants.

4.3 Methods

The results in this section were analysed using quantitative statistical methods. The statistics software package used was the IBM SPSS version 23 software package. Graphs were produced on Microsoft Excel (2016) or SPSS 23. Differences between groups were assessed using independent t-tests to explore whether there were overall differences between the two disease groups or sexes. ANCOVA testing was then carried out which takes into account another variable (or covariate) and corrects for this (in this chapter degree of disability, using the BADLS score). One condition of ANCOVA (the other assumptions and tests used before an ANCOVA analysis takes place are discussed in the Methods chapter) is that there is a consistent, continuous covariate which is comparable between the groups being tested. For that reason, degree of disability was used as a surrogate for severity (BADLS was used in both groups). UMSARS and PSPRS are not directly compatible and Hoehn and Yahr, though a comparable measure of severity in both groups, is categorical rather than continuous. Chi-squared tests of homogeneity were used to look for differences in proportions between groups where the variables are categorical or nominal e.g. mild, moderate and severe, or male and female. If there were insufficient numbers for chi-squared testing (requires five variables per group), Fisher's exact test was used instead and stated. Milestones were reviewed and plotted on graphs to visually represent their onset, such as speech problems, relative to diagnosis ('-' numbers signifying before diagnosis and '+' after). The diagnosis point '0' denotes when the patient was diagnosed with AP, not a prior, revised diagnosis such as PD. Median scores were used to describe these onset times as their distributions were not normal on visual inspection of histograms and Shapiro-Wilk (SW) tests.

4.4 Results

4.4.1 Demographics of patients

The overall patient-participant demographics are shown in table 4.1.

	Female	Male	Total Overall	Mean age (SD), years	Median Disease duration, months	Disease duration IQR, months
MSA	11	12	23	64.6 (10.1)	33.0	29.0
PSP	10	14	24	71.6 (6.8)	25.5	30.8
Overall	11	26	47	68.2 (9.2)	29.0	30.0

Table 4.1: Basic demographic information of patient-participants. SD-standard deviation. IQR-Interquartile range. Age is measured in years, duration of disease in months

4.4.2 Sex

There were 47 patient-participants enrolled into the study. There were 23 patients with MSA. Of these 11 were female and 12 were male. There were 24 patients with PSP, of which 10 were female. There was an even balance between sexes (with a slight male preponderance in PSP) in keeping with current thinking that the sexes in MSA and PSP are likely equally affected (Glasmacher *et al.*, 2017).

4.4.3 Duration of disease and age

Duration of disease was non-normally distributed. The median time since diagnosis was 29 months overall, with MSA patients at 33.0 months and PSP patients at 25.5 months. Interquartile range (IQR) was similar at 29.0 months for MSA and 30.8 for PSP. The mean overall patient-participant age was 68.2 years; in MSA 64.6 years and in PSP 71.6 years. As PSP is described as affecting individuals at an older age than MSA, this was expected. See tables 4.2 and 4.3. Duration of disease is considered from diagnosis of MSA or PSP. Although pre-diagnosis symptoms may precede diagnosis by varying amounts, diagnosis time was used for consistency.

	Median disease duration, months	Mean Age (SD), years	Disease duration IQR, months	Total N (%)
MSA-P	29.0	65.8 (10.8)	28.8	16 (69.6)
MSA-C	34.0	61.9 (8.2)	59.0	7 (30.4)
Total	33.0	64.6 (10.1)	29.0	23 (100)

Table 4.2: Duration of disease in months and age for subtypes of MSA.

SD = standard deviation IQR = Interquartile range

Using Mann-Whitney U tests, there was no significant differences between the subgroups of MSA in terms of duration of disease or age (p = 0.349).

	Median disease duration, months	Mean Age (SD), years	Disease duration IQR, months	Total N (%)
PSP-RS	21.0	71.8 (2.1)	24.5	13 (54.2)
PSP-P	28.5	71.0 (6.3)	53.0	10 (41.7)
PAGF	51	76 (-)	-	1 (4.2)
Overall	25.5	71.6 (6.8)	30.8	24 (100)

Table 4.3: Duration of disease in months and age for subtypes of PSP.

SD = standard deviation IQR = Interquartile range.

Using Mann-Whitney U tests, there was no significant differences between PSP-RS and PSP-P in terms of duration of disease or age (p = 0.693). PSP-PAGF was excluded as there was only a single case.

4.4.4 Severity

Severity for each condition was graded using disease-specific measures, the UMSARS and the PSPRS for MSA and PSP respectively. These are not directly comparable. For descriptive purposes, the Hoehn and Yahr scales for the participants are shown below. The Hoehn and Yahr staging was designed for grading the severity of Parkinson's disease but it is useful to consider the severity of Parkinsonism using this scale. The median score for both groups was 4 and there were no significant differences between the ranks of scores between the two disease types using the Mann Whitney U test (p = 0.116).

There were no participants at stage one of the Hoehn and Yahr (unilateral disease only). Stages 4 and 5 of the scale would be expected to be reached after 7.5-14 years on average with Parkinson's disease (Poewe, 2006). By contrast, 18 (78.3%) of MSA participants were Hoehn and Yahr stage 4 or 5, with a median duration of disease of only 33 months (2.8 years) and 21 (91.3%) of the PSP participants with a median disease duration of 25.5 months (2.1 years). See figure 4.1. This describes the rapid progression and accumulation of disability as discussed in Chapter 1.
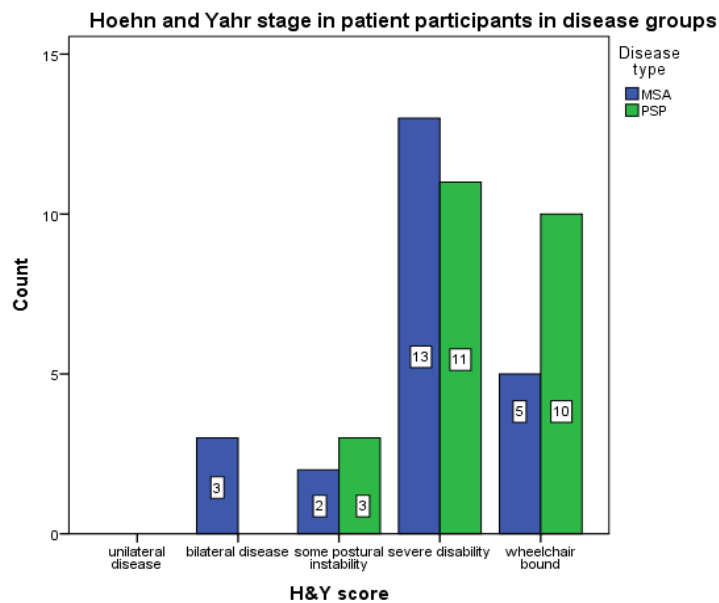
Figure 4.1: Hoehn and Yahr staging of severity of disease showing MSA patients (blue) and PSP participants (green). Mean score for MSA 3.9, median score 4. Mean score for PSP 4.3, median score 4.

All patient-participants answered questions regarding their symptom onset, diagnosis, the timing of ten key milestones relative to their diagnosis being made, and their medication. Other relevant results regarding depression and use of therapies, are included in this section.

4.4.5 Diagnosis

Overall, 22 out of 47 patients had a prior diagnosis before receiving a diagnosis of MSA or PSP. This project does not take account referrals to specialist centres or where/from which speciality they received the prior diagnosis. 11 out of 23 MSA patients were diagnosed with PD before their diagnosis was revised to MSA. The median duration between the original diagnosis and the final diagnosis was 41 months. All the MSA cases who previously had a PD label were MSA-P except for one case of MSA-C. 12 out of 24 PSP patients had a prior diagnosis before being diagnosed with PSP. Unlike the MSA group, several diagnoses were made. Nine cases were diagnosed with PD, seven of which were revised to PSP-P, the remaining two were revised to PSP-RS. One patient was diagnosed as having FTD, another mixed dementia and a third as 'stroke disease'. The latter three diagnoses were all later revised to PSP-RS. The median time to revision of diagnosis was also 41 months.

In the cases in which PD had been given as a prior diagnosis overall, the median time to revision to AP diagnosis was 36 months. 84.2% (N=16) were re-diagnosed as having the Parkinsonian variant of MSA or PSP, suggesting that early stages of these subtypes are more difficult to differentiate from PD in the early stages whereas PSP-RS was diagnosed as dementia in 23.1% (N=3) of the PSP-RS cases in this cohort, but none of the PSP-P cases.

4.4.6 Key symptoms

The ten key milestones used in this study were selected on the basis they were likely to be well-documented, memorable events which relate to the degree of severity and challenges patients face. These are listed in tables 4.4 and 4.5. The milestones were decided upon with reference to previous work in the literature and discussions with the lead supervisor of this project who is an expert in movement disorder (Ben-Shlomo *et al.*, 1997; O'Sullivan *et al.*, 2008; dell'Aquila *et al.*, 2013).

The presence or absence of these key symptoms was recorded for each subtype, as well the proportion who had these symptoms prior to their diagnosis of AP (see tables 4.4 and 4.5). One patient was excluded from the catheter category in the MSA group as he had received a catheter 26 years prior following prostate surgery. One patient was excluded from the PSP wheelchair category as they had required a wheelchair since a fall resulted in vertebral fractures 11 years earlier. It was considered unlikely that that these milestones occurred due to their AP; for transparency however, these results are taken into account in the tables below and are labelled with an asterisk.

Milestone	Milestone present	Onset prior to diagnosis	Median onset (months)	IQR
Falls	19	11	-1	30
Wheelchair	12	2	14.5	35
Autonomic	20	11	-5.5	56
Speech	21	7	10	33
Swallowing	7	0	23	64
PEG insertion	2 (pending)	-	-	-
Catheter	7 (8*)	1 (2*)	25 (21*)	27 (36*)
Acute Admissions	11	4	4	30
Institutionalization	3	0	46	57
Tracheostomy	0	-	-	-

*Table 4.4: Presence and median onset of milestones in MSA. * represents values if excluded patient milestones included. N=23*

Milestone	Milestone present	Onset prior to diagnosis	Median onset (months)	IQR
Falls	22	18	-18.5	50
Wheelchair	12 (13*)	1 (2*)	17 (16*)	28 (26*)
Autonomic	2	1	3.5	-
Speech	18	8	4	32
Swallowing	12	1	12.5	22
PEG insertion	0	-	-	-
Catheter	4	0	31	42
Acute Admissions	13	6	0	36
Institutionalization	1	0	-	-
Tracheostomy	0	-	-	-

*Table 4.5: Presence and median onset of milestones in PSP. * represents values if excluded patient milestones included. N=24*

At the time of review the most frequently present milestones reached in MSA were speech difficulty (defined as 'when others began to have trouble understanding me') at 91% of the MSA group, autonomic symptoms at 87% of the group and falls at 78%. In the PSP group, the most frequent milestones achieved were falls at 92%, speech difficulty at 75% and wheelchair requirement and swallowing difficulties were tied at 50%.

As the distribution of durations to milestones were non-normally distributed, median durations were calculated rather means. Negative values suggest the median onset occurred prior to diagnosis whereas positive values show median values tending to fall after diagnosis. This is represented graphically in figures 4.2 and 4.3, below for each disease-type.
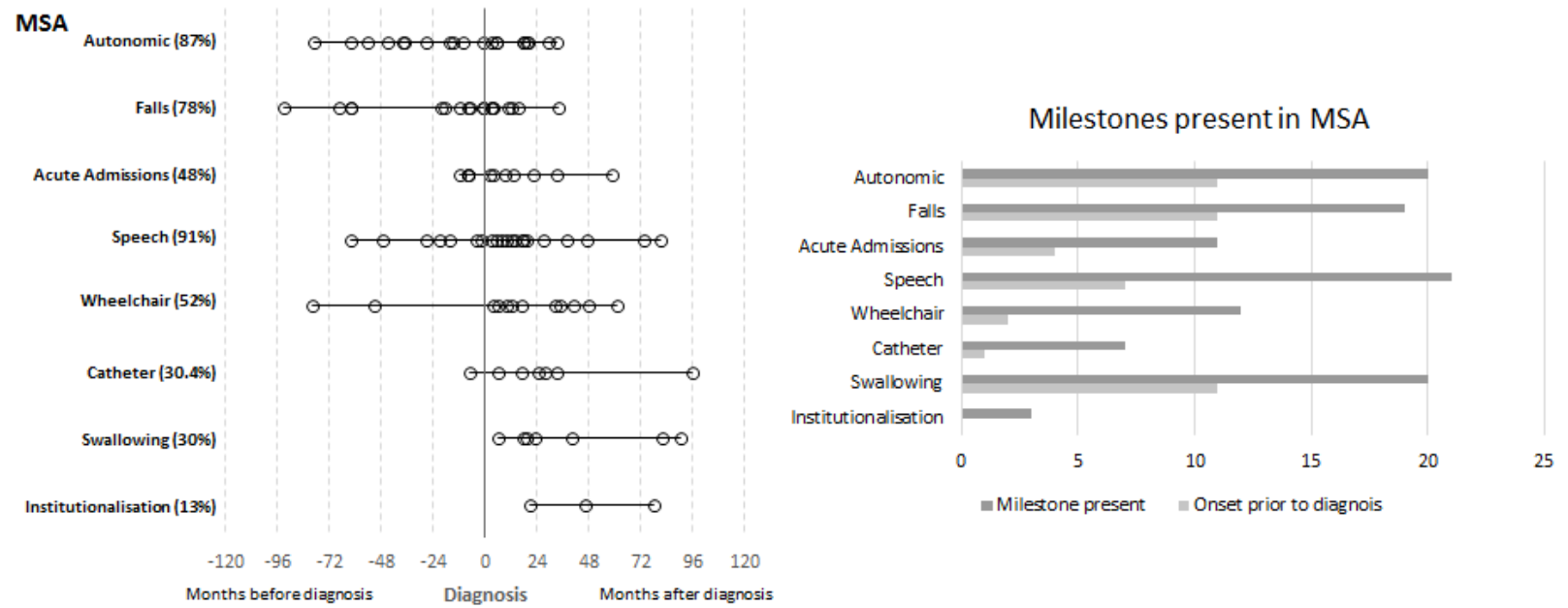
Figure 4.2: Timeline of onset of key milestones for each MSA patient (left) and proportion having reached milestone (right). One patient was excluded from the catheter category as they had received one 26 years earlier for prostate carcinoma.
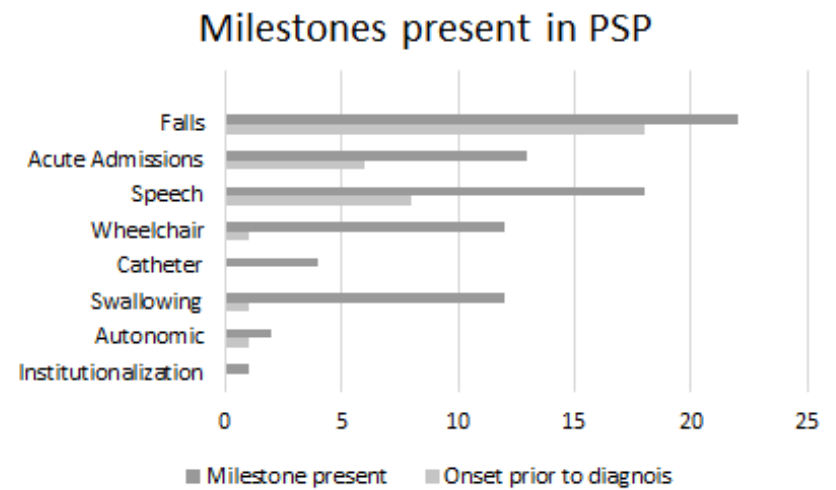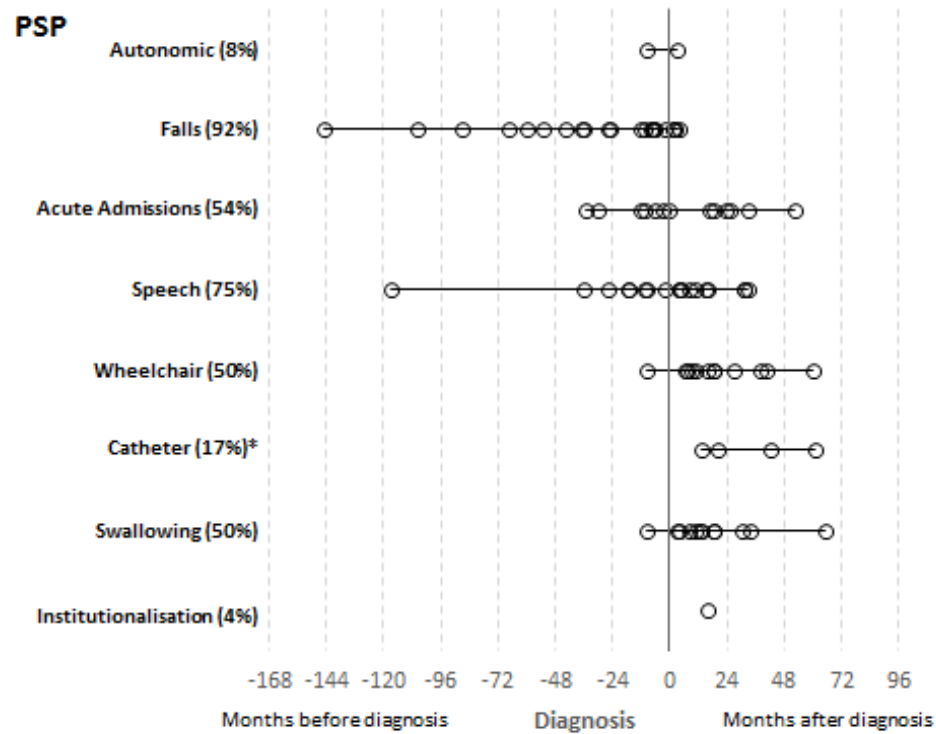
Figure 4.3: Timeline of onset of key milestones for each PSP patient (left) and proportion having reached milestone (right). One patient was excluded from the wheelchair category as they had required wheelchair since a fall resulted in vertebral fractures 11 years previously.

In the MSA group, two milestones had a median which fell before diagnosis; autonomic symptoms (median 5.5 months prior to diagnosis) and falls (median 1 month before diagnosis). All other median milestones occurred after diagnosis. In the PSP group falls had a median onset of 18.5 months prior to diagnosis.

4.4.7 Subjective Symptoms

All patient-participants were questioned on whether they had symptoms of pain, drooling, problems sleeping, anxiety or depression. It was made clear to the participants that they should answer according to whether they felt these symptoms were present rather than if they had been given a diagnosis, or symptoms had been identified by a clinician. This was asked as part of a designed proforma rather than a validated scale. These findings are summarised in tables 4.6 and 4.7.

	MSA Participants (N=23)				
	Present (%)	Absent (%)	Treated	Not treated (refused treatment)	Never acknowledged
Pain	17 (73.9)	6 (26.1)	12	5 (0)	0
Drooling	15 (65.2)	8 (34.8)	4	3 (8)	3
Sleep issue	10 (43.5)	13 (56.5)	7	3 (0)	0
Anxiety	10 (43.5)	13 (56.5)	8	1 (1)	1
Depression	10 (43.5)	13 (56.5)	9	0 (1)	0

Table 4.6: Presence of symptoms, whether acknowledged and if treatment given in MSA cohort. Treatment includes pharmacological and non-pharmacological therapies.

	PSP Participants (N=24)				
	Present (%)	Absent (%)	Treated	Not treated (refused treatment)	Never acknowledged
Pain	15 (62.5)	9 (37.5)	11	2 (2)	1
Drooling	19 (79.2)	5 (20.8)	9	3 (7)	3
Sleep issue	8 (33.4)	16 (66.6)	4	2 (2)	2
Anxiety	5 (20.8)	19 (79.2)	5	0	0
Depression	6 (25)	18 (75)	5	1	1

Table 4.7: Presence of symptoms, whether acknowledged and if treatment given in PSP cohort. Treatment includes pharmacological and non-pharmacological therapies.

4.4.8 Pain

In the MSA group, 17 (73.9%) patients experienced pain. Of these, 70.6% (12/17) were being treated for pain. All of the MSA patients with pain felt that their pain had been acknowledged by a professional though five were not receiving treatment.

In terms of pain in the PSP group, 62.5% experienced pain. 73.4% of these (11/15) had received treatment for pain, in one case non-pharmacological treatment. One patient did not feel that their pain had been acknowledged and was not on analgesia.

4.4.9 Drooling

65.2% of MSA patients had drooling. Of this group, 80% (12/15) had had this problem acknowledged by a health professional. 53.4% (8/15) of the MSA-drooling group had refused treatment for this symptom and 4 had received symptomatic treatment.

In the PSP group, 79.2% (19/24) reported drooling. This was acknowledged in 84.2% of cases (16/19) and treated 47.4% (9/19) of the time. 3 patients in the drooling group had not been offered treatment and 7 had refused it.

4.4.10 Sleep Problems

In the MSA group 43.5% (10/13) perceived problems with sleep which included rapid eye movement (REM) behaviour disorder, insomnia and fragmented sleep. All felt their sleep issues had been acknowledged by a professional and 70% of these had had treatment in an effort to address it.

In the PSP group 33.3 % (8/24) admitted to sleep difficulty. 75% (6/8) had this acknowledged and half of this total had received treatment (4/8). 2 had refused treatment and 2 had not received treatment.

4.4.11 Anxiety

In the MSA group 10/23 described anxiety (43.5%) with 9/10 (90%) acknowledged by health professionals. 5 had had their anxiety addressed with treatment, 1 had refused input and 3 had had non-pharmacological input.

In the PSP group, 5/19 of the cohort felt that they had anxiety (20.8%) and of these all had their anxiety recognised and all had received treatment with medication (4/5) or talking therapies (1/5).

4.4.12 Depression

Depression has been found to be an important factor in QoL and life satisfaction as assessed on varying scales in conditions such as renal failure and COPD as well as PD and AP (Karlsen *et al.*, 1998; Benrud-Larson *et al.*, 2005; Lee *et al.*, 2006; Schrag *et al.*, 2006c; Yoo *et al.*, 2016). In this study the DASS-21 scale was used to assess the presence of depression as well as anxiety and stress. However, as discussed in Chapter 3, the anxiety scale has some overlap with the physiological symptoms and may be less reliable than the depression or stress scores.

When patient-participants were asked whether they perceived themselves as having depression 43.5% (10) of the MSA patients felt that they did. Of these, nine participants were being treated for low mood with the remaining patient refusing treatment for low mood. In the PSP group, participants felt that they had low mood in 25% (6/24) of cases. Of these participants 84% (5/6) were treated for low mood. Only one participant with PSP who felt they had low mood had not received treatment and felt their mood problems had not been acknowledged.

When low mood was assessed objectively using the DASS-21 scale, 12/23 (52.2%) of the MSA group were found to have some depression as compared to the subjective 43.5%. None were categorised as having severe or very severe depression on the DASS-21. In the PSP group, the overall presence of depression on the DASS-21 scale was 9/24 (37.5%) of participants and 2/24 (8.4%) were in the severe category (compared with perceived low mood of 6/24 or 25%). As previously discussed, the DASS-21 is not a measure of suicidality and no patients were thought to have suicidal ideation during assessment. See figure 4.4.

Mann Whitney U tests looking for statistical differences between groups did not find any such differences in the degree of depression between MSA and PSP ($p = 0.798$), nor between male and female participants ($p = 0.715$).
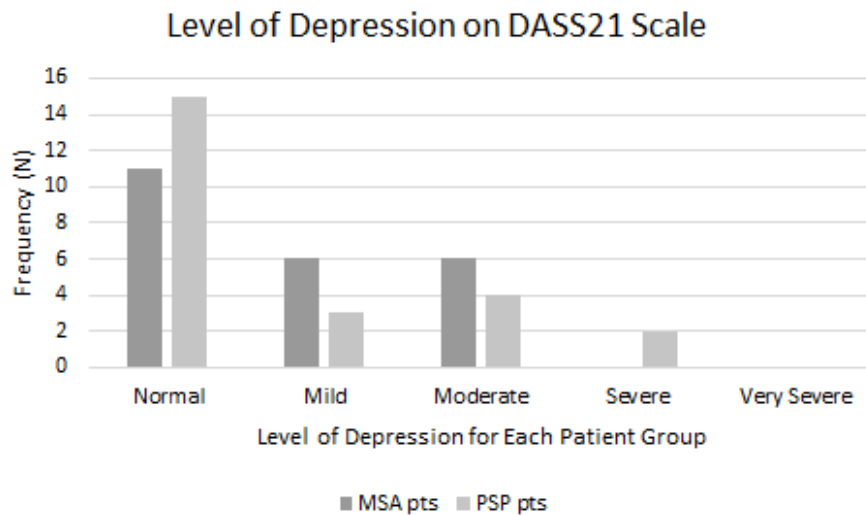
Figure 4.4: Levels of depression as shown on the DASS-21 scale for both disease groups

4.4.13 Treatments in MSA and PSP

Other treatments thought relevant to the multiple symptoms and issues were recorded and are shown in figure 4.5. These treatments were verified from history taking, patient notes and patient prescriptions where possible. It was not possible to verify treatments previously tried then discontinued as patient recollection and documentation was inconsistent. A greater proportion of MSA patients were taking dopaminergic therapies (78.3% or 18/23) than the PSP group (45.9% or 11/24). Similar proportions were taking analgesics, and bone protection. As might be expected from the symptom-profile in MSA, greater proportions of MSA patients compared to PSP were using medications for urinary symptoms and orthostatic hypotension (9/23 versus 3/24 and 5/23 versus 1/24 respectively). Only 6 patients overall were known to be on bone protection. Antidepressant use and medication for drooling was discussed previously but are also shown in figure 4.5.

This suggests that there may be better perceived dopaminergic treatment response in MSA groups than in PSP groups though the numbers here are small. This does not take into account previous responsiveness which may have been lost nor the fact that PSP patients may require higher doses to get any response (which means that side effects may preclude its use) (Brooks, 2002).
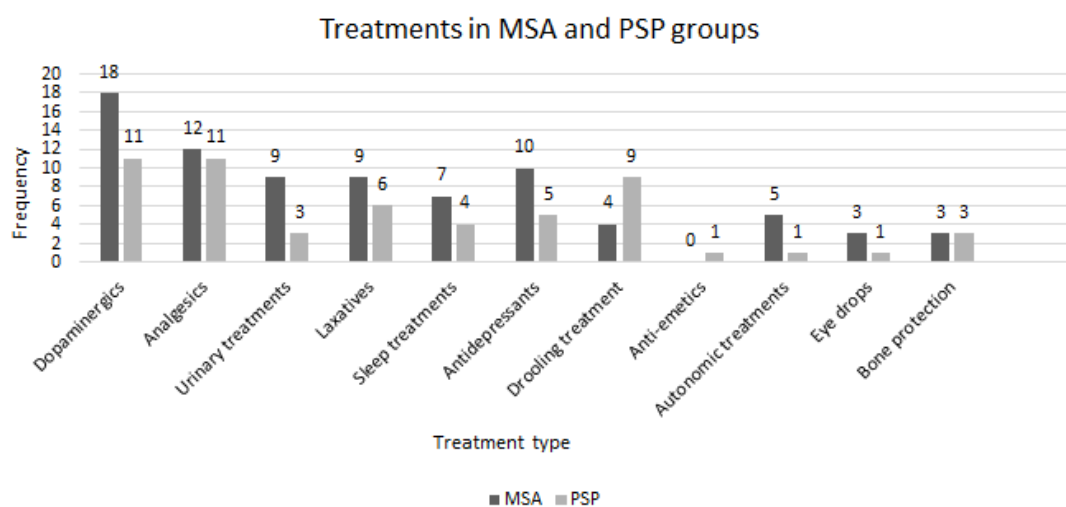
Figure 4.5: Numbers of patients from each disease group taking symptomatic treatments

More MSA patients were taking dopaminergic agents than patients with PSP. The majority of the patients with MSA taking dopaminergic medications felt they had some beneficial response to them (16/18, 88.9%). See figure 4.6. Of the 7 MSA-C patients, 5 were not taking dopaminergic medication. In the PSP group 11 patients, 5 PSP-RS and 6 PSP-P, were taking dopaminergic medication, and all of these patients felt they had some benefit from these medications. It should also be considered that stimulation of the dopaminergic reward centres could drive some subjective feeling of benefit rather than symptom improvement (Wolters *et al.*, 2008).

Some implications from this may be considering more rigorous assessment for depression in PSP, and reviewing why acceptability of treatments in drooling issues for MSA is poor. Have medications with fewer centrally-acting effects been considered, including non-pharmacological measures? In terms of dopaminergic therapy, the majority of people receiving it felt benefit (though this was subjective, which has limitations). This should be borne in mind that despite the higher incidence of poorer responsiveness, there is a possibility of a degree of benefit and these therapies should be at least trialled.
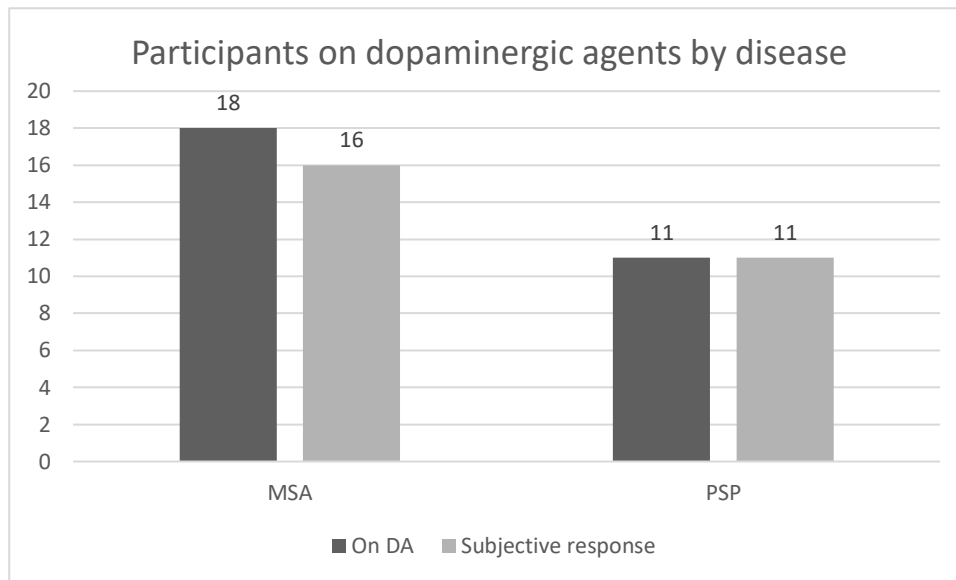
Figure 4.6: Comparison of participants taking dopaminergic treatments and whether there is subjective benefit compared across disease types

4.4.14 Palliative Care Need Using POS-S-PD Scale

The POS-S-PD scale was used as a surrogate of palliative care need in the context of symptoms associated with Parkinsonism. Previous work has included patients with MSA and PSP as well as PD. Saleem *et al.* (2013) whose paper introduced the POS-S-PD, described the score obtained on the POS-S-PD as the palliative care need with regards to symptoms relevant to Parkinsonism.

All 47 patient-participants in the study completed the POS-S-PD. The overall scores for all patients and for MSA and PSP groups separately were normally distributed on SW scores and visual inspection of histograms. The mean score of the POS-S-PD was 27.2 ± 11.5 (n = 47). In Saleem's study including advanced PD (with MSA and PSP) the mean score was 10.68 ± 3.89, for comparison. See table 4.8.

Overall POS Scores for Patient-Participants		
Participants	Mean (SD)	N
Overall (MSA and PSP)	27.2 ± 11.5	47
MSA	29.4 ± 11.5	23
PSP	25.2 ± 11.3	24

Table 4.8: POS scores for all patients, MSA and PSP subgroups. Mean scores shown with SD.

4.4.15 Differences between disease groups using POS-S-PD

An independent t-test was carried out to compare the POS-S-PD scores of the MSA group compared with the PSP group. No statistical differences were found between the two disease types in terms of overall POS-S-PD score [(95% CI, -2.4710 to 10.9203), t(45) = 1.271, p = 0.210]. There was also no influence on patient sex in terms of POS-S-PD score when independent t-tests were carried out [(95% CI, -1.224 to 12.086), t(45) = 1.643 , p = 0.107].

In order to assess the degree of palliative care need whilst accounting for the degree of disability (BADLS score), differences between the two disease groups POS-S-PD scores were explored using ANCOVA; removing any influence that disability has on POS-S-PD scores. No differences were seen between the two groups using the ANCOVA when amount of disability was accounted for; F(1,44) 2.431, p = 0.126, partial η^2 0.052, 95% CI (-1.469, 11.511). Therefore, in this study, the palliative need as measured by the POS-S-PD was not statistically different between MSA and PSP, which remained the case when the degree of disability was accounted for.

4.4.16 Highly-Rated Symptoms on POS-S-PD

The most highly nominated symptoms for the overall cohort were problems using legs, communication, falls, fatigue and difficulty with bladder control. This is shown in figure 4.7.
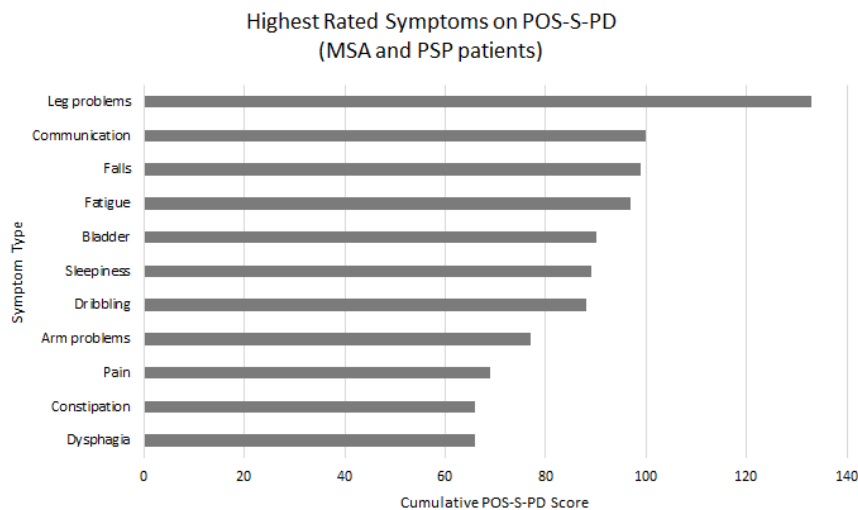
Figure 4.7: Ten most highly scored symptoms in whole cohort on POS-S-PD. Tied results included.

In both the MSA and PSP subgroups, problems with legs (including walking problems) was the most highly scored symptom. In the MSA subgroup, the greatest cumulative scored symptoms (as well as leg problems) were fatigue, bladder problems, communication issues and sleepiness. In the PSP group (as well as leg symptoms) falls, dribbling, communication issues and fatigue were the most highly scored. See figure 4.8.
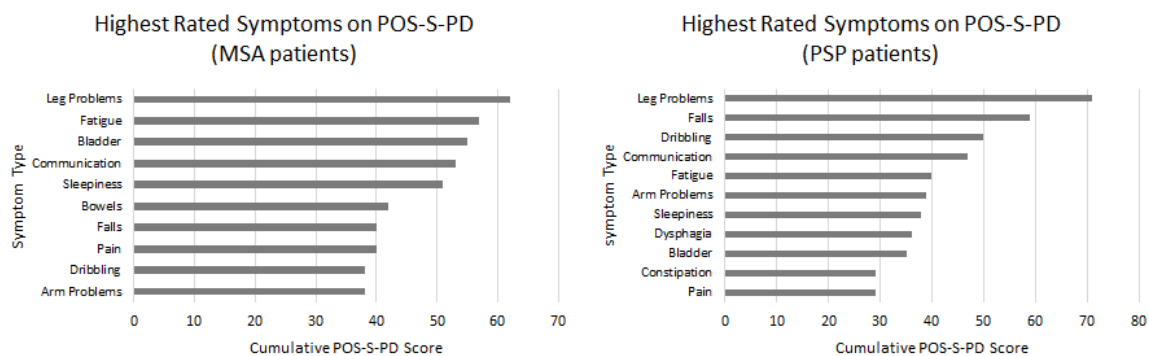
Figure 4.8: Ten most highly scored (cumulative score) symptoms in MSA group (left) and PSP group (right) on POS-S-PD. Tied results included.

A breakdown of median scores overall, median scores for each disease group, and frequency of responses for each degree of severity for symptoms is shown in table 4.9. Median scores have been used, as the POS-S-PD used a Likert scale.

