Anxiety in Parkinson's Disease

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Finally, I dedicate this thesis to Wiki – a bright light in our cohort who will be sorely missed. This is for you!

Thesis Portfolio Abstract

Evidence shows that non-motor symptoms of Parkinson's Disease are associated with reduced quality of life (QOL). Anxiety is one such symptom and it is highly prevalent among people with Parkinson's (PwP). A systematic review, incorporating a meta-analysis, was undertaken to review the relationship between anxiety and QOL in PwP. By pooling data from 17 studies, the meta-analysis established that the relationship was strong ($r = 0.53$). Additionally, a review of regression data from 20 studies highlighted that anxiety predicted significant variance in participant QOL in all but two studies. Given the significance of anxiety highlighted in the review, it is important that the experience of anxiety among PwP is well understood. Research was therefore undertaken using a modified Nominal Group Technique to better characterise the ways in which anxiety is experienced by PwP. The range of anxiety experiences was broad, with some experiences representing generic anxiety experiences that are not unique to the Parkinson's population. However, the majority of experiences related specifically to the symptoms of Parkinson's or had the potential to be aggravated by them. Additional findings are reported relating to the existing approaches taken by our participants to manage their anxiety. Theoretical and clinical implications for all findings are discussed.

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Chapter One: Introduction to Thesis Portfolio

Mental and physical health are closely interrelated and impact one another in a multitude of ways (Naylor et al., 2016; Prince et al., 2007). It is now recognised that people with chronic physical health conditions are two to three times more likely to experience mental health difficulties compared to the general population (Naylor et al., 2012). This comorbidity of physical and mental health conditions is associated with increased use of physical health services (Das-Munshi et al., 2007), poorer health outcomes (Felker et al., 2010) and reduced quality of life (QOL; Moussavi et al., 2007). In recognition of this, mental health services have been given greater responsibility to support the psychological needs of people with chronic physical health conditions (National Collaborating Centre for Mental Health, 2018; NHS Confederation, 2012). Related research stemming from these initiatives has repeatedly demonstrated the value of tailoring psychological interventions to acknowledge the complexity and heterogeneity of the comorbidity (Evers, Kraaimaat, van Riel, & de Jong, 2002; Greer et al., 2012; Johansson et al., 2019; Thieme, Flor, & Turk, 2006).

It is notable that there are no nationwide initiatives that specifically address the mental health needs of people with Parkinson's (PwP). Parkinson's Disease is a neurodegenerative disorder of unknown aetiology that is estimated to affect 0.3% of the entire population, a figure rising to 1.8% of people over the age of 65 (Mayeux, 2003). What is more, prevalence is anticipated to double by 2065 owing to an aging population (Parkinson's UK, 2017). Parkinson's is largely considered a disorder of the extrapyramidal system (a neural network that regulates and modulates motion) and is associated with impaired dopaminergic function (Chen & Swope, 2014). Consequently, there are a range of movement related symptoms that can be experienced in Parkinson's (Jankovic, 2008) (see Appendix A for full breakdown). It is typically defined by the presence of at least two of the following motor symptoms: shaking (tremor), slowness of movement (bradykinesia), muscle stiffness (rigidity) and difficulties with maintaining balance (postural instability) (Jankovic, 2008). There are known to be two distinct motor phenotypes in Parkinson's disease, namely tremor-dominant and postural instability gait difficulty (PIGD) dominant (Jankovic et al., 1990). Unlike tremor-dominance, which is experienced in the limbs, the PIGD-dominance presents in symptoms of the central body. These symptoms are

considered to be more disabling (van Rooden, Visser, Verbaan, Marinus, & van Hilten, 2009) and more greatly associated with non-motor symptoms (Ba, Obaid, Wieler, Camicioli, & Martin, 2016).

There are a range of non-motor symptoms of Parkinson's. These can be categorised as cognitive, neuropsychiatric, gastrointestinal, sleep-related and autonomic (Chaudhuri, Yates and Martinez-Martin, 2005) (see Appendix A for full breakdown). Neurotransmitters of the dopaminergic, glutamatergic, cholinergic, serotonergic, and adrenergic systems are implicated in the presence of these symptoms (Lim, Fox, & Lang, 2009; Willis, Moore, & Armstrong, 2012). Non-motor symptoms are common (Chaudhuri, Healy, & Schapira, 2006; Poewe, 2008) and impact patient QOL (Barone et al., 2009), but are typically less well recognised and addressed by health professionals (Chaudhuri & Schapira, 2009; Shulman, Taback, Rabinstein, & Weiner, 2002). This was well exemplified when researchers generated a ranked list of research priorities as identified by people with direct and personal experience of Parkinson's. One non-motor symptom in particular came to the fore as the study population named 'effective stress and anxiety management' as the second greatest of all research priorities (Deane et al., 2014).

The existing evidence base for the use of psychological therapy for anxiety in PwP is in its infancy. It has been argued that theoretical models and interventions of anxiety in this population should be augmented to address issues specific to Parkinson's (Egan, Laidlaw and Starkstein, 2015). In line with this, Egan et al. (2015) developed an augmented Cognitive Behavioural model of anxiety and depression in Parkinson's. This augmented CBT model sits alongside augmented CBT models in other areas of clinical neuropsychology and older adult psychology (Broomfield et al., 2011; Gracey, Longworth, & Psaila, 2016; Kishita & Laidlaw, 2017). It incorporates well-established CBT predisposing and maintaining factors of anxiety and depression including core beliefs (Beck, 2011), rumination (Ehring, 2008), hypervigilance relating to physical symptoms (Clark, 1986), counterproductive behaviours (Salkovskis, Clark, Hackmann, Wells & Gelder, 1999) and avoidance (Barlow et al., 2017), but adapts them to incorporate Parkinson's specific components. This adaptation includes the incorporation of specific categories of Parkinson's related cognitions, illness beliefs and cohort beliefs about disability.

Currently, anxiety in Parkinson's is poorly defined, researched, diagnosed and treated (Chen & Marsh, 2014; Egan et al., 2015; Pontone et al., 2009; Todorova, Jenner, & Chaudhuri, 2014), arguably providing insufficient evidence with which to evaluate the augmented CBT model of Egan and colleagues (2015). In particular, it has been argued that for anxiety in PWP to be better addressed, research should strive to better understand and characterise the anxiety (Pontone et al., 2019).

There are a number of factors that make it challenging to characterise the anxiety experienced by PwP. Firstly, chronic disease in general can contribute to anxiety through the reduction in sense of self, uncertainty about the future, challenges in relationships and social isolation (DeJean, Giacomini, Vanstone, & Brundisini, 2013). Yet, for those with Parkinson's, the anxiety experience is also known to relate in part to disrupted dopaminergic, noradrenergic, cholinergic and serotonergic pathways associated with the disease (Barone, 2010; Chaudhuri & Schapira, 2009). A further challenge to the characterisation of the anxiety in Parkinson's is that the anxiety can be intermittent, associated with variations in motor symptoms and antiparkinsonian medications (Siemers, Shekhar, Quaid, & Dickson, 1993; Witjas et al., 2002). It is also reported that an interaction occurs between the symptoms of Parkinson's and those of anxiety, whereby one can activate the other (Pontone, 2013). The symptoms of the two disorders can also be difficult to distinguish from one another, owing to the overlap in many of the symptoms (Higginson, Fields, Koller, & Tröster, 2001).

This thesis portfolio seeks to investigate the impact of anxiety on QOL for PwP and to better characterise their experience of anxiety. Chapter Two presents a Systematic Review which examines the relationship between anxiety and QOL for PwP. The Systematic Review has been written for publication in *Movement Disorders*. The review includes 22 studies, 17 of which were pooled in a correlation meta-analysis and 20 reviewed for their regression data. Chapter Three provides a link between the Systematic Review and Empirical Research Project. It also introduces the rationale for incorporating Patient and Public Involvement (PPI) into the project and for our choice of research methodology. Chapter Four presents the Empirical Research Project, which has also been written for publication in *Movement Disorders*. The project investigates the anxiety experienced by PwP to develop a detailed characterisation of the anxiety. Chapter Five describes the methodology

used in the Empirical Research Project in a level of detail not afforded by the *Movement Disorders* article word limit. Chapter Five specifically expands on the standardised clinical psychometric measures used and ethical considerations. Owing to word count restrictions of the empirical paper, additional results are presented in Chapter Six. Chapter Seven, the final chapter of this portfolio, integrates the findings from the Systematic Review and the Empirical Research Project, considering them in the context of wider psychological theory and literature in this area. It also provides a critical appraisal of the work, addresses clinical implications and makes suggestions for future research. Appendices spanning each of the chapters are provided at the end of the portfolio.

Chapter Two: Systematic Review

The Relationship Between Anxiety and Quality of Life Among People with Parkinson's.

Written for publication to *Movement Disorders*

(Author guidelines for manuscript preparation – Appendix B)

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Abstract

Anxiety management remains an area of unmet need for people with Parkinson's Disease (PwP) despite anxiety's high prevalence in this population. This systematic review explored the relationship between anxiety and quality of life (QOL) among PwP. Searches of CINAHL, MEDLINE and PsycINFO yielded 22 eligible studies. Included studies examined the correlation and/or regression of anxiety and QOL using validated measures in adults with idiopathic Parkinson's disease. The studies examined 3834 PwP. Participants were 63% male, mean ages ranged from 58 to 72 years, disease duration ranged from 2.1 to 9.93 years and average Hoehn and Yahr disease severity scores fell between 1.4 and 4. Quality was assessed using a modified National Institutes of Health (NIH) Quality Assessment Tool. Most items were well conducted but 21/22 studies failed to justify their sample size. However, 25% of those reporting regression statistics did meet established criteria for adequate sample size. Meta-analysis of correlation data of 17 studies showed a pooled effect size ($r = 0.53$, (95% CI 0.44-0.61), $Z = 9.96$, $p < 0.0001$) indicating a strong relationship between anxiety and poorer QOL. There was significant heterogeneity in this finding ($I^2 = 86.1\%$), likely due to the diverse range of participants and measures. Exploration of regression analyses identified that 18 out of 20 studies found that anxiety predicted significant variance in participant QOL. This review identified a strong correlation between anxiety and QOL, with regression identifying anxiety as a significant predictor of poor QOL. Therefore, more research is needed in anxiety management in PwP to address its negative impact.

Prospero Registration: CRD42019152793

Keywords: Parkinson's; anxiety, quality of life, correlation, regression

Introduction

Anxiety is a common non-motor symptom (NMS) in Parkinson's Disease,[1] with a prevalence of 31%.[2] This significantly exceeds the prevalence of anxiety disorders in the general population of older adults which is estimated to fall between 3.2% and 14.2%.[3,4] Unfortunately, anxiety in Parkinson's is also an important area of unmet need.[5]

Parkinson's research has established that quality of life (QOL) is significantly worse for those with NMS than for those without.[6] Anxiety is one such NMS that has been regularly implicated as a correlate or predictor of QOL. Studies exploring the relationship between anxiety and QOL in people with Parkinson's (PwP) typically study anxiety as one of multiple NMS investigated in relation to QOL, an approach which supports the development of a holistic understanding. However, no review has yet systematically brought the anxiety-QOL findings of each of these studies together for collective consideration. Given that people with personal and professional experience of Parkinson's have identified effective stress and anxiety management as their second greatest of all future research priorities in Parkinson's,[7] it is important that such a review is conducted.

Current Systematic Review

The aim of this study was to provide a systematic review of the relationship between anxiety and QOL in PwP. This includes a meta-analysis to provide an estimate of weighted pooled correlation coefficient effect sizes and an additional review of regression analyses.

Method

The review was registered with Prospero (CRD42019152793).

Inclusion Criteria

The review was restricted to papers written in English and published in full, in peer reviewed journals. Articles were included if their adult participants had a diagnosis of idiopathic Parkinson's Disease and if they directly explored the relationship between anxiety and QOL using standardised measures validated in this population. No date restrictions were applied.

Search Methods

A scoping search was conducted on 8th February 2019 through the Google Scholar Database using the search: 'Parkinson's Anxiety Quality of Life'. The results of the scoping search informed the MESH terms and keywords used in a systematic computerised search using CINAHL (EBSCO), MEDLINE (Ovid) and PsycINFO (EBSCO) databases. They were searched from inception of the databases to 9th March 2019. The search terms were Parkinson Disease AND Quality of Life AND Stress OR Anxiety. Full search strings used in each database are provided in Appendix C.

Study Selection

Duplicate articles were removed. Study titles and abstracts were examined to exclude obviously irrelevant studies, and then the remaining full texts assessed against the inclusion criteria by DC. Where there was any uncertainty about inclusion KD was consulted and inclusion agreed by discussion.

Data Extraction

Relevant data were extracted from the included articles by DC.

Quality Assessment

The quality of the included articles was assessed against five of the 14 criteria from the National Institutes of Health (NIH) National Heart, Lung and Blood Institutes Quality Assessment Tool for Observational, Cohort and Cross-Sectional Studies[8] (Appendix D). The quality criteria were selected to be relevant to the design and focus of this review. The wording of four items were taken verbatim from the NIH tool. An additional question regarding outcome measures was used that merged items nine and 11 from the NIH tool to create an item that did not make a distinction between independent and dependent variables. For the first item: 'population clearly defined', emphasis was placed on how representative the participants were of the whole Parkinson's population, i.e. the study's exclusion criteria and recruitment methods. We allowed studies to exclude comorbidities, non-idiopathic Parkinson's, Dementia, and significant sensory impairment. The quality of studies was assessed for each study by DC and for 50 percent of the studies by CIC (Appendix E).

Data Analysis

Meta-Analysis

Studies reporting a correlation coefficient (r) of the relationship between anxiety and QOL were meta-analysed using a random effects model. Positive correlation coefficients indicate that symptoms of anxiety are associated with impairment to quality of life. Higher values of r represent a stronger positive association between anxiety symptoms and impaired quality of life. Effect sizes were considered as small, medium and large using .1, .3 and .5 respectively.[9]

Some studies did not report the correlation coefficient (r) but instead reported the standardised beta coefficient (β) from regression analyses. A formula is recommended by which a relatively accurate estimate of r can be derived from β.[10] This formula was adopted in the current meta-analysis to convert β to r values such that they could be included in the meta-analysis.