Symptom	Median Score Overall	Median Score MSA, PSP	None N (%)		Slight N (%)		Moderate N (%)		Severe N (%)		Overwhelming N (%)	
			MSA	*PSP*	*MSA*	*PSP*	*MSA*	*PSP*	*MSA*	*PSP*	*MSA*	*PSP*
Pain	2	2, 0.5	6 (26.1)	12 (50.0)	3 (13.0)	2 (8.3)	7 (30.4)	4 (16.7)	5 (21.7)	5 (20.8)	2 (8.7)	1 (4.2)
Spasm/Cramp	1	1, 0	8 (34.8)	15 (62.5)	6 (26.1)	3 (12.5)	4 (17.4)	2 (8.3)	4 (17.4)	3 (12.5)	1 (4.3)	1 (4.2)
Fatigue	2	3, 2	0	5 (20.8)	5 (21.7)	6 (25.0)	6 (26.1)	7 (29.2)	8 (34.8)	4 (16.7)	4 (17.4)	2 (8.7)
Shortness of Breath	1	1, 0	8 (34.8)	14 (58.3)	5 (21.7)	4 (16.7)	7 (30.4)	5 (20.8)	3 (13.0)	1 (4.2)	0	0
Nausea	0	0, 0	13 (56.5)	19 (79.2)	4 (17.4)	2 (8.3)	4 (17.4)	1 (4.2)	1 (4.3)	2 (8.3)	1 (4.3)	0
Vomiting	0	0, 0	18 (78.3)	20 (83.3)	3 (13.0)	1 (4.2)	2 (8.7)	2 (8.3)	0	1 (4.2)	0	0
Poor Appetite	0	0, 0	14 (60.9)	16 (66.7)	7 (30.4)	3 (12.5)	1 (4.3)	1 (4.2)	1 (4.3)	3 (12.5)	0	1 (4.2)
Dysphagia	0	0, 0	2 (8.7)	6 (25.0)	13 (56.5)	7 (29.2)	7 (30.4)	5 (20.8)	1 (4.3)	5 (20.8)	0	1 (4.2)
Sleepiness	2	2, 2	0	8 (33.3)	6 (26.1)	2 (8.3)	9 (39.1)	6 (25.0)	5 (21.7)	8 (33.3)	3 (31.0)	0
Poor Sleep	1	1, 0	10 (43.5)	13 (54.2)	5 (21.7)	4 (16.7)	4 (17.4)	3 (12.5)	3 (13.0)	4 (16.7)	1 (4.3)	0
Constipation	1	2, 1	5 (21.7)	9 (37.5)	6 (26.1)	6 (25.0)	8 (34.8)	5 (20.8)	1 (4.3)	3 (12.5)	3 (13.0)	1 (4.2)
Problems with Bowel Control	1	2, 0	6 (26.1)	13 (54.2)	5 (21.7)	4 (16.7)	3 (13.0)	3 (12.5)	5 (21.7)	4 (16.7)	4 (17.4)	0
Problems with Bladder Control	2	3, 1.5	1 (4.3)	10 (41.7)	7 (30.4)	2 (8.3)	2 (8.7)	5 (20.8)	8 (34.8)	5 (20.8)	5 (21.7)	2 (8.3)
Problems with Arms	2	2, 2	6 (26.1)	6 (25.0)	5 (21.7)	4 (16.7)	4 (17.4)	8 (33.3)	7 (30.4)	5 (20.8)	1 (4.3)	1 (4.2)
Pressure Sores	0	0, 0	19 (82.6)	21 (87.5)	3 (13.0)	1 (4.2)	1 (4.3)	0	0	2 (8.7)	0	0
Problems with Legs	3	3, 3	2 (8.7)	1 (4.2)	2 (8.7)	1 (4.2)	3 (13.0)	5 (20.8)	10 (43.5)	8 (33.3)	6 (26.1)	9 (37.5)
Communication Difficulties	2	2, 2	1 (4.3)	6 (25.0)	3 (13.0)	2 (8.3)	10 (43.5)	6 (25.0)	6 (26.1)	7 (29.2)	3 (13.0)	3 (12.5)
Dribbling	2	1, 2	4 (17.4)	3 (12.5)	8 (34.8)	5 (20.8)	5 (21.7)	7 (29.2)	4 (17.4)	5 (28.8)	2 (8.7)	4 (16.7)
Falling	2	1, 3	5 (21.7)	4 (16.7)	7 (30.4)	2 (8.3)	3 (13.0)	5 (20.8)	5 (21.7)	5 (20.8)	3 (31.0)	8 (33.3)
Hallucinations	0	0, 0	19 (82.6)	20 (83.3)	3 (13.0)	3 (12.5)	0	0	1 (4.3)	0	0	1 (4.2)

Table 4.9: Median scores for each symptom on the POS-S-PD scale including median overall score for each disease type

Chi-squared tests of homogeneity (or Fisher's exact test where appropriate) were performed to analyse whether there was a statistical difference in the proportions of individuals with more severe symptom ratings compared to milder symptoms (none to moderate compared with severe to overwhelming) from the POS-S-PD assessment. The highest rated symptoms were included. There were no statistically significant differences in proportions between the two groups. There was a trend towards difference however in two symptoms; bladder problems and fatigue which all had a greater proportion of patients with MSA in the more severe category. See table 4.10.

Symptom	χ^2	p
Leg Problems	0.009	0.924
Falls	1.785	0.181
Fatigue	**3.670**	**0.055**
Communication	0.031	0.859
Bladder issues	**3.595**	**0.058**
Sleepiness	0.011	0.917
Dribbling	0.704	0.401
Arm Problems	0.537	0.464
Pain	0.173	0.677
Constipation	0.004*	1.000
Dysphagia	3.952*	0.097

Table 4.10: Chi-square tests of homogeneity comparing rated symptom severity between disease groups.

** = indicates Fisher's exact test used. Items shown in **bold** approach show a trend toward statistical significance*

4.4.17 Perceptions of Palliative Care

Patient-participants were asked if they understood what palliative care was. Their responses were recorded as yes or no. 27 participants felt that they understood the purpose of palliative care and 13 of those (48.1%) had actually received PC input of some kind (listed in table 4.11). None had refused PC input.

		Day Hospice	None	Macmillan Team	PC Clinic	Refused	Total
Understand what PC is	**Yes**	6	13	3	5	0	**27**
	No	4	12	1	2	1	**20**
	Total	10	25	4	7	1	**47**

Table 4.11: Cross-tabulation participants who felt they understood what PC was and whether they actually received it

20 participants felt that they did not know what PC was, though 7 of these had received some in the form of SPC clinics, day hospice or Macmillan team input. 13 of the 20 (65%) had not received PC intervention (1 having refused it); a greater proportion than those who felt they had some understanding of PC.

Participants were then asked what they thought palliative care as a service or concept meant, even if they had said they did not know above; some tried to give a definition. These definitions were taken down verbatim and were grouped into themes; seven similar definitions in total. If multiple themes were contained within a response, participants were asked what they thought the most important aspect of palliative care was and this was the definition used. 29 patient-participants gave a definition, 18 responded with 'do not know'. The second most frequent response was 'end-of-life' or 'easing suffering for the dying'. 41.1% of those who gave a definition felt that this was what PC was. The next most frequent response (34.5% of those who gave a definition) was grouped into 'help and care' which included 'extra help', and 'more caring medicine'. Only one person felt that PC was a service for people with a cancer diagnosis. See table 4.12 and figure 4.9.

	Frequency	Percentage
End of life/dying	12	25.5
Help and care	10	21.3
Serious/debilitating illness	2	4.3
Cancer	1	2.1
Making life easier	2	4.3
Pain and symptom control	1	2.1
Dignity	1	2.1
Don't know	18	38.3
Total	**47**	**100.0**

Table 4.12: Definitions for PC grouped into similar themes

Themes for Perception of Palliative Care in Patient-Participants

Legend:
- Don't know
- End of life/dying
- Help and care
- Serious/debilitating illness
- Cancer
- Making life easier
- Pain and symptom control
- Dignity

Pie chart labels: Don't Know (18), End of life/dying (12), Help and care (10)
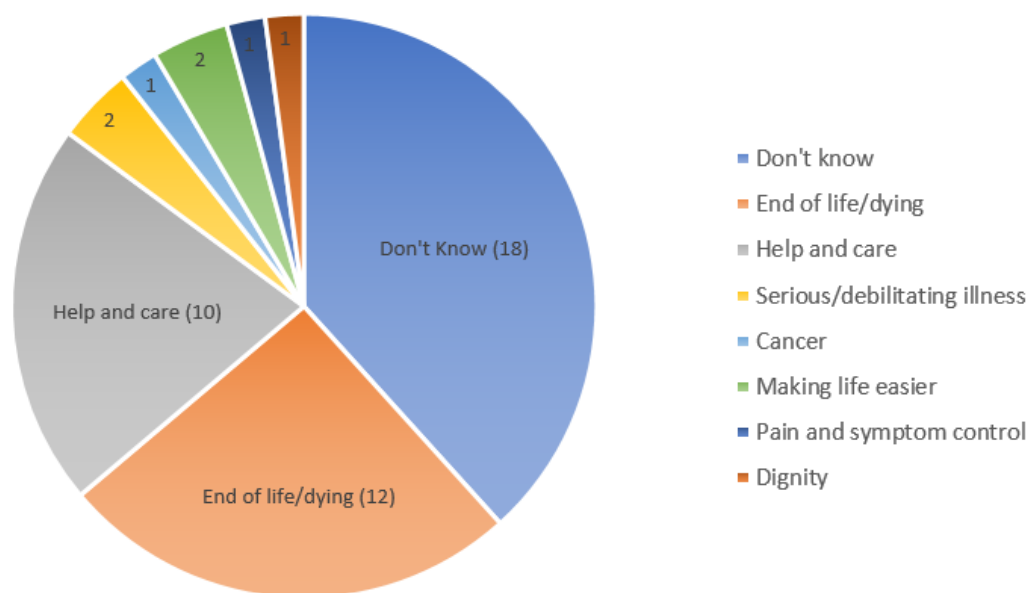
Figure 4.9: Pie chart of perception of Palliative Care by Patient-Participants grouped into similar themes

4.5 Discussion

In terms of recruitment, there was an even representation of individuals with MSA and PSP (n=23 and 24, respectively). The median disease duration was 33.0 months in MSA compared with 25.5 months in PSP, with the latter having a larger IQR of 30.8 months compared with 29 months. Over 2/3 of the MSA cases were MSA-P which is in keeping with proportions of MSA subtypes seen in European populations (Kollensperger *et al.*, 2010). The MSA-C subgroup had a longer disease duration than MSA-P at 34 compared with 29 months, respectively. Previous work has suggested that patients with MSA-C may have a modestly longer survival, which may account for this (Ben-Shlomo *et al.*, 1997). In the PSP group, over half had the PSP-RS form and only one pure akinesia with gait freezing. Again, this is in agreement with literature describing a predominance of PSP-RS and PSP-PAGF as a 'rare' phenotype, with PSP-RS having a shorter disease duration. PSP-RS has a more progressive course than the PSP-P variant (Williams *et al.*, 2005; dell'Aquila *et al.*, 2013). The mean ages of individuals with MSA was in their 60s whereas individuals with PSP were in their 70s, in keeping with work predicting older age of onset in PSP (O'Sullivan *et al.*, 2008). This suggests that the cohort recruited was representative of the disease groups in terms of subtypes and characteristics and that inferences are more likely to be generalisable.

In terms of severity of disease, despite the range of patients enrolled (from having been diagnosed 5 months ago to having carried a diagnosis for 17 years), 83% of the 47 enrolled patients were categorized as H&Y 4 or 5. This emphasises the relentless progression and early morbidity that patients with AP face. By contrast, patients with Parkinson's disease are expected to reach H&Y stage 4 at between 7 and 14 years after disease onset (Poewe, 2006).

When the milestones of disease were considered, falls overall were a key symptom which occurred prior to diagnosis and fits with previous work and recommendations that early falls are red flags for both conditions (Tada *et al.*, 2007; O'Sullivan *et al.*, 2008; Kollensperger *et al.*, 2010). However, in MSA, there was a median time of 1 month before a diagnosis was reached and in PSP 18.5 months. This may be because MSA is diagnosed in a timelier manner than PSP, or that PSP produces instability and a tendency to fall in advance of other features which might facilitate the diagnosis. Speech problems were more numerous in both conditions than swallowing issues and the latter tended to follow speech problems (though speech is arguably more subjective than swallowing problems). Approximately half of both groups had required acute hospital admissions related to their AP and half of each group needed a wheelchair for anything other than short distances.

Being able to predict the onset of key milestones such as early speech disturbance or falls, is not only helpful when seeking to make a diagnosis of AP but also in guiding clinicians on preparing patients and families for choices and challenges ahead in a timely way, such as the swallowing issues which may require patients to choose whether they would have a PEG tube or need for wheelchair triggering adaptations to their home. Therefore, these trends are helpful as a guide as to when, on average, problems might be expected to arise and how to plan with them, though work on larger cohorts is required.

An interesting finding was the suggestion that patients themselves underestimate the presence of low mood in the context of their disease, which has implications for clinicians asking about mood and depression and should be borne in mind as a complicating factor, even if patients initially feel their mood is not low. This was particularly so in the PSP group (though also to a lesser extent in the MSA group) where subjective depression was lower than objective depression using the DASS-21 scale.

This difference in the PSP group between perceived low mood and objective mood scores could be explained in several ways. If someone does not think they are depressed but score highly on a rating scale do they just not realise it? Can someone be depressed if they do not perceive it? It may be that the DASS-21 has detected apathy for example, rather than low

mood. Is there a 'distancing' effect i.e. are the frontal cognitive problems 'sparing' PSP patients some of the distress of reflecting upon progressing disease? Further work should explore different research tools measuring depression against measures of apathy and cognitive impairment in PSP and other diseases with this pattern of cognitive impairment, seeking validity in depression measurement for these groups.

The symptoms that were represented in the ten most highly scored issues in both disease groups were leg problems (incorporating walking), falls, difficulties using arms, dribbling, communication issues, sleepiness, bladder problems, and fatigue. In Chapter 7, which explores the experience of living with AP using qualitative methods, communication and speech was frequently discussed as a fundamental issue influencing QoL in both conditions, affecting the ability to connect to others and impacting the perception of self. Interestingly, though falls were present in 83% of MSA patient-participants, they were not thought to be one of the chief difficulties that MSA patients experience in terms of symptom-burden and came seventh. There was no significant difference between palliative symptom burden using POS-S-PD using t-tests nor when the degree of disability was accounted for using ANCOVA testing, suggesting that, at least in this small cohort, palliative need is equivalent in both conditions though different symptoms may predominate. When the symptoms with the highest cumulative scores in the POS-S-PD tool were compared between groups using chi-squared testing, there were not significant differences though there were trends towards greater urinary disturbance and fatigue in the MSA group. Finally, palliative care in terms of its meaning and whether patients received it was explored. Nearly half of the overall cohort had received some palliative input (22/47, 46.8%) including Macmillan nurse visits, day hospice access or SPC clinic. In fact, some patients were not aware that these services represented palliative care. Of those who had received some PC input, 7/22 or 31.8% could not define it. Does this matter if recipients of PC derive benefit from the service? An issue which may arise from a lack of public knowledge of the mandate of PC and the benefits it could bring, include anxiety should patients be referred and refusal due to this concern. It should be noted that nearly half of those who gave a definition, felt PC was 'end-of-life care', though a PC approach is increasingly being offered earlier in disease to maximise QoL in life-limiting conditions. Therefore, perceptions of PC as "just for the end-of-life" could be a barrier for patients who could derive benefit from it. It is of interest that seven participants who were receiving palliative care felt they could not give a definition for it, though they valued it nevertheless. This could mean that the holistic nature of PC is not explained well to

patients or possibly that explanations are not retained but nevertheless the essence of the care is appreciated.

In conclusion, the demographics of the study cohort appear to be representative of AP in terms of proportions, gender and subtypes, as described in previous work. Palliative symptom burden is high, almost double that shown in previous work made up mainly of PD (H&Y 4 and 5) and is not statistically different between disease type or gender. Leg problems, communication and fatigue were highly rated in common between both disease types and larger studies in future on AP should pay consideration to these concerns. Milestones which tended to occur prior to diagnosis in MSA were autonomic symptoms and falls and in PSP falls alone, but far earlier than the onset of MSA (a difference of 17.5 months in the median onset). Depression was not felt to be present as often as objective depression scores suggested, which may suggest deficiencies in the scales available for these patients and PC as a concept could not be explained by many patients and the most frequently-cited response given was 'end-of-life care'.

Chapter 5. Quality of Life in Patients with MSA and PSP

5.1 Background

As described in Chapter 1, QoL is increasingly recognised as an important area of research. How various factors can impact upon QoL in PD has been described though few similar studies have been carried out in atypical Parkinsonism.

In this study, three different QoL measures were used to assess patient participants; the disease-specific MSA-QoL designed for patients with MSA and the disease-specific PSP-QoL designed for patients with PSP. The details of these scales and how to administer them is given in Chapter 3. These are specific to the particular condition, but not comparable between groups. All participants also received the SEIQoL-DW, which is a general, subjective scale intended to represent a more holistic instrument as opposed to concentrating purely on how QoL is affected in relation to disease. In this chapter, the continuous overall output score from the SEIQoL-DW, MSA-QoL and PSP-QoL was used to establish associations and correlations and then explored using regression modelling, looking for factors predicting these QoL measures.

Later, the SEIQoL-DW will be analysed in terms of its descriptive components, looking at domains which patients nominated and found meaningful, and whether there were any differences between the two disease groups.

5.2 Aims

The aims of this chapter were to find associations with QoL measures in the patient groups, considered together and in the MSA and PSP disease subgroups. Differences between the MSA and PSP groups in terms of their quality of life were then investigated taking into account degree of disability. The SEIQoL-DW was then explored as a rich tool, which gives a wealth of information on subjective quality of life.

5.3 Methods

The results in this section were analysed using quantitative statistical methods. The statistic software package used was the IBM SPSS version 23 software package. Differences between groups were assessed using independent t-tests to explore whether there were overall

differences between the two disease groups. ANCOVA testing was then carried out, which takes into account another variable (or covariate) and corrects for this, as was used in Chapter 4. Correlations between variables were tested using Pearson's or Spearman's Rho (the former if normally distributed, the latter if not) and multiple linear regression methods were used to models whether factors could predict for outcomes. More details of these statistical tests are provided in Chapter 3: Methods.

5.4 Results

5.4.1 Associations between disease specific QoL and other factors

Disease-specific QoL scores for MSA and PSP were utilised in this study as they were constructed and validated to include issues that might be of particular concern to that group of patients e.g. questions on apathy in PSP-QoL and postural hypotension symptoms in the MSA-QoL.

As the two QoL scores are distinct and not directly comparable, tests of correlation were carried out on each of the QoL scores, seeking associations with key variables such as disease severity, duration and age. The MSA-QoL and PSP-QoL have a scoring system which rises as the disease-specific QoL falls.

5.4.2 Correlations with MSA-QoL

The MSA-QoL was tested for normality of distribution using histograms and the Shapiro-Wilk (SW) test was performed. The SW test did not violate the null hypothesis of normality (SW statistic 0.928, $p = 0.100$) though the histogram showed some skew. Other variables which were tested for their association with MSA-QoL were also assessed for normality using the same methods. If a non-normal distribution was found, correlation was assessed using Spearman's correlation. Correlations with dichotomous variables used point-biserial correlation. See table 5.1

Variable	Coefficient correlation	Significance (p-value)
Age	-0.140[R]	0.525
Sex (PBS)	-0.322[b]	0.134
BADLS (disability)	0.366[P]	0.086
Disease-specific severity	0.399[P]	0.59
Depression (DASS-D)	**0.821[P]**	**0.001**
Anxiety (DASS-A)	**0.711[P]**	**0.001**
Palliative need (POS-S-PD)	**0.772[R]**	**0.001**
Duration of disease (months)	0.308[P]	0.153

*Table 5.1: Correlation coefficients between MSA-QoL and other study measures. R=Pearson's correlation coefficient, P=Spearman's Rho correlation coefficient, b=point-biserial correlation. Rows in **bold** represent significant correlations between variable and MSA-QoL.*

There was a large, positive strength of association between MSA-QoL and depression (DASS-D), anxiety (DASS-A) and palliative need score (POS-S-PD), respectively. There was no significant association between disease-specific QoL, disability or severity (as measured on UMSARS), though there is a trend towards small-moderate level of correlation for the latter. When shown plotted on a scattergraph, visual inspection does not show a strong linear relationship (see figure 5.1).
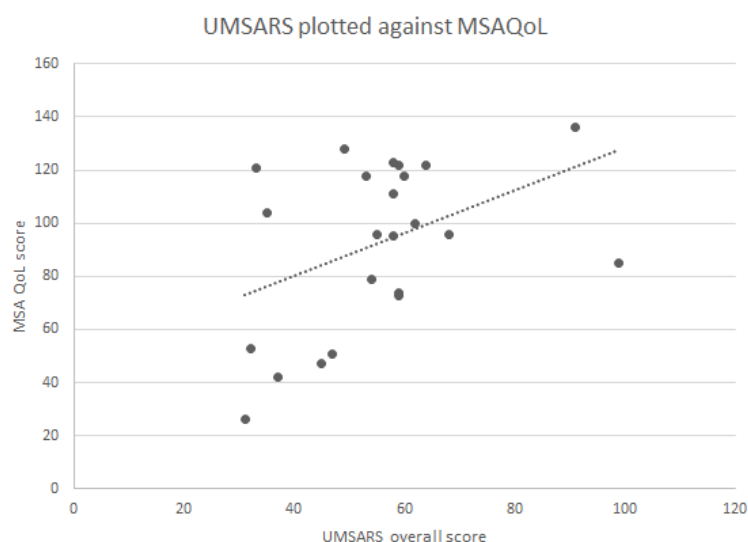
Figure 5.1: Scatterplot of MSA-QoL against UMSARS severity score. R=0.399

By contrast, MSA-QoL plotted against palliative care need or DASS-depression shows a good linear relationship (see figures 5.2 and 5.3)
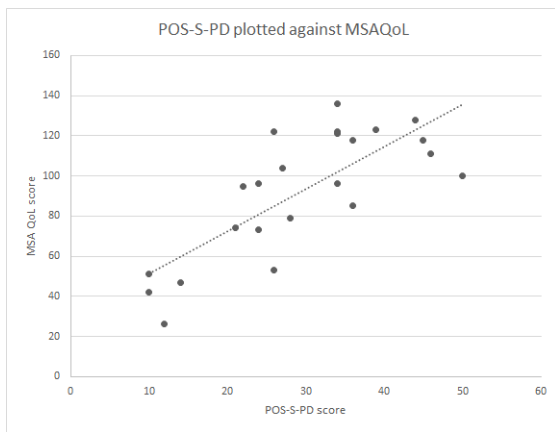
Figure 5.2: Scatterplot of MSA-QoL against palliative care need (POS-S-PD), R=0.772
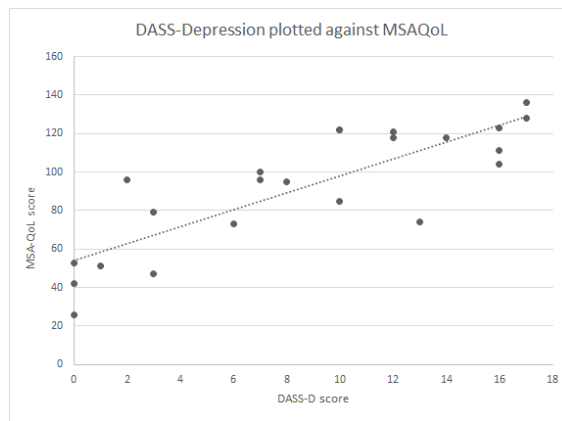
Figure 5.3: Scatterplot of MSA-QoL against DASS-depression score, R=0.830

5.4.3 MSA regression modelling

Multiple regression analysis was carried out using the three study variables which correlated with MSA-QoL score as independent variables (MSA-QoL being the dependent variable).

The method of multiple regression used was backwards elimination; all predictors (independent variables) are placed in a regression model and then eliminated to judge the significance of its removal. If the predictor is not making a significant contribution to the predictive value of the model, it is removed. The remaining predictors are then assessed in a similar way. Here, predictors were only included in regression models if they correlated with the dependent variable in question. Variables which had significant correlation were tested with univariate regression to ascertain if they could predict for MSA-QoL. They were then combined together into a backward elimination regression to obtain a basic model.

A basic model containing POS-S-PD and DASS-depression score gave an adjusted R^2 of 0.76 (76%), $F(3,22) = 35.896$, $p = 0.001$. DASS-anxiety did not contribute significantly to the model and was removed. Therefore, the POS-S-PD score, together with DASS-depression score, could explain 76% of the variance of the MSA-QoL score. The distribution of the residuals was approximately normal and the KS/SW tests of unstandardized and standardized residuals were not significant. See tables 5.2 and 5.3.

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	β	SE	p-value	95% CI		R² adj	F-value
				LB	UB		
POS-S-PD	**0.772**	**0.378**	**0.001**	**1.318**	**2.892**	**0.577**	**30.949**
DASS-depression	**0.830**	**0.642**	**0.001**	**3.049**	**5.721**	**0.675**	**46.607**
DASS-anxiety	**0.658**	**1.336**	**0.001**	**2.568**	**8.124**	**0.406**	**16.019**

*Table 5.2: Univariate regression coefficients for MSA-QoL. Significant results in **bold** text. SE= Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R² adj=R² adjusted value*

	β	SE	p	95% CI		R² adj	F
				LB	UB		
POS-S-PD	**0.401**	**0.375**	**0.009**	**0.312**	**1.877**		
DASS-depression	**0.569**	**0.726**	**0.001**	**1.489**	**4.520**	**0.76**	**35.896**

*Table 5.3: Overall basic regression model for MSA-QoL when non-significant predictors removed. Significant results in **bold** text. SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R² adj=R² adjusted value*

In this cohort of MSA patients, 76% of the variance of HR-QoL using the MSA-QoL can be predicted for by palliative need (POS-S-PD score) and depression (DASS-D).

5.4.4 Correlations with PSP-QoL

Similarly, the PSP-QoL was tested for normality of distribution using histograms and the Shapiro-Wilk (SW) test was performed. The SW test did not violate the null hypothesis of normality (SW statistic 0.986, p = 0.980) and the histogram demonstrated a normal distribution. Other study variables, such as age and severity, were also assessed for normality using the same methods. If a non-normal distribution was found, correlation was assessed using Spearman's correlation, correlations with dichotomous variables using point-biserial (PBS) correlation. See table 5.4.

Variable	Correlation coefficient	Significance (p value)
Age	-0.292^R	0.167
Sex (PBS)	0.000^b	0.998
BADLS (disability)	$\mathbf{0.680^R}$	**0.001**
Disease-specific severity (PSPRS)	$\mathbf{0.781^R}$	**0.001**
Depression (DASS-D)	$\mathbf{0.744^P}$	**0.001**
Anxiety (DASS-A)	$\mathbf{0.428^P}$	**0.037**
Palliative need (POS-S-PD)	$\mathbf{0.755^R}$	**0.001**
Duration of disease (months)	-0.092^P	0.670

*Table 5.4: Correlation coefficients between PSP-QoL and other study variables. R=Pearson's correlation coefficient, P=Spearman's Rho correlation coefficient, b=point-biserial correlation. Rows in **bold** represent significant correlations between independent variable and PSP-QoL.*

Disease-specific severity, disability, palliative need and depression had a strong positive correlation with PSP-QoL scores. Anxiety had a medium strength of positive correlation with PSP-QoL score. Scatterplots of the associations with disease-specific severity and palliative need are shown below to illustrate this (figures 5.4 and 5.5).
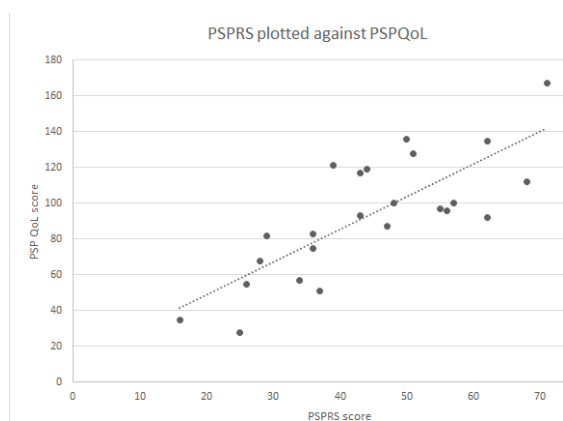
Figure 5.4: Scatterplot of PSP-QoL against PSPRS severity score, R=0.781
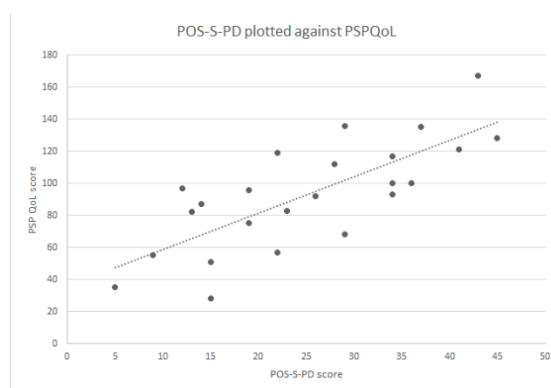
Figure 5.5 Scatterplot of PSP-QoL against POS-S-PD, R=0.755

5.4.5 PSP regression modelling

Backward multiple regression analysis was carried out using the four study variables which correlated with PSP-QoL score as independent variables (PSP-QoL being the dependent variable). Univariate analysis with each predictor variable was carried out (see table 5.5) and significant predictors were then considered together in a regression model (see table 5.6).

	β	SE	p	95% CI		R^2 adj	F
				LB	UB		
PSPRS	**0.781**	**0.313**	**0.001**	**1.183**	**2.480**	**0.592**	**34.339**
BADLS (disability)	**0.680**	**0.375**	**0.001**	**0.853**	**2.410**	**0.438**	**18.893**
DASS-depression	**0.708**	**0.780**	**0.001**	**2.050**	**5.285**	**0.479**	**22.111**
DASS-anxiety	0.346	1.532	0.098	-0.531	5.824	0.079	2.983
POS-S-PD	**0.755**	**0.418**	**0.001**	**1.395**	**3.130**	**0.551**	**29.245**

*Table 5.5: Univariate regression coefficients for PSP-QoL. Significant results in **bold** text. SE= Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R^2 adj=R^2 adjusted value*

	β	SE	p	95% CI		R^2 adj	F
				LB	UB		
POS-S-PD	**0.292**	**0.354**	**0.023**	**0.136**	**1.615**		
PSPRS	**0.474**	**0.253**	**0.001**	**0.584**	**1.638**	**0.82**	**36.029**
DASS-depression	**0.357**	**0.553**	**0.003**	**0.698**	**3.006**		

*Table 5.6: Overall basic regression model for PSP-QoL when non-significant predictors removed. Significant results in **bold** text. SE= Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R^2 adj=R^2 adjusted value*

The regression model containing PSPRS, POS-S-PD and DASS-depression score gave an adjusted R^2 of 0.820 (82.0%). Therefore, PSPRS and POS-S-PD, together with DASS-depression score could explain 82% of the variance of the PSP-QoL score. The distribution of the residuals was approximately normal and the KS/SW tests of unstandardized and standardized residuals were not significant.

5.4.6 SEIQoL-DW regression modelling

Associations with SEIQoL-DW were then tested using other study variables. It is worth noting, as discussed in the methods section that as QoL improves, SEIQoL-DW rises (compared to MSA-QoL and PSP-QoL which rise with *worsening* QoL). See table 5.7.

Correlations between SEIQoL-DW and study variables (combined and in disease subgroups)			
Variable	**SEIQoL-DW coefficient (p-value)**	**MSA SEIQoL-DW coefficient (p-value)**	**PSP SEIQoL-DW coefficient (p-value)**
BADLS (disability)	0.205[R] (0.183)	0.270[R] (0.225)	0.66[R], (0.770)
DASS-depression	**-0.323[P] (0.032)**	-0.239[P] (0.283)	-0.379[P]. (0.082)
DASS-anxiety	-0.225[P](0.142)	-0.156[P] (0.487)	-0.268[P], (0.228)
POS-S-PD	**-0.338[R] (0.025)**	-0.064[R] (0.777)	**-0.661[R], (0.01)**
Duration of disease	0.176[P] (0.253)	0.212[P] (0.343)	0.150[P] (0.506)

*Table 5.7: Correlations between SEIQoL-DW score and other study variables. Significant results shown in **bold** R=Pearson's coefficient, P=Spearman's Rho. Duration of disease shown in months.*

When MSA and PSP patients were considered together, the model containing POS alone predicted 9.3% of the variance of SEIQoL-DW and the model was significant. F (2,41) = 5.434, p = 0.025.

There were no independent variables which predicted for SEIQoL-DW scores in the MSA group. In the PSP group POS-S-PD score accounted for 40.9% of the variance in SEIQoL-DW in the PSP group, and was significant (p = 0.001); therefore, rising palliative need in the PSP group only produced a fall in subjective QoL. This suggests that the small predictive value of POS-S-PD for SEIQoL-DW in both groups combined, is driven by the moderate predictive value of POS in the PSP subgroup.

5.4.7 Differences between patient groups

As both MSA and PSP patient groups had completed the SEIQoL-DW, any differences in scores were investigated. 22 MSA and 22 PSP patients completed the SEIQoL-DW assessment. The mean MSA score was 55.3 (±22.4) and in PSP, 67.0 (±15.3). There was not a statistically significant difference between SEIQoL-DW score in patients with MSA and PSP using independent t-tests (95% CI -23.1 to 0.26), t(42) = -1.973, p = 0.055. However, there is a trend towards significance for MSA having a lower subjective QoL than PSP.

The SEIQoL-DW scores were then explored for differences between the MSA and PSP groups accounting for level of disability (standard severity scores UMSARs and PSPRS are disease-specific and not directly comparable. As most participants were at Hoehn and Yahr stage 4 or 5, this classification was less meaningful also. Therefore, the BADLS disability score was used to account for differences in level of disease and how this impacted activities of daily living. ANCOVA was used to compare the SEIQoL-DW scores between the disease

groups, using BADLS score as a covariate. Unadjusted means of SEIQoL-DW were 55.6 for MSA and 67.0 for PSP. Adjusted for disability, the mean scores were 55.9 for MSA and 66.7 for PSP. After the effect of disability was accounted for, there was no significant difference between the means of MSA and PSP SEIQoL-DW scores. $F(1,41) = 3.5$, $p = 0.068$, partial $\eta^2 = 0.079$. This is represented in figure 5.6. As the p-value is further from significance than using the t-test, this may suggest that degree of disability does account for some of the difference in QoL scores between the groups.
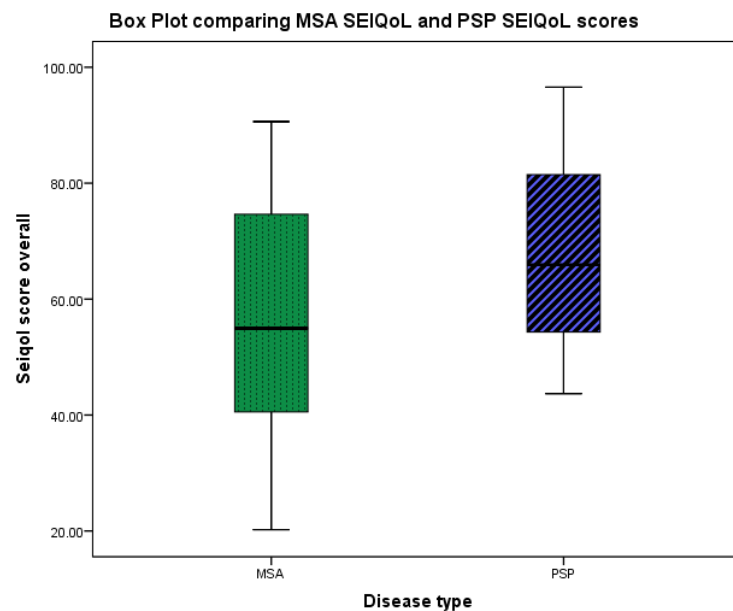
Figure 5.6: Box plots showing SEIQoL-DW scores between MSA (green) and PSP (blue) disease groups. There is overlap in their distributions.

5.4.8 SEIQoL-DW breakdown

The SEIQoL-DW is a flexible tool which can produces a great deal of information about different aspects of the participant's QoL beyond a continuous end-index. All patient-participants had the opportunity to take the SEIQoL-DW. This was timed (from the completion of the rater's explanation to the completion of the instrument). A judgement was then made by the rater as to the participant's understanding of the tool, degree of fatigue and therefore validity of the results. All assessments were done alone with the rater only to reduce the bias which may be produced from having a family member present e.g. may feel compelled to rate 'family' as having greater importance etc. The SEIQoL-DW administration data is given in table 5.8.

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Carers had the opportunity to take the SEIQoL-DW after it was added to the protocol using an ethical substantial amendment; in part due to the interest carers took in the process when applied to their family member and interest in trying for themselves. The carers' nominated domains will also be considered in this section for completeness sake.

Variable	MSA (N=22)	PSP (N=22)
Time taken, excluding explanation (minutes)	17.8 mean	23.3 mean
	16.0 median	24 median
	SD 6.43	SD 5.41
Assistance needed	None 14 (63.6%)	None 6 (27.3%)
	Part 4 (18.2%)	Part 10 (45.5%)
	Full 4 (18.2%)	Full 6 (27.3%)
Fatigue	None 19 (86.4%)	None 16 (66.7%)
	Some 3 (13%)	Some 4 (18.2%)
	A lot 0	A lot 2 (9.1%)
Understanding	Good 21 (95.5%)	Good 22 (95.7%)
	Some 1 (4.5%)	Some 0 (0%)
		Poor 1 (4.3%)
Validity	Valid 22 (100%)	Valid 20 (83.3%)
		Some 1 (4.2%)
		Questionable 1 (4.2%)

Table 5.8: SEIQoL-DW completion data for all patients.

Overall, 58 different domains were nominated when all groups were considered. These are shown in Appendix C. Although all statements of nomination of life areas were recorded, by necessity these had to be simplified into domains to allow analysis. There were 36 domains nominated by MSA patients and 36 by PSP patients; 24 of these domains were shared between the patient groups. In the MSA carer group 34 domains were nominated and in the PSP carer group 29 domains were nominated; 25 of these were shared between the carer groups. When domains were compared between the four groups, 19 were nominated in common. This suggests that QoL is made up of very diverse and broad categories according to individuals, but there is some overlap in concerns, even between different forms of AP and between patients and carers.

The most frequently nominated domains are shown in figure 5.7 below. In all groups, the most frequently nominated domain was 'family' (nominated by 82% of MSA patients and

77% of PSP patients and by 80% of MSA carers and 94% of PSP carers). Marriage or partner featured in all top five domains for each category (included tied positions) ranging from a frequency of 59% in PSP patients to 25% in PSP carers.
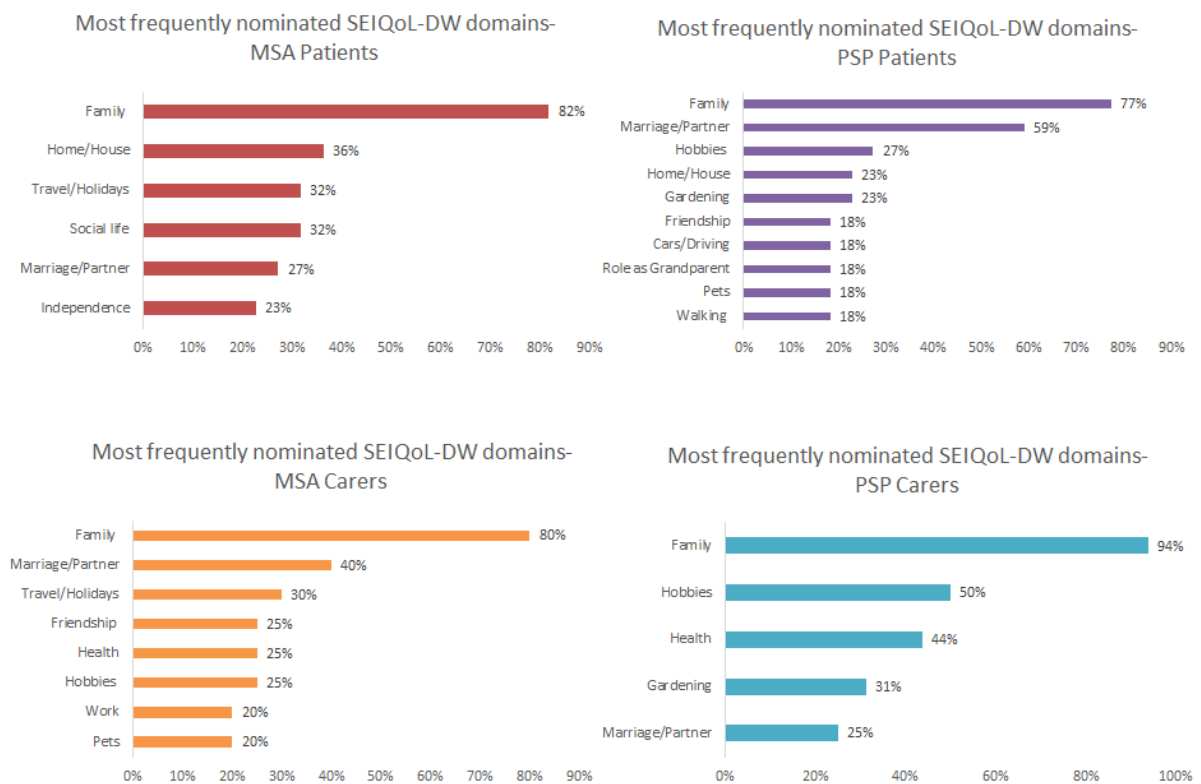
Figure 5.7: Bar charts showing most frequently nominated domains in SEIQoL-DW between respondent groups (5 most frequently nominated shown, tied totals included).

5.4.9 RAND-36 score comparisons

The RAND-36 comprises of eight sub-scores and two overall composite scores. This is explained in the methods section. These ten categories were compared between the groups using Mann-Whitney U testing. The scores which showed significant differences between the groups were the overall mental and physical composite scores (RAND-36 MCS and PCS), energy level and general health. The median scores for these domains are shown in table 5.9.

The categories which showed no significant differences between groups were physical, physical role, emotion, emotional role, social functioning and pain. The composite scores were derived by using the weightings described in Farivar *et al.* (2007). In terms of both physical and mental well-being, MSA patients had lower median scores representing poorer well-being compared to PSP patients. Of the eight sub-scores, energy levels, and general well-

being were significantly different between the two disease types. MSA had lower median scores than PSP in both of these subdomains also.

RAND-36 domain	Mann Whitney U (p-value)	Median score for disease groups if significant differences	
		MSA	PSP
Physical Composite Score	**0.049***	**27.1**	**31.3**
Mental Composite Score	**0.028***	**31.2**	**38.4**
Physical	0.464	0.0	5.0
Physical role	0.720	0.0	0.0
Emotional	0.359	64.0	72.0
Emotional role	0.447	0.0	16.7
Energy	**0.009***	**20.0**	**45.0**
Social functioning	0.244	12.5	25.0
Pain	0.280	45.0	57.5
General	**0.028***	**25.0**	**40.0**

*Table 5.9: Summary of Mann Whitney U comparisons between disease groups for RAND-36 domains. Significant results shown in **bold** and marked with * (p significance level = 0.05)*

5.5 Discussion

When disease-specific QoL was considered, palliative care need and depression were found to be predictive in MSA. While in PSP, palliative care need, depression and disease-specific severity were predictive of QoL. Some possible reasons for this include lesser cognitive impairment in MSA allowing greater insight into condition, which may cause distress earlier in disease course. Or, in contrast, these patients may have the cognitive capacity to adjust to their condition in later stages. Similarly, concrete thinking and frontal lobe dyscognitive symptoms in PSP could interfere with adjustment and acceptance, making the physical manifestations of illness impact more directly on QoL. Another possibility is that PSPRS as a scale reflects severity more accurately than the UMSARS scale, and therefore, has a greater predictive power in HR-QoL. This is probably unlikely as both scales are validated and widely used internationally in observational and randomised-controlled trials.

When subjective QoL was analysed (subjective and individual-focussed as opposed to HR-QoL which concentrates on QoL in relation to disease), there were far fewer associations seen with study variables or patient demographics. When all patients were considered together there was a small predictive effect of palliative care need. However, when MSA and PSP

patients were considered separately, it was found that there was a medium-sized predictive value for palliative care need in the PSP group and no predictions could be made in the MSA group. One possibility for this is that patients with PSP may be more impacted by physical symptoms, whereas in MSA there may be other factors influencing subjective QoL which have not been explored in this study. Maybe MSA patients focus on other aspects of life beyond disease symptoms due to their retained cognition, whereas PSP patients remain more fixed on the physical manifestations of their disease.

Some considerations are that SEIQoL-DW as an individual and subjective representation of QoL is much more heterogeneous and as such, straightforward relationships with any one measure might be less likely. SEIQoL-DW does not focus the patient on their disease and activities they can no longer do as a consequence, but is open to all aspects of the patients' life. This may act as a reminder of the factors which can improve QoL in the populations we care for. When it is considered that neither the MSA nor PSP patient groups considered 'health' as one of the most frequently nominated domains and that 'walking' was tied only 4th in the PSP group, there are significant areas of the patient experience which contribute to QoL beyond their disease. It must be noted that 'family' and 'marriage/partner' were the most highly rated domains across all both patient and carer groups. These are opportunities to enhance the patient experience in the face of a condition for which there is no disease-modifying therapy yet available. Palliative care, with its inclusive ethos of supporting families and carers during the disease course, and after the death of the patient, is well-suited to enhance these aspects of QoL for these patients, as well as the health-related symptom aspects which impact disease-specific QoL.

In terms of differences between the MSA and PSP groups, there were no significant differences in the overall SEIQoL-DW scores, though mean MSA scores were lower and there was a trend toward significance. When accounting for degree of disability using BADLS there were still no significant differences, though MSA patients had lower mean scores, both unadjusted and adjusted for disability. When RAND-36 scores were compared, there were significant differences between patient groups in terms of overall physical and mental well-being (Physical and Mental Composite Scores), energy and general health. In all RAND-36 scores where there were significant differences, MSA patients had lower ranked median scores (thus lower well-being) than PSP patients. These scores are generic, so not disease-specific but unlike SEIQoL-DW they take a fairly 'mechanistic' view to well-being, looking chiefly at functional abilities in each domain and not including reflection or judgement (the

key difference between health status and QoL scores). Therefore, MSA patients may reflect more upon their disability than PSP patients, again a possible consequence of the greater frontal cognitive deficits which tend to be seen in PSP.

Chapter 6. Carers of Individuals with MSA and PSP

6.1 Introduction

This chapter will explore associations and relationships found in terms of carers of participants with MSA and PSP. All but one participant (who had PSP-PAGF) had a carer who took part in the study. The patient was keen to take part and had input from a family member but they did not later attend to take part in the study. It was decided to retain and use the data collected by this patient-participant rather than exclude their contribution as their carer chose not to attend (his data was used in the analysis in Chapters 4, 5 and 7).

6.2 Aims

The aims of this chapter are to explore the descriptive data to describe similarities and differences in the care-givers of participants with MSA and participants with PSP, to find whether there are differences in the levels of strain and QoL (using various measures) between the MSA carer group and PSP carer group, and whether any associations existed between study variables collected, carer strain and carer QoL. Finally, comparisons will be made between patients and carers using generic measures, looking at whether certain groups have particular issues which may be of interest clinically.

6.3 Methods

In this chapter, comparison of variables between the MSA and PSP groups was carried out, first using independent t-tests and then using ANCOVA, accounting for disability in each case. This method makes adjustments for the variable being tested, accounting for a covariate and then looks for any significant differences. Fisher's exact test was used instead of chi-squared when proportions between groups were compared and there were scarce numbers in one category. Fisher's exact test generates a significance value only and no other test statistic. The statistical tests used in this chapter have been discussed in Chapter 3.

6.4 Results

6.4.1 Carer Demographics.

There were 46 carers who took part in this study and all were informal carers (*i.e.* not paid or employed to provide care), as required by the study criteria. As discussed in the introduction, there was a single patient-participant who did not have a carer.

There were 23 carers of participants with MSA and 23 PSP carers. Their demographic information is shown in table 6.1.

		Disease type		Total	Test of proportions χ^2 (p-value)
		MSA n (%)	PSP n (%)	n (%)	
Carer sex	Female	15 (65.2)	13 (56.6)	28 (60.9)	$\chi^2(1) = 0.546$
	Male	8 (34.8)	10 (43.5)	18 (39.1)	$p = 0.763$
Employment status	Employed	12 (52.2)	6 (26.1)	18 (39.1)	$\chi^2(1) = 3.286$
	Unemployed	0	0	0 (0)	$p = 0.130$
	Retired	11 (47.8)	17 (73.9)	28 (60.9)	
Driving	Driver	18 (78.3)	18 (78.3)	36 (78.3)	$\chi^2(1) = 0$
	Non-driver	5 (21.7)	5 (21.7)	10 (21.7)	$p = 1$
Relationship to patient	Spouse/Partner	18 (78.3)	19 (82.6)	37 (80.4)	
	Daughter/Son	4 (17.4)	3 (13.0)	7 (15.2)	$p = 0.724$ *
	Friend	0 (0)	1 (4.3)	1(2.2)	
	Sibling	1 (4.3)	0 (0)	1 (2.2)	

Table 6.1 Demographic information of carer-participants. Test of 2 proportions have used to detect differences between groups, *=indicates Fisher's exact test was used

There was a preponderance of female carers in both the MSA and PSP groups; 15 in the MSA group and 13 in the PSP group. A test of two proportions was performed, and this showed there was not a statistically significant difference between the two carer groups in terms of the proportions of male and female carers ($\chi^2(1) = 0.546$, $p = 0.763$). See table 6.1 and figure 6.1.
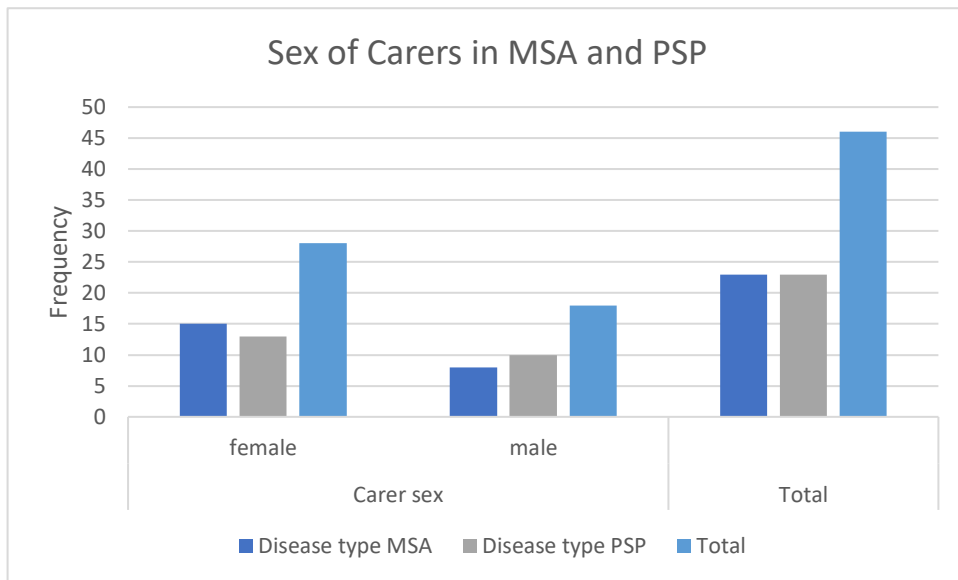
Figure 6.1: A cluster column chart showing frequency of carer sexes in MSA and PSP groups

6.4.2 Age

In terms of carer ages, the median age in the MSA group was 63.0 years (IQR 18.0) and in the PSP group, 69.5 (IQR 9.5). There was no statistical difference between the carer groups when the median ages were compared (using Mann-Whitney U tests due to their non-normal distribution). Nevertheless, more carers were in their 60s and 70s in MSA and in their 70s in PSP, as demonstrated by figure 6.2.
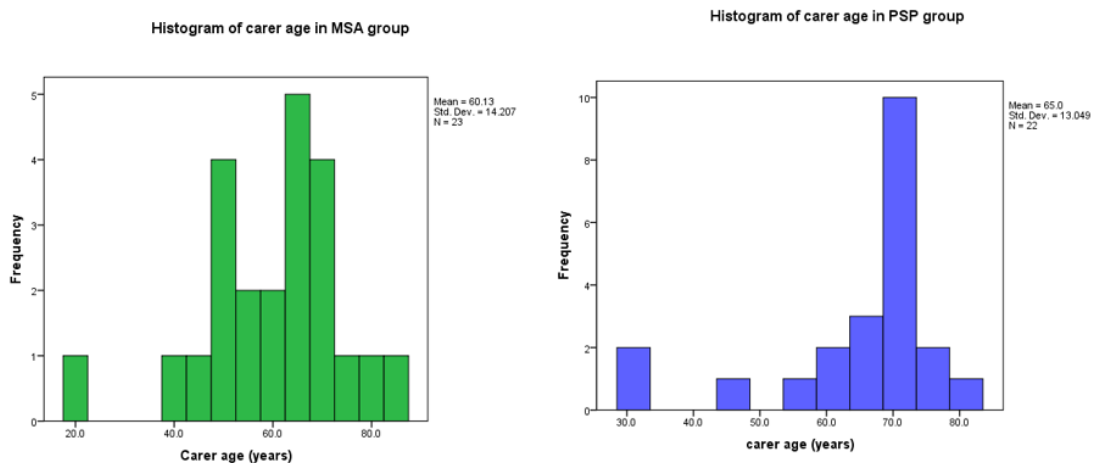
Figure 6.2: Histograms showing distribution of carer ages in MSA (green) and PSP (blue)

The median duration of care-giving was 36 months in the MSA group and 48 months in the PSP group so a trend was seen toward longer duration of care in the PSP group.

The distributions of care-duration for each condition were not normally distributed. Mann Whitney U tests were used to compare the distribution of care duration between the two disease types and no significant differences were found. The distribution was skewed toward a shorter duration of care of less than 100 months in both conditions, see figure 6.3.
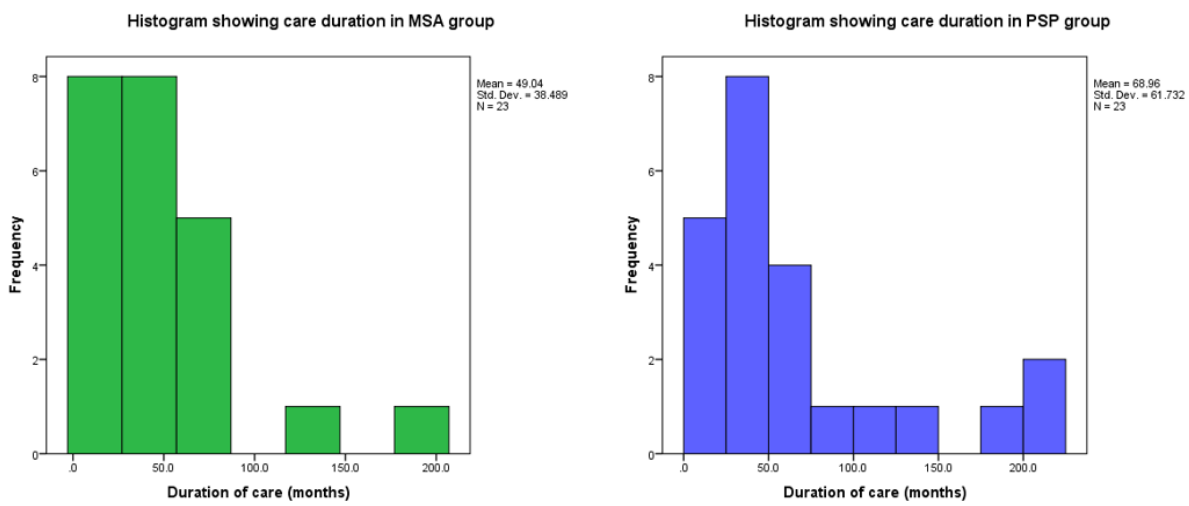
Figure 6.3: Histograms of carer age for MSA (green) and PSP patients (blue). Neither show a normal distribution.

6.4.3 Relationship to patient

The majority of carers who took part in the study were the partners or spouses of the patient. Of the 42 patient-partner pairs, there were 41 mixed-sex relationships and one same-sex relationship. This partner-as-carer majority reflects the previous literature which has found that partners (especially in degenerative diseases which tend to affect people in middle-age or older), tend to provide the bulk of unpaid care (Goldsworthy and Knowles, 2008; Greenwell *et al.*, 2015). Only one participant in the PSP group had a non-relative carer (who was not a partner). When comparing proportions between groups, there were insufficient numbers in each category to use chi-squared tests so Fisher's exact test was used to compare proportions between partners and non-partner groups (as Fisher's exact can only be used to compare 2 groups). There was no significant difference between groups, p = 0.724. See table 6.1.

6.4.4 Carer Employment

Carers were asked about their employment status. They were asked whether they were still working, seeking work/unemployed or retired. No participants defined themselves as unemployed. 52.2% of MSA carers were still in paid work compared with 26.1% of PSP carers. A test of two proportions did not find a significant difference in the proportions of carers still in work between the two disease groups though a greater proportion of MSA carers were still employed. ($\chi^2(1) = 3.286$, $p = 0.130$) See table 6.1 and figure 6.4.
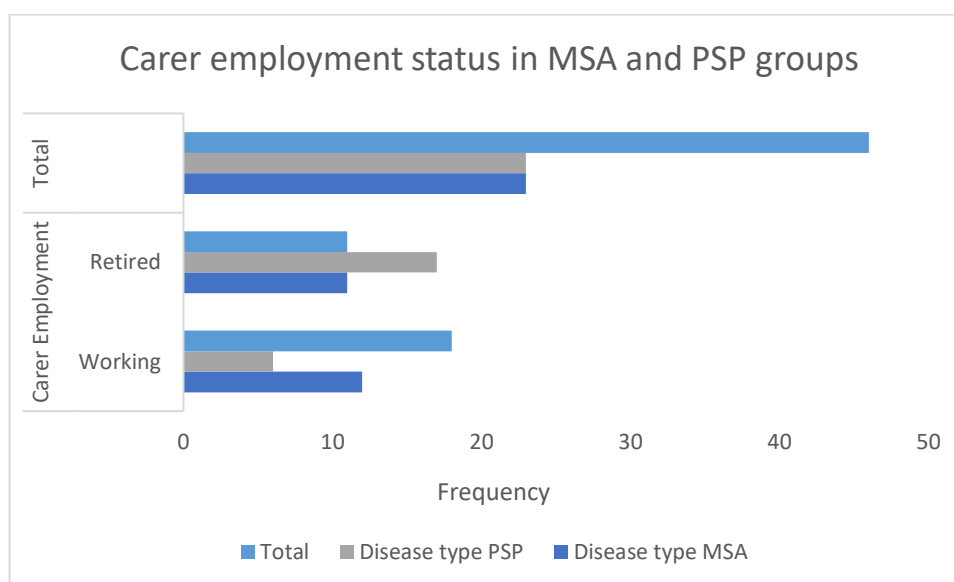
Figure 6.4: Bar chart of employment frequencies for carers in MSA and PSP groups

6.4.5 Driving

Driving, which may be important in terms of care-giving and mobility to hospital appointments and similar, had an equal distribution in the MSA and PSP groups. There was no significant difference between drivers and non-drivers between the MSA and PSP carer groups (see table 6.1). When a cross-tabulation was produced looking at the proportions of non-drivers by sex, 28.6% (8) women were non-drivers whereas only 11.1% (2) men were non-drivers. As the sample size was too small for a test of two proportions, Fisher's exact test was run. There was no statistically significant difference in proportions of men and women who were non-drivers, $p = 0.274$

6.5 Associations and Predictions

6.5.1 Carer strain (MCSI) associations and predictions

The first carer variable to be considered was strain using the MCSI. Overall, including all carers, the MCSI had an approximately normal distribution on histogram and SW testing did not show significance when carer groups were divided into MSA and PSP groups, therefore there was no evidence against normal distribution.

When mean scores of MCSI were compared using independent t-tests, there were no significant differences between carers of patients with MSA and PSP. MSA carers had a mean score of 13.4 ($\pm$ 6.4) and PSP carers a mean score of 12.9 ($\pm$ 6.1). Again, when independent t-testing was carried out between male and female carers there were no significant differences between mean scores for these categories (mean male score 13.2, $\pm$ 5.8, mean female score 13.1, $\pm$6.5).

An ANCOVA adjusting for degree of disability was carried out, looking for differences between MCSI score in MSA and PSP carers with the influence of degree of patient disability removed. Disease type did not affect MCSI score when disability was taken into account $F(1,43) = 0.233$, $p = 0.632$, $\eta p^2 = 0.005$.

MCSI was tested for associations with carer demographics such as gender, age, duration of time as a carer, care afforded per week, and duration of relationship. Previous work in other conditions has given mixed results on factors such as carer sex and age but has suggested that amount of time as a carer might impact on carer strain and QoL. Carer physical and mental well-being and patient variables tested in the study such as depression, disability and QoL were also tested, all of which have been investigated for associations with carer strain and QoL in other conditions including PD (Morley *et al.*, 2012; Corallo *et al.*, 2016). See table 6.2.

Independent variable	Coefficient correlation	Significance (p-value)
Carer sex (PBS)	0.019[b]	0.903
Carer age	-0.150[P]	0.327
Duration of care	0.119[P]	0.430
Care given per week	-0.047[P]	0.759
Duration of relationship	**-0.296[P]**	**0.046**
Carer physical well-being (RAND-36 PCS)	-0.094[P]	0.533
Carer mental well-being (RAND-36 MCS)	-0.232[R]	0.121
Carer subjective QoL (SEIQoL-DW)	-0.269[R]	0.107
Patient depression (DASS-21)	0.261[P]	0.080
Patient disability (BADLS)	0.188[R]	0.210
Palliative need score (POS-S-PD)	0.176[R]	0.241
Patient disease-specific QoL (MSA-QoL/PSP-QoL)	0.184[R]	0.402
	0.274[R]	0.206
Patient subjective QoL (SEIQoL-DW)	0.018[R]	0.910

Table 6.2: Correlations of MCSI with carer and patient variables. R=Pearson's correlation coefficient, P=Spearman's Rho correlation coefficient, b=point-biserial correlation. *Significant associations shown in* **bold** *text.*

The duration of relationship (measured in months) was the only significant association found between carer demographics and the amount of strain they reported on the MCSI scale. The duration of relationship was found to be negatively correlated with amount of strain experienced. This suggests that duration of relationship has a protective effect against carer strain. Duration has been tested before in this way but no associations have been found previously in American or Japanese cohorts of carers of people with PD (Tanji *et al.*, 2013). Sex, age and the amount of care given, in terms of overall duration and per week, had no statistically significant correlation nor did patient variables, such as degree of disability or QoL, though there was a non-significant trend in the case of depression.

Univariate analyses were then carried out on duration of relationship and patient DASS-depression, to see if they predicted for MCSI scores. See table 6.3.

	β	SE	p-value	95% CI		R² adj	F-value
				LB	UB		
Relationship duration	**-0.324**	**0.005**	**0.028**	**-0.022**	**-0.001**	**0.085**	**5.156**
DASS-depression	0.287	0.143	0.053	-0.004	0.573	0.062	3.956

*Table 6.3: Univariate regression coefficients for MCSI. Significant results highlighted in **bold** text. SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R² adj=R² adjusted value*

The overall basic regression model produced was in keeping with univariate analysis and contained only relationship duration as a significant predictor of carer strain, measured with MCSI. The adjusted R^2 was 0.085 (accounting for a variance of 8.5% of MCSI score), meaning that the duration of carer relationship could predict for 8.5% of the carer strain score assessed using the MCSI. Therefore, relationship duration is a significant predictor of carer strain but the effect size is trivial to small. See table 6.4.

	β	SE	p-value	95% CI		R² adj	F-value
				LB	UB		
Relationship duration	**-0.324**	**0.005**	**0.028**	**-0.022**	**-0.001**	**0.085**	**5.156**

*Table 6.4 Overall basic model of regression coefficients for MCSI. Significant results highlighted in **bold** text. SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R² adj=R² adjusted value*

6.5.2 Carer QoL (PQoLc) associations and predictions

The second variable to be tested was the QoL in the carer group and this was measured with PQoLc. This is a specific QoL measure which appraises QoL in the context of caring for a person with AP. Higher scores represent a lower QoL. PQoLc was found to be normally distributed on visual inspection of histograms and SW testing suggested a normal distribution for each group.

When PQoLc scores for MSA carers and PSP carers were compared using independent t-tests there were no significant differences between the two. MSA carers had a mean score of 43.9 (± 20.3) and PSP carers a mean score of 45.8 (± 24.6). The carers were then considered for differences between PQoLc scores in terms of sex. Again, there were no significant

differences between the groups. Male carers had a mean score of 43.3 (± 19.4) whilst female carers had a mean score of 45.8 (± 24.3).

An ANCOVA adjusting for degree of disability was carried out, looking for differences between PQoLc score in MSA and PSP carers. Disease type did not affect PQoLc score when the influence of patient disability was taken into account, $F(1,43) = 0.016$, $p = 0.901$, $\eta p^2 = 0.00$

PQoLc was then explored for associations with study variables including carer demographics, patient study variables and carer study variables. See table 6.5. When patient variables were examined for associations with PQoLc, duration of falls was also included, as literature has discussed falling as having an impact upon carer QoL in a previous British study in PD (Schrag *et al.*, 2006b).

Independent variable	Coefficient correlation	Significance (p-value)
Carer sex (PBS)	0.039[b]	0.799
Carer age	-0.192[P]	0.205
Duration of care	0.045[P]	0.764
Care given per week	-0.086[P]	0.570
Duration of relationship	**-0.334[P]**	**0.023**
Carer physical well-being (RAND-36 PCS)	**-0.535[P]**	**0.001**
Carer mental well-being (RAND-36 MCS)	**-0.700[R]**	**0.001**
Carer subjective QoL (SEIQoL-DW)	**-0.401[R]**	**0.014**
Patient depression (DASS-21)	**0.415[P]**	**0.004**
Patient disability (BADLS)	0.156[R]	0.302
Palliative need score (POS-S-PD)	0.231[R]	0.123
Patient disease-specific QoL (MSA-QoL/PSP-QoL)	0.163[R]	0.456
	0.339[R]	0.113
Patient subjective QoL (SEIQoL-DW)	0.267[R]	0.083
Duration of falls (months)	0.131[P]	0.415

*Table 6.5: Associations between study variables and PQoLc. R=Pearson's correlation coefficient, P=Spearman's Rho correlation coefficient, b=point-biserial correlation. Significant associations shown in **bold** text.*

As with MCSI, the only association seen with carer demographics was the duration of overall relationship between the patient with AP and their carer. Again, like MCSI, this relationship was a negative correlation; suggesting that as caring-specific QoL became poorer (using this instrument, a higher score) duration of relationship tended to decrease. Therefore, pairs with

longer relationships tended to have carers with a better carer-specific QoL (lower PQoLc score).

There were negative correlations between PQoLc and the carer general physical and mental well-being as measured by the RAND-36, medium and large respectively in terms of strength. There was also a negative, medium-sized association with carer SEIQoL (subjective QoL) and a positive medium-sized association with patient depression (DASS-21).

Univariate analysis with each of these measures which showed an association was performed and all showed some predictive value alone for PQoLc score. See table 6.6.

	β	SE	p-value	95% CI		R^2 adj	F-value
				LB	UB		
Relationship duration	**-0.346**	**0.18**	**0.019**	**-0.080**	**-0.008**	**0.100**	**5.976**
Carer PCS	**-0.485**	**0.300**	**0.001**	**-1.709**	**-0.499**	**0.218**	**13.532**
Carer MCS	**-0.700**	**0.230**	**0.001**	**-1.959**	**-1.032**	**0.479**	**42.360**
Carer SEIQoL	**-0.401**	**0.153**	**0.014**	**-0.709**	**-0.085**	**0.137**	**6.693**
DASS-depression	**0.380**	**0.499**	**0.009**	**0.355**	**2.364**	**0.125**	**7.435**

*Table 6.6: Univariate regression coefficients for PQoLc. Significant results highlighted in **bold** text. SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R^2 adj=R^2 adjusted value*

A basic overall model was produced using backward elimination regression, shown in table 6.7. All independent variables except for Carer MCS were removed as they did not contribute significantly to the model.

	β	SE	p-value	95% CI		R^2 adj	F-value
				LB	UB		
Carer MCS	**-0.706**	**0.273**	**0.001**	**-2.168**	**-1.058**	**0.484**	**34.804**

*Table 6.7: Overall basic model of regression coefficients for PQoLc. Significant results highlighted in **bold** text. SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R^2 adj=R^2 adjusted value*

The overall basic model produced for PQoLc after non-significant predictors were removed, contained only carer mental well-being (carer MCS). Carer mental well-being had an adjusted R^2 of 0.484 (accounting for 48.4% of the variance of PQoLc).

6.5.3 Carer SEIQoL-DW associations and predictions

The third variable to be tested was carer SEIQoL-DW. This is a general, subjective QoL measure. Higher scores represent a higher QoL. Carer SEIQoL-DW was found to be normally distributed on visual inspection of histograms and SW testing.

When SEIQoL-DW scores for MSA carers and PSP carers were compared using independent t-tests there were no significant differences between the two. MSA carers had a mean score of 65.6 ($\pm$ 18.4) and PSP carers a mean score of 62.2 ($\pm$ 27.8). The carers were then considered for differences between SEIQoL-DW scores in terms of sex. Again, there were no significant differences between the groups. Male carers had a mean score of 65.6 ($\pm$ 20.5) whilst female carers had a mean score of 61.9 ($\pm$ 24.3).

An ANCOVA to compare the two carer groups adjusting for degree of patient disability was carried out, looking for differences between SEIQoL-DW score in MSA and PSP carers. Disease type did not affect carer SEIQoL-DW score when disability was taken into account $F(1,34) = 0.172$, $p = 0.681$, $\eta p^2 = 0.005$.

Subjective carer QoL using the SEIQoL-DW overall index was then investigated. Associations were found with carer age, duration of relationship, carer mental well-being and patient depression (see table 6.8). There was an association found between disease-specific QoL in the PSP group only (PSP-QoL) though not in the MSA group (MSA-QoL).

Independent variable	Coefficient correlation	Significance (p-value)
Carer sex (PBS)	0.139[b]	0.413
Carer age	**0.400[P]**	**0.016**
Duration of care	0.280[P]	0.093
Care given per week	0.188[P]	0.264
Duration of relationship	**0.450[P]**	**0.005**
Carer physical well-being (RAND-36 PCS)	0.283[P]	0.089
Carer mental well-being (RAND-36 MCS)	**0.451 [R]**	**0.005**
Patient depression (DASS-21)	**-0.516[P]**	**0.001**
Patient disability (BADLS)	0.092[R]	0.589
Palliative need score (POS-S-PD)	0.254[R]	0.129
Patient disease-specific QoL (MSA-QoL/PSP-QoL)	-0.204[R]	0.389
	-0.569[R]	**0.017**
Duration of falls (months)	0.131[P]	0.415

Table 6.8: Correlations of carer SEIQoL-DW index with carer and patient variables.
R=Pearson's correlation coefficient, P=Spearman's Rho correlation coefficient, b=point-biserial correlation.
*Significant associations shown in **bold** text.*

Univariate regression analysis was carried out for each of these independent variables where an association had been found. For PSP-QoL, only the PSP subgroup was considered. See table 6.9.

	β	SE	p-value	95% CI		R^2 adj	F-value
				LB	UB		
Age	0.306	0.272	0.070	-0.043	1.061	0.067	3.510
Relationship duration	**0.398**	**0.23**	**0.015**	**0.012**	**0.105**	**0.134**	**6.578**
Carer MCS	**0.451**	**0.348**	**0.005**	**0.332**	**1.744**	**0.180**	**8.914**
DASS-depression	**-0.512**	**0.557**	**0.001**	**-3.094**	**-0.832**	**0.262**	**12.415**
PSP-QoL (subgroup only)	**-0.569**	**0.161**	**0.017**	**-0.774**	**-0.088**	**0.279**	**7.179**

*Table 6.9: Univariate regression coefficients for carer SEIQoL-DW. Significant results highlighted in **bold** text.*
SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound,
R^2 adj=R^2 adjusted value

When an overall basic regression model was produced with non-significant predictors removed, patient depression (using DASS-21) remained and had a R^2 of 0.300 (meaning

depression in patients measured by the DASS-21 accounted for 30% of the variance of carer subjective QoL using SEIQoL-DW). See table 6.10.