The meta-analysis was calculated using the MAVIS package version 1.1.3.[11] The correlation coefficients were extracted from each study and pooled to provide a weighted estimate of the size of the correlation between anxiety and QOL. These were reported alongside their 95% confidence interval values. Forest plots as well as Cochran's Q test[12] and the I-squared statistic[13] were used to assess heterogeneity. The Cochran's Q test reports the significance level of the heterogeneity within the studies. The I-squared provides a percentage of variation across studies attributed to heterogeneity as opposed to chance.

Sensitivity Analysis

Sensitivity analysis was undertaken to examine whether results were skewed by studies which required the conversion from beta coefficient (β) to correlation coefficient (r).

Review of Regressions

A number of studies completed regression analyses. As the types of regression differed substantially between studies, a quantitative synthesis of the findings was not feasible. Therefore, the results were extracted and reported together in a table. Each study was considered against established rules of thumb for adequacy of sample size ($N \geq 50+8m$ for testing the multiple correlations or $N \geq 104+m$ for testing individual predictors - where m is the number of independent variables).[14] As multicollinearity can contribute to the accuracy and precision of

regression coefficients,[15] the studies' acknowledgment and management of collinearity was also considered.

Results

This systematic search found 458 articles. An additional 24 articles were selected from the initial scoping search. This total of 482 articles was reduced to 317 following the removal of duplicates, and a further 213 articles were removed as it was evident from their titles and abstracts that they did not meet the inclusion criteria. The remaining 104 articles were obtained in full and 82 removed (Appendix F) as they did not meet the inclusion criteria. A total of 22 articles were included in this review, see Figure 1 for a PRISMA diagram of this process.

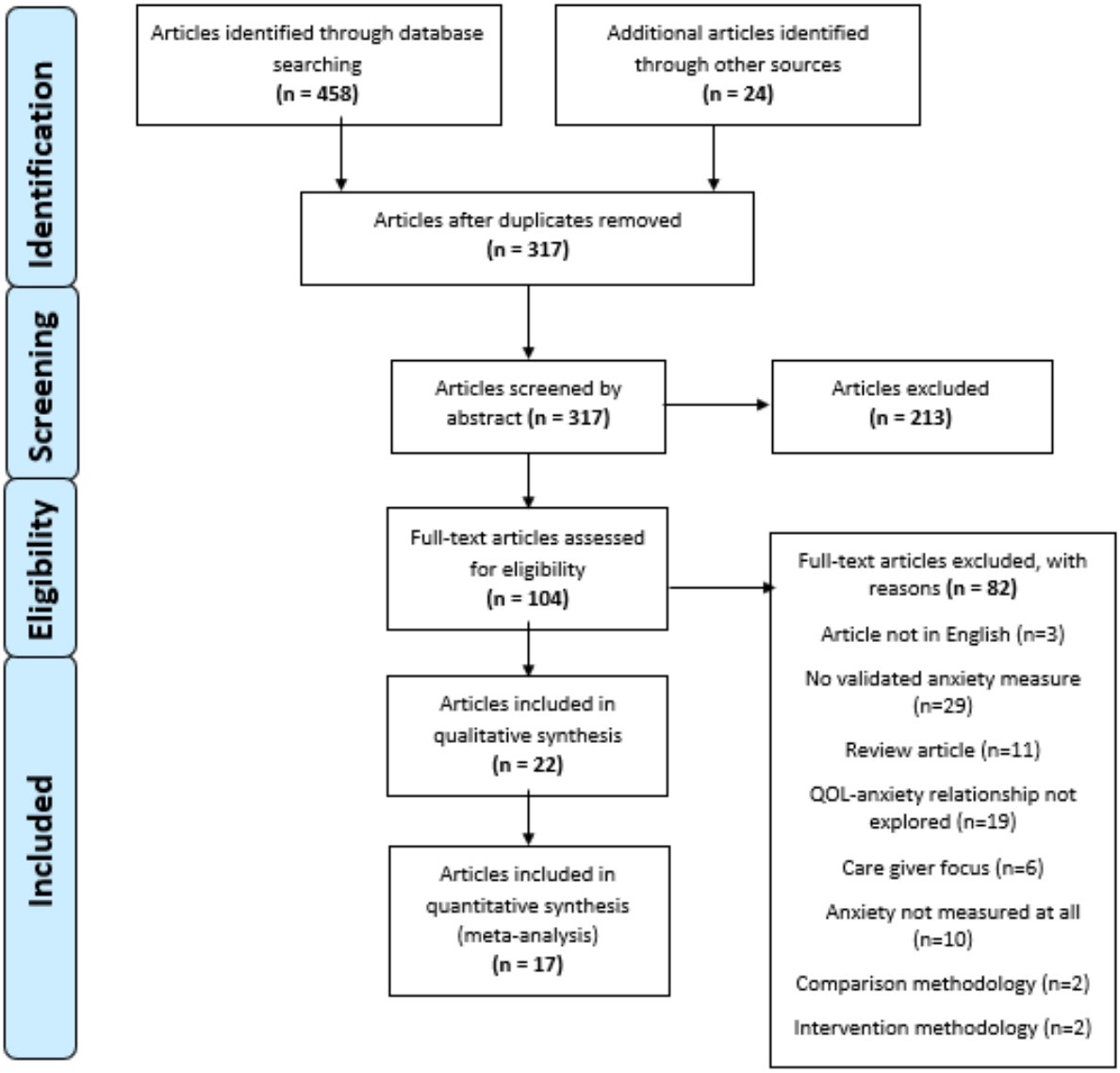

Figure 1. PRISMA diagram outlining the searching and exclusion process.

Characteristics of Studies

Characteristics of the 22 studies included in this review [16-37] can be found in Table 1. Every study employed a cross-sectional design, whereby participants completed standardised questionnaires at a single time point to determine the relationship between a range of non-motor symptoms (including anxiety) and QOL. Eleven reported both correlation and regression analyses. [16,18,21,22,23,26,31,32,33,34,35] Two reported correlational analyses only,[17,36] whilst nine reported regression analysis only. [19,20,24,25,27,28,29,30,37]

Participants

Participant characteristics are summarised in Table 1. Of the 22 studies, 19 reported the setting from which participants were recruited. Sixteen of these had recruited through specialist clinics related to neurology, movement disorders, or Parkinson's. Three of these studies additionally recruited from the community; namely a Parkinson's Disease Society group,[20] care for the elderly centre,[24] and Parkinson's support group.[26] Of the remaining three studies, two recruited from hospitals[22,25] and one from a Parkinson's Research Centre.[29]

Seventeen of the 22 studies reported their population's stage of disease through an average Hoehn and Yahr Score. Of these, 16 averaged a score between one and three on the rating scale, representing the early to mid-stages of the disease. Only one study[20] reported a mode of stage four and no studies reported stage five as an average score. This indicates that the more severe stage of the disease was not well represented by the studies included in this review.

Twenty of the 22 studies reported the gender of participants. Seventeen of these reported a higher number of male than female participants. A total of 63% of participants were male, which is slightly greater than the estimated percentage of males living with Parkinson's in the UK.[38] Twenty studies reported the mean age of participants, which ranged between 58 and 72 years.

Sixteen studies used the Parkinson's Disease Questionnaire 39 (PDQ-39)[39] as a measure of Quality of Life, whilst two studies used the shorter Parkinson's Disease Questionnaire 8 (PDQ-8).[40] The remaining studies used the Short Form Health Survey 36 (SF-36)[41], Short Form Health Survey 12 (SF-12)[42] and EuroQol five-dimensional descriptive system (EQ5D)[43]. All of the QOL measures were self-rated.

To measure anxiety, fourteen studies used the Hospital Anxiety and Depression Scale – Anxiety (HADS-A)[44]. The Beck Anxiety Inventory (BAI)[45] was used by three studies. The remaining studies used the Kouhout Anxiety Scale (KAS)[46], Leeds Anxiety and Depression Scale-Anxiety (LAD-A)[47], State Trait Anxiety Inventory-Trait (STAI-T)[48], Hamilton Anxiety Scale (HAS)[49], and Parkinson's Anxiety Scale (PAS)[50]. Just two of these scales (HAS and PAS) were observer rather than self-rated.

Quality Assessment

Individual quality assessment scoring for each study can be found in Appendix E, and an overview of these found in Figure 2. The decision was taken not to calculate overall quality scores, as not all items will have the same impact.[51]

Twelve studies had met the quality criterion for their recruitment as their participants reasonably represented the whole Parkinson's population. For six studies, it was unclear whether they met the criterion because they either did not provide sufficient detail on recruitment strategy[16,19,22,26,34] or did not adequately describe the clinical criteria used to identify participants.[20] Four studies did not meet the criterion as they excluded participants below the age of 65 [27] or selectively recruited those with a recent diagnosis.[29,33,36]

Five studies[16,20,23,29,37] met the quality criterion for participation rate as it was greater than 50%, whilst two[19,25] did not as their participation rates were less than 50%. For fifteen of the studies it was not possible to ascertain whether they met the criterion as they did not provide sufficient detail on the numbers invited to participate.

Twenty studies met the quality criterion of uniform recruitment and application of inclusion/exclusion criteria. For the remaining two it was unclear whether they met the criterion they did not report where they recruited patients from[19] or clearly specify inclusion/exclusion criteria.[20]

As part of our selection criteria we only included studies that used measures of anxiety and QOL that have been validated in Parkinson's populations. It was therefore unsurprising that all studies used clearly defined, valid and reliable measures. However, one study[19] had missing data from 7 out of 49 participants, so

we found the measures were not implemented across all study participants, meaning it did not meet this criterion.

In contrast, all but one study[21] did not justify their sample size and therefore did not meet this quality criterion. This meant that we were unable to ascertain if they had sufficient numbers of participants to ensure the statistical robustness of their findings.

Table 1

Summary of Studies Included in the Review

Reference	Country	Setting	Sample size	Mean age	Gender (%)	Hoehn and Yahr	Disease duration (years)	Anxiety measure	QOL measure	Relevant analysis
Chrischilles et al., 2002[16]	USA	Neurology clinic	193	68.2	M = 58.5, F = 41.5	2-2.5*	NR	KAS	SF-36	Pearson's correlation; Stepwise regression
Carod-Artal et al., 2007[17]	Brazil	Outpatient neurology department	144	62	M = 53.5, F = 46.5	2**	6.6	HADS-A	PDQ-39	Spearman's correlation
Carod-Artal et al., 2008[18]	Brazil	Outpatient neurology department	115	62.5	M = 56.5, F = 43.5	3**	8.7	HADS-A	PDQ-39	Spearman's correlation; Standard multiple regression
McKinlay et al., 2008[19]	New Zealand	NR	49	66.5	M = 63.3, F = 36.7	2.5*	6	HADS-A	PDQ -39	Hierarchical multiple regression
Rahman et al., 2008[20]	UK	Hospital for neurology and neurosurgery; Parkinson's Disease society	130	67	M = 65, F = 35	4*	9.28	BAI	PDQ-39	Stepwise multiple regression
Quelhas & Costa, 2009[21]	Portugal	Movement disorder consultation at hospital	33	72	M = 44, F = 56	2*	NR	HADS-A	SF-36	Spearman's correlation; Standard multiple regression
Gallagher et al., 2010[22]	UK	Hospital	94	67.5	M = 65, F = 35	2*	7.8	HADS-A	PDQ-39	Spearman's correlation; Stepwise multiple regression
Haviklova et al., 2011[23]	Slovakia	Outpatient neurology; hospitals	93	68	M = 49.5, F = 50.5	2***	6.1	HADS-A	PDQ-39	Pearson's correlation; Hierarchical multiple regression

Table 1

Reference	Country	Setting	Sample size	Mean age	Gender (%)	Hoehn and Yahr	Disease duration (years)	Anxiety measure	QOL measure	Relevant analysis
Hinnell et al., 2012[24]	UK	Neurology; Care for elderly centres	462	67.5	M = 64.9, F = 35.1	2*	5	HADS-A	PDQ-8	Hierarchical multiple regression
Dubayova et al., 2012[25]	Slovakia	Hospital outpatient	142	67.6	M = 73, F = 27	NR	7.6	HADS-A	SF-36	Stepwise multiple regression
Hanna & Cronin Golomb, 2012[26]	USA	Neurology clinic; Local PD support groups	38	62.1	M = 52.6, F = 47.4	2*	8.4	HADS-A	PDQ-39	Spearman's correlation; Hierarchical multiple regression
Skorvanek et al., 2013[27]	Slovakia	NR	106	NR	NR	NR	NR	HADS-A	PDQ-39	Standard multiple regression
Fereshtehnejad et al., 2014[28]	Iran	Movement disorders clinic	140	61.3	NR	NR	NR	HADS-A	PDQ-39	Standard multiple regression
Baig et al., 2015[29]	UK	Parkinson's Disease research centre	796	64.8	M = 66.1, F = 33.9	2*	2.9	LAD-A	EQ-5D	Logistic regression
Fereshtehnejad et al., 2015[30]	Iran	Movement disorder outpatient department	157	61.4	M = 68.8, F = 31.2	2**	6.8	HADS-A	PDQ-39	Standard multiple regression
Jones et al., 2015[31]	USA	Centre for movement disorders; Neurorestoration	107	64	M = 69, F = 31	2*	9	STAI-T	PDQ -39	Correlation (type NR); Stepwise multiple regression
Walton et al., 2015[32]	Australia	Parkinson's' Disease research clinic	203	66.8	M = 68, F = 32	2*	5	HADS-A	PDQ-39	Pearson's correlation; Standard multiple regression

Table 1

Reference	Country	Setting	Sample size	Mean age	Gender (%)	Hoehn and Yahr	Disease duration (years)	Anxiety measure	QOL measure	Relevant analysis
Wu et al., 2015[33]	China	Department of neurology	301	58.4	M = 54.8, F = 45.2	1.9***	2.1	HAS	PDQ-39	Correlation (type not specified); Stepwise multiple regression
Fan et al., 2016[34]	Taiwan	Movement disorder outpatient department	134	65	M = 63.4, F = 36.6	1.4***	7.9	BAI	PDQ-39	Pearson's correlation; Standard multiple regression
D'Iorio et al., 2017[35]	Italy	NR	84	65.4	NR	1.75***	9.3	PAS	PDQ-8	Pearson's correlation; Standard multiple regression
Yoon et al., 2017[36]	South Korea	Movement disorder clinic	89	NR	M = 52.8, F = 47.2	NR	NR	BAI	PDQ-39	Spearman's correlation
Prisnie et al., 2018[37]	Canada	Movement disorder clinic	224	67.5	M = 63.4, F = 36.6	NR	NR	HADS-A	SF-12	Standard multiple regression

Note. NR = not reported; * = mode; ** = median; *** = mean. *KAS* = Kouhout Anxiety Scale; *HADS-A* = Hospital Anxiety and Depression Scale - Anxiety; *LAD-A* = Leeds Anxiety and Depression Scale - Anxiety; *STAI-T* = State Trait Anxiety Inventory-Trait; *BAI* = Beck Anxiety Inventory; *HAS* = Hamilton Anxiety Scale (observer rated); P*AS* = Parkinson's Anxiety Scale (observer rated); *PDQ-39* = Parkinson's Disease Questionnaire 39; *PDQ-8* = Parkinson's Disease Questionnaire 8; *SF-36* = Short Form Health Survey 36; *SF-12* = Short Form Health Survey 12; *EQ-5D* = EuroQol five-dimensional descriptive system.