	β	SE	p-value	95% CI		R^2 adj	F-value
				LB	UB		
DASS-depression	-0.548	0.542	0.01	-0.3173	-0.969	0.300	14.574

*Table 6.10: Overall basic model of regression coefficients for carer SEIQoL-DW. Significant results highlighted in **bold** text. SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R^2 adj=R^2 adjusted*

When PSP-QoL was explored in just the PSP subgroup, carer age and patient depression remained in the model as significant predictors and PSP-QoL was removed as non-significant. See table 6.11. Therefore, in the PSP carer group only, both depression in the patient and age of the carer predicted for carer subjective QoL, accounting for 50.9% of the variance.

	β	SE	p-value	95% CI		R^2 adj	F-value
				LB	UB		
DASS-depression	-0.654	0.767	0.003	-4.423	-1.111	0.509	8.770
Carer age	0.422	0.425	0.036	0.077	1.902		

*Table 6.11: Overall basic model of regression coefficients for carer SEIQoL-DW (PSP sub-group). Significant results highlighted in **bold** text. SE=Standard error, CI=Confidence Interval, LB=Lower bound, UB=Upper bound, R^2 adj=R^2 adjusted*

6.5.4 Comparisons between four groups

Two scales were completed in common by all four groups in the study. These were the RAND-36 and SEIQoL-DW. A limited number of comparisons between all four groups were conducted to look at the differences in ranking in well-being and subjective QoL. As the RAND-36 composite scores were non-normally distributed, Kruskall-Wallis tests to perform comparisons were used rather than 1-way ANOVA. See table 6.12.

RAND-36 Category	Test statistic, H (df), p-value	Null hypothesis	Rank order (low to high)
RAND-36 PCS	39.185 (3), p ≤ 0.001	Rejected	MSA patient, PSP patient, MSA carer, PSP carer
RAND-36 MCS	12.894 (3), p = 0.005	Rejected	MSA patient, PSP patient, MSA carer, PSP carer

Table 6.12: Kruskall-Wallis H comparisons between patient and carer groups in RAND-36. Also shows order of ranked catagories (lower scores represent poorer health status).

In both categories which showed significant differences between groups, the ranked orders were the same; the lowest well-being in MSA patients, then PSP patients, then MSA carers with PSP carers having the highest well-being scores (the significant differences were not necessarily between all groups. The group differences are explored in tables 6.13 and 6.14 using Dunn's pairwise comparison to assess where the significant differences lay and are shown below.

Groups being compared	Kruskall-Wallis Test Statistic	Standard error	Adjusted significance
MSA patient, PSP patient	-10.833	7.875	1
MSA patient, MSA carer	**-36.087**	**7.959**	**0.001**
MSA patient, PSP carer	**-42.739**	**7.959**	**0.001**
PSP patient, MSA carer	**-25.199**	**7.875**	**0.000 (0.001)**
PSP patient, PSP carer	**-31.851**	**7.875**	**0.000 (0.001)**
MSA carer, PSP carer	-6.652	7.959	1

*Table 6.13: Pairwise comparisons using Dunn's procedure with Bonferroni correction for the RAND-36 Physical well-being composite score (RAND-36 PCS). **Bold** means significant differences detected between those two categories*

Groups being compared	Kruskall Wallis Test Statistic	Standard error	Adjusted significance
MSA patient, PSP patient	-17.124	7.876	0.178
MSA patient, MSA carer	**-21.978**	**7.959**	**0.035**
MSA patient, PSP carer	**-26.783**	**7.959**	**0.005**
PSP patient, MSA carer	-4.854	7.876	1
PSP patient, PSP carer	-9.659	7.876	1
MSA carer, PSP carer	-4.804	7.959	1

*Table 6.14: Pairwise comparisons using Dunn's procedure with Bonferroni corrections for RAND-36 Mental well-being composite score (RAND-36 MCS). **Bold** means significant differences detected between those two categories*

In the RAND-36 PCS composite score there were significant differences in ranked mean scores between the MSA and PSP patient groups and between patients and carers within disease groups.

When the RAND-36 MCS composite score was considered there were significant differences between MSA patients and MSA carers (and MSA patients and PSP carers) though not between the different patient groups.

6.5.5 SEIQoL-DW comparisons

The most highly nominated response for the SEIQoL-DW for respondents in both patient and carer groups was 'family'. Therefore, comparisons were made between the overall family cue (functioning) score and family weighting (importance) between groups. In both cases, there were no significant differences between any of the groups (cue 0.025, p = 0.999, weighting 1.568, p = 0.667). This is shown in figure 6.5.
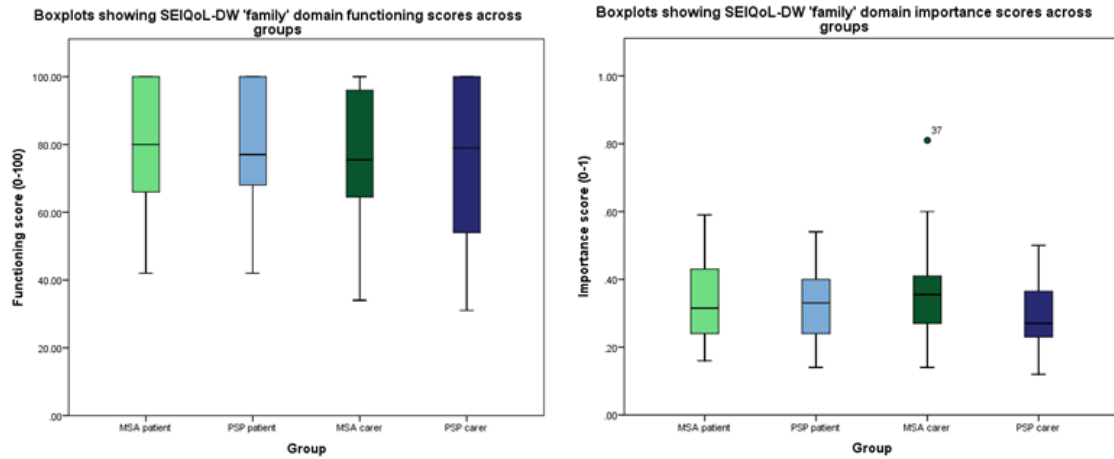
Figure 6.5: Boxplot comparisons showing similarities between family cue-level (functioning) and weight (relative importance) scores in SEIQoL-DW

6.6 Discussion

In the carer cohort, there was a trend toward older age in the PSP subgroup. PSP is a disease with a greater age of expected onset than MSA (O'Sullivan *et al.*, 2008). The differences were not significant however, likely because of the contribution of carers who were not spouses or partners of differing ages. There was a non-significant trend seen. Female carers were more common in both disease groups but there was not a statistical difference in the numbers of male and female carers between the MSA and PSP categories.

The median duration of care-giving in PSP was longer than MSA (4 years as opposed to 3 years). However, the duration of disease for each condition was approximately 3 years (40 months in each disease, see Chapter 4). One reason for this may be greater likelihood of more severe cognitive dysfunction in the PSP group necessitating more carer input and supervision from an earlier stage in disability than in the MSA group. The definition given for care was 'the point at which you felt you needed to offer support [to the patient] without which they would not easily cope'. This is obviously variable and subjective, but what individuals defined as 'care' as opposed to everyday help also varied. As this project considers the impact care-giving has on individuals, the subjective definitions of care are of value.

A greater proportion of MSA carers were in paid employment (52% compared with 26%). This might suggest several factors; one might be that as PSP carers tend to be older, more may have retired than the MSA carers. Another possibility may be that PSP patients require more care or supervision than MSA patients, so their carers tend to retire earlier. An

implication may be that PSP carers could be offered more care-input allowing them to retain paid work, should they wish to.

In terms of carer strain (measured by the MCSI), there were no differences between the two carer groups, nor between males and female carers. A single study in PSP has suggested that female carers may suffer more from the impact of care than males (Uttl *et al.*, 1998). However, this finding has not been replicated in other studies looking at carer strain in Parkinsonism generally (Schrag *et al.*, 2006b; Greenwell *et al.*, 2015). A small, negative association was found between carer strain and duration of the patient-carer relationship. A regression analysis found that duration of relationship did predict for carer strain (longer relationships predicted less carer strain). The effect was small though significant. More work to explore this association with greater numbers would be appropriate, also considering the quality of relationship, which has been suggested as having a buffering effect against carer burden in PD (Goldsworthy and Knowles, 2008).

QoL in terms of carer role using PQoLc demonstrated no differences between disease types or sex of carer. A number of associations were seen with PQoLc, including patient depression, physical and mental well-being of carers and duration of relationship. A basic regression model showed that once non-significant contributors had been removed, carer mental well-being accounted for 48% of PQoLc. Although the mental well-being score (RAND-36 MCS) does not provide information on individual aspects of mental health, it stands to reason that support of carers and treatment of mental health issues, such as depression, is important in maintaining carer QoL. It is possible that identifying mental health needs in carers and addressing them could allow care to continue and keep patients and their carers together in the community for longer.

In terms of overall subjective QoL in carers, after non-significant variables were removed, patient depression was found to predict 30% of the variance of SEIQoL-DW. This suggests that if the cared-for individual is depressed, this does not only affect the carer's experience in terms of their role in being a carer, but their whole individual experience (as SEIQoL is a general QoL tool, not limited to the carer experience, as PQoLc is). This finding suggests that depression in the patient is pervasive in the carer's outlook. This provides evidence for how important the recognition and management of depression is, not only to benefit patients but those who care for them. Interestingly, in PSP carers only, older age had some protective effect for subjective QoL. In Chapter 7, there will be a discussion of changing expectations and how this affects life plans (biographical disruption). It may be that older carers have more

of an expectation or preparation for serious illness, permitting adjustment, whereas this may not be the case in (generally) younger care-givers in the MSA group. From review of the literature, it is believed this demonstration of the impact of patient depression on subjective QoL in carers is novel.

Finally, some comparisons were made between the two patient groups and the two carer groups in terms of SEIQoL domains and RAND-36 scores (as all four groups completed these comparable and general tools).

The most commonly nominated response for all four groups was 'family'. There were no statistical differences between the groups when perceptions of family functioning nor the importance of family were compared.

In the RAND-36 tool, there were differences between overall composite scores with the significant differences between some (though not necessarily all) groups. For example, overall physical well-being (RAND-36 PCS) showed significant differences between MSA and PSP patients, with MSA patients having lower physical well-being and between MSA patients and their carers and PSP patients and their carers (though no differences between carer groups). In terms of mental well-being, MSA patients and carers had differences but PSP had not, nor did the two carer groups.

All RAND scores with significant differences had the same ranks; lowest being MSA patients, then PSP patients, then MSA carers, then PSP carers. It was interesting that this ordering was preserved across physical and mental well-being. PSP patients, with greater frontal lobe dysfunction may have lesser distress at their situation and decline than individuals with MSA, who tend to have lesser cognitive involvement and maybe more insight into their condition. Similarly, carers may suffer adversely if those they care for are distressed by their illness; which might explain why MSA carers might therefore could have lower well-being than PSP carers, overall.

It is vital to remember that individuals complete these tools according to their own perceptions. Therefore, if patients had marked disability but did not feel this was of concern to them, it was completed according to their outlook. It would be interesting in further work, for carers to complete these questionnaires as to how they felt the patient would respond, as it may be their perceptions of the experience of the person with illness and that of the individual themselves, are very different.

Chapter 7. Qualitative Exploration of Impact of AP on Patient and Carer Participants

7.1 Background

The implications of a diagnosis of a progressive and aggressive condition like MSA or PSP can be felt in both patients and carers, impacting markedly on QoL. To produce a rounded and holistic exploration of the experiences of the cohort in this study, qualitative methods were used (as discussed in Chapter 3: Methods) to try and gain a subjective view of living with MSA or PSP. These subjective insights can be helpful in not only gaining an understanding of the experiences of these participants but also how we might be able to tailor our approach and services to better manage these complex conditions.

7.2 Methods

The methods used for interviewing and data analysis were explored in depth in Chapter 3, Methods. Nineteen interviews were carried out, ten with patient-participants (four MSA and six PSP) and nine with carer participants (four MSA and five PSP). See table 3.6 in Chapter 3. Purposive sampling was used to obtain a range of viewpoints, including patients with severe speech difficulty, as this group has been poorly-represented in research. The interviews were conducted with open-ended questions from an interview guide (formulated for the study) which helped guide the interviewer and interviewee toward issues being studied. Interviews were recorded and transcribed verbatim and then coded to produce overall meaningful themes which pervaded the data. Thematic analysis was the method used for analysis and this is fully discussed in Chapter 3.

7.3 Results

The three main themes that were produced from the analysis of interviews were firstly 'Connection', encompassing speech as a means to communicate, how participants were able to connect to others and how they were perceived. Secondly, 'Transition' and the shift from one role or state to another, such as from spouse to carer or from independent individual to a person who is dependent on others. The last theme was 'Accessing Support' and what participants deemed as important and how they derived help from different sources.

7.4 Connection
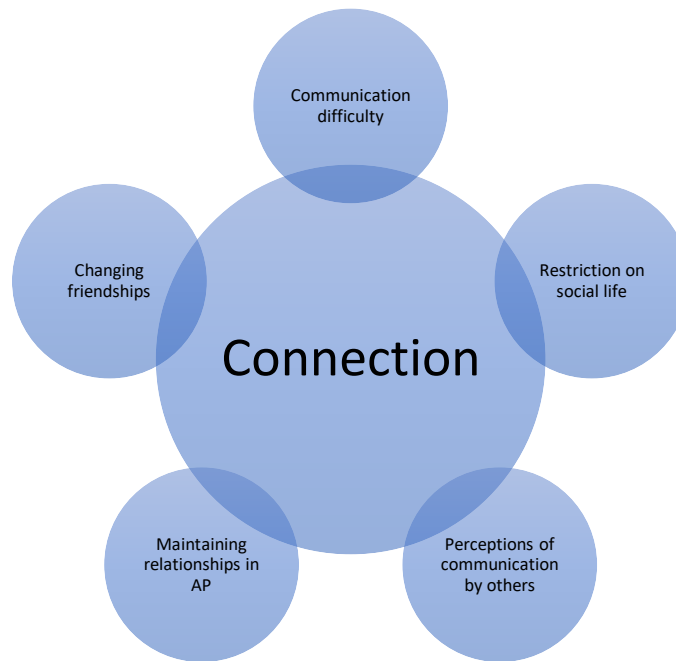
Figure 7.1: Key theme of "Connection" and associated sub-themes

A prevalent theme is that of connection to the world around, which encompasses many facets. The most obvious is that of communication, more specifically, speech. This had an impact not only on patients with marked speech deficits, but those whose speech remained intelligible. The concept of connection is broad and represents the ability of an individual to reach out and establish an understanding. In previous work in PD, connection as a theme encompassed speech and social ability (Hudson *et al.*, 2006), but I would argue connectedness also comprises of establishing meaning with oneself and others in this cohort, and is a deep, though difficult to define concept. This may be as part of a social interaction, in the workplace, or in the healthcare setting where an individual feels a professional has insight into their difficulties. The unifying principle behind feeling connected is not with whom, nor the setting, nor the mode of communication, but that others have the understanding, time, and patience so that the individual (whether patient or carer) feels part of the wider world. This section explores how the participants experience and interact with others and how they feel their disease or role affects that.

7.4.1 Communication difficulty

Although the speech of some patient-participants might have seemed clear and they had little difficulty in making themselves understood, their impression of their own voice, how it impacted upon their social interactions and perception of how they felt others saw them, was marked. Work in PD has shown that, given how key the ability to speak is in connecting to those around you, deficits do not need to be very severe to have a profound effect upon confidence as a communicator. However, individuals in this project also had marked speech problems requiring the use of electronic aids, in an effort to capture the impact varying speech abilities had upon the person. Sarah, below, could only produce single syllables intelligibly and this was not consistent.

> Interviewer: *So tell me what's hard for you now?*
> Sarah: **speaking**
> Interviewer: *speaking?*
> Sarah: *Yes… *indistinct muttering**
> Sarah, age 67, who has PSP (**bold** text indicates typed on an electronic device)

Feelings of control and frustration around being understood have been found to be an issue in PD. There was no association between the professional's assessment of how severe the speech problems were and perceived impact on the individual's ability to communicate (Miller *et al.*, 2011). This mismatch between how others saw participants' disability and how they perceived it themselves, emerged as a theme in both patients with MSA and PSP. Both Doris, a participant with MSA, and Gary, a participant with PSP, discussed their speech difficulty and how it had declined, in their own view. Their speech was clearly understandable to myself, when compared to participants like Sarah, above. Those around them maintained that their speech was understandable, possibly making comparisons with other patients with AP who may need communication aids. It could be that this was an attempt from others to reassure and encourage conversation, or that the speech genuinely did not seem abnormal in their view. However, this did not act to comfort these participants and may have produced frustration, as they felt their concerns were being dismissed. Gary described embarrassment as a consequence of the changes in his speech. This influenced his willingness to communicate and participate in a social life. Although not stated directly in the interview, Gary retired from his job when he felt he could no longer contribute in meetings due to his speech problems.

Other people… I'll ask them, "Do I come across...?" They always say, "Oh, you're fine." I don't believe them, but they always say I come across fine.

Doris, age 59, who has MSA

The social life has deteriorated because I'm scared I might be a bit caught short or not being able to speak properly. You said earlier that my voice seemed okay. To me, it doesn't seem okay. I'm not as confident as I used to be. I couldn't sit down at a meeting anymore, a complete meeting, because I feel embarrassed losing my voice.

Gary, age 58, who has PSP

During the interview with Gary, he spoke of the changes that he had experienced within himself which he felt were profound, but that others did not feel were severe or noticeable. What I, as a clinician, had thought of as reassurance (during a recent clinic) by saying his voice sounded clear, had minimised his concerns. This is a point which should be considered by clinicians and medical teams. Objective observations do not capture the internal experience and perception of the person living with a chronic condition. This has been seen in perception of swallowing in PD also; the severity of objective swallowing problems are not reflected in the experience of the patient, and may be subjectively much worse (or better) than the test result (Miller *et al.*, 2006a). These internal experiences impact upon the ability of individuals to connect to others socially, despite a range of objective speech ability. The value of communication aids as a means to enable speech, and allow entry into society, was discussed by both patients and carers for patients who were unable to speak intelligibly.

> *Interviewer:*   *And how…has the fact that she has to use the lightwriter to speak now, how has that impacted on both of your lives?*
>
> *Bob:*   *Oh, tremendous, great. Erm, beforehand, I would think, both of us, it was very, very frustrating. Erm, I would try and second-guess what she was trying to say to me, and because I was saying, well, say we're looking at a word, and I would say to her, "Shop?" "No, no, no." And then I would try something else. "No, no." Then she would get very irate at me.*

Bob, 69, carer of Mary who has PSP

The presence of the aid may also act as a symbol of illness, helping to explain the condition of the patient, acting as a visual cue of illness or disability. This might prepare others to make allowances for speech disability, if they see a device is needed. This may trigger allowances on behalf of others, socially.

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She took it [the light-writer] *on holiday. And we were sitting at the table, there was a couple sitting...and, erm, this woman straight away asked what it was, and [Mary]typed in that it was a communicator....and she says, "Oh," she says, "I tell you," she says, "I had a brother-in-law with Parkinson's," so that broke a bit of ice as well.*

Bob, age 69, carer of Mary who has PSP

There is however, difficulty using a device which requires verbal fluency and dexterity in a condition which is progressing in both physical and cognitive respects. With progression of disease comes greater difficulty in using the device, providing an increasingly tenuous means to communicate. This can be seen in problems in using the device and observations from family, together with concerns that the individual will not be able to use the aid in the future, further curtailing their ability to interact and communicate.

Interviewer*:*   *Do you think your main problem is... speech?*
Sarah*:*   *speech.... yes...*
Interviewer*:*   *probably the speech*
Sarah*:*   **typing sounds for 5 min**
Interviewer*:*   *I think I can read what...*
Sarah*:*   *mmmm...*
Sarah, age 67, who has PSP

First, I tried to put it down to the fact that she was doing this, but I don't think that is the case. I think she is starting to misspell words...and when it gets to, to, to press 'Do', sometimes she presses it, and it repeats and repeats and repeats. And I'd say, "No, the wrong- thing that's wrong is, you've pressed it too many times with your finger," and I don't think she realises...

Bob, age 69, carer of Mary who has PSP

Mary: **typing sounds* **I sometimes think** *typing sounds* ...people don't understand*
Interviewer: *What do people not understand that you want them to, can you pin that down?...*
Mary: ***that I'm not stupid***

Mary: **typing sounds* **it's very frustrating***
Interviewer: *how do people react to your speech as it is?*
Mary: **typing sounds* **most people just ignore me***
Interviewer*:*   *ignore you?*
Mary: ***yes***

*Mary, age 69, who has PSP (**bold** text indicates typed on an electronic device)*

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A participant who also has PSP with a similar degree of speech impairment to Sarah, is Mary. She uses a light-writer device which has a 'speech' function. Like Sarah, she has physical issues with stiffness and slowness, making typing difficult and is known to have some cognitive impairment (bradyphrenia literally is 'slow thought' which is common in PSP). She described frustration that she is ignored and feels she is perceived as stupid because she cannot respond quickly. This has serious implications for both the ability to connect socially for this group of people, but also in how medical care is provided. In the medical setting, the ability to communicate meaningfully with patients wherever possible, especially if they have these difficulties day-to-day, is very important. It allows patients to feel some empowerment and to feel considered in their care. It is also important to connect with patients to allow them to make decisions about their future if they wish to, while they are still able.

Interviewer:	*What do you think doctors and nurses, what do we do well and what do we do badly? Especially as you use a light-writer*
Mary:	**typing sounds** ***I sometimes think*** **typing sounds**
Interviewer:	*It is working its ticket, isn't it?*
Mary:	***People don't understand…that I'm not stupid****…*typing sounds* **people don't have the time to listen***

*Mary age 69, who has PSP (**bold** text indicates typed on an electronic device)*

Mary's statement in response to a question about how doctors and nurses could do better was framed around time and understanding. Without the time to allow her to respond as she wished, whether constrained by her physical ability to type or cognitive issues, she felt dismissed as 'stupid' and did not feel heard. This aspect of AP, with significant and objective loss of the ability to easily communicate, has implications for medical teams. To allow these individuals to connect, we need to provide time, space and where appropriate, technological support. Beyond this stage, should people be no longer able to connect via speech or written means, due to cognitive and/or physical decline, it is still important to try and maintain a connection with these individuals, and to speak to them, rather than to their carers, exclusively. Indeed, it may be that some communication *is* possible, despite significant barriers, if sufficient time can be given (if only with simple hand gestures).

In one interviewed participant who had PSP-RS, a pronounced lack of fluency was found. Despite having a previous career as a businessman, speech was very 'pared down' and to the point. Repeated use of 'yes' and 'no' responses, even when questions were not closed

suggested some 'concrete' thinking and lack of elaboration. Repeated use of the same phrase, often seen clinically in frontal cognitive syndromes was striking, despite efforts to widen the conversation up with open questions (Weder *et al.*, 2007). The phrase 'that's it' was used again and again, especially when Jack struggled to find words or lost his train of thought.

Interviewer:	*Do you and your wife ever talk about the way that the disease progresses?*
Jack:	*Yes.*
Interviewer:	*Is that hard to talk about?*
Jack:	*No.*
Interviewer:	*Have you thought about the future with your wife?*
Jack:	*Yes.*
Interviewer:	*Do you still take an interest in cars?*
Jack:	*Not really.*
Interviewer:	*Is that because you can't drive them as you did?*
Jack:	*That's it.*
Interviewer:	*Do you like going to see the consultant, or the nurses?*
Jack:	*Yes.*
Interviewer:	*Why is that, just to try and understand what we do well and what we do badly?*
Jack:	*Yes, that's it.*

Jack, age 71, who has PSP

7.4.2 Restriction on social life

Social activities and interaction with others is affected when speech becomes more effortful or difficult. Some individuals may voluntarily pull back from meeting with and speaking to people, as they may feel embarrassed and lose confidence in themselves. This has been shown to occur in patients with PD. One frequent concern of patients with Parkinsonism is maintaining the volume of their voice. Work has suggested that patients with PD may have impaired ability to detect low volumes in their own voice; feeling that they are shouting when they are, in fact, difficult to hear. This likely adds to social awkwardness and feelings of effort or struggle in conversation (Kwan and Whitehill, 2011; Miller, 2012). This may result in increased effort in being heard and the need to repeat things, impeding conversations and making them burdensome. This was seen particularly in participants with MSA who seemed to find it difficult to speak loudly or clearly enough, which from the example of Doris below, seemed demoralising.

I know my speech… nine times out of ten, I've got to repeat myself, and then I'll think, "Oh, I can't be bothered." It's not worth it usually.

Doris, age 59, who has MSA

Before I had MSA I was obviously quite a clear speaker, I could talk to anybody from the lowest of the low if I put it that way to a Duke, in my profession I'd talk to many people, many people in the population, wide variety of people...high flyers in business, don't think I could do that now. Couldn't have a long, intelligent conversation with a high flyer, would "pardon *name*, pardon".

Matthew, age 64, who has MSA

Matthew identified himself as a communicator, his job as a solicitor involving interaction with important and articulate people seemed an intrinsic part of how he saw himself. The transitions which people felt have occurred due to their disease are discussed in the next section. When his speech was impaired by MSA, this had a profound effect upon him. His voice was his means to connect to all kinds of people and this had been affected by his disease. His comment *'couldn't have a long intelligent conversation with a high-flyer'* suggests that he felt he had lost a key skill which had opened up opportunities for him in his working life. Similarly, to Doris and Gary, Matthew could still be understood. However, he felt that the change in his voice affected the quality of his interactions with others. In AP, which affects speech earlier and more severely than PD, the impact on social life and relationships may be more extensive and occur earlier.

A frequent barrier to social interaction, be it formal occasions or routine conversation, was the inability to make oneself understood or worry that one was less intelligible than before. This could be due to voice changes leading to a low volume resulting in withdrawal from social situations, taking more of a 'spectator' role, rather than being an active participator. This has also been described in patients with speech impairments from a number of causes including AP (Walshe and Miller, 2011).

If I went to things, like the royalty dinners and things, there came to a certain point where really, I couldn't take part in the conversation. 'Course you'd have a big round table. People were talking of course backwards and forwards, and they didn't, couldn't hear me. So, I tended to just sort of sit back and just let things go on in front of me, and that was it, so I changed quite a bit

Rose, age 71, who has MSA

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Therefore, patients may be experiencing distress as they are less able to connect to others by speech; even if families and medical staff are not aware of any problem. The shift may be fairly innocuous, such as Rose's gradual shift during social dinners to sitting back and letting the conversation flow around her, as she realised her voice was becoming less able to cut through many voices in a loud social setting.

7.4.3 Perceptions of communication by others

There was concern from patient-participants that speech problems could be misinterpreted by others as memory problems. This stigma of the perception of cognitive impairment, and how speech could be a sign of this, is apparent in both patients who feel they have some cognitive problems (Gary, below) and those who do not (Rose, first quote below). Miller *et al.* (2006b) discusses the effect that speech problems have on PD patients. Listeners not waiting for replies, answering for them, or assuming they are cognitively impaired, explained how those affected with speech difficulties interacted with and felt judged by, others. Some respondents welcomed humour and flexibility in an attempt to facilitate conversation, despite difficulties, such as Rose when there was problems picking up her quiet voice on the recording device in her second quote below.

Gary*:*	*Yes. I feel as it's difficult. The others will take what I say and they'll understand it, but then they'll question it.*
Interviewer*:*	*What do you mean, Gary?*
Gary*:*	*It's the way you say things to people. Words get jumbled up. They'll then say they understood me, but they didn't.*

Gary, age 58, who has PSP

...you have people sort of waiting whilst I slowly spoke to them. I didn't want them to think that I'd sort of- I think everybody thinks when you've got that and you slow down it might be a mental thing, which obviously it isn't because inside your head, it's all, it's really going on

Interviewer:	*I think I'm going to put the microphone a little bit closer so that it can pick your voice up.*
Rose:	*Very quiet, is it?*
Interviewer:	*Yes, yes.*
Rose:	*Are people there? Are you receiving me?*
Interviewer/Rose:	*(Laughter)*

Rose, age 71, who has MSA

The use of humour on the part of Rose may have been to detract from embarrassment, either of herself or to relieve what she may perceive as uneasiness in others, because of her speech problems. She may, based upon her previous statement, also use wit to reassure others that she is cognitively astute. A qualitative study in neurological disorders in Canada found that humour was a strategy that participants used to maintain a positive sense of self in the face of challenges (Roger *et al.*, 2014).

7.4.4 Maintaining relationships in AP

Relationships and how they succeed or fail beyond a diagnosis of AP, was a frequent theme. Relationships with others were frequently discussed within interviews. These relationships did not only include that between patient and carer (in this study, spouses) but also with other family members, friends, and with medical professionals. Relationships are intrinsically about connection, the definition being: *'The way in which two or more people or things are connected, or the state of being connected'. Oxford English Dictionary (2017)*

Some carers were very aware of speech issues, either because their partner's disease had impacted speech more, or because their disease was more advanced. Bill, who described a previously active social life which he shared with his wife, Doris, had noticed the impact of MSA on Doris' voice. Like the quote above in which Doris describes having to repeat herself and finding it effortful, Bill saw the effort that she had to make to speak clearly and how this had affected the quality of the social life they had shared.

> Interviewer: *It sounds like you were both pretty social people, pretty outgoing?*
> Bill: *Yes, very social, very social. That's one of the problems that I have now.*
>
> *Her voice, oh God. I say, "What? What?" She's never been a loud talker, but she's really quiet now. She just whispers and mutters away*
>
> Bill, age 57, carer of Doris who has MSA

> *So, the people that run the PSP [meeting] come and talk because they spend time, they're used to it. But the other people may not talk to- They'll talk to me, not to [her]. And that must be frustrating for [Sarah].*
>
> Tom, age 70, carer of Sarah who has PSP

Tom observes that in an environment with an awareness of the issues that AP can cause (a PSP support meeting), people take the time and effort to communicate with his wife Sarah, who has minimal speech and uses a tablet device to type on and 'speak' with. Outside of this 'safe space' however, people speak to him rather than his wife, reflecting the ability to connect to others falling away as disease progresses. The reasons for this were not explored by Tom, but from Sarah's interview, the pauses required to allow typing of responses were long and it was, from my own perspective, difficult not to interrupt. People may find it quicker or less socially awkward to bypass Sarah and speak directly to her carer, Tom. Tom did acknowledge the impact of possible frustration on his wife. Communication between patient and carer is seen as something very valuable, and when this breaks down or becomes more difficult, this seems to have a profound effect upon QoL for both parties. Previous work in PD suggests that the quality of the relationship between the individual with PD and their carer, has a protective effect on carer well-being and that patient and carer QoL have an association. In Chapter 6, analysis in this cohort of carers suggested that there was a small predictive influence between longer relationships between carer and patient, and reduced carer strain. As communication is so fundamental to relationships, the ability to have meaningful interactions with a partner seems very important in maintaining that relationship (Goldsworthy and Knowles, 2008; Greenwell *et al.*, 2015). This can be seen with Jackie, a carer who feels he can still communicate meaningfully with his wife, Rose, and with Sally, whose spouse is less able to speak (and was not able to give an interview) but she feels they are still able to communicate with each other.

> *Well deep down, no, it doesn't matter at all. We can have a nice night in together and we can communicate with one another. [Rose] loves talking although she has difficulty talking now and I have difficulty hearing her. She is a little bit deaf, you might have noticed that but I think quality of life, it is defining quality of life. When you get to real hardcore values, they're probably undiminished in my view but you have to be single minded to be able to identify that and I count myself fortunate*

> *Jackie, age 73, carer of Rose who has MSA*

> *Came back on the Sunday, I went straight to see [my husband]; tell him all about it and blah, blah, blah. He's happy to hear…we have quality time. We have meals together. I take him out; we go for a beer. I'm falling in love with him again.*

> *Sally, age 70, carer of husband with PSP*

Some of the discussions suggested that the relationship between participants with AP and their spouse were challenged by their diagnosis. Matthew felt that dealing with his illness was an injustice for his wife, Emma, whom he had married soon before his diagnosis, and that given the option, he would have preferred to shoulder the burden of his progressing disease alone, to spare her. Emma who was also interviewed, described loneliness as an effect of Matthew's diagnosis. It may be that in an effort to relieve Emma of worry, by bearing it alone, Emma feels isolated as Matthew's attention is taken up with coping with his illness. By contrast, other couples such as Tom and Sarah, and Rose and Jackie, who maintain as much open communication as possible, there is a loss of connection between Matthew and Emma, as a consequence of trying to protect the other.

> *It's affected my marriage very badly, very badly indeed… certainly if I'd known I had MSA coming on I wouldn't have married [Emma-my wife… I would have stayed single, it's not fair doing this to any woman*

> *Matthew, age 64, who has MSA*

> *Eeehhh-no, (laughs), it would be nice to say, that this has brought us together or something like that, you know I love him, I love him so much, but I don't know that I love him more, it's hard to say isn't it? And he's changed as well, but, there again, it's quite lonely because of his preoccupation with his illness, and I don't know that's because of his character*

> *Emma, age 61, carer of Matthew who has MSA*

Julia, a participant with MSA, spoke positively of the impact her marriage and the relationships with her family had on maintaining home life with a degenerative disease. The use of the term 'rock' is an interesting one, suggesting her husband keeps her tethered or connected despite her illness.

> *Exactly. Which is why I always refer to him as my rock. Because he is a stable influence in my life. He is just so down-to-earth, his feet are just so firmly cranked on the ground. He keeps saying, "That's no bother. That's no bother"*

> *Julia, age 62, who has MSA*

> *The relationship [changing]? No, not really. Still love each other.*

> *Tiberius, age 66, carer of Julia who has MSA*

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Similarly, Julia's husband, Tiberius, as he simply put it, didn't feel that the quality of his relationship with his wife had changed, despite the change in her health and abilities and that they still loved each other. This support for people with chronic conditions is very valuable and may trigger medical and social teams to consider patients and carers more as a pair; supporting both, as the well-being of one is so fundamental to the other.

> *...I love my wife. I cannot say that 53 years has been the Hollywood movie because we've certainly had problems but we've always resolved them by caring for one another and really getting on with it.*

> *Jackie, age 73, carer of wife with MSA*

Jackie, describes 'getting on with it'. He felt that certain types of people are better equipped to cope with problems. However, it may be that the ability to cope and adapt may be in part, due to secure relationships with others rather than being intrinsic to individuals.

Family is known to be very important to both patients and to carers in terms of support and reassurance. In Lee *et al.* (2006) in the context of PD, family was the most frequently nominated category in the SEIQoL-DW by patients, and in Chapters 4 and 6 it is also worth noting, that this was also the case in both disease groups, in patients and carers in this study.

In the case of patients with PSP who were interviewed, some family members used avoidance strategies, possibility out of fear or difficulty adjusting to the diagnosis, whilst others may not have understood the extent or severity of the illness. This was seen when Earl tried to discuss the gravity of his wife, Helen's, diagnosis of PSP with his daughter, who had minimized her problems to just having problems with her leg. Bob who was the carer for his wife, Mary, felt the child that had the most difficulty coming to terms with Mary's illness, was their daughter who had a medical background. He believed that this was because she understood some of the implications of the diagnosis and was therefore using avoidance strategies not to discuss it.

> *See my daughter who is lovely at 41 when I told her, her expression was of absolute bewilderment. She said, and this is word perfect, "Dear me, Dad. I thought all that Mam had was a gammy leg".*

> *Earl, age 70, carer of wife with PSP*

Er, the one that's- the [daughter] that's a nurse, I think she- because she knows what it is.
'Cause there's times when I say things, erm, about Mam, she'll, erm, go rather cold. And I
think it's because she knows exactly what's what, but is she, erm, not wanting to accept it?

Bob, age 69, carer of wife with PSP

Other patients and carers, such as Julia, have described the importance of support from
family, including spouses and the value that they bring, especially when the pre-existing
family relationships are close. To that end, Earl mulled over the difficulties patients must face
without a strong family network in place.