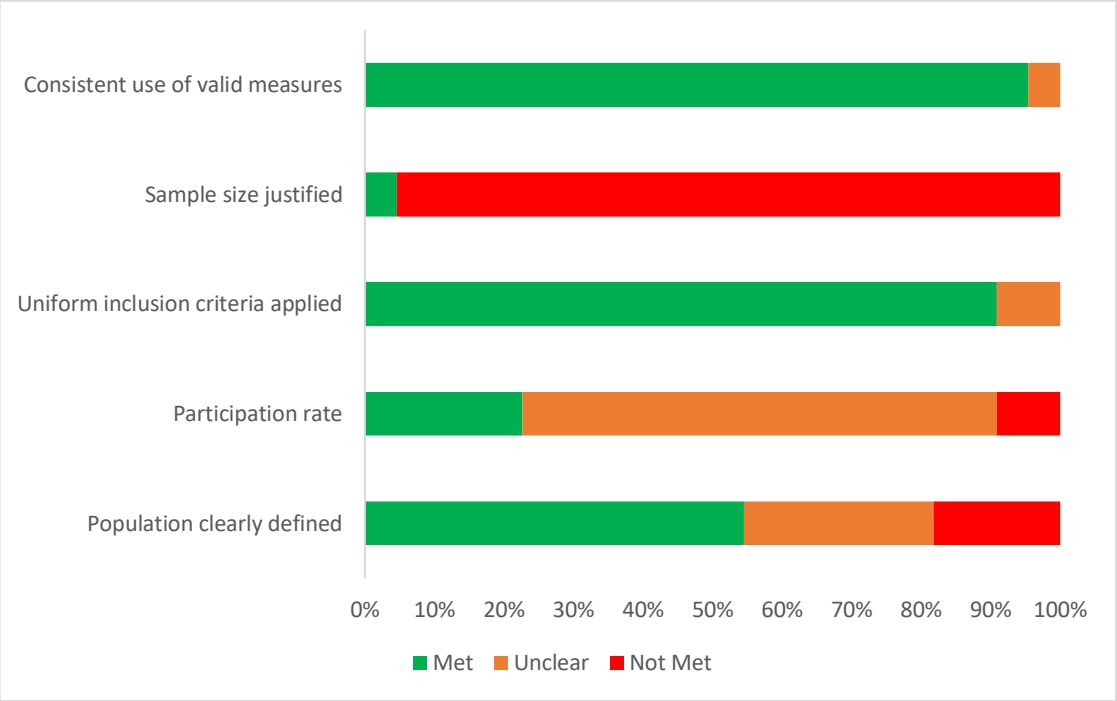

Figure 2. Proportion of studies that met each of the quality assessment criteria.

Meta-Analysis

Five studies could not be included in the meta-analysis as they did not report their data in a manner that could be incorporated into the analysis[16,25,28,29,37]. A total of 17 studies were included in the meta-analysis, based on data from 2332 participants. The correlation coefficients included were taken directly from 12 studies, whilst for the remaining five studies an estimate of the correlation coefficient was calculated from the β value. The distribution of coefficients is presented in Figure 3. Anxiety was strongly correlated with QOL ($r = 0.53$, (95% CI 0.44-0.61), $Z = 9.96$, $p < 0.0001$). The test of homogeneity of variance indicated significant heterogeneity across studies: [$Q(16) = 115.45$, $p < 0.0001$, $I^2 = 86.1\%$]. The potential sources of heterogeneity included the mean disease duration ranging from 2.1 to 9.3 years, mean age ranging from 58.4 to 72 years old, and the gender split ranging from 44% to 69% males. Additionally, five measures of anxiety: HADS, BAI, HAS, PAS, STAI-T and three measures of QOL: PDQ-39, SF-36, PDQ-8 were used.

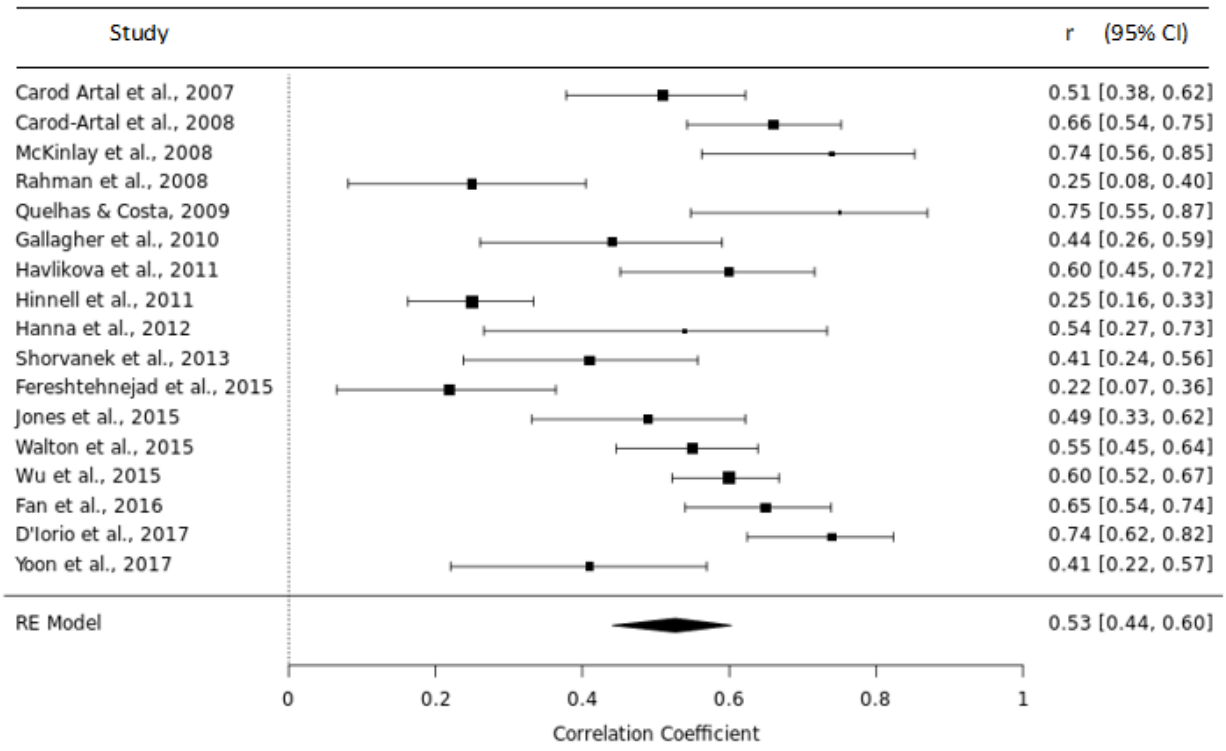

Figure 3. Forest plot estimating pooled correlation effect size.

Sensitivity Analysis

Converting β to an estimate of r allowed the inclusion of studies into the meta-analysis that would otherwise have been omitted. The increased breadth of research designs and increased number of correlation coefficients that this approach affords is associated with respective reduction in the size of non-sampling and sampling errors. Sensitivity analysis was undertaken to examine whether results were skewed by studies which required the conversion from beta coefficient (β) to correlation coefficient (r). When those studies were removed from the correlation, the analysis identified that the range of r's (0.44 to 0.75) was smaller. Anxiety remained strongly correlated with QOL [r = 0.58, (95% CI 0.52-0.63), Z = 15.73, p < 0.0001]. The test of homogeneity again indicated significant heterogeneity across the studies: [$Q(11) = 24.84$, $p < 0.05$, $I^2 = 55.7\%$].

Based on this sensitivity analysis, the decision was taken to include all 17 studies in the meta-analysis. A number of factors influenced this decision. Firstly, when the beta-converted studies were added to the analysis, the correlation effect size remained strong. Secondly, given that there was a slight overall reduction in effect size when the studies were added, we have confidence that their incorporation did not inflate the effect size. With this in mind, the addition of these five studies and

their data for 897 participants was considered a valuable addition to the meta-analysis. However, it is important to acknowledge that the inclusion of these additional data increased the heterogeneity of variance across the studies.

Regression

The twenty studies that completed regression analyses are summarised in Table 2. Four different types of multivariate regression were used: standard, [18,21,27,28,30,34,35,37,] stepwise, [16,20,22,25,31,32,33] hierarchical, [19,23,24,26] and logistic [29]. Eighteen of the studies found that anxiety predicted QOL. Anxiety is consistently among the studies' variables (motor and non-motor) that are most predictive of QOL and contribute significant unique variance in QOL. Five of those eighteen studies[18,24,30,32,37] met the rule of thumb for appropriate sample size[14] and reported consideration of multicollinearity between predictors and which invites increased confidence in the findings from these studies.

Two studies[22,33] did not find anxiety to be a significant predictor of QOL. Consideration should be made regarding the observer rated anxiety measure (Hamilton Anxiety scale) that was used by the latter study. It is possible that the observers did not sufficiently capture the anxiety as well as a self-report study. Further, for regression analyses, it divided the population in half according to disease phenotype, so this may have limited the power to find an effect. The former study[22] also had a concerningly small sample size (n=94) for the nine variables entered into the regression.

Table 2

Summary of Regressions where Reported

Study	Type of multivariate regression	Adequate sample size	Collinearity consideration reported	Anxiety statistics	All factors in model
Chrischilles, 2002[16]	Stepwise	✓	X	Mental QOL (R^2 = 0.303, p < 0.05); Physical QOL (NS – NR)	As no summary score of QOL was included, we report no further details.
Carod-Artal, 2008[18]	Standard	✓	✓	(B = 2.3, p < 0.0001)	Disability (B = 1.1, p < 0.001); **anxiety (β = 2.3, p < 0.0001).**
McKinlay, 2008[19]	Hierarchical	X	X	(β = 0.69, p < 0.001)	1. Motor symptoms (tremor), motor symptoms (non-tremor). 2. **Anxiety (β = 0.69, p < 0.001);** apathy (NS); fatigue (NS); depression (β = 0.51, p < 0.01); sleep (NS); hallucinations (β = 0.39, p < 0.01).
Rahman, 2008[20]	Stepwise	X	X	(β = 0.478, p < 0.0005)	1. Age of PD onset; disease stage; disability; disease duration. 2. Depression (β = 0.409, p < 0.0005; UV = 40.8%). 3. **Anxiety (β = 0.478, p < 0.0005, UV = 17%).**
Quelhas & Costa, 2009[21]	Standard	X	X	(β = -0.36, p < 0.05)	Disease stage (β = -0.28, p<0.05); depression (NS); **anxiety (β = -0.36 p < 0.05)**

Table 2

Summary of Regressions where Reported

Study	Type of multivariate regression	Adequate sample size	Collinearity consideration reported	Anxiety statistics	All factors in model
Gallagher, 2010[22]	Stepwise	X	✓	Anxiety is not a significant predictor of QOL (value not reported)	Autonomic symptoms (β = 0.49, p < 0.001); depression (β= 0.22, p < 0.005), fatigue (β = 0.18, p < 0.01); sleep (β = 0.17, p < 0.05); psychosis (NS), pain (NS); sleep quality (NS); **anxiety (NS)**, motor symptoms stage (NS).
Havlikova, 2011[23]	Hierarchical	X	X	(β = 0.38, p = 0.001)	1.Age; gender and disease duration. 2. Motor symptoms (β = 0.48, p < 0.001). 3. **Anxiety (β = 0.38, p = 0.001, UV = 28%)**. 4. Depression (NS). 5. Sleep quality sleep quality (β = 0.31, p < 0.001). 6. Daytime somnolence (NS).
Hinnell, 2012[24]	Hierarchical	✓	✓	(β = 0.196), p < .001)	1.Age, comorbidities, independence, disease duration, dopaminergic medication. 2. Cognitive ability (NS); motor symptoms (β = 0.148, p < 0.001, UV= 1.3%); **anxiety (β = 0.196, P < .001, UV = 2.2%);** other non-motors symptoms (β = 0.232, p < 0.001, UV = 3.7%; depression (β = 0.308; p < 0.001, UV = 5.6%).

Table 2

Summary of Regressions where Reported

Study	Type of multivariate regression	Adequate sample size	Collinearity consideration reported	Anxiety statistics	All factors in model
Dubayova, 2012[25]	Stepwise	✓	X	Mental QOL (β = -0.24, p < 0.01); Physical QOL (β = -0.19, p < 0.05)	As no summary score of QOL was included, we report no further details.
Hanna, 2012[26]	Hierarchical	X	X	(β = 0.34, *P* < .05)	**1. Anxiety (β = 0.34, *P* < .05, UV = 29%).** 2. Depression (β = 0.37, *P* < .05, UV = 10%). 3. Overall cognition (NS).
Skorvanek, 2013[27]	Standard	X	X	(β = 0.36, P < .001)	**Anxiety (β = 0.36, P < .001)**; depression (β = .21, P < .05); education (β= 0.18, p < 0.05); disease duration (β =.18, p < 0.05); disease progression (motor) (β = 0.24, p < 0.01). NS = age, gender, apathy, dopaminergic medication.
Fereshtehnejad, 2014[28]	Standard	X	X	(*B* = 0.6, *P* = 0.003)	**Anxiety (*B* = 0.6, *P* = 0.003)**; depression (B = 1.5, p < 0.001). NS = early onset, sex, education level, comorbidity, disease stage, nutritional status.

Table 2

Summary of Regressions where Reported

Study	Type of multivariate regression	Adequate sample size	Collinearity consideration reported	Anxiety statistics	All factors in model
Baig, 2015[29]	Logistic	X	X	(OR = 4.89 p < 0.001)	Pain (OR = 13.7, p < 0.001) and depression (OR = 6.76, p < 0.001), **anxiety (OR = 4.89, p < 0.001).** Remaining 20 non-motor symptoms (see paper for full list), had lower OR than anxiety.
Fereshtehnejad, 2015[30]	Standard	✓	✓	(β = 0.17, p < 0.01)	**Anxiety (β = 0.17, p < 0.01)**; depression (β = 0.32, p < 0.001); activities of daily living (β = 0.43, p < 0.001); UPDRS parts I, II, IV (NS); motor symptoms (NS), fatigue (NS), nutritional status (NS). (Added to baseline covariates of sex, level of education, comorbidity score and PD duration).
Jones, 2015[31]	Stepwise	X	✓	(β = 0.472, p < 0.001)	1. Age, global cognitive ability, and disease severity. 2. **Anxiety (β = 0.472, p < 0.001)**; depression (NS - data not provided); apathy (NS - data not provided).
Walton, 2015[32]	Stepwise	✓	✓	(B = 1.041, p < 0.001)	1. Dopaminergic medication use; time since diagnosis. 2. Freezing of Gait (B = 0.955, p < 0.001, UV = 9.4%); depression (0.527, p < 0.001, UV = 4.4%); **anxiety (B = 1.041, p < 0.001, UV = 4.2%)**; sleep I (B = 0.842, p < 0.001, 3.2%); sleep II (B = 0.283, p < 0.05, 1%); stage of disease (NS).

Table 2

Summary of Regressions where Reported

Study	Type of multivariate regression	Adequate sample size	Collinearity consideration reported	Anxiety statistics	All factors in model
Wu, 2015[33]	Stepwise	✓	X	Anxiety is not a significant predictor of QOL (NR)	1. Motor phenotype, age, gender, comorbidity, disease duration, treatment, UPDRS III score, disease stage. 2. Depression (β = 0.646, p < 0.001). **NS = anxiety**, cognitive function, 'other non-motor'.
Fan, 2016[34]	Standard	X	✓	(*B* = 0.95, *p* = 0.001)	**Anxiety (*B* = 0.95, *p* < 0.005)**; depression (B = 0.70, p < 0.001), ADL (B = 1.47, p < 0.001); mental state (B = -1.97, p < 0.019). NS = sex, disease duration, disease stage, dopaminergic medications, disease stage (UPDRS parts I, III, IV, V, VI,) sleep.
D'Iorio, 2017[35]	Standard	X	✓	(*B* = 0.389, p < 0.001)	**Anxiety (*B* = 0.389, p < 0.001)**; apathy (executive) (B = 0.251, p < 0.05); cognitive function (B = 0.283, p < 0.05); depression (NS); global functioning (NS); apathy (cognitive/behaviour initiation) (NS).
Prisnie, 2018[37]	Standard	✓	✓	Mental QOL (B = -1.09, p < 0.0001); Physical QOL (B = 0.25, p > 0.05) (NS)	As no summary score of QOL was included, we report no further details.

Note. NS = non-significant at p < 0.05; *UV* = unique variance in QOL accounted for by variable; *NR* = not reported; *OR* = odds ratio; *ADL* = activities of daily living.

Discussion

This systematic review is the first to review the relationship between anxiety and QOL in PwP. Twenty-two studies were identified, with a combined total of 3834 participants. Overall, the quality of the studies was deemed relatively high. However, just one study[21] provided a power calculation. So individually the studies may have been at risk of identifying spurious relationships, but this may be mitigated by entering their results into a meta-analysis. Seventeen of these studies (n = 2332) informed a meta-analysis that indicated a strong positive relationship (r = .53) between anxiety symptoms and impacted QOL (i.e. higher anxiety is associated with lower QOL). Whilst the relationship is strong, causality cannot be inferred from this relationship. It is possible that relationship is bidirectional, or that the presence of artifacts inflates the result. To extend our review beyond bivariate correlational relationships, 20 studies (n = 3601) that completed regression analyses, were reviewed, with all but two studies finding anxiety to account for significant variance in participant QOL. The unique variance in QOL accounted for by anxiety, and its position among the consistently strong predictors, also brings its role to the fore.

The findings of this review highlight the significance of the role of anxiety in Parkinson's. The indicated impact of anxiety may explain why those with personal experience of Parkinson's have prioritised the need for research on stress and anxiety management techniques in Parkinson's.[7] The findings are also consistent with the body of research outside of Parkinson's, which indicates that anxiety disorders have a significant impact on QOL.[52]

The extent of this relationship between anxiety and QOL appears comparable to that present among other long-term physical health conditions including respiratory[53], cardiac[54], diabetic[55] and stroke[56]. However, patients with these conditions now have greater access to condition-specific anxiety and depression focused psychological interventions provided by primary care mental health services.[57-59] This allocation of resource stemmed from the acknowledgement that untreated mental health in physical health patients can exacerbate symptoms and increase cost expenditure in the health care system.[60] Yet, no such tailored support is provided for those with Parkinson's. By highlighting the significant role of anxiety in QOL for PwP, it is hoped that the disparity in care is highlighted.

Limitations

Whilst overall the quality of included studies was good, not every study clearly reported participation rate or clearly defined their participants. The omission of sample size justification was the biggest threat to study credibility, but this was managed through our retrospective sample size calculations and review of collinearity measures. It is also notable that some of multiple regression studies did not report standardised beta values. This meant that, for these studies, predictive ability of variables could not be compared. This restricted conclusions for these studies.

It is important that the findings are considered in the context of significant heterogeneity across these studies, likely reflecting the range of differences in samples and methodologies.[13] The range in population demographics, such as mean disease duration (2-9 years) and age (58-72 years) are an example of the heterogeneity of the samples. In the meta-analysis the sensitivity analysis highlighted that heterogeneity increased following the addition of studies where standardised beta was converted to r. We also acknowledge that the introduction of these papers may also have impacted the accuracy of the correlation effect size estimate.

A significant methodological consideration is that the studies are not specifically designed to explore the experience of an anxious population. Therefore, the anxiety experience within and between studies is broad and the conclusions about 'disorders' of anxiety are limited. Further, six different measures of anxiety were used, including two that were observer rated. The validity and reliability of observer rated measures may be problematic given the known challenges in identifying and diagnosing anxiety in this population.[5] Additionally, four different measures of QOL were used. The overall diversity of both the QOL and anxiety measures is such that they may have been assessing different facets of anxiety and QOL relationships.

As can be seen from the PRISMA diagram (Figure 1), articles that were not written in English were excluded, and no 'grey literature' or additional literature was sought. We acknowledge that this increases the risk of publication bias in this review. Finally, the screening of full text papers according to eligibility for inclusion in this study was carried out by the principle author and not replicated by a second

author. A full independent replication of the screening process may have provided increased confidence in the review.

Clinical and Research Recommendations

As this study did not assess a clinical intervention, no specific recommendations can be made. However, the review does highlight a significant negative impact of anxiety on QOL. Placed within the wider context of anxiety in this population being highly prevalent yet poorly defined, diagnosed and treated,[5,61,62] this finding emphasises the importance of further research being conducted. This research should target improved conceptualisation, diagnosis and treatment of anxiety among PwP. Based on the quality assessment of the papers included in this review, we would also encourage future research to consistently report participation rate, clearly define participants and justify sample size.

Conclusion

The current review identified a strong correlation between anxiety and QOL. It also identified that anxiety is a significant predictor of poor QOL. In the context of the unmet therapeutic needs of PwP with anxiety, the findings highlight the importance of more research in the area.

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Chapter Three: Bridging Chapter

Overview of Chapter

This chapter provides a bridge between the Systematic Review in Chapter Two and the Empirical Research Project in Chapter Four. It also introduces the rationale for incorporating Patient and Public Involvement (PPI) input into the empirical project, as well as detailing how PPI enhanced the project. Finally, it includes information on the decision-making process that led to our choice of research methodology.

Introduction

The systematic review in Chapter Two established a strong relationship between anxiety and quality of life in participants with Parkinson's. It also identified their anxiety to be a significant predictor of poor QOL. It follows that appropriate conceptualisation, diagnosis and intervention for anxiety among people with Parkinson's (PwP) is important.

As outlined in Chapter One, anxiety in Parkinson's has a complex symptomology. Yet, research attempting to capture the experience of anxiety in Parkinson's has typically used the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV; American Psychiatric Association, 1994), a standard classification of mental disorders used by mental health professionals. Consequently, many PwP do not meet the diagnostic criteria for an anxiety disorder despite having clinically significant anxiety (Chen et al., 2010; Leentjens et al., 2011; Pontone et al., 2009). It is argued that if the anxiety symptoms could be characterised beyond the restrictions of such standardised anxiety criteria and measures, it would significantly improve the diagnosis and subsequent treatment of anxiety in this population (Dissanayaka et al., 2017).

In recognition of this, our research team sought to design an empirical research project that could explore the potentially broad and nuanced content of anxiety experiences among PwP. We felt it important not to be led by, or indeed restrict participant experiences to, predetermined symptom criteria. Instead we wanted to generate a participant led understanding of their symptomology. The aim of the study was not only to capture the experiences of PwP, which it did using Nominal Group Technique (NGT), but also for PwP to support every step of the

research. Accordingly, the project incorporated Patient and Public Involvement (PPI).

Patient and Public Involvement

PPI refers to the process whereby research is conducted 'with' or 'by' patients, carers, service users, services or their representatives, rather than 'to, 'about' or 'for' them (Hayes, Buckland, & Tarpey, 2012). It is increasingly recognised as instrumental in improving the quality, relevance and impact of research projects (Ocloo & Matthews, 2016). Crucially, PPI can shift research attention to areas that most concern health service users (Brett et al., 2014; Crowe, Fenton, Hall, Cowan, & Chalmers, 2015). Further, PPI input to the creation of plain English participant facing documents has been found to widen the acceptability and accessibility of the documents (Brett et al., 2014). Similarly, more effective dissemination has been achieved through PPI involvement in presentation of findings (Baxter et al., 2016). It has also been reported that the exchange of expertise between researchers and PPI members promotes reciprocal learning (Staley & Barron, 2019). The mutual benefit extends further, such that PPI volunteers can feel empowered through skill development and contribution to progress whilst researchers are reported to better understand patient experience and are increasingly motivated to develop the research (Hanson & Hanson, 2017; Wilson et al., 2015). Understandably then, incorporation of PPI into health research is increasingly promoted (Wilson et al., 2015) and it has been more recently argued that PPI should be extended to doctoral research (Tomlinson, Medlinskiene, Cheong, Khan, & Fylan, 2019).

It was decided that PPI volunteers would be recruited to join the empirical project steering group from the beginning of the research process. This was achieved through liaison with the Research Involvement Officer at Parkinson's UK and subsequent completion of application documents. A total of two volunteers were recruited, both had Parkinson's and experience of anxiety that affected their quality of life. We were fortunate to recruit one male and one female. One had tremor dominant Parkinson's and one postural instability gait difficulty dominant (PIGD) Parkinson's. This gave our team a range of expertise of the impact of the symptoms of Parkinson's and anxiety. They were given an hour-long training session on the role of PPI volunteers in research processes and an outline of the research project by

KD. KD has previously developed PPI training materials for Parkinson's UK and promotes its utility in all her research. They were also able to contact Parkinson's UK for further support and training as they wished.

Their role included attendance of quarterly steering group meetings. They reviewed and amended all participant-facing documents. This included the participant information sheets, consent forms, and two online surveys. They supported the qualitative analysis of the first survey responses and subsequent development of summary statements for second survey. Finally, they helped with interpretation of results of the second survey. Due to their substantive input to the design and conduct of the research they will be authors on the peer reviewed journal articles to be published from the empirical findings. They will also aid the team in reporting study findings in lay reports to Parkinson's UK and in press releases.

We experienced the mutual benefit of incorporating PPI into the project. As the principal researcher, conversations with our volunteers about their experiences of both anxiety and of Parkinson's reinforced the importance of beginning with open-ended survey questions to capture the nuances of experiences. It also provided the entire steering group with a renewed sense of the importance of the research and made the process exciting. Their editing of patient facing documents and shift to plain English increased their acceptability and accessibility. Further, their piloting of questionnaires helped to maximise the content of the survey without it becoming a burden for participants. These benefits were highlighted to us by a participant from the first survey who contacted us to "congratulate the designers/programmers of the survey" as it did not have the "problems (ambiguity, etc)" associated with other surveys they had completed. Alongside the principle investigator, one of the PPI volunteers (BC) presented a piece at the UEA Health Sciences Festival 2019 about his experience of the benefits of PPI. He reported feeling a sense of achievement and reward not just from his involvement, but also from the success of the project and positive feedback. He found it interesting to compare survey responses with his own situation. Finally, he enjoyed the social aspect and found it fun to be part of the steering group.

Choice of Method

The steering group met to discuss ideas for a research method that would best enable us to achieve the aims of the study (summarised in Table 1). Firstly, given the limited characterisation of anxiety among people with Parkinson's, it was important that the chosen method gave participants the opportunity to present any and all aspects of their anxiety experiences. Crucially then, the method could not be restricted to the exploration of predetermined factors in the way that a purely quantitative style questionnaire would be (Pothas, De Wet, & De Wet, 2001). Choosing a methodology with a qualitative component was therefore key. It was also important that the method enabled the experiences of a large number of participants across the UK to be gathered to capture the breadth of the anxiety experience in PwP. Qualitative methods such as focus groups and interviews, which are typically time consuming, limited to a small number of participants and restricted by geographical location, were therefore not appropriate. Finally, beyond capturing just the breadth and detail of anxiety experiences, it was important that the method enabled us to generate some form of consensus about which experiences were most common. Interviews and purely qualitative questionnaires would not be able to achieve this. Accordingly, this led us to consider the more novel methodologies, namely the Nominal Group Technique (NGT), Concept Mapping and the Delphi method. These methodologies have distinct qualitative process, but can also be used on a large scale and allow researchers to summarise the data quantitatively.