...the family, I must be honest, I think God gave me a family, the sort of family that you
need to have if you are to face hurdles in life. Because the family is more supportive and
without their support and without their understanding of me, I just don't think I would have
survived at the time I have done

Julia, age 62, who has MSA

[illness] is a very personal heart-aching thing and lots of the elderly haven't got the
backup of families and friends and finances to help through some of the more difficult
things

Earl, age 70, carer of Helen who has PSP

7.4.5 Changing Friendships

Friendship was cited less in the SEIQoL-DW compared with family. Four PSP participants
nominated friends as one of their five important domains, whilst five MSA carers nominated
friends or friendship. Interviewed participants discussed the difficulties in maintaining
friendships, which seemed to be multifactorial. The nature of friendship, and even the friends
themselves, seemed to shift or change with diagnosis and increasing symptoms. Bryce, a
participant with PSP, who was the only interviewed participant who had no spouse or partner,
felt that certain friends were only interested in socializing when he was well enough to do so
and lost interest in him when he became less physically able. However, he found he
increasingly spent time with other acquaintances, to whom he had become closer due to their
shared experience of chronic illness and disability. This suggests the importance to some
people of peer support with others who can relate to their condition. This will be discussed in
the 'Accessing Support' section.

Bryce*:*   *No, because- well, your friends yes, used to be. When you were all right your friends used to come around and see you. Since I've took bad I never see them.*

Interviewer*:*   *Do you know why?*

Bryce*:*   *Yes, because they don't care. That's my opinion like.*

Bryce*:*   *Yes, she'll say, "By, you went round the shops better today", you know what I mean? It gives you that bit of push. Poor lassie, she's got cancer, so we sort of help each other in different ways. We call it our moaning day on a Friday because we always moan about everything. We moan about the shops, we moan about the taxi, we moan about the traffic.*

Interviewer*:*   *So, having somebody to have a moan to, to complain to, that helps?*

Bryce*:*   *Yes, have a good moan as we call it.*

Bryce, age 76, who has PSP

Matthew and Doris found an element of their social isolation and difficulty interacting with friends, to be self-imposed due to fatigue, speech difficulty, and self-consciousness around their symptoms. Doris, in particular, found that the safety of her home and being alone, was easier than coping with company, despite her retained desire to make contact with friends. Emotional lability (rapidly shifting emotions leading to tears or laughter) was also discussed by Matthew, as a source of embarrassment in terms of his social life.

I get so emotional about it, which I've never experienced before, on any topic, about people with death, birth or marriage or anything else, I don't understand why I get so emotional

Matthew, age 64, who has MSA

He [husband, Bill] does try to get me out, but it's much easier for me to just stay put. So, because of that, I don't really see much of my friends. Sometimes, they do want to come and visit. That puts me in a panic, and I don't know why, because all they're going to do is turn up at my door and have a cuppa. I think, a lot of the time, I'd just rather be on my own.

Doris, age 59, who has MSA

Friendship, unlike family ties, is frequently associated with common interests and activities. When the ability to carry out these activities or the enthusiasm is no longer there, these bonds may fall away, leaving a void and possibly, a sense of abandonment. A study examining the loss of friendships after stroke, found a number of factors involved in shrinking down the friendship networks that people had enjoyed prior, such as fatigue, speech difficulty, and the perceptions of others, as well as the physical disability caused by the stroke. These factors are

of relevance to AP too, with the difference that these issues are progressive and relentless. Whereas in stroke, the changes are sudden but fixed with a possibility of improvement (Northcott and Hilari, 2011). Carers too, found it more difficult to find the time to meet with friends, and if they did, might find it harder to connect with them due to the impact of their care-giving. Emma, who speaks later about the constant need to present a brave face on caring in the 'Transitions' section, found that even in what could be thought of as a 'safe space' with good friends, she was loathe to confide in them about the problems she faced as a carer. The reason is alluded to in the quote; it may be hard to put that brave face back on after sharing how she feels with her friends.

> *Unless they're very close to you… it's hard to click back into the "hi, yes how you today?" when the day before you broken down in tears over coffee, but I find that even, with my good friends which I think I mentioned to you, that you think twice about opening up to them. I hardly see any friends.*

> *Emma, age 61, carer of Matthew who has MSA*

The sense of self and being able to connect, not just to others but to accept changes to oneself, encompasses some other themes which were found in this study; which were grouped into the overarching theme, transition.

Connection to others is key in any relationship; to a spouse, friend or even a doctor-patient relationship. The participants in this study with AP felt that their condition reduced their ability to make connections; speech became impaired affecting confidence and intelligibility, which in turn, reduced the ease and pleasure of social contacts. As the existence of those with AP contracts, their carer, also trying to support someone with increasing dependence, has less contact with the world outside. This shrinking reality containing fewer people is noteworthy; and this is why trying to facilitate communication between medical teams and patients (with measures such as longer appointments or differently-structured clinics to allow the time for communication to be effective) is important. Equally, maintaining connection between individuals and their carers (despite speech problems) and keeping a channel of communication between patients and those they are closest to, has the potential to greatly affect the experience of people living with AP.

7.5 Transition
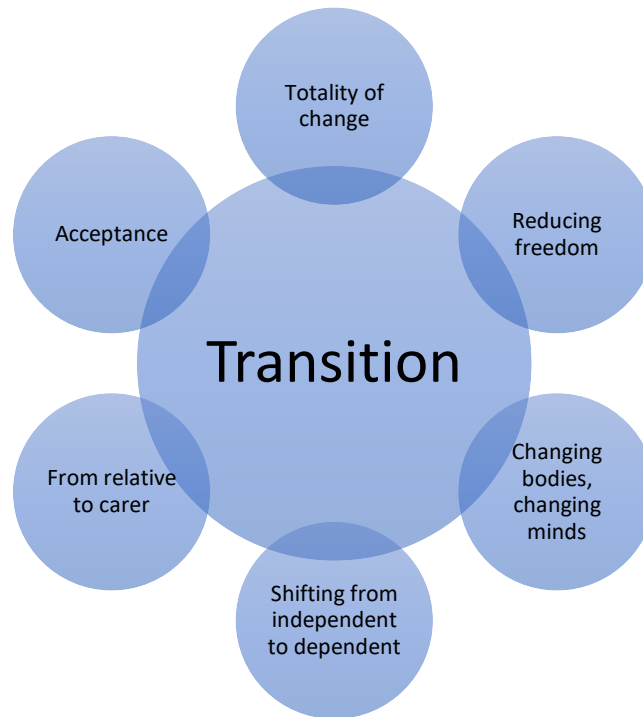
Figure 7.2: Key theme of "Transition" and associated sub-themes

A frequently cited issue during this study was that of change or transition.

7.5.1 Totality of change

Different aspects of change were discussed, but often change was described in terms of totality of experience when in context with a diagnosis of AP. This complete transition in life was not just found in patient-participants, but in carer-participants also; meaning that the all-encompassing impact of diagnosis affects not only those with the disease, but their relatives and carers who share in that experience.

> *It [the condition] changes you, every aspect of you is changed, it's physical…physical and mental.*
>
> *Matthew, age 64, who has MSA*

Here, Matthew describes the shift he felt in his life as a result of his condition. He felt it touched on every aspect of his self. Interestingly, he describes the change as a personal thing; the disease has changed him rather than things having changed *for* him. This may emphasise the intensity of the impact of the transition, as not only do patients have to adjust to a

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difference in lifestyle, they themselves may have changed as a response to their diagnosis. Patients may have difficulty relating to themselves after this transformation. This can be seen by Mary's quote, in which she found a shift in her whole being as a result of feeling cut-off from others by her lack of speech. This produced a boundary between who she was and who she is now.

Mary*:*	*typing sounds* **it's very strange to have someone talking to you and you can't talk back…**
Interviewer:	*can't talk back…?*
Mary:	*typing sounds* **it's affected my whole life, I used to be a very outward type of person**

*Mary, age 69, who has PSP (**bold** text indicates typed on an electronic device)*

Mary describes how her diagnosis has changed not only her functional abilities (most obviously manifested in her inability to speak without the use of a communication device), but how this has transformed her personality and her self-image. She also describes the change she has experienced from her disease in terms of its completeness. Her whole life has been affected, culminating in the transformation of who she is and how she views herself. Previously, she perceived herself as 'outward' and she is no longer the person she used to be.

Carer-participants tended to describe the changes they have experienced in terms of lifestyle and in expectations. Emma, whose husband had a fairly early diagnosis of MSA, found that his diagnosis seemed to produce a sense of continual discomfort in which there was never any sense of restfulness. She remarked that time together was no longer relaxed and there is a sense of the knowledge of the disease pervading all aspects of the relationship they share.

I think it just affects so many things…everything, everything just everything, life is just never normal, I don't think we ever have any kind of really relaxed time together

Emma, age 61, carer of Matthew who has MSA

She, like Matthew, her partner, described how complete the sense of change has been to both of them. She uses the word 'everything' three times to emphasis her point. Earl, who cares for his partner, Helen, described the alteration in expectations since Helen's diagnosis and again, described the totality of the change in their lives since the diagnosis and progression of Helen's disease. He pulls back from using the word 'significant' for the degree of change they have experienced as a couple and instead uses the word 'totally' and that the effect of this upon their lives has been 'savage'.

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Shrunk. They have shrunk to, the horizons, I mean a holiday abroad now is, is a pie, pie in the sky and sorry for the pun…it's, so how has it affected us? Significant? I don't think significant. Totally? I don't think significant describes it. It is, erm, savage really.

<div align="center">

Earl, age 70, carer of Helen who has PSP

</div>

Earl also describes a 'shrinking world' as the horizons narrow with Helen's growing disease-burden, producing increasing disability and limiting their possibilities, changing how they expected their lives to be. Contraction of social spheres has been described in both physical illness and in carers of those with chronic illness (Sacks, 1984; Öhman and Söderberg, 2004).

7.5.2 Reducing freedom

Similar to Earl's experience as a carer feeling shut off from certain places that he and his partner had previously enjoyed, Rose who has MSA, felt that her physical problems prevented her from accessing the places and activities which had been important to her. This separation from places or activities which previously had meaning, or were sources of enjoyment, was a recurrent theme amongst people with MSA and PSP who were interviewed.

Once I was diagnosed, then life changed completely because I was limited to where I could go and what I could do.

<div align="center">

Rose, age 71, who has MSA

</div>

Julia spoke of how important her contact with nature has been for her; her ability to walk in wooded areas and to take her dog to places that she found beautiful, such as the seaside. She then described how her access to nature is now detached or 'indirect' as she has to be taken to these places by others and is distanced from them as a spectator, unable to interact or 'be' in those places, as she is confined to her wheelchair. There is emerging evidence of the health and social benefits of green spaces; and empirical studies continue to further elucidate the strength of the association between natural environments and health (The Hague, 2004).

[nature] always, for me, sparked an interest in life… [now]it is something I can't get involved with directly…the only way I can get into it, unfortunately is indirectly is if somebody takes us out and I am sitting in a wheelchair and there are certain areas I can't visit anymore, can't walk anymore, can't visit anymore because it is not wheelchair-accessible.

<div align="center">

Julia, age 62, who has MSA

</div>

There were some positive aspects to the changes in expectations or previous lifestyles, at least in part, described by some of the participants. Tom discussed that since Sarah, who has PSP, required more care; they have spent much more time together, which he did feel was a good change. However, the same issues discussed above were present; disability limiting travel or easy access to areas, often tempered these positive factors.

> *I spend more time with [Sarah], which is good, but the sad thing is, whereas we planned to travel and do things, now we can't...so your time that you were looking forward to has changed...there's a different view of your life together.*

> *Tom, age 70, carer for Sarah who has PSP*

Tom who had worked all over the world, had discussed in his interview that he had assumed that in retirement he and Sarah would travel together. This thread of disruption of plans or changed expectations, recurs in interviews, with both patient and carer-participants who had invested not only financially, but also emotionally, in the idea of an enjoyable and active life after retirement. This phenomenon is known as 'biographical disruption' - the interference with life, including social networks and the envisioned future which illness can bring (Bury, 1982). The unpredictable onset and rapid progression of AP is seen as having taken this opportunity, which Earl again describes as an almost visceral loss, below.

> *It was very, very, it was a very hard fact of trying to come to terms with the change in circumstances, of things that we had taken for granted and enjoyed were no longer open to us. It was really a severe kick in the guts yes.*

> *Earl, age 70, carer of Helen who has PSP*

Sally, whose partner required nursing home care, described the plans that she and her husband (who attempted but was unable to interview due to cognitive and speech problems) had formulated during their working lives. They had particularly wanted to drive across continents, a physically demanding endeavour. Sally evoked a theme that was recurrent across the interviews; that of plans of travel after retirement, delayed due to work, family or financial commitments, which then were impossible due to the diagnosis of AP. There was almost a sense of feeling 'cheated' out of these plans.

Overland to Australia in a Land Rover… people had done it and we read this book and thought, we're going to do that on day…blah, blah, blah…when the kids are [grown] up. But then you couldn't afford it because our business was da, da, da, da, da…and then you retire. And then you get ill.

Sally age 70, carer of husband (not interviewed) who has PSP

Although Sally and her husband had dreamed of extensive travel across the world, other participants discussed how their freedom of movement and travel had become constrained so that even a night in hotel was not possible, nor was going out for dinner. This suggests that not only 'big dreams' of the future are affected by the diagnosis of a disease such as MSA and PSP, but the smaller, more routine pleasures of life can become so difficult as to not be enjoyable or even possible any more. This again alludes to the 'shrinking' of existence and the constriction of choices that AP brings to individuals and those who care for them.

I think the superficial elements of quality of life have obviously changed for the worse. I mean I would love to go away to a hotel, we used to go away for two days…to a nice hotel in Peebles…a nice view of the river behind the hotel…that's gone…somebody else to make the meals, we don't get out even for a meal now which is a little bit sad.

Jackie, age 73, carer of Rose who has MSA

Jackie, a carer in the quote above, describes trips to hotels and to restaurants as 'superficial' parts of QoL. He later goes on to describe what he feels are more fundamental or deeper constituents of QoL (the quality of the relationship and the conversations he shares with his partner, Rose). This was discussed in the 'connection' section. Therefore, if the ability to connect to others by being able to communicate adequately and maintaining quality of relationships can help to ameliorate the loss of functional ability, this should be prioritised more in terms of care, support and research. Some studies on adjustment have found benefit in expressing emotion and interventions, such as writing therapy and cognitive behavioural therapy, may reduce distress in patients with cancer. It should be noted that a diagnosis of the most aggressive cancers is associated with poorer adjustment overall, perhaps suggesting that time to accept these changes or transitions is needed. This may mean that patients with more aggressive diseases with rapid or uncertain trajectories such as AP should be prioritised for interventions which may support adjustment (de Ridder and Schreurs, 2001).

7.5.3 Changing bodies, changing minds

AP is made up of conditions which are variable in terms of their symptoms, progression and impact on abilities. This study considered only MSA and PSP, but even these two conditions show a great deal of diversity in how they affect personality and cognition. Due to these diseases being rare and information on them not being so readily available as in more 'common' diseases, people with the disease and those around them may struggle to understand the effects of AP.

Although the physical changes of disease are most obvious to others and are often clearly visible, either as the direct result of illness e.g. tremor or use of an aid such as a wheelchair or stick, cognitive or personality changes are hidden and can be less easy for others to recognise or understand. AP, like PD and some other movement disorders, has the added challenge of having both prominent physical and cognitive aspects but, unlike PD, being rapidly progressive.

One transition that a number of participants struggled with was a loss of drive or energy. It was difficult to distinguish from people's personal experience whether this was due to a loss of physical energy because of their disease, loss of confidence or intrinsic change in personality or cognition due to (pathological) apathy, which is well described in AP. This affected participants in a range of ways; affecting their view of themselves as a person, such as Helen below:

> Helen: *But when I wake up I think I should be full of life and I'm not.*
> Interviewer: *And is that a big change from how you were before?*
> Helen: *Oh yes, completely.*
> *Helen, age 68, who has PSP*

Within the theme of changing personality there was a subtheme of withdrawal, from being less outgoing and acting as an instigator, to taking a back-seat and delegating responsibilities to others. This transition from participant to spectator can also relate to the theme of connection. Individuals who have related to others by their leadership or a very active style of interacting, may feel disenfranchised and detached should they then be obliged to take a 'back-seat' due to cognitive, energy or personality change.

I just haven't been so active and then being like the leader of things and a person who
pushed things forward, I found that I really had to just- couldn't do it. I had to leave it up
to other people to do things.

Rose age 71, who has MSA

This transition to a more introverted state may also obligate the carer or partner to take on unfamiliar roles in addition to their growing responsibilities as care-giver. For example, some male carers might have found increasing housework responsibilities which may have been previously shared or performed mainly by their female partner. Above, Rose described herself as the person who 'pushed things forward'. Below, from the carer point-of-view, Tom describes how the burden of maintaining social contacts, which used to be shared or mainly undertaken by his wife, must now be done by him; the instigation or motivation to do so is no longer there.

We still see our friends and family, but not as often as we could do. Although we could do
more, it's all got to come from me, so it's all instigated by me. And that's… whereas
before, it was both of us, or mainly [Sarah].
Tom, age 70, carer of Sarah who has PSP

These less obvious responsibilities, sometimes called 'emotional labour' may then be taken up by carers if the person with AP is no longer able to do it. Especially if these tasks have never been done by the care-giver before, these produce an added strain. There is a recognition that this role has been frequently, though not invariably, filled by women (James, 1992). Doris who has MSA, still tried to organise social contacts, remember and respond to birthdays and prompt her husband, Bill. However, her progressing disease made this duty, which used to be easier for her, more challenging, leading her to use technology like computerised reminders.

One time [Doris] used to remember, but not now. She's got everything written down on a
calendar and on her computer system, so it prompts her…a couple of times she'd forget
because I never remember, I'm useless at it: birthdays, dates of birth, even my grandkids'
names.
Bill, age 57, carer for Doris who has MSA

One side-effect of these changes may be that social life for people with AP and their partners may be more restricted, if the affected individual tended to cultivate family and social relationships more than the other.

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Changes in personality can also be more obviously apparent to others. In both MSA and PSP, but particularly in the latter, frontal lobe changes can produce a range of effects from withdrawal and apathy to disinhibition. Disinhibited behaviour is usually not perceived by the affected individual to be abnormal, so may cause frustration in relatives, particularly if at that point no diagnosis has been reached. These behaviours may be frightening or embarrassing, as described by Sally, whose husband had prominent behavioural changes before he was diagnosed with PSP.

> *I didn't know, I just knew there was something going on, "for God's sake, don't say…" [I would say] and I used to tell him off… "don't do that again. You upset people"… and I was, sort of, treating him as a person without an illness.*
>
> *The man I married changed dramatically in to a bit of an- he needed motivating all the time.*

> *Sally, age 70, carer of husband (not interviewed) who has PSP*

Although apathy and disinhibition can be thought of as somewhat 'opposite', Sally's experience shows that lack of restraint and withdrawal can co-exist. These behaviours, especially if they are very different to the personality that individuals had before, might be very troubling. Equally, without knowledge or understanding that there is an underlying disease producing the behaviour, this might lead to guilt over blame that was shifted to the individual before diagnosis. There can be varying amounts of insight from individuals as to how their behaviours might have changed because of their illness. In the case of Sally's husband (not interviewed), there was none, so Sally seemed to bear the brunt of the social consequences. However, others might have awareness of how their public conduct has been altered by their disease. Emotional control and being easily moved to tears (or less often, laughter) was frequently cited as problematic for participants. This is a common problem in PSP, but MSA participants were also troubled by it.

> *Part of the condition as well, which I've have found, it makes you very emotional, even if you're watching something that's daft on the TV, you start- tears start welling in your eyes. You think, "Why the hell am I crying for this for?". It's- I don't know. That can become embarrassing.*

> *Gary, age 58, who has PSP*

Friends have stopped asking me how I am personally as I just break into tears which is
quite rude of me I think… in some respect… but they understand.

Matthew, age 64, who has MSA

Although some participants had difficulty communicating and used communication aids, whilst others struggled with slower thinking and fluency, the participant whose interview demonstrated the greatest degree of cognitive change which is typical of frontal lobe problems was Jack, who has PSP. Despite efforts to 'draw him out', using open questions, he struggled with description and abstract thought. He tended to close down lines of questioning into 'yes/no' answers, even if dichotomous answers weren't always appropriate and used repetition of the same phrase. This 'catch-phrasing' is another feature of frontal lobe problems (Weder *et al.*, 2007). However, given time and space, Jack did spontaneously respond meaningfully to questions or had insights (which did not necessarily relate to the question asked).

Interviewer*:*	*How has [your wife] adjusted to the change in your social life?*
Jack:	*She's adjusted very well, but basically there's been no real change, she didn't socialise. I [used to] go to the pub every night, I used to have more conversations in the pub, I don't anymore.*
Interviewer:	*[Would you] go if you were helped to the pub?*
Jack:	*No. I just don't enjoy it anymore*

Jack, age 71, who has PSP

In one of the few parts of the interview which Jack spontaneously spoke without prompting, he was able to articulate the challenges of change, not only from a physical point of view of disease, but how his disease has changed his ability to enjoy a previous pleasure of drinking with friends. This loss of being able to speak with fluency, tying in with apathy and cognitive change and how this has affected his social life, is one of the most complete of the participants.

7.5.4 Shifting from independent to dependent

Physical changes were the most ubiquitous of the changes discussed by all individuals; those with AP and their carers. Physical changes were often the most visible landmark of decline and progressing disease and more readily perceived by others, as opposed to cognitive and emotional problems, which were more hidden. As individuals became less mobile, their

physical disability prevented a number of activities. However, even more sedentary activities such as eating, a very social experience, is affected by physical limitations such as dexterity, as discussed by Pat who found the physical reminders of her husband Gary's deterioration upsetting**.**

> *Erm, eating, erm, even, erm, some things, he finds difficult to swallow, so I'm mindful of that. Erm, the cutlery he uses, it does, so he uses a large version of children's cutlery. (Emotional)*
>
> Pat, age 62, carer for Gary who has PSP

The description of Gary having to use a knife and fork akin to a child, suggests regression and loss of abilities. There is a sense of these basic functions being 'taken away' from Pat's point of view. Eating and difficulty in doing so, captures a number of the concerns and challenges in AP; loss of dexterity, embarrassment at the perceptions of others, loss of functions once considered so fundamental such as swallowing, and requiring help for an intimate activity. Sarah found challenges in eating which encompasses the gamut of physical problems which co-exist in AP (PSP in particular). As well as struggling with the co-ordination needed to cut up her food and handle cutlery, she had the visual problems in PSP (blurring of vision, especially on looking down). This can make the process of eating uncomfortable and unpalatable.

> Sarah: **typing sounds* **I tend to sit close to what I am doing for example when I am using my iPad or when I am eating** *indistinct* **everything is blurred, [my husband] has to cut up my food for me and also put food on my fork or spoon for me***
>
> Interviewer: *so, your husband has to cut up your food and put it on your fork and spoon? How does that make you feel?*
>
> Sarah*: *typing sounds* **terrible***
>
> Sarah, age 67, who has PSP (**bold** text indicates typed on an electronic device)

The changes produced by AP are accompanied by a myriad of challenges in responding to these, by those who have the condition and those caring for them. These included experiencing or witnessing decline in a number of ways, physical and cognitive, the emotional burdens of care, and coping with the perception of others.

One key difficulty cited by patients and by carers, was growing dependence of the individual with disease upon their carer and families. This was alluded to by Sarah above, who cannot cut up her food due to her motor problems and cannot get her spoon to her mouth due to

problems with blurred vision. This results in ever-growing reliance on others, with a recognition that advancing disease will result in reducing ability to care for oneself, was commented on as being an inhumane aspect of illness.

> *My independence is the biggest thing I have lost. Before I could always do things for myself but now I can't do it [it's the hardest thing] in my life having to be dependent on other people and that I find bad. I find that very difficult to cope with. A human being should be able to perform functions without having to be reliant on another human being.*

> *Julia, age 62, who has MSA*

A thread running through the discussions of experiences by patients and carers was the alteration of the person and the disturbance of expectations of what someone is able to do or expected to be, compared with before their illness. Julia above, who discusses throughout her interview her adjustment to illness, has found that the loss of her physical autonomy and independence difficult to accept. When describing 'functions' she adopted a knowing tone and expression, not captured by the transcript, suggesting intimate care. During the study visit and after the interview, Julia struggled to mobilise to the bathroom alone, refusing assistance offered by her husband. This seemed to capture Julia's resistance to her body's decline and her belief in the right of the person to be able to self-care.

Similarly, Doris wanted to retain whatever function and independence she could, despite inconvenience and slowness. In this case, Doris had recognised the challenge of walking as her MSA progressed, but was unwilling to use a walking aid until she absolutely had to. As well as being a symbol of dependence, one element of this could have been perception. Doris was one of the youngest participants and the use of a walking aid is often associated with old age.

> *It's too much, even though my other half's got me a walking stick, a frame thing, so I can plonk myself down if I get tired, but I'm not using that. Not until I really have to.*

> *Doris, age 59, who has MSA*

AP was described as something taking from independence or abilities. Sometimes participants described 'feeling' like an older person, or their disease having affected their youth. Gary described his perspective of AP as advancing old age, as opposed to the disease taking youth away, which is how Matthew viewed his circumstances. When the challenges described by

participants were considered, such as loss of social life, reduced mobility, cognitive decline, and a fear of growing reliance, one can relate this to perceptions that many have of isolated and frail, elderly people. The visibility of a condition is a double-edged sword; if there is obvious manifestation of illness, it can confer legitimacy to the individual; unlike the people who have purely hidden illnesses, or like Sally's husband who had early symptoms which were not understood as disease, but as strange behaviour (Bury, 1991). The downside is of course, as physical disability moves on, it cannot be concealed and people may feel 'labelled' or defined by it.

> *I get very frustrated because I used to be a very fit young man, athletic and sporty, I can do very few things now although I'm still independent*
>
> *Matthew, age 64, who has MSA*

> *That's scary because basically you meet…- old age is another thing that gets you and PSP pushes that old age to you. I feel that is part of it. With the PSP, old age seems sooner than it is.*
>
> *Gary, age 58, who has PSP*

As disability progresses and independence is lost, many patient-participants were concerned that they were a burden to others, particularly to their carer or family. Others who were more mildly affected were concerned about this eventuality in the future. This ties in with Gary's comment that AP pushes 'old age' forward and these very ubiquitous fears of physical and mental deterioration, with a need for their loved ones to support and care for them, even attending to their most basic needs, which ageing is often associated with. Feeling like a burden and requiring continual assistance also led to attempts to try to maintain privacy and self-sufficiency. Sarah felt that she was under constant surveillance, which limited her freedom and left her frustrated. Helen found the lack of alone-time so off-putting that she had begun depriving herself of fluids so that the number of toilet trips, with their incessant monitoring, could be reduced. This antagonism between a patient's desire for self-governance and privacy and a carer's aim of reducing risk and trying to enable patients, can be seen particularly around mobility and falling.

> **typing sounds 2mins* **it makes me feel like I'm a burden to others…I feel like I'm being watched over constantly and I'm not allowed to do anything.***
>
> *Sarah, age 67, who has PSP (**bold** text indicates typed on an electronic device)*

Oh, it's, it's horrible. It's even when I get up on a night to go the toilet, he's there, he stands, he gets up with me, he walks me to the toilet and I think, "Gee creepers". I've even cut down my drink during the day to try and see if I cannot get up [for] the toilet.

Helen, age 68, who has PSP

7.5.5 Shift from relative to carer

Another transition that carers described, was the move towards the role of a 24-hour carer from that of spouse or partner, with its continual emotional as well as physical responsibilities.

The lack of freedom to move around, make choices or take risks which are part of everyday life, was something that participants with PSP in particular, felt affected by. The added complication of this is that PSP can produce recklessness (because of frontal lobe involvement). This can lead to a risk of falls, which carers repeatedly described as something they feared and tried to avoid wherever possible. This can lead to conflict between patients who feel constrained and frustrated (which may be compounded by their frontal lobe problems) and carers who want to protect their relatives from injury. Falling was a prevalent and emotive subject which almost all of the carer-participants returned to. There was a combination of devastation when their partner fell and hurt themselves, and an undercurrent of feeling judged for providing inadequate care.

Because he has some horrendous falls…when he was at home before I went off for some respite he'd had- oh, he'd fallen and he was bruised. He looked like a car crash. He was always bumping into walls and stuff and falling back over and cracking his head. But I managed to keep him reasonably safe and intact as best I could

Sally, age 70, carer of partner with PSP

What happens if I am not here, if she falls over?"

Earl, age 70, carer of Helen who has PSP

I said, "Every fall to me, it kills me." I shout at [Sarah], "There's a reason for your falling, you [can't lean on the] door handle.

if you don't use your walker, you'll have a fall. And falls vary: sometimes she stumbles, which is almost fine, but the bad falls… It's bruises…it's…

Tom, age 70, carer for Sarah who has PSP

There is a sense of the constant vigilance which is required; the 24-hour nature of care and the fear that any lapse in attention or period of absence could result in a fall which the carer feels responsible for. When the duties of a household are considered, if it is too difficult for the person receiving care to leave the house, how are everyday tasks achieved? Most of the participants interviewed had no or very little respite input, either from professional carers or informal care from family or friends. Essentials, such as shopping, become hard, and free-time for carers almost unthinkable as the guilt of being away from their partner and the worry of harm they could come to whilst away, overwhelms any enjoyment of a break. As Earl said, 'What if I'm not here?". Even if someone was standing in for him to provide support to his wife, if something happened whilst he was away, he would feel responsible for it. This lack of relief from the pressure of caring, obviously weighed heavy on the carers interviewed. Especially poignant was Tom's comment that each fall that his wife Sarah had 'kills me' and that he tries to stop the behaviours that lead to the falls. Sarah, who interviewed herself, felt a lot of frustration at being governed in this way, but has had numerous falls and often does not use her walking aids, reflecting the conflict between the couple and their prerogatives.

Carers describe being subsumed by the care they needed to provide, reflecting the transition from partner or spouse to care-giver. As the partner of the patient, the care required was not confined to the physical. Carers felt obliged to reassure, support and maintain the social lives of their partners, a demanding role. Carers also seemed to push their own health, social and psychological needs into the background, as they prioritised their partner.

> There's a physical side of it, but I think, of the whole lot, the mental side is bigger than the physical. Erm, because I have went and said to the doctor, I need to go to the gym to put muscles on, so that I can lift my wife up. But I've had to go to the doctor's and say, "I need tablets, 'cause I cannot cope." And that is the difference between physical and mental.

> *Bob, age 69, carer of Mary who has PSP*

> I think it's just the, for me, the constant, the constant feeling of responsibility, and I feel that I'm very, very much needed, and in the supporting role... because I know how much he depends on me, and I think that's just very tiring

> it's hard to keep enthusiastic and pretend, I feel I have to pretend... I'm all steeled-up, jolly... it's, you put on, like a shield...but it's not the real person, really

> *Emma, age 61, carer of Matthew who has MSA*

In both the cases of Bob and Emma, they had made efforts to hide their difficulties from their partners. Bob had hidden from his partner that he was now taking antidepressants for depression, which he felt arose from the strain of becoming a carer. Emma described putting on a shield to hide how she really felt, which gave an external impression of positivity. This shield was described as being 'up' both for the benefit of the public, including hospital staff, as well as Matthew, her partner, to disguise the weariness she felt. This suggests that the pressures carers feel to hide the impact of the caregiving role are from every angle; not only do they feel they need to provide consistent and multifaceted support to their relative, but also to protect them from the effect of the strain they experience, as a consequence.

This forced transition from relative or spouse to carer has implications for the carer's identity and well-being. Some carers attempt to maintain some of their former selves by continuing to work or continuing with a hobby. In some cases, patients try to encourage their carer's continuing outside lives. In other cases, carers felt pulled back to the carer environment either by the needs of their partner or their own anxieties about them, such as Earl's remark on falling above.

> *I've always been a grafter. She wants us to sell it. She wants us to get out. She wants [me to stop the club] and she wants me to sell my business. What am I going to do? Sit there? I cannot sit [7 days and 24 hours] I love her, but I can't do that.*

> *Bill, age 57, carer of Doris who has MSA*

> *I feel as though I can still add value into what I do at work, and I get value from it, and that value helps me as a person, so maybe although it is quite tough going, I can come away with it, with a strength, that I might not have, if I was a carer 24/7, at this moment in time.*

> *Pat, age 62, carer for Gary who has PSP*

> *At the same time, I think in a way, now I wouldn't say it to [Jackie] but I'll say it to you, I've tried to get him to keep doing the things that he was doing before I was ill, but I don't want to stop him having a life.*

> *Rose, age 71, who has MSA*

In the case of Bill, he seemed to be struggling with the conflicting drives to be there in a supporting role to Doris, who had withdrawn by a combination of self-consciousness over her

condition and physical limitations, and stayed in the home the majority of the time. His perception of himself was as a 'grafter', a man whose work is tied up with who he is. He also had an active social life and a position in the organising committee of a recreational club. The pressure that he felt from Doris to sell his business, seemed to represent for him the loss of the life outside his role as carer. This tension between 'his' life outside and the carer life indoors, was clearly something he struggled with. He felt he could not reconcile between Doris' needs and his own. Pat, meanwhile, although she seemed to foresee that the role of carer might become more prominent in her life as Gary's disease progressed, appreciated her work-life enabling her to hold on to her individual identity. She also felt that despite the inevitable pressures of balancing a full-time job with caring, this division between these two roles was empowering; that she would not be as able to cope with caring and with Gary's PSP, without her job, and the personal satisfaction it gave her. Finally, Rose described her efforts to maintain her husband's interests outside of the home and care for herself. Rose used the phrase 'I wouldn't say it to [him]' which out of the context of the interview seems strange, but within the context, she wanted to keep his interests outside of the home alive because she could foresee a time beyond her own death, when friends and an active social circle could help Jackie continue. This marks the ultimate transition from the carer's point of view, from relative to carer and then to widow/er. Sudden loss of a feeling of purpose and difficulties in re-constructing a life after being a carer, has been described in PD; continued interests and links outside the caring-life may act to buffer against a complicated grief reaction (Hasson *et al.*, 2010).

7.5.6 Acceptance

In contrast to change imposed upon the participants, whether physical or cognitive symptoms in participants with AP, or the transition from partner to carer, adjustment seemed to be distinct in its generation from within the person as a force for change, rather than externally imposed. Although the adjustment could have been triggered by the external force, adjustment and acceptance seemed to be a way of re-establishing control of a narrative which had the disease in charge, up until that point.

> *As with everything, I tend to be in life organised. So I find when somebody tries to*
> *disorganise it, such as illness. I try to get it back in order again as quickly as I can so I can*
> *take over again. In that way I feel I have got some control of the illness. I am not letting the*
> *illness control me, I am controlling the illness.*
>
> *Julia, age 62, who has MSA*

I was feeling fine with it. I was helping other people get through it. They would get upset, and I would say, "Well, deal with it. Man up." Like my other half. He was getting upset, and I'm thinking, "It should be me, not you." So, I think I dealt with it okay. I think I still am

Doris, age 59, who has MSA

Julia interprets her illness as disruptive and has tried to adapt to the changes it has imposed. To her, order is important, so her efforts are to control and to feel that she has some mastery over the illness. As the illness continues to progress, to maintain this feeling of order, Julia may feel the need to predict and plan for this. Julia had made practical plans within her home for her further decline, in advance. These two aspects of change fit with the discussion above of the chaotic nature of change due to circumstances (in Julia's case, diagnosis and progression of MSA) and change in oneself, in response to an event to re-impose order and adjustment, allowing change to be more on one's 'own terms'.

Doris, who had previously been a medical librarian, put a lot of emphasis on information and facing truth. When discussing her diagnosis and discovering her prognosis, she felt that she faced the reality of her disease and rather than becoming upset, spent her time comforting family. The statement 'it should be me, not you' refers to her husband coming to terms with his feelings about the diagnosis of MSA. Her last statement "I think I still am" reflects the truth about adjustment to a progressing condition; it is not a process to be completed. Adjustment and acceptance are continual and cyclical things, and the added difficulty of progressive disease is that once you have adjusted to how things are right now, after a period there will be further change, requiring more adjustment. Some aspects of acceptance may be easier than others for different people. Changing strategies in the face of disease moving on, is recognized to be part of the adaptive process (Bury, 1991).

Accepting that death would be hastened by AP was discussed by patients and by carers. For some participants, the offer of palliative support triggered the realisation that AP is a life-limiting condition. The internet as an information source (be it reliable or not) was the way in which some participants such as Doris above or Mary below, found out that their disease would bring their lives to an earlier close.

Mary:	**I researched it** (repeats on light-writer several times)
Interviewer:	online?
Mary:	**my husband did**
Interviewer:	the research you did, what did you find out about PSP, the two of you?
Mary:	**that I'd have a much shorter life** (repeated on light-writer several times)

*Mary, age 69, who has PSP (**bold** text indicates typed on an electronic device)*

He's an amazing man. Considering what he's got to put up with. He just accepts his fate. Now I think I would be a nightmare if it was me. I wouldn't accept it…

Sally, age 70, carer of husband (not interviewed) who has PSP

Sally admired her husband's acceptance, his thinking about his future and facing the prospect of death. As he moved from being independent to increasingly reliant, now residing in supported living, Sally remarked upon how peaceably he has accepted these changes and how she doesn't feel she could. This respect for her husband seems to have helped her make the transitions necessary to become his carer, and the change in their lifestyle.

(Sighs) I think the main challenges for me, is to make sure I change whatever I need to change, at the right time for him, so to be there more for him. Erm, without pushing him too much, to do things, to understand, you know, seeing if he can't do it now. Erm, to accept certain things. (Emotional)

Pat, age 62, carer for Gary who has PSP

Oh, yes. Oh god. I think the world's still so good. You have your little bit of time, and that's it. It's good. The world has been very good to me, I have to say, and now I think we're getting to the end of the line, and it doesn't frighten me. It doesn't scare me or anything. You just take every day and accept it as a good day, and that's the way it goes.

Rose, age 71, who has MSA

Ultimately, for Pat, the challenge in accepting her husband Gary's illness was to maintain a balance. As his needs increased she wanted to be there to support him, though she emphasised that she wanted to time things correctly. She did not want to do things for him when he was still able, but was not forcing him to take on tasks he could no longer cope with. This compromise between facilitating independence and assistance included, for her, helping him to gradually adjust to his changing condition. Clearly however, this was a difficult process for

her. Rose, as someone with MSA, spoke frankly about her life coming to an end. Earlier in the interview she had described how she wanted her husband to continue with his hobbies and pursuits as something to support him, and in terms of her own condition she was resigned to her own death, and took every day as 'a good day' no matter what it brought. This suggests that when acceptance is more 'complete' and expectations have adjusted as a consequence, time that patients have is of better quality, as previous expectations have shifted to encompass the new reality.

Transitions and change were an integral part of the experiences of all the participants' narratives. This comprised of the move from a person with symptoms to a person diagnosed with an aggressive condition, a shift to uncertainty and away from plans and dreams often made over years. Carers found themselves in that role, sometimes insidiously, sometimes quickly, but their contribution increased as their partner's status from an independent individual to a more dependent one took place. Finally, some interviewees described a more active way of coping with the uncertainty of progressive illness in adaptation and adjustment; a more 'active' way of responding to change. This may enable some feelings of mastery over their lives, especially the patients, as they themselves become less physically or socially able.

7.6 Accessing Support
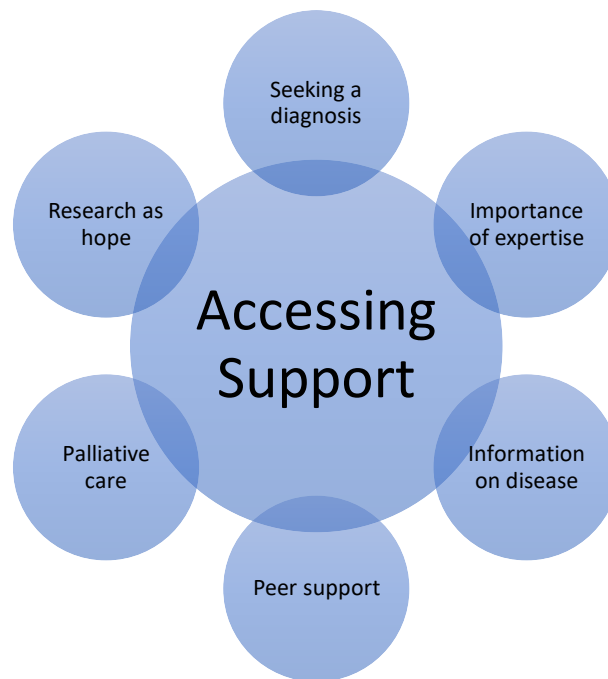
Figure 7.3: Key theme of "Accessing Support" and associated sub-themes

The theme of support and its availability was prevalent as an overall theme in the study and different aspects were discussed.

7.6.1 Seeking a diagnosis

The first need for expert support, guidance and input was in seeking a diagnosis. The difficulties that were described by every participant, both patients and carers, were that of achieving the correct diagnosis, not knowing who the correct specialists were and moving beyond the GP to find the expertise to get them their diagnosis. In some cases, this process took many visits to the GP, referrals to different medical specialities and required revisions in their diagnosis. Coming to terms with a life-changing diagnosis such as PD requires time, acceptance and adjustment. The upheaval of then having this diagnosis overturned and replaced with another which is more sinister, was an extreme experience after a long period of frustration. Earl discusses the process that his wife Helen had, in which their GP attempted to facilitate Helen's diagnosis by referring to what he felt was the correct specialist. As AP has a myriad of presentations it can be very variable in appearance and in Helen's case, by the time

she received a diagnosis, she and her husband had been struggling with her progressing disability for half a decade.

> *The diagnosis itself took an awful long time… five years, which involved being referred to various consultants by the doctor who…was struggling and floundering with her symptoms, [she] went to various consultants and after three months to wait to see them…to get a letter back… "Nothing to do with me" and we'd be referred back to the [GP] who then took another best guess.*

> *Earl, age 70, carer for Helen who has PSP*

> Interviewer: *There was a bit of a rocky road when you were diagnosed.*
> Rose: *Yes, that took quite a while. It took a long time actually, and I saw my doctor I don't know how many times because [my husband] had noticed how shuffly I was and how tired. They just said, "Oh, look, you're just completely exhausted from looking after your mother."*
> *Rose, age 71, who has MSA*

In some cases, the journey to receive their diagnosis was a very long one, such as for Helen and Earl. Rose had a similar experience in which her advancing symptoms were thought to be a reaction to caring for her mother who happened to have Parkinson's disease (which has some features in common with MSA). Rose re-presented to her GP despite reassurances, as her physical condition continued to decline, seeking answers and the correct input. Sometimes the diagnosis was only received due to the efforts of carers. An extreme example was Sally, whose husband was diagnosed as having dementia, but requested a referral to movement disorder services after a friend suggested that her husband had features of PSP, which she had encountered in her work as a hospice volunteer.

> *[the consultant said] "Your [GP]'s very good because not many people can blah, blah, blah." And I said, "Well don't give her all the credit it was [my friend] who works in a hospice who had come across it down in Oxford."*

> *Sally, age 70, carer for husband (not interviewed) who has PSP*

7.6.2 Importance of expertise

The scene for trying to seek support and services in AP may be set by the initial, often protracted battle to get a diagnosis in the first place. The difficulty in reaching the appropriate specialist and how they were diagnosed, may impact upon the reactions people had to it. Many participants felt relief that they finally had answers, though the impact of hearing they

had a life-limiting condition (and if the diagnosis was a revision from PD to AP, hearing they had something worse) was difficult. Work has been done showing the devastation that a diagnosis of PD brings (Phillips, 2006). Having this then changed to a related but more aggressive diagnosis, is likely to combine further upheaval after an initial coming-to-terms, with shock and fear. How the news was imparted was important to participants; face-to-face breaking of bad news seems to have been appreciated. In one case, diagnosis by letter caused upset and distress.

> *The way he told me… like a fireside chat…I was very impressed with him, I read up about him on the internet, I knew who to expect and what to expect…but his manner was wonderful, he …well…he has my complete confidence*

> *Matthew, age 64, who has MSA*

> *After the, after the DAT scan and everything, we actually got a letter, informing us what it was, I just gave [Mary] the letter, and I went in the back kitchen, came back out, and she was in a flood of tears. So, I says, "What's the matter?" and she gave me her letter*

> *Bob, age 69, carer for Mary who has PSP*

The contrast between these two stories can show the difference that expertise and support can provide to a patient who has heard difficult news. This could impact upon trust given to professionals by patients and carers throughout the disease process. A more traumatic, unsupported diagnosis might lead to greater difficulties in adjustment. Matthew's diagnosis, though not the news he wanted, and like many other participants, delayed and revised from an earlier diagnosis of PD, was given by a clinician he had faith in and felt reassured by. He had the ability to ask questions from a respected source. Mary however, had little time to prepare, no knowledgeable professional to hand to ask, and as a result, her experience of diagnosis was not a positive one. After receiving a diagnosis, there was a theme of feeling left to deal with the condition after the intensity of the diagnostic testing and bad news. There was a sense of feeling abandoned to deal with the disease alone from the participants.

> *I think in the hospital once you were diagnosed, that was it. You were out and you had to get on with it. So it went very short from having a lot of input to nothing to taking your prescription and leaving and getting on with it*

> *Rose, age 71, who has MSA*

Well, I was told it's a totally separate condition (from PD) and they couldn't do anything about it. There was no magic cure for it. Basically, I'd have to manage the PSP with help from the hospice.

Gary, age 58, who has PSP

Gary's experience of hospice input was very positive and pervaded his interview. However, at this point in his narrative, he had no experience of PC and his diagnosis was coloured by the impression that his illness had no cure and that only the hospice could offer him anything. From perceptions of PC (Chapter 4), the most frequent response of participants who had a diagnosis of AP (some of whom had already received PC) was being unable to define what PC was and the next most frequent response was that it was a service for the dying. Therefore, hearing that you had a more progressive condition than PD and that you would be referred for hospice care was likely to be a frightening one. The phrase 'they couldn't do anything about it' again suggests withdrawal of active management and abandonment, without explanation of how PC might be able to help. In a review exploring giving a diagnosis of cancer, the importance of setting, ample time, and a face-to-face delivery is emphasised as beneficial and helpful in reducing the suffering of patients, as well as avoiding nihilistic comments like 'we cannot help you' (Baile *et al.*, 2000).

7.6.3 Information on disease

After diagnosis, participants on the whole, sought more information about their disease, though the amount they wanted to know varied. There was a realisation that the condition they had was not well known generally, including amongst health care professionals. A theme amongst the carer-participants was to try and disseminate information in their local community, possibly in the hope that this might benefit their partner if more people were aware of their condition. Of note, this theme of carers distributing information on their partner's illness was seen in the male and not female carer group. Possibly, male carers felt that this activity was a way of actively addressing the root of the problem of poor public information, as opposed to female carers.

Even nurses and doctors don't even know what the hell it is, man. I just say, "Not a problem. I'll send you a pack." And I do it. I get in touch with the [MSA] Trust and say, "Send them a pack." Or I'll take them any leaflet in I've got, and I've got leaflets in my reception for people to read because a lot of people don't know what it is.

Bill, age 57, carer for Doris who has MSA

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I've taken magazines down, and I've put them in the doctor's surgery for people, the public to see, so that the public are, become aware.

Bob, age 69, carer for Mary who has PSP

The information that was available tended to be either from specialist organisations, like the MSA Trust and UK PSP Association, or information from the internet, whether from official sources or not. Aside from these support groups and the internet, only one participant had heard of MSA or PSP before the diagnosis was made; Sally, from her friend, prompting her to seek further referral, above. Her GP had not heard of the diagnosis prior to her raising the issue. Information and making information more available through various means, be it open communication within communities, medical education or charity outreach, was a universal issue for all participants, patients and carers. There is a suggestion that bringing their disease out into the public understanding might make constant explanations less necessary and increase the understanding of their situation. Work into rare diseases in Australian families has shown that there is a desire for as much reliable information as possible, which becomes more vital the more unheard-of the disease is and aid in connecting to others who can offer peer support (Anderson *et al.*, 2013).

Well I think PSP is so unheard of. Even in the medical situation. My doctor had never heard of it. It's just so unheard of. I think it needs a little bit more publicity but it's such a rare thing, you know.

Sally, age 70, care for her husband (not interviewed) who has PSP

Like everyone knows about Parkinson's and everyone knows about cancer. I would like everyone to know about [PSP] so that they would have more of an understanding of daft people like me.

Helen, age 68, who has PSP

Specialist services, who were knowledgeable about AP, were important to the well-being of the participants interviewed. This not only comprised of medical services who had experience of AP, like specialist nurses, but also charitable organisations like the PSP Association or MSA Trust. Participants found that access to a number of experts and agencies were required to help them navigate the problems which arose through their disease. Matthew, who felt well-informed and supported since diagnosis, thought having to cope without them would be

very detrimental. These groups not only provided the guidance and networking which can be so useful in finding useful contacts and advice in rare, complex conditions, but in finding other people to connect with. This is especially important for individuals who feel that the symptoms of their disease, such as speech problems or socially-difficult symptoms such as continence issues, are shared and understood by others.

> *I wouldn't have known what I'd been missing, but...it would be pretty awful. It's such a horrible disease to have and the more back-up you've got, the more support the better it is, and...living in this area, you get tremendous encouragement.*

> *Matthew, age 64, who has MSA*

> *That was the time I went and sat in that group, and, er, got very emotional that night, actually, that I told them that… [Mary] didn't have Parkinson's, but it was something on a darker, down a side road, and I got really upset that night, expressing myself to them, and they were all really supportive of us.*

> *Bob, age 69, carer for Mary who has PSP*

The role of the group meeting and the peer support which is provided, appears immediately applicable to patients who share the same features of disease, but carers too, described the benefits of having access to people who were dealing with similar pressures of care-giving. Not all of these groups were specific to AP. Some were general carers groups of people with long-term illnesses, and some were Parkinson's carers groups. However, finding people who you could confide in, and who you felt had the life-experience to empathise with you, appeared important to this group of participants.

7.6.4 Peer support

Peer support was not only found in support groups but also from palliative care services, from other patients with various life-limiting illnesses, as well as from staff who attempted to provide more holistic care for the whole person. Therefore, the care provided by PC services may not only have relieved symptoms from physical issues, but gave time and access to other people, staff and patients, thus addressing psychosocial and spiritual needs.

It helps due to the fact that people- you're in with a group of people who's going to have the same endings you are. I'm not saying it's going to be quicker or time-wise, but psychologically you feel that you're on par with them, and they help you and you help them in different ways.

<p align="center">*Gary, age 58, who has PSP*</p>

When participants described experiences that they had had with PC services, they tended to describe the human interactions, rather than specifically the treatments received or services provided. PC is a varying 'package', be it day hospice, home visits or clinic appointments, in keeping with the heterogeneous presentation of AP and different elements which constitute QoL, shown in Chapters 4 and 6. This suggests that some of the benefits participants derive from PC are from the extra time and service design allowing greater connection with others. This includes meeting other patients, one-to-one nursing and volunteer input, protracted and more frequent clinic reviews with continuity of care, and personalisation. Gary experienced this from his time in day hospice, where he could relate to the others in the group, though their conditions and trajectories might vary.

7.6.5 Palliative care

The contribution of generalists, such as GPs using a palliative approach, was also described. Sally's GP who had not heard of PSP before making a referral, as described earlier, had become informed on PSP and maintained continuity of care with Sally's husband. This had culminated in her helping Sally's husband with advance care planning so his wishes were respected as he approached the last days of his life. Sally found the process difficult, though the discussions seemed to orientate and began to prepare her for the future. She seems to have a great deal of gratitude to the GP for her work with her husband, using the word 'incredible' which might allude to the journey the GP has made to educate herself on the disease so she could apply a palliative approach to improve his care.

My doctor [GP] was incredible. I mean she has gone, and we've done his end-of-life thing, where he can tell you what he wants. I had to walk out of the conversation because I was…I sort of pulled myself back together and went back in.   And I suppose that's when the word palliative hit me. The meaning of the word palliative hit me. I think that was it. And I now know that he won't live forever.

<p align="center">*Sally, age 70, carer for her husband (not interviewed) who has PSP*</p>

I think it means people like nurses who are coming and sort of help you to do things, talk to you about your disease, check on your medication, perhaps advise on maybe a bit of extra help and say things that you can do to make your life easier

Rose, age 71, who has MSA

Rose had not had any input from PC but was open to the possibility and that it could enhance her experience. This is contrasted with participants who felt PC was the last refuge before death and seemed to fear it or dismiss it as unhelpful to them at their point in their illness. Viewpoints varied between the perception of PC as extra support and as a staging post, a referral to PC being made when your doctor felt you were dying. It can be seen that in this later group, especially if PC as a concept is not fully and openly explained from an early stage in the disease process, that people might defer engaging with the service out of fear; losing the opportunity to benefit from it in the ways discussed by Gary, Sally and Rose. Matthew appears to fit into this category. Doris seems between these two viewpoints, as though she is in transition between anticipating her advancing illness and beginning to appreciate that PC may have a role to play in enhancing her QoL. This appreciation for PC and its outlook into facing the future, possibly mirrors participants' adjustment to their diagnosis.

I don't think I need the help. I might later on. I don't know. Like now, some people might be in bits, talking like this, but I know what to expect.

Doris, age 59, who has MSA

I would say the end of your life, er, that sort of care is offered, I've heard of organisations…I don't know whether if I've reached that stage

Matthew, age 64, who has MSA

In terms of adjustment and acceptance, the expectations of research from participants may vary (as seems to be the case with opinions on PC). Some participants were involved in multiple types of research. There appeared be widespread solace in the fact that though there was, as yet no curative treatment for AP, active research was going on seeking to address that.

Interviewer: *So you think being informed about the research and things, does that help you?*
Rose: *Yes. It makes you feel if you hang on long enough there'll be something out there. At least if you don't, well, there'll be something, if you can help a little bit, there'll be something for somebody else later on. Mightn't be in my time, but I'm sure like the cancer research, it'll come.*

Rose, age 71, who has MSA

7.6.6 Research as hope

Motivations, however, varied from envisioning cures which would come about quickly and effect a cure, to wanting to contribute to the possibility of a cure for others in the future. The cure seemed to be tied up with the notion of hope, though Rose for example did not seem to have lost hope, despite not foreseeing a cure for herself; rather she has shifted the hope from herself onto others. Bryce particularly discussed the need to have the possibility of a cure as a reality. To dispel this idea or to suggest that this might not come to pass for him was seen as a cruelty on behalf of doctors, destroying hope. One doctor who suggested that he might consider the future if, by chance a cure was not found, was considered in his words a "menace" for dispelling his prospect of being healthy again. This indicates that an 'absolutist' attitude to always telling patients all the facts may be harmful. There is a delicate balance to assessing how and when to convey information to patients when they are ready. This allows them to prepare and plan. In some cases, divulging the full truth may damage patients' well-being (Begley and Blackwood, 2000). Expectations of cures and interventions may have changed perceptions of mortality in illness, making the concept and idea of death and dying unexpected and frightening; leading to a 'dehumanised' and medicalised dying (Clark, 2002).

> *A cure … I just think it's all lies, you can get cured. I'm not saying you're going to get cured tomorrow or the next day or next week but in years to come…. as long as people like them stupid doctors don't turn around and say you're never going to get cured. Give you a bit of hope.*

Bryce, age 76, who has PSP

> Interviewer*:*   *is there are a lot of discussion of cures and research in the house?*
> Emma*:*   *all the time, all the time… he'll present me with the latest thing he's been reading about …-I think that, he's clinging to this to give him hope.*

Emma, age 61, carer for Matthew who has MSA

Emma describes Matthew's avid scrutiny of the medical literature, desperate for news of a new effective treatment as a means to maintain hope in the face of his disease. This may be in tandem with his current position on palliative input; he is not yet ready to consider that a cure may not be found. It may be that this is a position he could come to in the future, he might then be open to PC input (though these two viewpoints may not be mutually exclusive). This balance between hope for curative treatment and embracing a different kind of care, encompassing holistic management and looking to the future, is something that all physicians

and care teams will face, as medical technology increases. It also become more important as our knowledge of the needs beyond the traditional biophysical model grows (Clark, 2002).

7.7 Discussion

The main themes that pervaded this qualitative study were connection, transition and accessing support. The first two lead very much into the last; connectedness allowing access to support and in turn, increasing the feeling of connection for patients and carers as transitions lead to the need to access services.

Connection was described as the ability to relate to others by speech, communication generally, quality and maintenance of relationships, and being able to relate to oneself and how identity can be affected by such a pervasive disease. Identity was profoundly affected in the patient-participants; some described the strangeness or oddness of what the disease had done to them, especially in terms of personality or cognitive changes. Others withdrew, either voluntarily from social interactions due to self-consciousness about their progressing disability, or felt that this withdrawal was imposed upon them as their voices faded, and became weaker; literally, in terms of volume, but also metaphorically, as fatigue and the burden of their illness weighed them down. Participants emphasised that the voice of the patient and of the carer was not heard and that the public was not aware of the struggle they faced with a rare, little-known illness, as the demands of the condition severed the connections and ties to their previous lives. Pre-morbid poor social networks have been seen in work on stroke to predict for poor outcomes. The influence of the social network in neurological disease has been found to have such an impact on the outcome of patients that incorporating key members of the network into clinical discussions has been found to improve health behaviours and influence depression (Boden-Albala *et al.*, 2005; Dhand *et al.*, 2016). Patients and relatives should be considered together; what impacts one will influence the other, especially true of the sole spouse-carer with a limited family network for wider support. Connectedness is as important for carers as for patients. AP has more rapid and devastating effects upon speech and communication than PD and in the latter, Hudson described the social sphere shutting down to just the patient and carer. However, as communication became more difficult even between them, both ended up being cut off from meaningful human contact (Hudson *et al.*, 2006; Miller *et al.*, 2011; Rusz *et al.*, 2015). Carers are frequently isolated from their social networks by the 24-hour nature of care, and this was captured particularly by the carer's fear of the patient falling. It should be a priority to keep

the channels of communication open to patients and to carers as long as possible. This encompasses speech therapy, technological devices and trained staff to recognise communication difficulty, but also simple, meaningful measures such as eye contact with a mute patient, speaking to patients themselves rather than their carer, and asking carers about their well-being and signposting them to sources of support.

The transition theme also recognises the link between patients and carers. Both groups endured a narrative of change which has been described in the literature as 'biographical disruption' - chronic illness causing the defined path of life up until that point and the projected or expected course after, to deviate in unexpected ways. This disruption is associated with chronic illnesses, particularly when associated with uncertainty and part of acceptance is coming to terms with this impact upon the planned life and adjusting to the new unexpected reality (Williams, 2000). This alteration to the planned life affected the partnership of patients and carers. The bond between the patient and the care-giver appeared key to coping and adjustment. However, there was tension inherent in these relationships which was shown particularly clearly in patients with frontal cognitive problems and motor recklessness. The aims of maintaining independence and keeping ambulant in these patients (especially as there may be loss of insight about the risk of injury) and the conflicting objective of carers keeping their partner safe whilst promoting their well-being, often downplaying the increasing amount they need to do to keep their partner going, were sometimes in opposition. This view of the life together and the contribution of each person to the relationship has been described as the 'biographical we' (Aasbo *et al.*, 2016). Carers have this 'safety versus independence' dilemma, which is often not seen by the patient and pervades the whole relationship with ongoing worry.

The nature of the changes or transitions made in response to illness can be seen as reactive due to the demands of the illness (be it from patient or carer), or proactive as a consequence of shifting one's own expectations and adjusting to the new reality. In terms of how this can be seen narratively, the changes imposed by disease can be seen as chaotic and out of the person's control, further cementing the impact that the disease has upon the person's reality. This could be seen from the retreat of patient-participants from the active roles and social circles due to their disease silencing their voices, slowing their thoughts and bodies, and from carers whose social outlets are trimmed away as the needs of their partner grow. By contrast, the internal changes described by participants, of outlook, expectations and viewpoints, mirror acceptance and adjustment. These transitions seek to limit the power the chaotic disease has

upon the participants as they shift their expectations. These adjustments are difficult to maintain in the face of uncertain disease, but participants whose interviews evoked the themes of adjustment and acceptance, seemed to fix their gaze beyond the immediate challenges as they arose, almost as though they were prepared for a difficult journey with obstacles, the ending of which they were prepared for. This perception of chronic illness as a quest to the final destination of death, with its alternative as a tumultuous imposition of events upon the person, is described by Frank (2013) in his narrative on the illness journey. These narratives are not exclusive, and individuals can simultaneously experience the buffeting of the chaos narrative, and learning about themselves and their illness in the quest narrative or, pass from one to the other.

The nature of MSA and PSP is complex and seemed to affect multiple elements of the person; physical, cognitive, psychosocial and spiritual. For this reason, the transitions that individuals (both patients and carers) endure and impose upon themselves in the course of their illness-journey, are many and varied. The 'totality of change' is therefore a good descriptor of the transitions made during the course of the illness; seeking a diagnosis, experiencing the changing self, and the shift from relative to carer.

These two previous themes feed into the access of support theme. Support seeks to make transitions easier, to address the 'shrinking down' of horizons, and re-open the door to the outside world via peer support, addressing a lack of information, helping with symptoms and engaging with research as a source for hope into the future. Palliative care stood as a beacon for some, enabling this re-connection and helping the journey to acceptance. For others it was a symbol of decline and loss, preparing for a future without a cure. Palliative care is envisioned as a multi-system, holistic and individual approach to the well-being of people with chronic or life-limiting illness (World Health Organisation, 2002). As the prevalent threads of this qualitative work have shown, much distress from the cohort interviewed springs from lack of information, perceived expertise, time and loss of social networks. A palliative approach, by its very remit is better equipped to salvage quality from the lives affected by AP than the traditional biomedical model.

7.8 Reflections

I have reflected upon the analysis in this chapter using criteria described by Yardley (2000), as was discussed in the Methods chapter.

As part of the requirement of qualitative work is commitment and rigour, necessitating immersion, I tried hard to engage with the experiences of the participants. This was on some levels difficult to do, as clinicians are encouraged to have some professional detachment from their patients, but in the context of the research, I sought to consider the participant's experiences not from a medical-practitioner standpoint but from a neutral stance so best to appreciate their story. Equally, some participants who had known me from clinical work prior to the study, regarded me as a doctor primarily, which at times influenced their interview responses. They may have assumed I would want to hear more 'technical' and medical details rather than their own concerns and narratives. This required frequent reminders and guides to the participant to give their own story rather than listing appointments and tests. However, during interviewing and analysis, I was conscious of my tendency to try to 'diagnose' issues interviewees described, rather than allow participants to discuss them in terms of their own experience. Consequently, I needed to constantly check and review my interviewing to ensure I was not interviewing as a doctor rather than as a researcher. However, I accept that this background likely coloured the interactions with participants and influenced the tone of the analysis.

As well as my standpoints and beliefs influencing the study, there were impressions made on me from the project and working with its participants. Compared to my clinical work, the qualitative part of the project allowed me to understand the participants better, gaining insight into other aspects of their disease beyond the 'safe space' of the clinic. This has positive sides in that it may help me to gain perspective when considering difficulties and patient needs in clinical care and planning of service provision in the future. Potential negative impacts were due to the greater relationship developed between myself and these participants. Seeing these patients progress and, in some cases, die whilst still reviewing their words in written interview format and hearing their voice recordings was, at times, difficult. Previous interaction with patients and carers has had a fairly defined boundary in clinical practice; when invited into people's homes to take very personal interviews, these individuals made a far deeper impression and their subsequent deterioration was challenging to deal with. Debriefings with KB were helpful in this regard.

Chapter 8. Discussion

8.1 Discussion

There is a growing body of work exploring QoL in chronic, progressive disease, with the aim of giving individuals and their families the best possible experience as they live with their condition. Rare illnesses, like MSA and PSP, may have unique symptom profiles and the added burden of delayed diagnosis and fewer practitioners with experience of managing the disease (Moore and Guttman, 2014; Wiblin, 2017).

Although some studies have explored QoL in MSA and PSP, and scales have been developed to measure it, there has been a paucity of studies looking at subjective QoL; HR-QoL tends to measure well-being related only to illness and is limited in assessing how other factors in the individual's life influence patient satisfaction (Schrag, 2005; Schrag *et al.*, 2006a; Schrag *et al.*, 2006c; Meissner *et al.*, 2012; Pekmezovic *et al.*, 2015).

Palliative care aims to maximise QoL by embracing all aspects of the person and alleviating distress and managing symptoms wherever possible, including psychological distress, and taking carers and families into account (up to and beyond the patient's death) (Sepulveda *et al.*, 2002; World Health Organisation, 2002). The palliative approach, which as discussed in Chapter 1, can be used by anyone, not just doctors or nurses working in Specialist Palliative Care. It advocates a style which is personalised to the individual, incorporating future planning and preparation but only at a pace determined by, and according to the wishes of, the patient. Greater complexity may involve liaison with or referral to SPC services, and part of the palliative approach is recognising when this is required (Ghoche, 2012; Miyasaki, 2015).

PC has been increasingly recognised as helpful in neurodegenerative disease such as PD and dementia, in part due to the example of MND which incorporates PC into best practice from diagnosis with improvement in QoL consequently (Borasio, 2013; Veronese *et al.*, 2015; Oliver *et al.*, 2016). There has been little work which considers the use of PC in MSA and PSP nor the PC needs of these conditions, the majority being in PD alone or PD together with some AP (Higginson *et al.*, 2012; Saleem *et al.*, 2013).

This study aimed to describe QoL in MSA and PSP both in terms of HR-QoL and subjective QoL and compare the two groups. It also assessed QoL in the carers of MSA and PSP-affected participants. Symptom profiles were explored using a palliative symptom questionnaire and subjective symptom onset was recorded to give a view of retrospective

symptom trajectories over time. Interviews were carried out with a sample of participants to allow a nuanced and rich view of participants' experiences with MSA and PSP.

Depression and palliative care need (using DASS-21 and the POS-S-PD) were shown to predict HR-QoL (using MSA-QoL) in MSA whilst depression, palliative care need *and* disease-specific severity predicted HR-QoL (PSP-QoL) in PSP. This is the first evidence we are aware of looking specifically at palliative care requirement as a predictor for QoL in MSA and PSP. Furthermore, the difference highlighted between the two conditions in terms of how severity impacts HR-QoL (significant effect on QoL in PSP though not in MSA). Subjective QoL showed diverse and varied domains in patients and carers, highlighting that QoL is heterogeneous. The importance of relationships was the most frequently nominated issue in all patient and carer groups: Family/family-life was most nominated and marriage/partner second overall. Scores on subjective QoL showed no significant differences between MSA or PSP (between patients or between carers), though MSA patients had lower mean scores than PSP patients. MSA carers also had lower mean scores than PSP carers. Possible reasons for this include the possibility that greater cognitive involvement might afford some relative 'protection' from considering the future implications of a progressive disease (which might make PSP patients' QoL more reliant on direct physical impact of disease, such as HR-QoL being affected by severity). Similarly, carers for MSA patients may have greater distress if the people they care for are more distressed. Work in PD has suggested that age does not seem to affect care-giver burden, though the carers in the two disease groups in this study showed different characteristics (Greenwell *et al.*, 2015; Navarta-Sanchez *et al.*, 2016). PSP carers were older and almost all were retired. In the MSA group, carers and patients tended to be younger and some carers were still in employment. It may be that disruption of plans and expectations and the subsequent adjustments required, were more substantial and demanding in the MSA group, leading to greater impact on all aspects of QoL and well-being. The SEIQoL-DW is a powerful tool which can capture complex data on subjective, individualised QoL. Although SEIQoL has been used to generate continuous scores in AP cohorts together with PD, there is currently no literature which explores subjective QoL in MSA or PSP. As there are no current treatments which can prolong life or have a disease-modifying effect in these conditions (and indeed in any other neurodegenerative disease at present), looking at ways to improve the experience of these people beyond symptom control should be sought. As QoL means different things to different individuals, a personalised approach, possibly with social as well as medical input, may be required, but more work should be done in future to explore the benefits of this.

From a carer perspective, other than a single paper in 1998, there has not been any work looking into QoL, strain or well-being of carers of people with MSA or PSP (Uttl *et al.*, 1998). Clearly this is a group who deal with a complex disease affecting physical and cognitive health as well as the fairly unique pressures of delayed diagnosis and the 're-diagnosis' from PD, which is a frequent emotional aspect of dealing with these conditions. This project not only used generic tools to look into carer well-being, but also specific carer QoL scores for this group of diseases and subjective QoL scores which allowed comparison between carer groups and between carers and the people they cared for. The findings suggest some protection afforded by a longer relationship-duration between patient and carer. As the predictive value is modest and the qualitative work in this project produced findings that emphasised the importance of connecting to others and particularly, a meaningful relationship with a partner and family, it is possible that the *quality* of the relationship between patients and carers have a more profound influence on QoL. Exploring this and how quality relationships could be preserved or enhanced would be a logical progression in future work, which could also have implications for well-being and service planning for other conditions.

Exploration of palliative symptom profiles showed that burden was higher than in previous work (PD with some MSA and PSP patients) using the same tools. There were no significant differences in palliative symptom severity between MSA and PSP, though there was a trend toward greater urinary disturbance and fatigue in the MSA group. Symptom profiles were similar, suggesting that services for both MSA and PSP patients are appropriate, though assessment of individual concerns is important. How patients' palliative or symptom needs can be addressed in different locales depends very much upon the culture of the team and geography of the area. It may be that teams could be fully integrated, with movement disorder services and palliative care teams sharing the care of patients as well as physiotherapists, occupational therapists etc. Other regions may have rehabilitation teams incorporating a palliative ethos, as symptom control is part of routine care for neurological conditions such as Multiple Sclerosis in rehabilitation medicine. In very rural conditions, nursing teams or palliative care nursing and therapy teams in the community could keep patients and carers connected to their specialists; be they neurologists, elderly care consultants or specialist palliative care consultants. Increasingly, as hospitals try to concentrate on outpatient care and reducing admissions to hospital, more creative solutions to provide care and support to patients need to be trialled for efficacy and patient satisfaction. These include community outreach clinics, possibly held in hospice or community hospital settings or virtual clinics using video-conferencing (which could link up multiple disciplines together whilst the patient

does not have to leave their home - which can be very difficult in advanced disease). Exploration of technology and community work and how they could benefit people with AP would be a meaningful subject for research and service improvement projects.

Qualitative interviewing and analysis revealed three main themes; connection, transition and seeking support. Connection was concerned with relating to others and how this is affected by the impact of AP affecting speech, cognition and concerns about how one is perceived. Transitions comprised of subthemes of changing roles, shifting physical and mental conditions, and adjustment to these changes. Finally, seeking support highlighted the difficulties in obtaining a diagnosis and getting appropriate help and assistance with a rare disorder which is poorly understood. These themes related to each other (i.e. support could help individuals undergoing particular transitions re-connect to others, such as family or peer groups). Interestingly there was some cross-over between the SEIQoL-DW domains and interview themes (see Appendix C), particularly in the emphasis patients and carers placed on how relationships were affected by disease, the nature of 24-hour care, and the burden this produces and delayed diagnoses. However, the interviews tended to discuss experiences people had had whilst the SEIQoL-DW tended to focus on the more positive aspects that participants had.

8.2 Limitations and future perspectives

This study comprised of a relatively small sample and was cross-sectional in design. In order to gain greater insight and more definite conclusions on QoL, palliative care needs and symptom profiles, further work should be done with larger groups and on a longitudinal basis. Assessing the validity of depression scores in patients with MSA and PSP, taking into account a measure of apathy, might also be helpful in better assessing the mood of this patient group.

Another limitation of this work was the lack of formal cognitive testing. Although it is well-described in standard medical texts and the research literature that cognitive dysfunction tends to be more severe in PSP than MSA, it would have been helpful to have a measure to ascertain how different cognitive scores were between groups and whether these profiles impacted upon QoL (and QoL of care-givers).

MSA and PSP have profound effects on the QoL of patients and carers. Palliative symptom burden appears higher than PD at an equivalent H&Y stage, and participants were particularly troubled by the impact of their condition upon relationships. Depression and palliative burden

impacted on QoL. SPC seemed to be of benefit to patients, though prior perceptions of PC were often that it was a service for cancer, or the imminently-dying. Service provision should consider the benefits of a blended approach with palliative care integrated from the beginning. Depression and symptoms such as drooling and pain, should be sought as much as motor symptoms in neurological reviews to improve QoL. When communication is impaired, efforts should be made to retain the patient's input, such as prior sessions to obtain concerns and issues with volunteers or therapy staff, and more time in clinic. Measures to support carers should be researched in the future, as caregiver-burden in chronic disease is sizeable, growing and their well-being is intrinsically connected with that of the patient.