NGT provides a methodology to generate and subsequently rank ideas from a given population (Boddy, 2012). This approach has been described as 'semi quantitative and qualitative' (Perry & Linsley, 2006) and thus some authors class it as a mixed method design (Potter, Gordon, & Hamer, 2004). Typically, participants are presented with a question(s) and are invited to provide a written response containing their ideas. Each participant response is anonymous, and the contribution of each participant is given equal weighting (Harvey & Holmes, 2012). The responses of the individuals are then pooled into a list and shared among the group, with the goal that the group will prioritise each item on the list according to predetermined criteria (Boddy, 2012). Essentially, this process can be divided into two phases; brainstorming and prioritisation. The benefits of this approach to brainstorming are numerous. Firstly, the generation of ideas as individuals is more productive than as a group (Taylor, Berry, & Block, 1958). A number of reasons for

this have been cited, including: openness of response due to participant preference for anonymity (Boddy, 2012), absence of the wasted time and stunted creativity that can be associated with turn taking in groups (Nijstad & Stroebe, 2006), and space for reflection and creativity being greater without the presence of the noise of a group (Campbell, 1999). In sum, the quality and quantity of ideas generated have been found to be significantly greater using NGT than other forms of brainstorming groups (Mullen, Johnson, & Salas, 1991). With regards to ranking ideas using NGT, this is reported to generate more structured data than other methods, such as focus groups (Claxton, Ritchie, & Zaichkowsky, 1980).

NGT has been previously used in Clinical Health Psychology research studies to identify service user priorities or needs (e.g. Sanderson, Hewlett, Richards, Morris, & Calnan, 2012) or to develop greater understanding of clinical difficulties (Elliot & Shewchuk, 2002). NGT has been modified recently, with face-to-face contact increasingly replaced with large scale online surveys (Deane et al., 2014). The steering group agreed that the modified NGT methodology met all of our desired criteria. Crucially, the qualitative stage means that participant answers are not restricted to the exploration of predetermined factors. It also enables a ranking process and results in data that are easy to quantify. Further, as participant input is only required at two phases, participant input would be relatively quick. Finally, if NGT was modified to use online surveys for the brainstorming and prioritisation phases would enable us to reach over 300 participants nationwide. This would represent a characterisation of anxiety in PwP on an unprecedented scale.

Concept mapping is a multi-staged, mixed methods approach designed to develop understanding of complex issues (Kane & Trochim, 2007). The method involves a process of multiple stages which, through collection of participant generated ideas and application of multivariate analysis, generates an interpretable visual map of ideas (Flaherty, 2014). The map prioritises ideas, clusters them within a circle or box and identifies links between clusters through connecting lines (Davis, 2011; Kinchin, Streatfield, & Hay, 2010). Aspects of this approach that were suitable for this project were that it was not restricted to the exploration of predetermined factors, data can be easy quantified and the information can be ranked. However, other aspects meant it was less suitable. Firstly, participant input is typically required for the majority of the six stages of this process (Burke et al., 2005), meaning that

participant burden well exceeded that of other comparable methods. This burden seemed unjustified, particularly as the linking of clusters was not required to answer our research questions. Concept mapping also stipulates that participants are asked just one question at the brainstorming phase of the process. This was at odds with our desire to ask multiple questions to best capture the detail of their experience. At the ranking phases of thesis process, concept mapping requires that the number of items within each cluster are approximately equal. It was felt that this was not well suited to the anxiety experience where some clusters may justifiably differ in size to others. Finally, the experience of concept mapping with people with Huntington's disease (Smith et al., 2015) highlighted that the clustering and ranking stages of the process require significant cognitive capacity. Given that a significant percentage of our target population may have some level of mild cognitive impairment (Chaudhuri, Yates, & Martinez-Martin, 2005) we were concerned that this might impact on participant ability to complete these stages online.

The Delphi technique is an approach which seeks to generate consensus among a group (Lynn, Layman, & Englebardt, 1998). This is an iterative process, typically spanning a number of rounds of data collection and analyses (Green, Jones, Hughes, & Williams, 1999). Round one typically requires the participants to provides answers to open ended questions, which are then processed presented to each participant through a questionnaire at the next round (Keeney, Hasson, & McKenna, 2001). The results are then prepared and then presented in another questionnaire and feedback round, a process that continues until a consensus is reached (Beretta, 1996). In many ways the Delphi was well suited to our project. It is not restricted to predetermined factors, data can be easy quantified, the information can be ranked, it is suited to large scale data collection and multiple questions can be asked at brainstorming the phase. However, we felt that the Delphi method placed too great an emphasis on consensus. Whilst we considered it useful to have the patient experiences ranked in some way, our principle objective was to identify the breadth of anxiety experiences in Parkinson's, not to emphasise a consensus. The multiple rounds taken to achieve consensus is also criticism of this method as it is synonymous with participant drop out in the later stages (Keeney et al., 2001).

Table 1

Comparison of Methodologies Against Project Requirements

Methodology	Suitable for large scale UK wide representation n > 300	Data easily quantifiable	Can identify new experiences as well as pre-determined	Ranking/ Prioritisation achieved	Participant input < 1 hour	Participants can be asked multiple questions
Modified NGT	✓	✓	✓	✓	✓	✓
Concept mapping	✓	✓	✓	✓	X	X
Delphi	✓	✓	✓	✓	X	✓
Focus group	X	X	✓	✓	✓	✓
Interviews	X	X	✓	X	✓	✓
Qualitative questionnaire	✓	X	✓	X	✓	✓
Quantitative questionnaire	✓	✓	X	✓	✓	✓

Approach to Modified Nominal Group Technique

The steering group established that the modified Nominal Group Technique using online surveys would best enable us to achieve the aims of the study. The qualitative brainstorming phase would be achieved through an online survey of open-ended survey questions created by the steering group. The questions would ask participants to describe their anxiety, its impact and the role of medication. Then a series of prompting questions to encourage participants to expand on their answers. These prompts, informed by the Five Areas CBT assessment model (Williams,

2001), would ask about triggers, thoughts, behaviours, physical sensations, emotions. This model has high acceptability in a variety of healthcare settings (Williams & Whitfield, 2001) and accesses patient problems across a range of domains such as to provide a clear conceptualisation of the difficulties (Wright, Williams, & Garland, 2002). Our lay advisors also felt it would be a good way to capture experiences. Questions regarding the impact of anxiety and the role of Parkinson's medication would also be used. The analysis of all collected submissions would be influenced by the protocol established by the James Lind Alliance (2018b). The submissions would be reviewed, such that duplicate or similar responses are grouped to create representative summary statements. The PPI volunteers would give advice to the research team on the clarity, relevance, and uniqueness of each statement. They would ensure that all aspects raised by the brainstorming respondents are represented in the second rating survey. These statements would then be taken to the quantitative phase of the process: a second online survey, to be rated by participants according to the extent to which they are typical of their experience.

Chapter Four: Empirical Paper

The Anxiety Experiences in Parkinson's Disease: A Mixed Methods Investigation.

Written for publication to *Movement Disorders*

Author guidelines for manuscript preparation – Appendix B

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Abstract

Objective: Anxiety is highly prevalent among people with Parkinson's Disease (PwP), yet it is poorly characterised and treated. This project aimed to better characterise the anxiety by surveying the detailed insights of PwP with anxiety.

Method: With the support of Patient and Public Involvement volunteers, modified Nominal Group Technique methodology facilitated data collection across two online surveys. Participant with a diagnosis of Idiopathic Parkinson's Disease and experience of significant anxiety were recruited through the Parkinson's UK Research Support Network, Parkinson's UK Support Groups and on the Parkinson's UK website.

Results: The first brainstorming survey collected the anxiety experiences of 205 PwP. These experiences were deduplicated and converted to 137 unique representative statements for a second survey. Here 341 participants Likert rated the extent to which each item is typical of their experience. The range of anxiety experiences identified is beyond anything previously captured by research in this population. Whilst some of the anxiety experiences are similar to those of anxiety disorders in the general population, the majority of items were related specifically to, or exacerbated by, Parkinson's symptoms.

Conclusions: This is the largest survey ever conducted characterising anxiety in Parkinson's. It identifies the anxiety's complexity and the significant impact of Parkinson's on the expression of the symptoms. The strong relationship between Parkinsonian and anxiety symptoms likely requires therapists with Parkinson's-specific knowledge and the support of a multidisciplinary clinical team.

Keywords: Parkinson's; Anxiety, Characteristics, Nominal Group Technique, Patient and Public Involvement.

Introduction

Anxiety is a common non-motor symptom of Parkinson's Disease. With 31% of people with Parkinson's (PwP) experiencing clinically significant anxiety,[1] the prevalence is greater than that reported in the general population.[2] Yet, anxiety in Parkinson's remains poorly characterised, underdiagnosed and undertreated.[3,4] Anxiety disorders negatively impact both quality of life (QOL) [5,6] and self-perceived health status.[7] Unsurprisingly, people affected by Parkinson's identified stress and anxiety management as their second highest research priority.[8]

There is a paucity of research into the treatment of anxiety for people with Parkinson's (PwP) whether pharmacological or psychological.[9] For effective psychological therapy the character of Parkinsonian anxiety needs to be well understood.[10] It has been identified that many different anxiety disorders such as social phobia, panic disorder and generalised anxiety disorder are common among PwP.[11,12] However, a significant percentage of anxiety experienced by PwP is classified as 'Anxiety Disorder Not Otherwise Specified (NOS)' [4,13,14] i.e. anxiety that affects QOL, but does not meet criteria for a specific anxiety disorder. It is hypothesised that NOS anxiety among PwP stems from clinical anxiety features that are unique to Parkinson's.[13] Yet, there is a dearth of research investigating this 'Parkinson's specific' anxiety. This is unfortunate given that it has been identified as way to improve understanding, diagnosis and treatment of anxiety in Parkinson's.[9]

The aim of the present study is to enhance the existing characterisation seeking the detailed insights of PwP who have experience of such anxiety.

Research Questions

1. What are the characteristics of anxiety experienced by PwP?
2. To what extent are each of these characteristics typically experienced?

Method

Design

We used a modified Nominal Group Technique (NGT), which is a methodology that incorporates both qualitative and quantitative components. [14,15] The modifications were influenced by the approach of the James Lind Alliance (JLA), a partner organisation of the National Institute for Health Research (NIHR).

They have used the approach to identify, prioritise and publish uncertainties in over 100 areas of health and care that could be better understood and answered by future research. The JLA Priority Setting Partnership (PSP) guidebook[16] provides a step by step framework for how to conduct and analyse modified online NGT in a PSP. This provided a useful blueprint for our methodology, albeit with some adaptations in instances where their emphasis on priority setting was not relevant to our research questions. Our emphasis on the qualitative steps facilitated the collection of rich, representative descriptions of anxiety on a large scale, whist the more condensed qualitative step established a sense of the extent to which each characteristic was experienced. Patient and Public Involvement (PPI) volunteers were involved in all steps of this research process.

The first step involved setting up a steering group. Two fully trained PPI volunteers (BC and JM), with experience of significant anxiety since their Parkinson's diagnosis, were recruited to the steering group from the Research Support Network at Parkinson's UK. Their roles included attendance of quarterly steering group meetings, reviewing all participant-facing content, and supporting with the design and analysis of both surveys. Their expertise provided an important additional perspective to the steering group which also included perspectives of a Clinical Psychologist, a Cognitive Behavioural Therapist, and a Health researcher with over 20 years expertise in Parkinson's and personal experience of a functional movement disorder.

In line with the next step of the JLA approach, the steering group then developed an online survey to gather participant experiences. In this case, we used open-ended questions about the participants' experience of anxiety since their Parkinson's diagnosis. This facilitated the qualitative 'brainstorming' element of this NGT methodology. The survey asked participants to describe their anxiety, its impact, and the role of Parkinsonian medications. In line with the Five Areas CBT assessment model,[17] subsequent questions asked about triggers, thoughts, behaviours, physical sensations and emotions. The steering group, including PPI volunteers, agreed that these questions were an appropriate way to prompt participants to consider the anxiety experiences across a range of domains.

Once participant responses had been submitted, a series of analysis steps from the JLA guidebook were followed (see analysis), with steering group input and

verification at each step. The analysis enabled the generation of 'indicative' statements that represented the major themes identified in the participant responses. The aim was that the statements would capture what the participants had meant, whilst being concise and easily understood.

Once the indicative statements had been generated, they were incorporated within a second online survey. Participants were invited to rate the representative statements on five-point Likert scales according to the extent to which they typically experience each one ('Never or almost never', 'Rarely' 'Sometimes' 'Often' 'Always or almost always'). Full listing of all advertisements, information sheets, consent forms and questions used in both surveys are available in (Appendices G-L). The JLA focus heavily on prioritisation, in particular establishing a final 'top 10' items at a priority setting workshop. This step was not required or appropriate for answering our research question and was therefore omitted.

Participants

Parkinson's UK advertised the surveys on its website and to its online Research Support Network, which has over 5000 members interested in Parkinson's research. The advertisement was also distributed to the Parkinson's UK support groups nationwide. Participants were required to be over the age of 18, able to read and write in English, have a diagnosis of Parkinson's and have experienced anxiety that impacted on QOL since diagnosis. Those with dementia were excluded.

Measures

Both surveys also gathered information on participant demographics and clinical status; physical and mental health, level of independence and access to psychological or psychiatric treatments. Two standardised psychometric measures were used; the Parkinson's Disease Quality of Life Questionnaire-8 (PDQ-8)[17] and the Parkinson's Anxiety Scale (PAS)[28]. These measures were validated in Parkinson's populations. [19,,20,21]

Procedure

For each of the surveys, participants accessed a project information sheet, consent form and the online survey through hyperlinks in the advertisement. Paper

copies of these documents were available on request. The first survey was open February-March 2019, and the second survey June-September 2019.

Ethical Considerations

Ethical approval was granted by the Faculty of Medicine and Health Sciences Research Ethics Committee at the University of East Anglia on 10/01/2019, Reference Number: 201819-046 (Appendix M). The British Psychological Society (2010)[22] guidelines for the conduct of psychological research were adhered to.

Data Analysis

The approach taken to NGT analysis was influenced by guidance from the JLA Guidebook.[16] Each step of the analysis process was first completed by the principle author (DC) then reviewed by the steering group before final decisions were made.