This work produced some findings that show the importance of identifying and treating depression and how symptoms often classified as 'palliative' such as drooling can influence QoL in MSA and PSP. It also explored the differences that different scales purporting to measure the same construct ('QoL') look at different aspects of a complex concept and are complementary rather than alternatives. Disease-specific QoL tools cannot capture the same holistic and individual meaning as subjective QoL tools, but in turn would not pick up personal concerns around these unique diseases and their specific symptoms. It is therefore reasonable to suggest that future work exploring QoL should incorporate both HR-QoL and subjective, more reflective measures of QoL, not only to capture a fuller picture, but to see what influences different aspects, and how they can be improved.

Similarly, the majority of tools used in this study were validated for AP (or at least PD). The depression scales have not been validated in AP and there seemed to be no consensus on which measure was best suited to frontal dyscognitive problems. As it can be difficult to distinguish apathy and depression from each other clinically, work to verify the most suitable tool, with apathy measures such as the Lille score and a clinical psychiatric assessment, would be extremely useful to find the most reliable ways to measure depression when apathy is also present.

Finally, I worked with supportive neurologists and palliative care physicians to complete this project. In the future, medical specialities may consider training physicians to acquire palliative care expertise within their own area to complement and work with SPC teams as our awareness of patient needs grow.

Appendix A: Questionnaires

Patient Demographics

Age

Sex   Female ☐   Male ☐

Diagnosis   MSA ☐   PSP ☐

Age at diagnosis

Age at (perceived) onset

Ethnicity

Marital state: Married/Partner/Widowed/Single

Occupation

Hoehn and Yahr Stage: 1 2 3 4 5

Medications:

Key Symptoms:

1. Frequent falls (more than or equal to 2/yr or documented freq falls)
2. Wheelchair
3. Postural drop/other autonomic
4. Speech problems
5. Swallowing problems
6. PEG insertion
7. Catheter insertion
8. Emergency admission to hospital for symptom control/sequelae of disease
9. Admission to institutional care
10. Tracheostomy

Do you have pain   Yes ☐   No ☐

If yes, type and any treatment

Do you have drooling?   Yes ☐   No ☐

If yes, type and any treatment

Do you have poor sleep?   Yes ☐   No ☐

If yes, type and any treatment

Do you have anxiety?   Yes ☐   No ☐

If yes, any treatment?

Do you have depression?   Yes ☐   No ☐

If yes, any treatment?

Memory problems?   Yes ☐   No ☐

Do you know what PC is?   Yes ☐   No ☐

What is it?

Have you had any palliative care input?   Yes ☐   No ☐

Details

Carer Demographics

Age

Sex   Female ☐   Male ☐

Caree Diagnosis: MSA ☐   PSP ☐

Ethnicity

Occupation

Marital status: Married/Partner/Widowed/Single

Lives with caree?   Yes ☐   No ☐

Driver: Yes ☐   No ☐

Length of time they've known participant/patient:

Length of time as caregiver/carer:

Length of time spent per week as caregiver:

PSPRS

I. History (Score 0-24)

1. Withdrawal (relative to baseline personality)
   0) None
   1) Follows conversation in a group, may respond spontaneously, but rarely if ever initiates exchanges
   2) Rarely or never follows conversation in a group
2. Irritability (relative to baseline personality)
   0) No increase in aggressiveness
   1) Increased, but not interfering with family interactions
   2) Interfering with family interactions
3. Dysphagia for solids
   0) Normal; no difficulty with full range of food textures
   1) Tough foods must be cut up into small pieces
   2) Requires soft solid diet
   3) Requires pureed or liquid diet
   4) Tube feeding required for some or all feeding
4. Using knife and for, buttoning clothes, washing hands and face (rate the worst)
   0) Normal
   1) Somewhat slow but no help required
   2) Extremely slow; or occasional help needed
   3) Considerable help needed but can do some things alone
   4) Requires total assistance
5. Falls (average frequency if patient attempt to walk unaided)
   0) None in the past year
   1) <1 per month; gait may otherwise be normal
   2) 1-4 per month
   3) 5-30 per month
   4) >30 per month (or chairbound)
6. Urinary incontinence
   0) None or few drops less than daily
   1) A few drops staining clothes daily
   2) Large amounts, but only when asleep; no pad required during day
   3) Occasional large amounts in daytime; pad required
   4) Consistent, requiring diaper or catheter awake and asleep
7. Sleep difficulty
   0) Neither 1° or 2° insomnia (i.e. falls asleep easily and stays asleep)
   1) Either 1° or 2° insomnia; averages at least 5 hours sleep nightly
   2) Both 1° and 2° insomnia; averages at least 5 hours sleep nightly
   3) Either 1° or 2° insomnia; averages less than 5 hours sleep nightly
   4) Both 1° and 2° insomnia; averages less than 5 hours sleep nightly

II. Mental exam (Score 0-16)

Items 8-11 use this scale: 0 = Clearly absent, 1 = Equivocal or minimal, 2 = Clearly present, but not affecting activities of daily living (ADL), 3 = Interfering mildly with ADL, 4 = Interfering markedly with ADL

8. Disorientation
9. Bradyphrenia
10. Emotional incontinence
11. Grasping/imitative/utilizing behaviour

III. Bulbar exam (Score 0-8)

12. Dysarthria (ignoring palilalia)
    0) None
    1) Minimal; all or nearly all words easily comprehensible (to examiner, not family)
    2) Definite; moderate; most words comprehensible
    3) Severe; may be fluent but most words incomprehensible
    4) Mute; or a few poorly comprehensible words
13. Dysphagia (for 30-50cc of water from a cup, if safe)
    0) None
    1) Fluid pools in mouth or pharynx, or swallows slowly, but no choking/coughing
    2) Occasionally coughs to clear fluid; no frank aspiration
    3) Frequently coughs to clear fluid; may aspirate slightly; may expectorate frequently rather than swallow secretions
    4) Requires artificial measures (oral suctioning, tracheostomy or feeding gastrostomy) to avoid aspiration

IV. Supranuclear ocular motor exam (Score 0-16)

Items 14-16 use this scale. Rate by inspection of saccades on command from the primary position of gaze to a stationary target. 0 = Not slow or hypometric; 86-100% of normal amplitude, 1 = Slow or hypometric; 86-100% of normal amplitude, 2 = 51-85% of normal amplitude, 3 = 16-50% of normal amplitude, 4 = 15% of normal amplitude or worse

14. Voluntary upward saccades
15. Voluntary downward saccades
16. Voluntary left and right saccades
17. Eyelid dysfunction
    0) None
    1) Blink rate decreased (<15/minute) but no other abnormality
    2) Mild inhibition of opening or closing or mild blepharospasm; no visual disability
    3) Moderate lid-opening inhibition or blepharospasm causing partial visual disability
    4) Functional blindness or near-blindness because of involuntary eyelid closure

V. Limb exam (Score 0-16)

18. Limb rigidity (rate the worst of the four)
    0) Absent
    1) Slight or detectable only on activation
    2) Definitely abnormal, but full range of motion possible
    3) Only partial range of motion possible
    4) Little or no passive motion possible
19. Limb dystonia (rate worst of the four; ignore neck and face)
    0) Absent
    1) Subtle or present only when activated by other movement
    2) Obvious but not continuous
    3) Continuous but not disabling
    4) Continuous and disabling
20. Finger tapping (if asymmetric, rate worse side)
    0) Normal (>14 taps/5 sec with maximal amplitude)
    1) Impaired (6-14 taps/5 sec or moderate loss of amplitude)
    2) Barely able to perform (0-5 taps/5 sec or severe loss of amplitude)

21. Toe tapping (if asymmetric, rate worse side)
    0) Normal (>14 taps/5 sec with maximal amplitude)
    1) Impaired (6-14 taps/5 sec or moderate loss of amplitude)
    2) Barely able to perform (0-5 taps/5 sec or severe loss of amplitude)
22. Apraxia of hand movement
    0) Absent
    1) Present, not impairing most functions
    2) Impairing most functions
23. Tremor in any part
    0) Absent
    1) Present, not impairing most functions
    2) Impairing most functions

VI. Gait/Midline exam (Score 0-20)

24. Neck rigidity or dystonia
    0) Absent
    1) Slight or detectable only when activated by other movement
    2) Definitely abnormal, but full range of motion possible
    3) Only partial range of motion possible
    4) Little or no passive motion possible
25. Arising from chair
    0) Normal
    1) Slow but arises on first attempt
    2) Requires more than one attempt, but arises without using hands
    3) Requires use of hands
    4) Unable to arise without assistance
26. Gait
    0) Normal
    1) Slightly wide-based or irregular or slight pulsion on turns
    2) Must walk slowly or occasionally use walls of helper to avoid falling, especially on turns
    3) Must use assistance all or almost all the time
    4) Unable to walk, even with walker; may be able to transfer
27. Postural stability (on backward pull)
    0) Normal (shifts neither foot or one foot)
    1) Must shift each foot at least once but recovers unaided
    2) Shifts feet and must be caught by examiner
    3) Unable to shift feet; must be caught, but does not require assistance to stand still
    4) Tends to fall without a pull; requires assistance to stand still
28. Sitting down (may touch seat or back but not arms of chair)
    0) Normal
    1) Slightly stiff or awkward
    2) Easily positions self before chair, but descent into chair is uncontrolled
    3) Has difficulty finding chair behind him/her and descent is uncontrolled
    4) Unable to test because of severe postural instability

Total Score 0-100

UMSARS

Part I: Historical Review

1. Speech
   0) Not affected
   1) Mildly affected. No difficulties being understood
   2) Moderately affected. Sometimes (less than half of the time) asked to repeat statements
   3) Severely affected. Frequently (more than half of the time) asked to repeat statements
   4) Unintelligible most of the time
2. Swallowing
   0) Normal
   1) Mild impairment. Choking less than once a week
   2) Moderate impairment. Occasional food aspiration with choking more than once a week
   3) Marked impairment. Frequent food aspiration
   4) Nasogastric tube or gastrostomy feeding
3. Handwriting
   0) Normal
   1) Mildly impaired, all words are legible
   2) Moderately impaired, up to half of the words are not legible
   3) Markedly impaired, the majority of words are not legible
   4) Unable to write
4. Cutting food and handling utensils
   0) Normal
   1) Somewhat slow and/or clumsy, but no help needed
   2) Can cut most foods, although clumsy and slow; some help needed
   3) Food must be cut by someone, but can still feed slowly
   4) Needs to be fed
5. Dressing
   0) Normal
   1) Somewhat slow and/or clumsy, but no help needed
   2) Occasional assistance with buttoning, getting arms in sleeves
   3) Considerable help required, but can do some things alone
   4) Completely helpless
6. Hygiene
   0) Normal
   1) Somewhat slow and/or clumsy, but no help needed
   2) Needs help to shower or bathe; or very slow in hygienic care
   3) Requires assistance for washing, brushing teeth, combing hair, using the toilet
   4) Completely helpless
7. Walking
   0) Normal
   1) Mildly impaired. No assistance needed. No walking aid required (except for unrelated disorders)
   2) Moderately impaired. Assistance and/or walking aid needed occasionally
   3) Severely impaired. Assistance and/or walking aid needed frequently
   4) Cannot walk at all even with assistance
8. Falling (rate the past month)
   0) None
   1) Rare falling (less than once a month)
   2) Occasional falling (less than once a week)
   3) Falls more than once a week
   4) Falls at least once a day (if the patient cannot walk at all, rate 4)

9. Orthostatic symptoms (Syncope, dizziness, visual disturbances or neck pain, relieved on lying flat)
    0) No orthostatic symptoms
    1) Orthostatic symptoms are infrequent and do not restrict activities of daily living (ADL)
    2) Frequent orthostatic symptoms developing at least once a week. Some limitation in ADL.
    3) Orthostatic symptoms develop on most occasions. Able to stand >1 min on most occasions. Limitations in most of ADL
    4) Symptoms consistently develop on orthostasis. Able to stand <1 min on most occasions. Syncope/presyncope is common if patient attempts to stand
10. Urinary function (urinary symptoms should not be due to other causes)
    0) Normal
    1) Urgency and/or frequency, no drug treatment required
    2) Urgency and/or frequency, drug treatment required
    3) Urge incontinence and/or incomplete bladder emptying needing intermittent catheterization
    4) Incontinence needing indwelling catheter
11. Sexual function
    0) No problems
    1) Minor impairment compared to healthy days
    2) Moderate impairment compared to healthy days
    3) Severe impairment compared to healthy days
    4) No sexual activity possible
12. Bowel function
    0) No change in pattern of bowel function from previous pattern
    1) Occasional constipation but no medication needed
    2) Frequent constipation requiring use of laxatives
    3) Chronic constipation requiring use of laxatives and enemas
    4) Cannot have a spontaneous bowel movement

Part II: Motor examination scale

1. Facial expression
    0) Normal
    1) Minimal hypomimia, could be normal ("Poker face")
    2) Slight but definitely abnormal diminution of facial expression
    3) Moderate hypomimia; lips parted some of the time
    4) Masked or fixed facies with severe or complete loss of facial expression, lips parted 0.25 inch or more
2. Speech (The patient is asked to repeat several times a standard sentence)
    0) Normal
    1) Mildly slow, slurred, and/or dysphonic. No need to repeat statements
    2) Moderately slow, slurred, and/or dysphonic. Sometimes asked to repeat statements
    3) Several slow, slurred, and/or dysphonic. Frequently asked to repeat statements
    4) Unintelligible
3. Ocular motor dysfunction (Eye movements are examined by asking the subject to follow slow horizontal finger movements of the examiner, to look laterally at the finger at different positions, and to perform saccades between two fingers, each held at an eccentric position of approximately 30°. The examiner assesses the following abnormal signs: (1) broken-up smooth pursuit, (2) gaze-evoked nystagmus at an eye position of more than 45°, (3) gaze-evoked nystagmus at an eye position of less than 45°, (4) saccadic hypermetria. Sign 3 suggests that there are at least two abnormal ocular motor signs, because Sign 2 is also present)
    0) None
    1) One abnormal ocular motor sign
    2) Two abnormal ocular motor signs
    3) Three abnormal ocular motor signs
    4) Four abnormal ocular motor signs

4. Tremor at rest (rate the most affected limb)
    0) Absent
    1) Slight and infrequently present
    2) Mild in amplitude and persistent. Or moderate in amplitude, but only intermittently present
    3) Moderate in amplitude and present most of the time
    4) Marked in amplitude and present most of the time
5. Action tremor (Assess postural tremor of outstretched arms (A) and action tremor on finger pointing (B). Rate maximal tremor severity in Task A and/or B (whichever is worse), and rate most affected limb)
    0) Absent
    1) Slight tremor of small amplitude (A). No interference with finger pointing (B)
    2) Moderate amplitude (A). Some interference with finger pointing (B)
    3) Marked amplitude (A). Marked interference with finger pointing (B)
    4) Severe amplitude (A). Finger pointing impossible (B)
6. Increased tone (Rate the most affected limb. Judged on passive movement of major joints with patient relaxed in sitting position; ignore cogwheeling.)
    0) Absent
    1) Slight or detectable only when activated by mirror or other movements
    2) Mild to moderate
    3) Marked, but full range of motion easily achieved
    4) Severe, range of motion achieved with difficulty
7. Rapid alternating movement of hands (Pro-supination movement of hands, vertically or horizontally, with as large an amplitude as possible, each hand separately, rate the worst affected limb. Note that impaired performance on this task can be caused by bradykinesia and/or cerebellar incoordination. Rate functional performance regardless of underlying motor disorder)
    0) Normal
    1) Mildly impaired
    2) Moderately impaired
    3) Severely impaired
    4) Can barely perform the task
8. Finger taps (Patient taps thumb with index finger in rapid succession with widest amplitude possible, each hand at least 15 to 20 seconds. Rate the worst affected limb. Note that impaired performance on this task can be caused by bradykinesia and/or cerebellar incoordination. Rate functional performance regardless of underlying motor disorder)
    0) Normal
    1) Mildly impaired
    2) Moderately impaired
    3) Severely impaired
    4) Can barely perform the task
9. Leg agility (Patient is sitting and taps heel on ground in rapid succession, picking up entire leg. Amplitude should be approximately 10cm, rate the worst affected leg. Note that impaired performance on this task can be caused by bradykinesia and/or cerebellar incoordination. Rate functional performance, regardless of underlying motor disorder)
    0) Normal
    1) Mildly impaired
    2) Moderately impaired
    3) Severely impaired
    4) Can barely perform the task

10. Heel-knee-shin test (The patient is requested to raise one leg and place the heel on the knee, and then slide the heel down the anterior tibial surface of the resting leg toward the ankle. On reaching the ankle joint, the leg is again raised in the air to a height of approximately 40cm and the action is repeated. At least three movements of each limb must be performed for proper assessment. Rate the worst affected limb.)
    0) Normal
    1) Mildly dysmetric and ataxic
    2) Moderately dysmetric and ataxic
    3) Severely dysmetric and ataxic
    4) Can barely perform the task
11. Arising from chair (Patient attempts to arise from a straight-back wood or metal chair with arms folded across chest)
    0) Normal
    1) Clumsy, or may need more than one attempt
    2) Pushes self up from arms of seat
    3) Tends to fall back and may have to try more than once but can get up without help
    4) Unable to arise without help
12. Posture
    0) Normal
    1) Not quite erect, slightly stooped posture; could be normal for older person
    2) Moderately stooped posture, definitely abnormal; can be slight leaning to one side
    3) Severely stooped posture with kyphosis; can be moderately leaning to one side
    4) Marked flexion with extreme abnormality of posture
13. Body sway (Rate spontaneous body sway and response to sudden, strong posterior displacement produced by pull on shoulder while patient erect with eyes open and feet slightly apart. Patient has to be warned)
    0) Normal
    1) Slight body sway and/or retropulsion with unaided recovery
    2) Moderate body sway and/or deficient postural response; might fall if not caught by examiner
    3) Severe body sway. Very unstable. Tends to lose balance spontaneously
    4) Unable to stand without assistance
14. Gait
    0) Normal
    1) Mildly impaired
    2) Moderately impaired. Walks with difficulty, but requires little or no assistance
    3) Severely impaired. Requires assistance
    4) Cannot walk at all, even with assistance

Part III. Autonomic examination

(Supine blood pressure and heart rate are measured after 2 minutes of rest and again after 2 minutes of standing. Orthostatic symptoms may include lightheadedness, dizziness, blurred vision, weakness, fatigue, cognitive impairment, nausea, palpitations, tremulousness, headache, neck and "coat-hanger" ache.)

Systolic blood pressure   Supine____/Standing (2 minutes)____/Unable to record

Diastolic blood pressure   Supine____/Standing (2 minutes)____/Unable to record

Heart rate   Supine____/Standing (2 minutes)____/Unable to record

Orthostatic symptoms   Yes/No

Part IV. Global disability scale

1. Completely independent. Able to do all chores with minimal difficulty or impairment. Essentially normal. Unaware of any difficulty
2. Not completely independent. Needs help with some chores
3. More dependent. Help with half of chores. Spends a large part of the day with chores
4. Very dependent. Now and then does a few chores alone or begins alone. Much help needed
5. Totally dependent and helpless. Bedridden

RAND-36

1. In general, would you say your health is:
   1) Excellent
   2) Very good
   3) Good
   4) Fair
   5) Poor
2. Compared to one year ago, how would you rate your health in general now?
   1) Much better now than one year ago
   2) Somewhat better now than one year ago
   3) About the same
   4) Somewhat worse now than one year ago
   5) Much worse now than one year ago

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Yes, limited a lot [1]

Yes, limited a little [2]

No, not limited at all [3]

3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports
4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf
5. Lifting or carrying groceries
6. Climbing several flights of stairs
7. Climbing one flight of stairs
8. Bending, kneeling or stooping
9. Walking more than a mile
10. Walking several blocks
11. Walking one block
12. Bathing or dressing yourself

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health? Yes [1]/No [2]

13. Cut down the amount of time you spent on work or other activities
14. Accomplished less than you would like
15. Were limited in the kind of work or other activities
16. Had difficulty performing the work or other activities (for example, it took extra effort)

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? Yes [1]/No [2]

17. Cut down the amount of time you spent on work or other activities
18. Accomplished less than you would like
19. Didn't do work or other activities as carefully as usual

20. During the past 4 weeks, to what extent has your physical health of emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?
    1) Not at all
    2) Slightly
    3) Moderately
    4) Quite a bit
    5) Extremely
21. How much bodily pain have you had during the past 4 weeks?
    1) None
    2) Very mild
    3) Mild
    4) Moderate
    5) Severe
    6) Very severe
22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
    1) Not at all
    2) A little bit
    3) Moderately
    4) Quite a bit
    5) Extremely

These [next] questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

All of the time [1]
Most of the time [2]
A good bit of the time [3]
Some of the time [4]
A little of the time [5]
None of the time [6]

23. Did you feel full of pep?
24. Have you been a very nervous person?
25. Have you felt so down in the dumps that nothing could cheer you up?
26. Have you felt calm and peaceful?
27. Did you have a lot of energy?
28. Have you felt downhearted and blue?
29. Did you feel worn out?
30. Have you been a happy person?
31. Did you feel tired?

32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?
    1) All of the time
    2) Most of the time
    3) Some of the time
    4) A little of the time
    5) None of the time

How TRUE or FALSE is each of the following statements for you?

Definitely True [1]

Mostly True [2]

Don't Know [3]

Mostly False [4]

Definitely False [5]

33. I seem to get sick a little easier than other people
34. I am as healthy as anybody I know
35. I expect my health to get worse
36. My health is excellent

MSA-QoL

[0] No Problem

[1] Slight Problem

[2] Moderate Problem

[3] Marked Problem

[4] Extreme Problem

In the last 4 weeks have you:

1. Had difficulty moving?
2. Had difficulty walking?
3. Had problems with your balance?
4. Had difficulty standing up without support?
5. Had difficulty speaking?
6. Had difficulty swallowing food?
7. Had too much saliva or drooling?
8. Had difficulty with handwriting?
9. Had difficulty feeding yourself?
10. Had difficulty drinking fluids?
11. Had difficulty dressing yourself?
12. Needed help to go to the toilet?
13. Had to stop doing that you liked to do, e.g. your hobbies?
14. Had difficulty doing things around the house, e.g. housework?
15. Experienced bladder problems?
16. Experienced problems with constipation?
17. Experienced dizziness when standing up?
18. Suffered from cold hands or feet?
19. Experienced pain in your neck or shoulders?
20. Experienced pain elsewhere, e.g. in your legs or your back?
21. Had difficulty getting comfortable during the night?
22. Had difficulty breathing during the night?
23. Been feeling tired very quickly (without exerting yourself)?
24. Experienced lack of energy?
25. Experienced slowness of thinking?
26. Had difficulty with your concentration, e.g. reading or watching TV?
27. Felt frustrated?

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28. Felt depressed?
29. Experienced a loss of motivation?
30. Been feeling incapable?
31. Worried about the future?
32. Worried about your family?
33. Felt on your own or isolated?
34. Experienced loss of confidence when interacting with others?
35. Felt that your role in your family or among friends has changed?
36. Experienced difficulty seeing your friends?
37. Had to give up social activities, e.g. going out for a meal, participating in events?
38. Had difficulty talking to friends about your illness?
39. Been embarrassed to talk to people?
40. Felt that life has become boring?

Visual Analog Scale (1-100) to indicate how satisfied you feel overall with your life at the moment

PSP-QoL

[0] No Problem

[1] Slight Problem

[2] Moderate Problem

[3] Marked Problem

[4] Extreme Problem

In the last 4 weeks have you:

1. Had difficulty moving?
2. Had difficulty walking?
3. Had difficulty climbing stairs?
4. Had difficulty turning in bed?
5. Had falls?
6. Had problems moving your eyes?
7. Had problems opening your eyes?
8. Had difficulty eating?
9. Had difficulty swallowing?
10. Had drooling of saliva?
11. Had problems communicating?
12. Had difficulty with your writing?
13. Had difficulty grooming, washing or dressing yourself?
14. Had difficulty using the toilet on your own?
15. Had difficulty holding urine?
16. Had difficulty reading?
17. Had difficulty doing your hobbies e.g. playing chess or an instrument?
18. Had problems doing things around the house, e.g. housework, DIY?
19. Had difficulty enjoying sports, including gardening or walking?
20. Had difficulty going out to see a play or film?
21. Had difficulty going out for a meal?
22. Had difficulty using public transport?
23. Felt not in control of your life?
24. Felt frustrated?

25. Felt a bit down, sad or depressed?
26. Felt pessimistic about the future?
27. Felt anxious?
28. Felt isolated?
29. Had difficulty sleeping not due to problems moving?
30. Found yourself crying?
31. Become more withdrawn?
32. Felt stuck at home?
33. Felt embarrassed in public?
34. Felt you cannot show your feelings?
35. Found your personality is different compared to before your illness?
36. Felt the relationship with your spouse/partner has changed?
37. Felt your relationship with other family members has changed?
38. Seen family less than before you had this condition?
39. Had problems with your memory?
40. Found yourself repeating things a lot?
41. Found your thinking is slower than before the illness?
42. Found your thinking is muddled?
43. Felt confused?
44. Felt not motivated to do things?
45. Found it difficult to make decisions?

Visual Analog Scale (1-100) to indicate how satisfied you feel overall with your life at the moment.

DASS-21

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you **over the past week**. The rating scale is as follows:

[0] Did not apply to me at all

[1] Applied to me to some degree, or some of the time

[2] Applied to me to a considerable degree, or a good part of time

[3] Applied to me very much, or most of the time

1. I found it hard to wind down
2. I was aware of dryness of my mouth
3. I couldn't seem to experience any positive feeling at all
4. I experienced breathing difficulty (e.g. excessively rapid breathing, breathlessness in the absence of physical exertion)
5. I found it difficult to work up the initiative to do things
6. I tended to over-react to situations
7. I experienced trembling (e.g. in the hands)
8. I felt that I was using a lot of nervous energy
9. I was worried about situations in which I might panic and make a fool of myself
10. I felt that I had nothing to look forward to
11. I found myself getting agitated
12. I found it difficult to relax
13. I felt downhearted and blue
14. I was intolerant of anything that kept me from getting on with what I was doing
15. I felt I was close to panic
16. I was unable to become enthusiastic about anything

17. I felt I wasn't worth much as a person
18. I felt that I was rather touchy
19. I was aware of the action of my heart in the absence of physical exertion (e.g. sense of heart rate increase, heart missing a beat)
20. I felt scared without any good reason
21. I felt that life was meaningless

BADLS

Thinking of the last 2 weeks, tick the box that represents AVERAGE ability

1. Preparing food
   a) Selects and prepares food as required
   b) Able to prepare food if ingredients set out
   c) Can prepare food if prompted step by step
   d) Unable to prepare food even with prompting and supervision
   e) Not applicable
2. Eating
   a) Eats appropriately using correct cutlery
   b) Eats appropriately if food made manageable and/or uses spoon
   c) Uses fingers to eat food
   d) Needs to be fed
   e) Not applicable
3. Preparing drink
   a) Selects and prepares drinks as required
   b) Can prepare drinks if ingredients left available
   c) Can prepare drinks if prompted step by step
   d) Unable to make a drink even with prompting and supervision
   e) Not applicable
4. Drinking
   a) Drinks appropriately
   b) Drinks appropriately with aids, beaker/straw, etc.
   c) Does not drink appropriately even with aids but attempts to
   d) Has to have drinks administered (fed)
   e) Not applicable
5. Dressing
   a) Selects appropriate clothing and dresses self
   b) Puts clothes on in wrong order and/or back to front and/or dirty clothing
   c) Unable to dress self but moves limbs to assist
   d) Unable to assist and requires total dressing
   e) Not applicable
6. Hygiene
   a) Washes regularly and independently
   b) Can wash self if given soap, flannel, towel, etc.
   c) Can wash self if prompted and supervised
   d) Unable to wash self and needs full assistance
   e) Not applicable
7. Teeth
   a) Cleans own teeth/dentures regularly and independently
   b) Cleans teeth/dentures if given appropriate items
   c) Requires some assistance, toothpaste on brush, brush to mouth, etc.
   d) Full assistance given
   e) Not applicable

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8. Bath/Shower
   a) Bathes regularly and independently
   b) Needs bath to be drawn/shower turned on but washes independently
   c) Needs supervision and prompting to wash
   d) Totally dependent, needs full assistance
   e) Not applicable
9. Toilet/Commode
   a) Uses toilet appropriately when required
   b) Needs to be taken to the toilet and given assistance
   c) Incontinent of urine or faeces
   d) Incontinent of urine and faeces
   e) Not applicable
10. Transfers
    a) Can get in/out of chair unaided
    b) Can get into a chair but needs help to get out
    c) Needs help getting in and out of a chair
    d) Totally dependent on being put into and lifted from chair
    e) Not applicable
11. Mobility
    a) Walks independently
    b) Walks with assistance i.e. furniture, arm for support
    c) Uses aids to mobilise i.e. frame, sticks, etc.
    d) Unable to walk
    e) Not applicable
12. Orientation – Time
    a) Fully orientated to time/day/date etc.
    b) Unaware of time/day etc. but seems unconcerned
    c) Repeatedly asks the time/day/date
    d) Mixed up night and day
    e) Not applicable
13. Orientation – Space
    a) Fully orientated to surroundings
    b) Orientated to familiar surroundings only
    c) Gets lost in home, needs reminding where bathroom is, etc.
    d) Does not recognise home as own and attempts to leave
    e) Not applicable
14. Communication
    a) Able to hold appropriate conversation
    b) Shows understanding and attempts to respond verbally with gestures
    c) Can make self understood but difficulty understanding others
    d) Does not respond to, or communicate with others
    e) Not applicable
15. Telephone
    a) Uses telephone appropriately, including obtaining correct number
    b) Uses telephone if number given verbally/visually or predialled
    c) Answers telephone but does not make calls
    d) Unable/unwilling to use telephone at all
    e) Not applicable
16. Housework/Gardening
    a) Able to do housework/gardening to previous standard
    b) Able to do housework/gardening but not to previous standard
    c) Limited participation with a lot of supervision
    d) Unwilling/unable to participate in previous activities
    e) Not applicable

17. Shopping
    a) Shops to previous standard
    b) Only able to shop for 1 or 2 items with or without a list
    c) Unable to shop alone, but participates when accompanied
    d) Unable to participate in shopping even when accompanied
    e) Not applicable
18. Finances
    a) Responsible for own finances at previous level
    b) Unable to write a cheque. Can sign name & recognises money values
    c) Can sign name but unable to recognise money values
    d) Unable to sign name or recognise money values
    e) Not applicable
19. Games/Hobbies
    a) Participates in pastimes/activities to previous standard
    b) Participates but needs instructions/supervision
    c) Reluctant to join in, very slow, needs coaxing
    d) No longer able or willing to join in
    e) Not applicable
20. Transport
    a) Able to drive, cycle or use public transport independently
    b) Unable to drive but uses public transport or bike, etc.
    c) Unable to use public transport alone
    d) Unable/unwilling to use transport even when accompanied
    e) Not applicable

POS-S-PD

Please put a tick in the box to show how you feel each of these symptoms has affected you and how you been feeling over the **past week**.

[0] Not at all

[1] Slightly

[2] Moderately

[3] Severely

[4] Overwhelmingly

1. Pain
2. Spasms
3. Fatigue or lack of energy
4. Shortness of breath
5. Nausea (feeling you are going to be sick)
6. Vomiting (being sick)
7. Poor appetite
8. Problems swallowing
9. Feeling sleepy
10. Difficulty in sleeping
11. Constipation
12. Difficulty in bowel control
13. Difficulty controlling urine
14. Pressure sores
15. Problems using your arms

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16. Problems using your legs
17. Difficulty communicating
18. Dribbling of saliva
19. Falls
20. Hallucinations
21. Any other symptoms

Which symptom has affected you the most?

Which symptom has improved the most?

MCSI

Please [choose the options] that apply to you.

[0] No

[1] Yes, sometimes

[2] Yes, on a regular basis

1. My sleep is disturbed (e.g. the person I care for is in and out of bed or wanders around at night)
2. Caregiving is inconvenient (e.g. helping takes so much time or it's a long driver over to help)
3. Caregiving is a physical strain (e.g. lifting in or out of a chair; effort or concentration is required)
4. Caregiving is confining (e.g. helping restricts free time or I cannot go visiting)
5. There have been family adjustments (e.g. helping has disrupted my routine; there is no privacy)
6. There have been changes in personal plans (e.g. I had to turn down a job; I could not go on vacation)
7. There have been other demands on my time (e.g. other family members need me)
8. There have been emotional adjustments (e.g. severe arguments about caregiving)
9. Some behaviour is upsetting (e.g. incontinence; the person cared for has trouble remembering things; or the person I care for accuses people of taking things)
10. It is upsetting to find the person I care for has changed so much from his/her former self (e.g. he/she is a different person than he/she use to be)
11. There have been work adjustments (e.g. I have to take time off for caregiving duties)
12. Caregiving is a financial strain
13. I feel completely overwhelmed (e.g. I worry about the person I care for; I have concerns about how I will manage)

PQoLc

When answering, please think about your role as a carer. Please tick one box to show how much of a problem you are having, if any with the following.

[0] No Problem

[1] Slight Problem

[2] Moderate Problem

[3] Marked Problem

[4] Extreme Problem

In the last 4 weeks:

1. Do you find it a physical strain to look after your relative/partner?
2. Do you find it difficult to look after your own health needs?
3. Has your own health suffered e.g. have you suffered back or joint pain?
4. Do you find caring a stressful job?
5. Do you feel fatigued or tired?
6. Do you feel frustrated or fed up?
7. Do you feel sad?
8. Do you feel alone or lonely?
9. Do you feel angry or betrayed?
10. Do you feel stressed?
11. Do you feel your sleep is disturbed?
12. Do you worry about your relative/partner?
13. Do you find it emotionally difficult to deal with your relative's/partner's physical problems?
14. Has your ability to communicate with your relative/partner suffered?
15. Has your relationship to your relative/partner changed?
16. Do you find it difficult to deal with your relative's/partner's changed personality?
17. Do you find it difficult to deal with a change in roles between you and your relative or partner?
18. Do you feel your privacy has been invaded?
19. Do you feel trapped?
20. Do you feel you do not do much for yourself now?
21. Has it become difficulty to do things spontaneously?
22. Do you find life boring?
23. Do you see friends and family less?
24. Has your family life been affected?
25. Do you find you have to take more responsibility than you should?
26. Do you find there is not enough support for you?

Visual Analog Scale (1-100) to indicate how satisfied you feel overall with your life at the moment.

What is your relationship to the patient?

Spouse/Partner

Daughter/Son

Other

Does your relative or partner live:

With you?

On his or her own?

Or in a nursing home?

How much time do you spend with your relative partner?

____hours per day or ____% of the day

SEIQoL-DW

Administration Procedure

Step 1: Introduction

Read the following to the respondent:

"For each of us, happiness and satisfaction in life depends on those parts or areas of life which are important to us. When these important areas are present or are going well, we are generally happy but when they are absent or going badly we feel worried or unhappy. In other words, these important areas of life determine the quality of our lives. What is considered important varies from person to person. That which is most important to you may not be so important to me or to your husband/wife/children/parents/friends (mention one or two of these groups as appropriate)… and vice versa".

"I am interested in knowing what the most important areas of your life are at the moment. Most of us don't usually spend a lot of time thinking about these things. Indeed, we often only notice that certain things are important when something happens to change them. Sometimes it is easier to identify what is important by thinking about the areas of life that would (or do) cause us most concern when they are missing or going badly".

Step 2: Eliciting the Five Most Important Aspects of Life (Cues)

Ask the respondent:

"What are the five most important areas of your life at present – the things which make your life a relatively happy or sad one at the moment… the things that you feel determine the quality of your life?"

If the respondent does not understand what is required the question may be rephrased in the following ways:

"What parts of your life are most important?/What things are most important?/The most important things in my life are..?"

Elicit areas NOT individuals e.g. marriage, not wife. Do not give examples.

The meaning of each cue for the respondent must be documented at this stage on the Cue Definitions Record Form. Establish what the respondent means by each quality of life area named as being important. For example, if an individual were to name "golf" as a cue, this may relate primarily to leisure activity, but equally it may represent social activity, or physical mobility. Similarly, if "religion" were named as a cue it might relate to the respondent's spiritual life, but might equally relate to being physically able to get to church, or to the social dimension of meeting one's friends at church. This is particularly important for subsequent review of data, and of obvious relevance when respondents must be re-assessed at some future date in order to ensure that the same cues are being considered.