Survey One

The participants' open-ended responses regarding their anxiety experiences were downloaded. Combined, the participant responses totalled 16,503 words. The principal author then familiarised themself with the participant responses. Any parts of participant responses that clearly did not address the questions were separated, reviewed by the rest of the steering group and ultimately removed. The remaining data were then systematically analysed by the principal author through coding. An inductive approach to coding was adopted, whereby codes were driven by what was in the data. This approach can be likened to phase two of the thematic analysis process as described by Braun and Clark.[23] The codes enabled duplicate or similar responses to be grouped together. This process occurred iteratively as the data were analysed and resulted in 75 distinct codes being identified (detailed in Appendix N). Unsurprisingly given the nature of the survey's prompting questions, the codes sat within broader themes of 'triggers', 'thoughts', 'behaviours', 'physical', 'emotion' and 'impact'. The coding of the data was reviewed by the steering group. An example of a participant response is given below and the coding of this response is outlined in Table 1.

"Because it affects my breathing, I tend to avoid going out to meet people and avoid social situations. I start thinking if people are looking at me then it makes my symptoms worse ie dyskinesia, when it kicks in increases. The anxiety will last until I

take myself out of the situation. It has a big effect; I have to try to not think about it. but I have been known to fake feeling ill & not go out. I hate the thought that people may look at me".

Table 1

Coding Example

Participant Response	Code Label	Code Name
It affects my breathing	P1	Fight or flight
I tend to avoid going out to meet people & avoid social situations	B7	Avoid social situations
I start thinking if people are looking at me	TH6	Social evaluation
It makes my symptoms worse i.e. dyskinesia, when it kicks in increases	I6	Increases Parkinson's symptoms
The anxiety will last until I take myself out of the situation	B5	Escape
I have to try to not think about it	B14	Attempt to distract from anxiety
I have been known to fake feeling ill and not go out	B7	Avoid social situations
I hate the thought that people may look at me	TH6	Social evaluation

The steering group met again with the aim of converting the 75 codes into 'indicative statements' that could be presented to participants of the second survey. It was important that each statement represented the items captured by the code and was easy for participants to read. In many cases this meant that more than one statement was used per code. For example, code TH13 (toileting) was summarised with two indicative statements, 'I worry about the embarrassment of having a toileting accident (being incontinent)' and 'I am embarrassed by the frequency and urgency with which I need to urinate'. In total 137 'indicative' statements were generated and agreed upon. This process included a PPI volunteering piloting the statements in survey form. The analysis process is summarised in Figure 1.

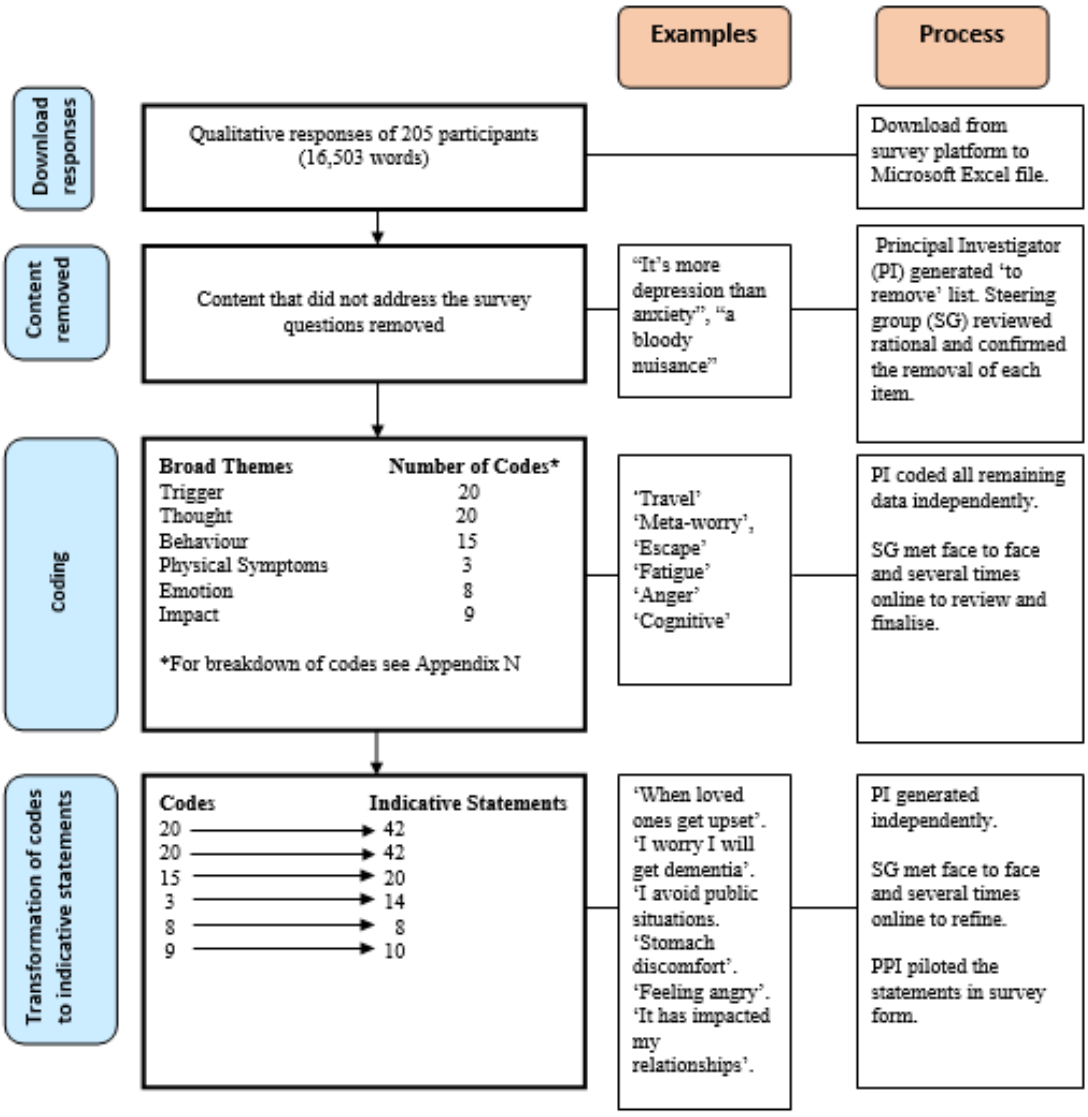

Figure 1. Flow chart providing overview of phase one of analysis.

Survey Two

Compared with the labour-intensive qualitative analysis of the survey one responses, the quantitative analysis of survey two was far simpler. Descriptive statistics were used, with participant Likert responses totalled for each item, then median values calculated for each. The median scores were then ranked in order from highest to lowest to establish an overall ranking of the items. The demographics of participants from both surveys were also analysed and reported using descriptive statistics.

Results

Two-hundred and five participants completed the first brainstorming survey, and 341 completed the second rating survey. The demographics and clinical characteristics of participants in both surveys is presented in Table 1. The respondents were reasonably representative of the membership of Parkinson's UK i.e. slightly younger, less advanced in their Parkinson's, and with less ethnic diversity than the whole UK population of people with Parkinson's.[24] We allowed PwP who had historic experience of anxiety to participate in this survey, but in each survey, at least 70% of participants exceeded the PAS threshold for anxiety disorder.

Table 2

Participant Characteristics

Variable	Survey one percentage (%) of participant sample (n = 205)	Survey two percentage (%) of participant sample (n = 341)
Gender		
Female	49.8	43.4
Male	50.2	56.3
Age		
18-30	0	0
31-50	9.3	3.3
51-64	34.6	34.8
65-80	52.2	58.7
81+	3.9	2.1
Ethnicity		
White	94.1	99.1
Black and Minority Ethnic	4.4	0.9
Prefer not to say	3.0	0
Years since diagnosis (mean and (SD)	5.1 (4.6)	5.7 (4.6)
Parkinson's Anxiety Scale (% above threshold)	74.1	72.1
PDQ-8 score* (mean and (SD)	11.0 (5.9)	10.8 (5.5)
Fallen (past 12 months)	37.6	41.6
Freezing of gait (past month)	30.7	30.8
Problematic Tremor	47.8	43.7
Difficulty with repetitious movements (past week)	74.1	74.8
Anxiety diagnosis from medical professional	40.5	33.7
Received psychological support for anxiety	26.3	28.4
Prescribed medication to help with anxiety	34.1	28.7
Has additional mental health diagnosis	12.2	11.1
First time anxiety impacted QOL	(not asked)	
Pre PD		45.7
Post PD		54.3

Note. * = *from maximum score of 32.*

A total of 137 descriptive statements were generated following the analysis of the first survey and then rated by participants of the second survey. At the rating

stage, the rate of missing data was between 0.3% and 2.1%. One hundred and six of the items are presented in Tables 2-4. These are the items with a median score of at least 3 points (where 3 was described as "sometimes" on the Likert scales). For the items relating to 'impact', those with a median of at least 4 ('agree') are included. All items that have lower median values can be found in Appendix O.

The items listed in this paper have been grouped as Triggers (32), Thoughts (32), Behaviours (15), Physical sensations (8), Emotions (8), Impact (11). Across the groups, 12% of the items were directly related to Parkinson's (P), e.g. 'When I see others at the later stage of Parkinson's'. In contrast, 27.5% of the items seemed to represent anxiety experiences common outside of the Parkinson's population (N), e.g. 'I try to distract myself from the anxiety'. The remaining 60.5% of items, whilst common outside of Parkinson's population, are likely exacerbated by the Parkinson's experience (EP). It is also noteworthy that, among the items with the highest median score 'often', the percentage of items directly related to Parkinson's increases to 40%. In the 'often' category, this equals the percentage of items that are likely exacerbated by Parkinson's (40%) and is double the percentage of those common outside of Parkinson's (20%).

Table 3

Rated List of Anxiety Triggers

Triggers	N	Median Likert Score	Theme
When I feel time pressured (for example making it to an appointment in time or at a supermarket till where I have to coordinate tasks quickly)	339	4	EP
When I am not able to perform a task or role that I previously would have been able to	339	4	EP
When I see others at the later stage of Parkinson's	336	4	P
My anxiety was triggered or made worse in the period just after my diagnosis of Parkinson's	339	3*	P

Table 3

Rated list of Anxiety Triggers

Triggers	N	Median	Theme
When I am not occupied/busy	331	3	P
At night	332	3	N
When I am tired	335	3	EP
When I have tremor	338	3	P
When I have difficulty with movement or coordination	339	3	P
By being outside my home	334	3	EP
When in confined or enclosed spaces	339	3	N
When in public settings	336	3	EP
When I am in crowded and/or noisy places	339	3	EP
If people are too close and I feel my movement is restricted	339	3	EP
When I am travelling	337	3	EP
When I am in social situations (where one may be observed or evaluated by others, such as speaking in public or meeting new people)	338	3	EP
When I am ignored in social situations	338	3	EP
When I eat in public	337	3	EP
When I am unsure if I can reach a toilet in time	336	3	EP
When others do not understand what I am experiencing	334	3	EP
When loved ones get upset	339	3	EP
When I have disagreements with others or am criticised by others	336	3	EP
When I am stressed by life or work (e.g. when a number of tasks fall together)	334	3	EP
When I do not meet demands or expectations	336	3	EP
When trying to organise myself and make decisions	337	3	EP
When I am having a medical consultation/appointment	339	3	EP
When reading about Parkinson's	333	3	P
I am not aware what the trigger is or why the anxiety occurs	332	3	N

Table 3

Rated list of Anxiety Triggers

Triggers	N	Median	Theme
When I have difficulties with sexual performance	178	3	EP
When I am in pain	267	3	EP
When I am alone	332	3	N
When the ground looks slippery	337	3	EP

Note. P = directly related to Parkinson's; N = normal for anxiety outside of Parkinson's EP = common anxiety experience but likely exacerbated by Parkinson's. Likert Scale: 1 = Not at all, 2 = Rarely, 3 = Sometimes, 4= Often, 5 = Always. *= ranked against different labels, 1 = strongly disagree, 2 = Disagree, 3 = Neither Agree or Disagree, 4= Agree, 5 = Strongly Agree.

Table 4

Rated List of Anxious Thoughts

Thoughts	N	Median	Theme
I worry about the rate at which my Parkinson's symptoms progress and how I will cope at their worst	340	4	P
I worry about the impact of my Parkinson's on my family and how they will cope	340	4	P
I compare my current abilities to my past abilities	337	4	EP
I worry about small things that never used to bother me as much	337	4*	N
I view my anxiety as a proportionate and rational response to the difficulties I experience with Parkinson's	337	4*	P
There is no fixed focus to my worry; I worry about anything, including irrational things, things I have no control over	338	4*	N
I compare my health status to those who are in better health	337	3	EP
I worry about falling and/or the consequences of falling	338	3	P
I worry about my speech (e.g. not speaking clearly or being understood)	338	3	P
I worry I will get dementia	337	3	EP
I worry that I am not able to contribute and will let others down or become a burden	337	3	EP
I worry about my death	335	3	EP

Table 4

Rated List of Anxious Thoughts

Thoughts	N	Median	Theme
I worry I will Lose control and not be able to do my everyday tasks	340	3	EP
I worry I will lose my identity	333	3	EP
I worry about my future ability to be an effective parent or carer for those who need my support	335	3	EP
I view my anxiety as largely irrational and out of proportion	334	3*	N
I feel out of control with my worry and find it hard to stop	334	3*	N
I blow things out of proportion and make mountains out of molehills*	338	3	N
I worry about having to go into a care home and the quality of the care I would receive there	339	3	EP
I worry about upsetting those close to me or making things difficult for them	339	3	EP
I worry how others will perceive my Parkinson's symptoms and that they will judge me negatively	336	3	P
I worry about eating in public and that others will judge me negatively	338	3	EP
I am embarrassed by the frequency and urgency with which I need to urinate	334	3	EP
I worry about the embarrassment of having a toileting accident (being incontinent)	339	3	EP
I worry that I will be not be able to function properly in public situations (e.g. on escalators, in supermarkets, in pubs)	339	3	EP
I worry about feeling anxious; how long it will last for, whether it will impact on my health, or how I will cope with it	337	3	EP
I worry about what is causing my anxiety	337	3	N
I worry that others will notice I'm anxious	338	3	N
I think about past events over and over again	336	3	N
I worry about the possibility of failing or making a mistake	337	3	N
I worry about the possibility of being late to appointments	339	3	EP
I worry about the welfare of others	337	3	N

Note. P = directly related to Parkinson's; N = normal for anxiety outside of Parkinson's EP = common anxiety experience but likely exacerbated by Parkinson's. Likert Scale: 1 = Not at all, 2 = Rarely, 3 = Sometimes, 4= Often, 5 = Always. *= ranked against different labels, 1 = strongly disagree, 2 = Disagree, 3 = Neither Agree or Disagree, 4= Agree, 5 = Strongly Agree.

Table 5

Rated List of Anxious Behaviours, Physical Sensations, Emotions, and Impact

Behaviours	N	Median	Theme
I am more argumentative or short tempered	339	3	N
I try to disguise my anxiety	339	3	N
I try to distract myself from the anxiety	336	3	N
I plan things in great detail, including how to get out of a situation/location quickly (e.g. sit near the exit or toilet)	339	3	EP
When I enter an anxiety provoking situation I try to get in and out of the situation as quickly as possible	337	3	N
I prefer to be accompanied by someone familiar when going into new places/situations	340	3	EP
I withdraw and isolate myself	338	3	N
I avoid giving an opinion or disagreeing with others	339	3	EP
I avoid decision making and/or positions of responsibility	336	3	EP
I avoid social interactions	337	3	EP
I over-analyse or check over things more than I need to	336	3	EP
I avoid public situations	340	3	EP
In public, I select food or drink that is easier to manage or I avoid eating or drinking altogether	338	3	EP
I avoid busy or crowded places	339	3	EP
I avoid confined spaces or places that are not easy to escape from	338	3	EP
Physical Sensations			
Fatigue or tiredness	339	4	EP
Changes to body temperature	333	3	EP
Increased sweating	333	3	EP
Muscle tension	336	3	EP
Stomach discomfort (churning/butterflies)	335	3	EP

Table 5

Rated List of Anxious Behaviours, Physical Sensations, Emotions, and Impact

Physical Sensations	N	Median	Theme
I need to use the toilet	334	3	EP
Restlessness	336	3	N
Increased Heart Rate	332	3	N
Emotions			
Feeling overwhelmed	338	3	EP
Feeling of dread	338	3	N
Feeling nervous	339	3	N
Feeling panicked	335	3	N
Feeling frightened/scared/terrified	338	3	N
Feeling upset	336	3	N
Feeling irritated	333	3	N
Feeling angry	337	3	N
Impact			
Has restricted me and impacted my freedom and independence	337	3	EP
Has made my Parkinson's symptoms worse	337	3	P
Has impacted my sleep	337	3	EP
Has impacted my relationships	337	3	EP
Has made me more isolated	338	3	EP
Has made it harder to complete daily tasks	339	3	EP
Has made it hard to think clearly	336	3	EP
Has impacted my confidence	338	3	N
Has made it hard to express myself	339	3	EP
Has impacted my ability to work	167	3	EP
Has impacted my ability to be an effective parent or carer for those who need my support	183	3	EP

Note. P = directly related to Parkinson's; N = normal for anxiety outside of Parkinson's EP = common anxiety experience but likely exacerbated by Parkinson's. Likert Scale: 1 = Not at all, 2 = Rarely, 3 = Sometimes, 4= Often, 5 = Always.

Discussion

The present paper represents the largest study to date examining the nature of anxiety in Parkinson's. Two online surveys, co-created with PPI volunteers, were used to identify the anxiety experiences of a total of 394 PwP. It is the first paper to capture the broad (137 distinct statements) and the nuanced nature of these experiences. It highlights why characterising anxiety in Parkinson's through traditional anxiety frameworks has posed a challenge. Whilst recognising that that there is no 'one size fits all' characterisation of anxiety for PwP, this research methodology enabled the rating of the anxiety experiences to highlight those most commonly experienced. It has also facilitated the identification of a number of common themes among the items which ultimately have significant implications for research and clinical practice.

A common thread throughout the listed items is that a significant proportion of the anxiety mirrors that of a non-Parkinson's population. The strong presence of safety seeking and avoidance behaviours, the presence of meta-worry, negative comparison to past abilities, catastrophising of anxiety symptoms, fear of social judgement and fear of failure are all examples of this.[25] This is encouraging as it may indicate that some of the guiding principles of existing evidence-based psychological interventions may be applicable to the experience of anxiety in PwP.

In contrast, many of the most prominent anxiety experiences are those which are specific to the experience of Parkinson's. Similarly, the majority of items are likely exacerbated by the Parkinson's experience. The identification of these items in this study aligns with the paradigm that the mainstream conceptualisation and treatment of anxiety could benefit from augmentation with Parkinson's-specific considerations in order to maximise effectiveness.[10] It also invites reflection on the services supporting these patients and the expertise required to deliver the treatment. For example, a psychological practitioner considering a trigger such as 'when I feel time pressured (for example making it to an appointment in time or at a supermarket till where I have to coordinate tasks quickly)', would likely benefit from Parkinson's-specific knowledge of the possible impact of motor, cognitive and sensory symptoms

of Parkinson's that may influence the feeling of time pressure. Similarly, they would be better placed to consider the possibility that the physical experiences of fatigue, restlessness, muscle tension may be Parkinsonian symptoms, as opposed to anxiety.

Integrated, multidisciplinary care models have already been found to be beneficial for the treatment of other Parkinson's symptoms.[26] There is a growing argument that a more integrated and multidisciplinary approach to anxiety care is this population is required.[9] Given the Parkinson's-specific nature of much of the anxiety reported by participants, the findings of the present study support this. They also indicate that anxiety symptoms can be triggered by other Parkinson's symptoms and vice versa. This provides further support for a multidisciplinary approach that joins up these previously fragmented treatment pathways. This study also highlights that "seeing others at the later stage of Parkinson's" is a prominent trigger for many, thus a traditional group intervention format involving patients at a range of disease stages may impact attendance, attrition and efficacy of the intervention.

Further, it may be useful to consider whether some of the anxiety experiences may have commonality with anxiety in other 'long-term health conditions'. Moss-Morris[27] calls for 'unified theory' in chronic diseases. For example, the existing body of work focusing on adjustment to diagnoses of long term conditions[28] may be applicable to those identifying with anxiety being 'worse in the period just after my diagnosis of Parkinson's'. Similarly, worry about 'becoming a burden' or 'how family will cope' may benefit from existing interventions relating to anxieties regarding progression of disease.[29]It is also apparent how many of the anxiety items involve those close to the PwP, whether as thoughts ('I worry about the impact of my Parkinson's on my family and how they will cope', triggers ('When loved ones get upset') or behaviours ('I prefer to be accompanied by someone familiar when going into new places/situations'). With this in mind, interventions that consider the family may be valuable. Early support for this notion was provided by a partner-assisted CBT intervention, which resulted in reduced anxiety and caregiver burden.[30]

Limitations

The study provides a broad description of common experiences of anxiety in PWP, but we recognise that there are sub-populations that may have quite different experiences of anxiety when compared to each other. We have plans for further

analysis to examine these issues and to determine what characteristics group and correlate with each other.

Online recruitment and participant input was central to achieving large scale participation nationwide, as was access to the Parkinson's UK Research Support Network and support groups. However, it is likely this will have biased the population to have limited representation of those with more severe disease, lower socioeconomic status, or from ethnic minorities.[8]

Recommendations for Future Research

Links to CBT conceptualisations and interventions dominate the discussion because they have the greatest evidence base in Parkinson's at this time. However, psychological conceptualisations such as acceptance and commitment and compassion focussed approaches may all glean valuable insight from this data. There is indeed some support for the utility of these therapeutic modalities in the treatment of anxiety in PwP,[31,32] but more research is required.

Conclusions

This is the largest survey characterising anxiety in Parkinson's. Anxiety in Parkinson's is complex with generic, Parkinson's-specific and Parkinson's-enhanced aspects. It is hoped this characterisation can inform the design of future assessment and psychological therapies, possibly enhancing efficacy.

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Chapter Five: Extended Methodology

Overview of Chapter

This chapter relates to the methodology of the empirical project, building on the information presented in Chapter Four. It includes information about the measures used and ethical considerations.

Measures

In each survey, two standardised clinical psychometric measures were used to characterise the participant sample. The Parkinson's Disease Quality of Life Questionnaire 8 (PDQ-8; Jenkinson, Fitzpatrick, Peto, Greenhall, & Hyman, 1997) measured participant health related quality of life through eight self-report items. Each item is rated on a five-point scale ('never', 'occasionally', 'sometimes', 'often', 'always – or cannot do at all'). This is a valid and reliable (Cronbach's alpha = 0.81) measure of health-related quality of life for people with Parkinson's (Tan, Lau, Wing, Au, & Luo, 2007). It has also been used by other researchers as a measure of quality of life in PwP (Martinez-Martin et al., 2004). As it is not designed to give prescriptive scores it has no prescribed cut off scores for determining 'caseness', but potential scores range from zero to 32. The Parkinson's Anxiety Scale (PAS; Leentjens et al., 2014) was used to measure anxiety in people with Parkinson's. The PAS measures anxiety on a 12-item patient-rated scale with three subscales for persistent anxiety, episodic anxiety, and avoidance behaviour. Each scale item consisted of five responses. A total score of above 13-14 is deemed indicative of the presence of an anxiety disorder. This is a valid and reliable measure of anxiety in a Parkinson's population with internal consistency (Cronbach's coefficient of 0.91).

Ethical Considerations

The project was granted ethical approval by the Faculty of Medicine and Health Sciences Research Ethics Committee at the University of East Anglia on 10/01/2019, reference number: 201819 - 046 (Appendix M). The research adhered to The British Psychological Society (2010) guidelines for the conduct of psychological research.

Before completing the online survey at either phase of this project, participants were required to read the information sheet and complete a consent form (Appendices H, I, K, L). The consent forms provided the participant an opportunity

to confirm that they understood and agreed to the information provided in the information sheet regarding the research process. The ability to access our online link and complete the surveys, or indeed to contact the lead author for a paper copy to be sent to them was taken as indicative of appropriate mental capacity.

For the online survey and online ranking form, participants were made aware that, because their data were non-identifiable, it would not be possible for data to be withdrawn once provided. They were however reminded that until they submitted their responses, they could still withdraw their involvement. There was a small possibility that some participants might experience distress when completing the surveys. In view of this, contact details of supporting agencies were signposted at every stage of the process. The signposting was to their local GP, and the free and confidential helplines offered by Parkinson's UK, The Samaritans and SANE.

All data were stored in line with the General Data Protection Regulation (2018). The research methodology was such that the participants were not identifiable by their responses. At each phase of data collection, participants were given the option to provide their contact details if they wanted to be involved in the next phase of data collection, or to receive information about the findings of the research when complete. Where provided, these personal details were never linked to their responses. The participant responses and participant contact details were always stored separately and securely either on password protected online survey databases. Contact details will only be kept for 2 years after the participants have completed the surveys. This will allow for the results of the study to be distributed to them in a lay report. All anonymised data will be kept for 10 years on the secure UEA server.

Participants were made aware that their participation in any of the phases of data collection was voluntary and that they were not obliged to take part. The methodology was such that deception was not required in this study. A short debrief statement was placed prior to the point at which participants submitted their responses. This included researcher contact information and signposting information.

For the involvement of PPI volunteers, the Health Research Authority (HRA; 2016) have clarified that because PPI volunteers play an advisory and planning role that is distinct from that of the participants, ethical approval is not required for their

involvement. Prior to agreeing to take part in the project they were provided with information about the project and their role. Travel expenses were refunded.

Chapter Six: Additional Results and Discussion

Overview of Chapter

This chapter outlines additional findings obtained from the empirical research project, which have not been reported in the Empirical Paper. Firstly, anxiety experiences that were not included in the empirical paper will be reported and briefly discussed. However, most of the chapter is dedicated to the responses to additional questions included in the first survey, that were not discussed in the empirical paper. These relate to participants' methods of anxiety management. The results are listed, but these are preceded by an introduction to this line of enquiry.

Additional Anxiety Experiences

As was outlined in the Empirical Paper, participants rated the anxiety experience on a Likert scale from one to five. Following analysis, those experiences with a median score of two ('rarely') or below were not included in the empirical paper so have been listed in Table 1.

The medians of these 31 items suggest that, taken as a whole population, they occur rarely or have limited impact. It is notable that key themes identified in the empirical paper also appear to be present in these items. It appears that some of these anxiety experiences are generic anxiety experiences common to the general population (29%) whilst others are a direct result of Parkinsonian presentation (10%) or at least exacerbated by it (61%). The ratio of items falling into each of these categories is also comparable to that of the Empirical Project.

Table 1

Rated Anxiety Statements Not Reported in Empirical Paper

Triggers	N	Median	Theme
When I am at home	334	2	N
When exercising	332	2	EP
When walking	333	2	EP
When I am unhappy about the healthcare I am receiving	336	2	EP
When I wake up	334	2	EP
By specific seasons or extremes of weather	333	2	EP
When I have hallucinations	75	2	P
Around menstruation	6	1.5	N
When I drink caffeine	337	1	N
When I smell strong smells or odours	334	1	N
Thoughts			
When experiencing physical symptoms of anxiety, I worry that they mean something more catastrophic	332	2	N
I worry that I stand out as different	338	2	EP
I worry about dribbling and that others will judge me negatively	338	2	P
I worry that someone will knock me over in busy places	340	2	EP
I focus too much on my medication (e.g. when its due, side effects, whether it's working)	334	2	EP
I am worried that others are embarrassed to be with me	338	2	EP
I fear being left alone because others are not able to cope with my symptoms	336	2	EP
I worry about money and my ability to maintain financial security	339	2	EP
I worry I will freeze (stop moving) in hazardous situations	337	2	P
I worry about my employability	333	1	EP

Table 1

Rated Anxiety Statements Not Reported in Empirical Paper

Behaviours	N	Median	Theme
I avoid driving	328	2	EP
I avoid some methods of travel (e.g. public transport, car travel, plane travel, etc.)	337	2	EP
I avoid leaving home	333	2	EP
I drink alcohol to try to reduce my anxiety and/or Parkinson's symptoms	337	1	EP
I physically harm myself when anxious	336	1	N
Physical Symptoms			
Difficulty breathing	336	2	N
Feeling very alert and focused	226	2	EP
Headache	332	2	EP
Feeling disorientated or dizzy	337	2	N
Nausea	336	2	EP
Chest discomfort	332	2	N

Note. P = anxiety symptom directly related to Parkinson's presentation; *N* = anxiety experience common outside of Parkinson's population; *EP* = anxiety experience common outside of anxiety population but likely exacerbated by Parkinson's presentation. Likert Scale: 1 = Not at all, 2 = Rarely, 3 = Sometimes, 4= Often, 5 = Always.