Having defined what the respondent means by the cure, it is important that the cue, as labelled by the individual, be used by the interviewer and not the interviewer's interpretation of what the respondent is saying.

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Should the respondent volunteer cues which resemble "quality of life" in meaning (e.g. satisfaction, life quality), the interviewer should probe for more specific cues. Cues such as "happiness", "attitude to life", "morale" are acceptable.

If it is absolutely necessary to make some suggestions, then read the following list, excluding any cues already mentioned – family, relationships, health, finances, living conditions, work, social life, leisure activities, religion/spiritual life. This list is derived from our findings with a range of populations and represents the cues most commonly elicited, in descending order of frequency. It provides for consistency across the interviewers where such prompting is absolutely necessary.

Step 3: Determining Levels

Say to respondent:

"Now that you have named the five most important areas in your life, I am going to ask you to rate how each of these areas are for you at the moment. First I will show you an example of how the rating is done".

Place the Sample Cue Levels Record Form between you and the respondent so that the respondent can clearly see how you carry out the rating.

"First look at this box (indicate). As you can see, there are spaces at the bottom in which I can write the five important areas of my life (indicate), and there is a scale along the left hand side (indicate). The scale ranges from 'worst possible' on the bottom to 'best possible' on the top, and passes through levels such as 'very bad' – 'bad' – 'neither good nor bad' – 'good' – and 'very good' between the two extremes.

The first important area of my life is X (use a cue not already nominated by the respondent and write it in the first space at the bottom of the rating box) and if this is going very well at the moment, I can show this by drawing a bar like this (draw a bar approx. 80mm high). I am using the scale (indicate) to decide how high my bar should be. The nearer I draw the bar to the bottom line, the poorer my rating of that area of my life. A mark in the middle range would indicate that I am rating life as neither good nor bad, but somewhere in between".

Now proceed with the ratings for the remaining cues:

Second cue – "if X_2 (use a cue not already nominated by the respondent and write it in the second space) is going well as is possible, I would rate it by drawing a bar like this…" (draw a bar 100mm high).

Third cure – "if X_3 (use a cue not already nominated by the respondent and write it in the third space) is going very badly, I would rate it like this…" (draw a bar approx. 15mm high).

Fourth cue – "if X_4 (use a cue not already nominated by the respondent and write it in the fourth space) is just all right, or 'fifty/fifty', I would rate it like this…" (draw a bar approximately 50mm high).

Fifth cue – X_5 (use a cue not already nominated by the respondent and write it in the fifth space) – (draw a random rating).

"This provides a picture of life as I might think of it as the moment".

Step 4: Elicit Rating of Present Life

Place the Cue Levels Record Form between you and the respondent. Write the respondent's five cues in the appropriate spaces under the box. Give the respondent a pen or pencil.

Say to the respondent:

"Now I want you to rate the five most important areas of your life, as you see presented here (indicate). Firstly, draw a bar which represents how you would rate yourself on each of this areas at the moment. As in the example I've just shown you, the nearer you draw the bar to the bottom line, the poorer you are rating that area of your life and the nearer you draw it to the top line, the better your rating of that area of your life".

Have respondent draw bars.

Step 5: Direct Weighting Procedure

Say to respondent:

"I would like you to show me how important the five areas of life you have nominated are in relation to each other by using this disk (indicate SEIQoL-DW). People often value some areas in life as more important than others. This disk allows you to show me how important each area in your life is by giving the more important areas a larger area of the disk, and the less important areas a smaller area of the disk. In my life, for example, X (name cue not already chosen by respondent) is about this important (manipulate disk so that X represents 30% of space available). X_2 however is less important that X, so it has only this much of the pie (manipulate disk so that X_2 represents 20% of the space available). X3 on the other hand is more important than X, so it has this much of the pie (manipulate DWP so that X_3 represents 40% of space available). Finally, X_4 and X_5 are the least important areas of life for me, and I value them about the same (manipulate disk so that X_4 and X_5 represent 5% each of space available). Now thinking about the five areas of life you mentioned (write the name of each cue along the cut edge of one of the 5 coloured disks with a non-permanent marker [disks may also be marked with stick-on 'post-it' labels indicating the cues if preferred]), I would like you to show me how important these areas are in relation to each other by moving the disks around until their relative size represents your view of their importance".

Appendix B: Semi-Structured Interview Guides

Patient interview guide

Prior to your diagnosis, what was life like?

Tell me how you came to be diagnosed?

        - What would have helped?

        - What was difficult?

Has your life changed? (work, relationships, leisure)?

How is your relationship (partner, friends, family)?

        - Has it changed?

        - How?

What parts of (MSA/PSP) do you find most difficult to deal with?

        - Has that changed over time?

        - How

What help would you have wanted?

        - At diagnosis?

        - Now?

Tell me about your contact with doctors, nurses and others

        - What do you think works well?

        - How could things be done better?

What is your understanding of palliative care?

        - How do you think you would feel if you were offered it?

        - What if it was mentioned at diagnosis?

Carer interview guide

How did you meet X?

Tell me about the process of diagnosis

        - What would have helped?

        - What was difficult?

Has your life changed (work, relationships, leisure)?

How is your relationship (partner, friends, family)?

        - Has it changed?

        - How?

Which parts of caring do you find most difficult to deal with?

        - Has that changed over time?

        - How?

What help would you have wanted?

        - At diagnosis?

        - Now?

Tell me about what you think troubles X most?

Tell me about your contact with doctors, nurses and others

        - What do you think works well?

        - How could things be done better?

What is your understanding of palliative care?

            - How do you think you would feel if you were offered it?

            - What if it was mentioned at diagnosis?

How do you feel about the future?

Appendix C. SEIQoL-DW Domain Details

MSA Patients Domain	Proportion nominated (N)	PSP Patients Domain	Proportion nominated (N)
Family	81.8% (18)	**Family**	77.3% (17)
Home/House	36.4% (8)	**Marriage/Partner**	59.1% (13)
Social life	31.8% (7)	**Hobbies**	27.3% (6)
Travel/Holidays	31.8% (7)	**Gardening**	22.7% (5)
Marriage/Partner	27.3% (6)	**Home/House**	22.7% (5)
Independence	22.7% (5)	**Walking**	18.2% (4)
Sports	18.2% (4)	**Pets/Animals**	18.2% (4)
Hobbies	18.2% (4)	**Grandchildren**	18.2% (4)
Pets/Animals	13.6% (3)	**Cars/Driving**	18.2% (4)
Television	13.6% (3)	**Friendship**	18.2% (4)
Health	13.6% (3)	Happiness	13.6% (3)
Food/Cooking	13.6% (3)	Music/Singing	13.6% (3)
Work	13.6% (3)	Travel/Holidays	13.6% (3)
Outdoors/Nature	13.6% (3)	Finance	13.6% (3)
Reading/Books	13.6% (3)	Health	13.6% (3)
Cars/Driving	9.1% (2)	Television	13.6% (3)
Connectedness	9.1% (2)	Independence	13.6% (3)
Organising/Planning	9.1% (2)	Reading/Books	9.1% (2)
Friendship	9.1% (2)	Going out/Trips	9.1% (2)
Grandchildren	9.1% (2)	Sports	9.1% (2)
Music/Singing	9.1% (2)	Social life	9.1% (2)
Walking	9.1% (2)	Routine	4.5% (1)
Happiness	9.1% (2)	"Light nights"	4.5% (1)
Sexual intimacy	4.5% (1)	Organising/Planning	4.5% (1)
Sunshine	4.5% (1)	Food	4.5% (1)
Environment	4.5% (1)	Writing	4.5% (1)
Birds	4.5% (1)	Outdoors/Nature	4.5% (1)
Beach	4.5% (1)	Freedom	4.5% (1)
Staying together	4.5% (1)	Nursing home staff	4.5% (1)
Cleanliness	4.5% (1)	Security	4.5% (1)
Nostalgia/Memories	4.5% (1)	Caring for appearance	4.5% (1)
Keeping informed/News	4.5% (1)	Sense of humour	4.5% (1)
Sympathy	4.5% (1)	Comfort	4.5% (1)
Gardening	4.5% (1)	Quality of life	4.5% (1)
Theatre/Cinema	4.5% (1)	Faith	4.5% (1)
Finance	4.5% (1)	Birds	4.5% (1)
Communicating	4.5% (1)		

Table C.1: All domains nominated and proportion that nominated them for MSA patient-participants (left) and PSP-patient participants (right).) Bold and shaded area represents top five domains for that group (including ties)

MSA Carers Domain	Proportion nominated (N)	PSP Carers Domain	Proportion nominated (N)
Family	80.0% (16)	**Family**	93.8% (15)
Marriage/Partner	40.0% (8)	**Hobbies**	50.0% (8)
Travel/Holidays	30.0% (6)	**Health**	43.8% (7)
Hobbies	25.0% (5)	**Gardening**	31.3% (5)
Health	25.0% (5)	**Marriage/Partner**	25.0% (4)
Friendship	25.0% (5)	Happiness	18.8% (3)
Pets/Animals	20.0% (4)	"Alone Time"	18.8% (3)
Work	20.0% (4)	Walking	18.8% (3)
Connectedness	15.0% (3)	Travel/Holidays	18.8% (3)
"Alone Time"	15.0% (3)	Staying together	12.5% (2)
Cars/Driving	15.0% (3)	Freedom	12.5% (2)
Freedom	15.0% (3)	Finance	12.5% (2)
Walking	15.0% (3)	Pets/Animals	12.5% (2)
Finance	15.0% (3)	Reading/Books	12.5% (2)
Gardening	15.0% (3)	Music/Singing	12.5% (2)
Home/House	15.0% (3)	Connectedness	12.5% (2)
Spouse well-being	10.0% (2)	Outdoors/Nature	12.5% (2)
Staying together	10.0% (2)	Social life	12.5% (2)
Food/Cooking	10.0% (2)	Grandchildren	6.3% (1)
Sports	10.0% (2)	Faith	6.3% (1)
Nostalgia/Memories	10.0% (2)	Food/Cooking	6.3% (1)
Pub	5.0% (1)	Home/House	6.3% (1)
Music/Singing	5.0% (1)	Work	6.3% (1)
Phone	5.0% (1)	Car	6.3% (1)
Outdoors/Nature	5.0% (1)	Birds	6.3% (1)
Beach	5.0% (1)	Independence	6.3% (1)
Birds	5.0% (1)	Sports	6.3% (1)
Faith	5.0% (1)	Spontaneity	6.3% (1)
Happiness	5.0% (1)	Culture	6.3% (1)
Sleep	5.0% (1)		
Reading/Books	5.0% (1)		
Role model	5.0% (1)		
Conversation	5.0% (1)		
Independence	5.0% (1)		

Table C.2: All domains nominated and proportion that nominated them for MSA carer-participants (left) and PSP carer-participants (right). Bold and shaded area represents top five domains for that group (including ties)

Participant	SEIQoL-DW five nominated domains	Interview themes
Matthew (MP1)	Marriage, sexual intimacy, conversation, walking, food (being able to eat and drink)	Change, guilt for needing help from spouse, decline, hope for cure, loss of speech
Emma (CM1)	Not performed	Carer identity, protecting partner from strain on self, concealing difficulty, transition from wife to carer
Sally (CP1)	Not performed	Delayed diagnosis, changing personality of husband, 24-hour caring, rediscovering relationship and self, planning for the end
Bryce (PP3)	Happiness, family, good health, pets, value of friendship	Grief, loss of abilities and abandonment by friend-groups, blame, information as cruel, need for cure
Doris (MP2)	Not performed	Decline, embarrassment, safety of home, withdrawing, making family understand challenges of MSA
Bill (CM2)	Not performed	Frustration, seeing loved one suffer, value of work in maintaining own identity, need for social interaction, little-known disease
Rose MP3	Family, connectedness, environment, cleanliness, keeping informed on progress	Acceptance, hope for progress beyond own death, physical change, speech and perception of others, care for spouse after own death
Jackie (CM3)	Not performed	Importance of carer's identity, being a problem-solver, relationships as true QoL, communication as key for happiness
Julia MP7	Marriage, family support, home, human contact/social, outdoors and nature	Acceptance, faith and family as a source of support, the patient-carer as a team, importance of nature, talking about death
Tiberius (CM7)	Marriage, family, financial security, home life, walking	Duty, strain on own health as a carer, the value of PC to patients and to carers, the resilience of relationships in illness
Sarah (PP4)	Family, marriage, being a grandparent, gardening/outdoors, happiness	Communication difficulty, frustration, being limited by body and speech, loss of freedom
Tom (CP3)	Not performed	Communication when speech is limited, disruption of retirement dreams, loss of spouse motivation, new obligations as a carer
Helen (PP18	Marriage, family (unity), being positive, security, independence	Individuality, resisting dependence, struggle for diagnosis, judgement of others, feeling barred due to lack of access for those with disability
Earl (CP17)	Family, alone time, food, holidays, time with partner	24hr caring, need for more than 'material' support for patients and carers, breaking bad news, truth, PC as vital
Mary (PP24)	Family (love), marriage, home, hobbies (crafting), birds (symbolise escape)	Speech and communication difficulty, feeling judged as 'stupid', as silent, personhood being taken away, need for more time from clinicians
Bob (CP23)	Marriage, family, community, nature, freedom	Need for sensitive delivery of news, constant worry and vigilance, respite, peer support, communication, teaching others about disease
Gary (PP20)	Family (deep bonds), financial security, friendship (peer support), travel, hobbies (sport)	Truth and transparency, the holistic needs PC addresses in incurable illness, becoming closer to family, legacy and future planning
Pat (CP19)	Happiness, security, family, health (to allow caring), alone time	Personhood and carer identity, value of work in preserving identity, conversation and connection, importance of expertise and time for patients
Jack (PP19)	Marriage, family, driving (just me and the road), reading ('go to' new places), social life	Speech difficulty, changing desires and changing self, the strangeness of disease, difficulty in maintaining a conversation

Table C.3: Participant SEIQoL-DW domains and their individual interview themes

Appendix D. Coding Web
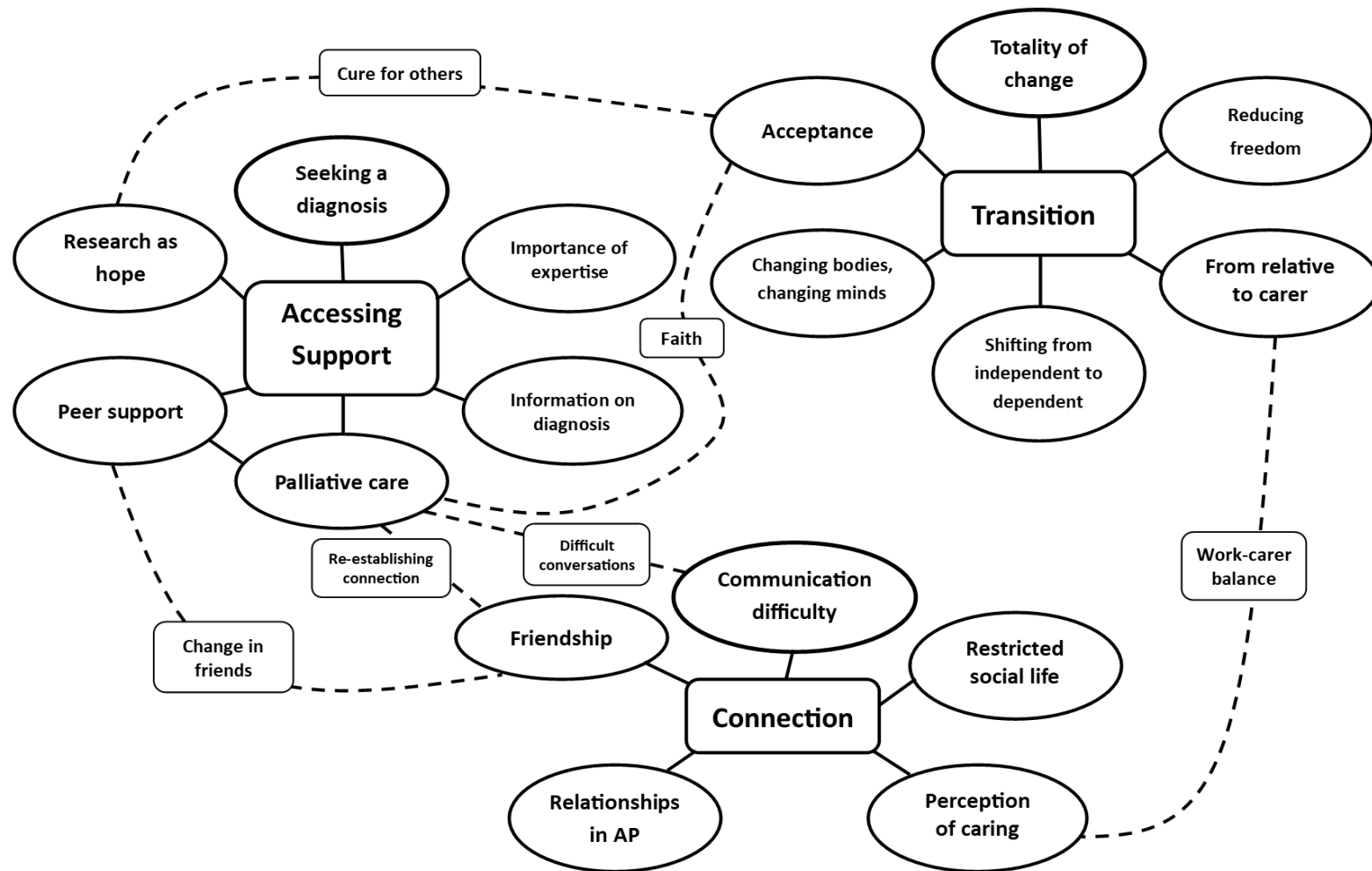
Figure D.1: Overall coding structure for thematic analysis
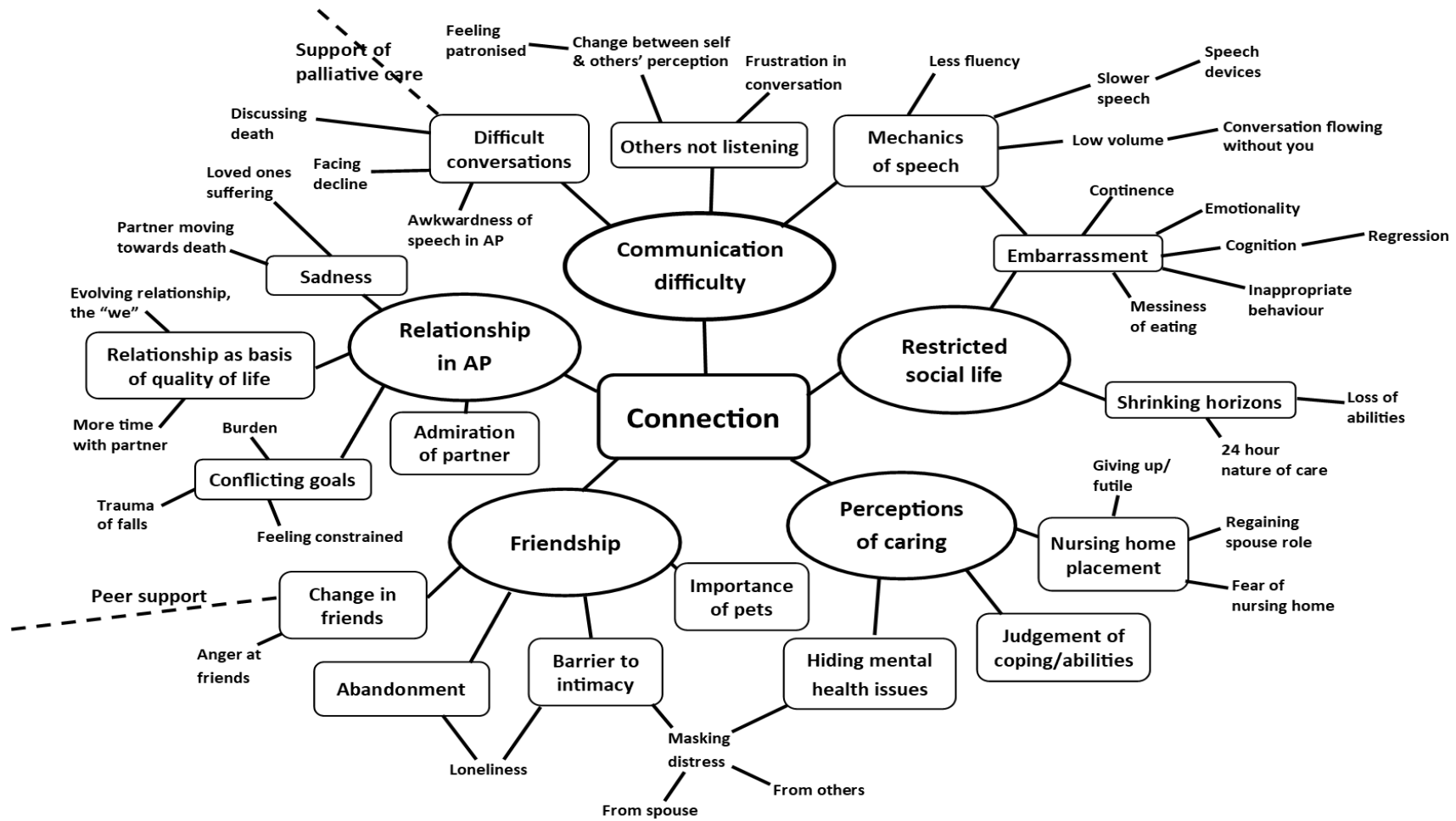
Figure D.2: Detailed Connection coding structure

Palliative care   Research as hope

Faith as support

Adjustment is a process not an event

Anticipation & preparation for future

Life as a journey

Cure for others and not self

The diagnosis as part of me

Acceptance

Biographical disruption   Loss of future together

Changed expectations

Stability is key   Cut off from nature   Fewer new experiences

Changing world

Cannot relate to self

The loss of self   New ill persona

Totality of change

Disability access

Loss of autonomy

Reducing freedom

Shrinking horizons

Transition

Quickness fading

Cognitive Decline   Fear of "losing mind" — Loss of focus — Lost memories

Becoming driving force of couple

Work-carer balance

Change in identity

Emotional labour

From relative to carer

Insidious gain of responsibility

Less romance

Changing bodies, changing minds

Physical Decline   Mobility loss — Becoming "old" — Changing appearance — Symptoms of disease

Relationship Shifts

Shifting from independent to dependent

Delaying the inevitable

Vulnerability

Sense of loss

Jealousy of other's abilities

Symbols of dependency   Need for wheelchair — Walking stick

Figure D.3: Detailed Transition coding structure

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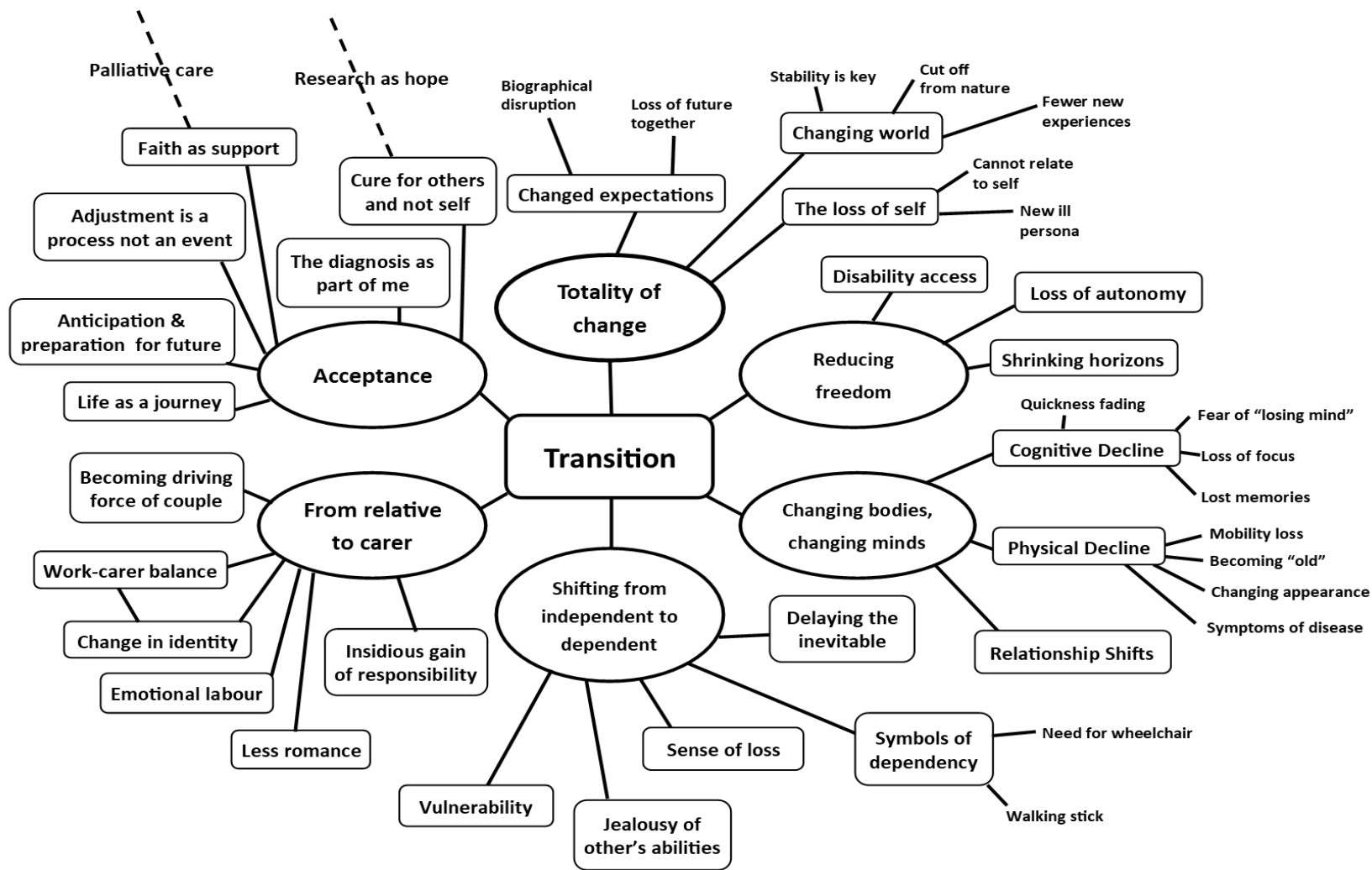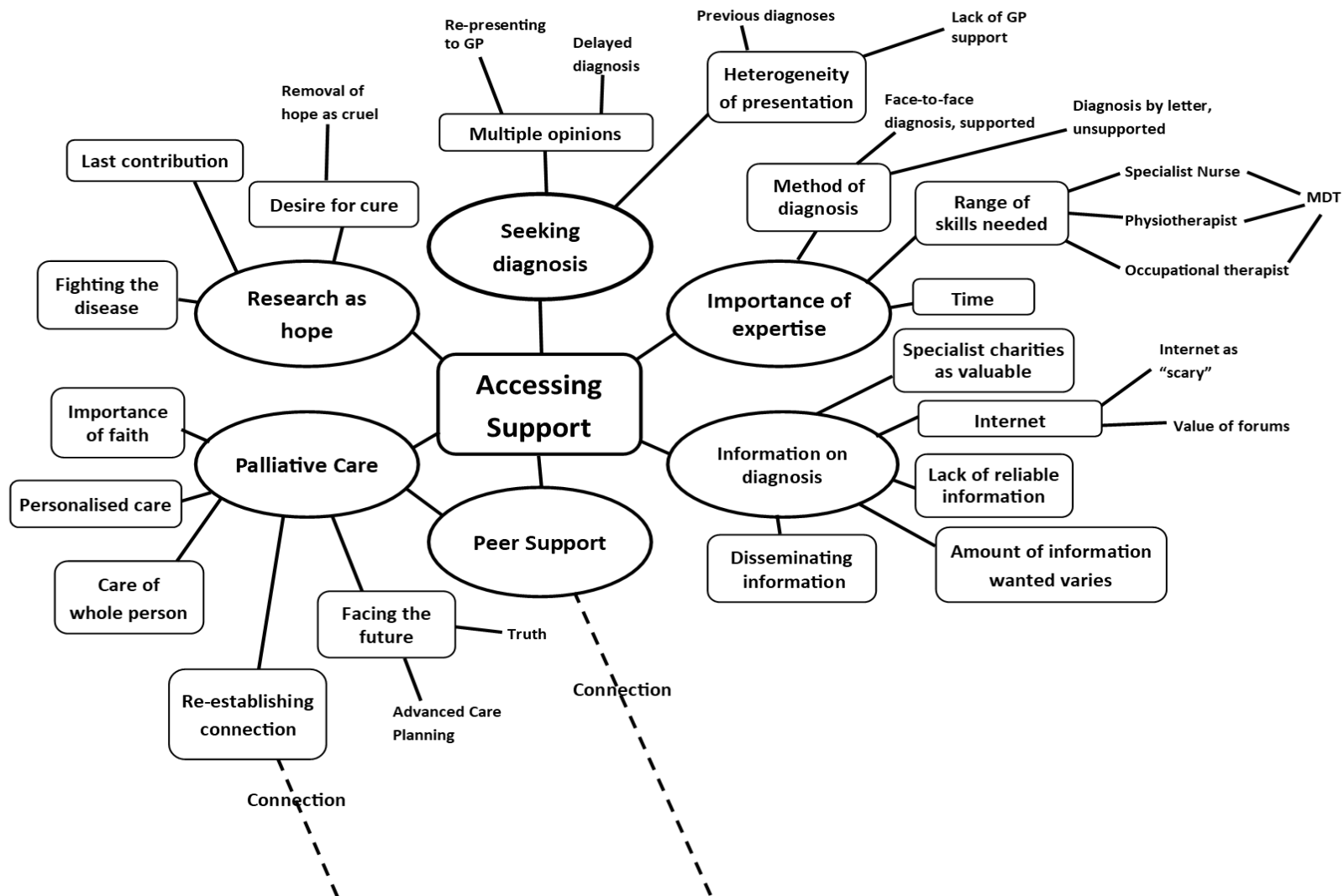*Figure D.4: Detailed Accessing Support coding structure*

Appendix E. COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

Domain 1: Research team and reflexivity

Personal Characteristics

1. **Interviewer/facilitator**
   - Which author/s conducted the interview or focus group?
   - *Louise Wiblin (LW) conducted all interviews in this study. The interviews were one-to-one to exclude peer pressure bias.*
2. **Credentials**
   - What were the researcher's credentials? E.g. PhD, MD
   - *LW is medically qualified (MBBS, MRCP, SCE neuro) and had three years of specialist in AP. LW was formally trained in interview techniques and qualitative analysis by Newcastle University.*
3. **Occupation**
   - What was their occupation at the time of study?
   - *Clinical research fellow in movement disorder neurology.*
4. **Gender**
   - Was the researcher male or female?
   - *Female.*
5. **Experience and training**
   - What experience or training did the researcher have?
   - *Medical degree and 8 years clinical experience (3 years in neurology), training courses in qualitative methods and interview techniques.*

Relationship with participants

6. **Relationship established**
   - Was a relationship established prior to study commencement?
   - *Some patients had encountered LW researcher before in a clinical capacity in a clinic setting or presenting at charity outreach events (MSA Trust and PSP Association).*
7. **Participant knowledge of the interviewer**
   - What did the participants know about the researcher? e.g. personal goals, reasons for doing the research
   - *Participants aware that project was part of an MD project.*
   - *That the aim of the work would be to build evidence to improve clinical services and to guide future research.*
   - *That findings would be disseminated to charities such as PSP Association and presented at conferences and journals.*
8. **Interviewer characteristics**
   - What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic
   - *Participants were aware of the topics of interest, namely QoL and palliative care.*
   - *They were aware of LW's role as a neurology doctor as well as researcher.*
   - *All participants knew that AP had been an interest of LW before the conceptions of the project.*

Domain 2: Study design

Theoretical framework

9. Methodological orientation and theory
- What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis
- *A thematic approach to analysis of semi-structured interviews was used. A thematic approach retains the production of codes from data to describe themes. Unlike grounded theory however, without the constraints of needing to build up all theory from the data without prior theories or focused aims.*

Participant selection

10. Sampling
- How were participants selected? e.g. purposive, convenience, consecutive, snowball
- *Participants were selected by purposively. There was an element of convenience sampling, as those well enough to interview during the interview phase were those who participated.*

11. Method of approach
- How were participants approached? e.g. face-to-face, telephone, mail, email
- *Participants were approached face-to-face in clinic by LW or by their consultant or specialist nurse, then then contacted by telephone (by LW) after permission for this was obtained.*

12. Sample size
- How many participants were in the study?
- *There were 19 participants; 10 patients and 9 carers.*

13. Non-participation
- How many people refused to participate or dropped out? Reasons?
- *14 participants were approached to give an interview which did not take place due to ill-health or conflicting time-tables. No-one approached for interview after consent refused for other reasons.37 of the 47 patients consented to be approached for interview and 40 of the 46 consented.*

Setting

14. Setting of data collection
- Where was the data collected? e.g. home, clinic, workplace
- *The data was collected in clinical settings (CRESTA clinic or St Benedict's) or the patient's home; depending on their preference.*

15. Presence of non-participants
- Was anyone else present besides the participants and researchers?
- *Family members could not be present for the interview so that the interviewee did not feel coerced or anxious talking about their true thoughts and feelings which might potentially worry or offend a relative.*

16. Description of sample
- What are the important characteristics of the sample? e.g. demographic data, date
- *Sex, age, previous occupation, patient or carer role and disease-type were the demographics collected as well as any relationship between participants.*

Data collection

17. Interview guide
- Were questions, prompts, guides provided by the authors? Was it pilot tested?
- *A semi-structured guide was produced and scrutinized. It was pilot-tested on the first two interviewees but no further changes were felt to be desirable as it seemed to elicit a full and natural account.*

18. Repeat interviews
- Were repeat interviews carried out? If yes, how many?
- *Only single interviews were carried out.*

19. Audio/visual recording
- Did the research use audio or visual recording to collect the data?
- *Audio recordings were made. No-one refused audio recordings.*

20. Field notes
- Were field notes made during and/or after the interview or focus group?
- *Field notes were made after the interview (as LW wanted greater immediacy and attention on the subject). Field notes were made immediately after and within 24-48 hours, with the benefit of listening back to the recording.*

21. Duration
- What was the duration of the interviews or focus group?
- *Interviews ranged from 20 minutes to 4 and a half hours (depending on how much they wished to say and speech difficulty). Participants were reminded before and during they should stop when they wished or rest if they needed to.*

22. Data saturation
- Was data saturation discussed?
- *Data saturation was discussed during briefings between LW, KB and ML. Interview transcripts and codings were used to verify whether any new meaningful content was being generated.*

23. Transcripts returned
- Were transcripts returned to participants for comment and/or correction?
- *No; as participants had been assured their spouse would not see their recordings, sending them back when patient is vulnerable and dependent on their carer to read for them would have compromised patient confidentiality and ethical approval for this project.*

Domain 3: Analysis and findings

Data analysis

24. Number of data coders
- How many data coders coded the data?
- One coder and one debriefer.

25. Description of the coding tree
- Did authors provide a description of the coding tree or system?
- *Coding network included.*

26. Derivation of themes
- Were themes identified in advance or derived from the data?
- *Entirely derived from the data.*

27. Software
- What software, if applicable, was used to manage the data?
- *QSR International NVIVO version 11 for Mac was used together with a card and paper web-system.*

28. Participant checking
- Did participants provide feedback on the findings?
- *See point 23.*

Reporting

29. Quotations presented
- Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number
- *Quotations were presented throughout the analysis to illustrate findings and identified according to the pseudonym assigned on the demographic table.*

30. Data and findings consistent
- Was there consistency between the data presented and the findings?
- *LW with the supervision and collaboration of KB, ML and DJB feel that the quotations and pervading themes were well-integrated and that the former illustrated the latter.*

31. Clarity of major themes
- Were major themes clearly presented in the findings?
- *Three overarching themes with five or six subthemes derived from codes were used to describe findings in discrete sections, though feeding into one another, their inter-relationships and impact upon each other commented upon.*

32. Clarity of minor themes
- Is there a description of diverse cases or discussion of minor themes?
- *Subthemes were stated rather than being alluded to and were shown diagrammatically for each of the three main themes.*

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