Introduction to the Management of Anxiety

In 2014, Deane and colleagues established that the second greatest of all future research priorities identified by participants with direct and personal experience of Parkinson's was 'effective stress and anxiety management'. The importance of this research direction was also echoed by our PPI volunteers in our early steering group meetings. As described in previous chapters, the steering group believed that an important step towards this research goal was to first of all develop a more comprehensive characterisation of anxiety in Parkinson's. It was hypothesised that a greater characterisation would provide a foundation for development of appropriate intervention. The methodology used to achieve this improved characterisation has been described in the empirical paper.

In addition to characterising the anxiety, the steering group believed it was important to gain an improved understanding of means by which PwP currently attempt to manage their anxiety. There is some published research exploring the role of psychosocial interventions (Yang, Sajatovic, & Walter, 2012) for anxiety in PwP as well as anecdotal accounts from our PPI volunteers and beyond about the benefits of activities such as dancing and boxing. However, to our knowledge, no research has yet sought to capture the detailed insights of how PwP currently attempt to manage their anxiety.

The importance of developing a more comprehensive characterisation of methods that PwP use to manage anxiety in Parkinson's is evident. So, a secondary aim of the study described in the empirical paper was to enhance the existing characterisation by seeking the detailed insights of PwP who have experience of such anxiety. The research questions were 'What methods of anxiety management do PwP currently use?' and 'How would PwP rank such methods in terms of effectiveness?'. The steering group aimed to address these research questions by incorporating questions about anxiety management into the online surveys previously described in the empirical paper (Appendices I and L). The questions included in the brainstorming survey were open ended, exploring anything that participants may have found helpful to manage or reduce anxiety. The questions also prompted participants to consider lifestyle choices, therapies, communication types and anything else they have found helpful (Appendix I). The planned methodology was the modified Nominal Group Technique (NGT) approach described in Chapter 4.

Anxiety Management Analysis

The participants' open-ended responses regarding their 'anxiety management' were downloaded. Combined, the participant responses totalled 8968 words. The principal author then familiarised themself with the participant responses. Any parts of participant responses that clearly did not address the questions were separated, reviewed by the rest of the steering group and ultimately removed. The remaining data was then systematically analysed by the principal author through coding. An inductive approach to coding was taken, whereby codes were driven by what was in the data. This approach can be likened to phase two of the thematic analysis process as described by Braun and Clark (2006). The codes enabled duplicate or similar responses to be grouped together. This process occurred

iteratively as the data was analysed and resulted in 27 distinct codes being identified (detailed in Appendix P). Unsurprisingly given the nature of the survey's prompting questions, the codes sat within broader themes of 'communication', 'lifestyle' and 'therapies'. The coding of the data was reviewed by the steering group. An example of a participant response it written below, whilst the coding of this response is outlined in Table 2.

"Talking to others with Parkinson's is helpful as you realise you're not the only one to feel this way. I do a lot of paper crafting and find it very relaxing. Exercise and my hobbies help to relax me".

Table 2

Coding Example

Participant Response	Code Label	Code Name
Talking to others with Parkinson's is helpful as you realise you're not the only one to feel this way	C4	Parkinson's specific
I do a lot of paper crafting and find it very relaxing.	L5 and L6	Staying Occupied. Hobbies/leisure
Exercise and my hobbies help to relax me	L7 and L6	Exercise Hobbies/Leisure

The steering group met again with the intention of converting the 27 codes into 'indicative statements' that could be presented to participants of the second survey. However, it was clear from our previous experience that generating statements that represented the items captured by the codes would significantly increase the size of the second survey. Concerns were raised that, if the survey was to include these additional items, it would be too time consuming and burdensome for participants to complete. Therefore, at this point, the PPI volunteers piloted the second survey without the inclusion of any 'anxiety management' items. Following

the pilot, the decision was taken not to proceed with the process of converting the codes to 'indicative statements'. It was accepted that addressing the second research question described above was beyond the scope of the current project. The analysis process is summarised in Figure 1.

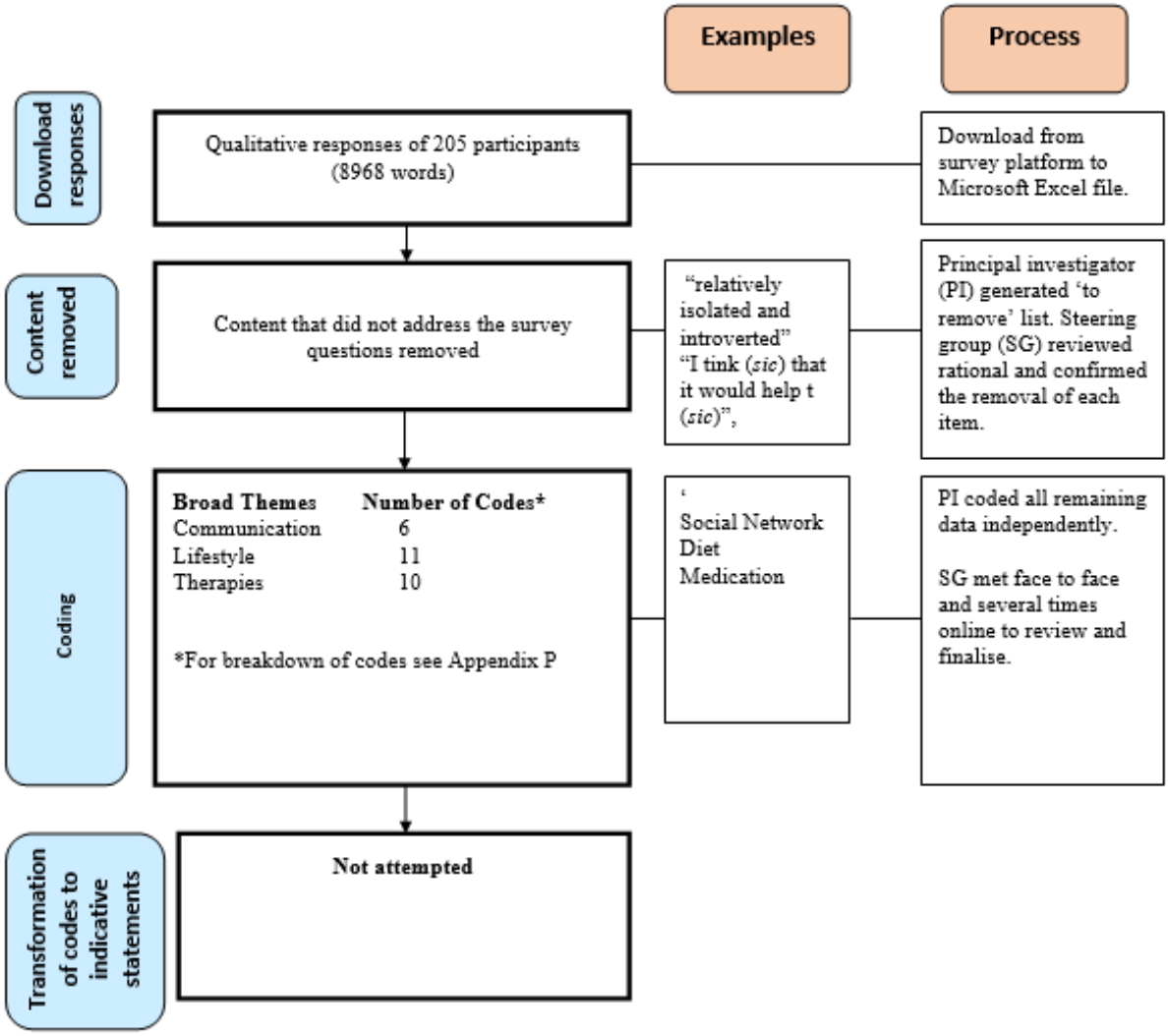


Figure 1. Flow chart providing overview of phase one of additional analysis.

Anxiety Management Results

Although anxiety management codes were not converted to representative statements and taken to the second survey, it is important to report a summary of the anxiety management strategies that were reported. The steering group has therefore deduplicated the anxiety management strategies within each code, and made a summary statement for each. These are listed below (Tables 3-5). A total of 192 unique items were generated. For the purposes of reporting the findings, they have

been broadly grouped into three categories: communication (33), lifestyle (85) and therapies (74).

Table 3

Means of Communication for Anxiety Management

Communication
General
Communication in general
Letting others know if I am having difficulties
Talking with others who experience anxiety
Talking to others who share their anxiety experiences
Being open and honest about what I am experiencing
Communication with select people
Explaining my symptoms to people who don't know me very well
Social Network
Talking to trusted friends
Talking to close family members
Connecting in the community (non-Parkinson's related)
Online communication (such as emails, chat forums, social media)
Professionals
Talking to a Parkinson's specialist professional (such as a Parkinson's nurse or consultant)
Talking to non-Parkinson's specialist professional (such as a support worker, GP or carers support)
Parkinson's Specific
Attending support groups for Parkinson's
Talking to others who have Parkinson's
Talking to others who DO NOT have Parkinson's
Communication with Parkinson's UK
Talking to people at Parkinson's specific events
Communication with people who understand Parkinson's
Support groups are not a useful means of communication as those attending have such different attitudes to me

Table 3

Means of Communication for Anxiety Management

Communication
Not Helpful
Communicating in a support group environment
Talking to others
Talking to others makes the anxiety worse
Communicating with others with Parkinson's makes the anxiety worse
Communication has no long-term benefit on my anxiety
Do Not Talk
I choose not to talk with others about my difficulties
I do not feel the need to communicate with others
I would like to communicate more but I am not sure of the required steps to gain such support
I find that others do not want to talk with me about my difficulties
I find it hard to find the words to talk to others about my experience
I do not talk about my experience because I find it do not want to draw attention to myself
I do not talk to those close to me about how I am feeling as I do not want to upset or burden them
I do not communicate because the anxiety is too severe to talk through

Table 4

Lifestyle Choices for Anxiety Management

Lifestyle
Managing Demands
Not overloading myself with commitments, demands or pressures
Pacing myself and not overdoing things
Keeping an organised schedule of appointments
Taking time away from work or retiring
Sticking to a routine
Dedicating time to myself
Speaking to employment professionals
Being in a quiet or calm environment
Breaking down complex tasks into smaller more manageable steps
Not thinking too far ahead, instead taking each day as it comes

Table 4

Lifestyle Choices for Anxiety Management

Lifestyle
Diet
Maintaining a healthy and satisfying diet
Alcohol consumption
Avoiding alcohol consumption
Sticking to a specialist diet
Weight management
Sleep
Having a good sleep routine
Getting good sleep
Having one or more daytime nap or sleep
Not sleeping in the day time
Laying down completely flat on the floor for a short while
Having a relaxing quiet time to rest
Sleeping alone
Taking medication to aid sleep
Occupying myself when I am struggling to sleep
Connection
Being around other people
Having sex
Being around friends, family or other familiar people
Socialising with other people who have Parkinson's
Helping or supporting others
Spending time with my pets or with animals
Staying Occupied
Taking part in anything that is absorbing and engages my mind
Keeping my mind active with things such as quizzes, puzzles, playing cards
Keeping occupied and busy
Keeping my hands busy as it reduces the tremor
Driving

Table 4

Lifestyle Choices for Anxiety Management

Lifestyle
Hobbies/Leisure
Engaging in one or more hobbies
Attending a choir or singing group
Listening to music
Attending a Parkinson's singing class
Planning and taking holidays or day trips
Holidays and daytrips help my anxiety as long as I am accompanied
Exercise
Any form of exercise
Gentle exercise
Moderate exercise
Intense exercise
Specialist exercise classes for those with Parkinson's (for example dancing, PD warrior, PD attack, PD gym and fitness, Active with Parkinson's programme)
Living an active lifestyle
Cycling (outdoor or on machines)
Home based exercise
Swimming
Boxing
Running
Golf
Badminton
Horse riding
Football
Going to the gym
Circuit training
Weight training
Outdoor bowls
Exercise classes
Dancing

Table 4

Lifestyle Choices for Anxiety Management

Lifestyle
Mind-Body Exercises
Pilates
Yoga
Tai-chi
Qigong
Yoga for Parkinson’s
Skype yoga
Being Outdoors
Spending time outdoors in the fresh air
Being among nature
Gardening
Being by the sea
Being in the countryside
Relaxation
Relaxation techniques
Taking baths
Audio relaxation recordings
Lavender oil
Aromatherapy oils
Other
Faith or prayer
Not doing any medical reading at night
Laughter
Sitting on my hands
Staying well informed about Parkinson's (through reading, lectures, courses etc)
Try to keep things as they were before so as to maintain a sense of normality
Meeting new people and facing anxiety provoking situations

Table 5

Therapies and Anxiety Management

Therapies
Psychological Therapies
Cognitive Behavioural Therapy
Counselling
Talking therapy
Psychological therapy
Course on resilience
Psychiatrist appointment
Psychotherapy
Therapy
Compassion Focussed Therapy
Cognitive Analytic Therapy
Self-Management Group
Neuropsychology
Physical Therapies
Occupational therapy
Neurophysiotherapy
Speech therapy
Live loud (PUK speech communication support)
Physiotherapy
Group physiotherapy
Physical health specialists
Parkinson's UK therapy centre
Mindfulness
Meditation
Mindfulness
Guided meditation
Breathing exercises
Progressive muscle relaxation (body scan)
Mindful colouring

Table 5

Therapies and Anxiety Management

Therapies
Medication
Medication
Adjustments to medication
Alternative Medicine
Homeopathy
CBD oil
Serotone 5htp supplements
Other
Maintaining positive mindset
Using imagery of a 'safe space'
Self-talk/rationalising
Trying to ignore the anxiety
Concentrating on achievements
Being kind to myself
Trying to stay calm
Getting on with things
Reminding myself it's not my fault
Waiting for it to pass
Not dwelling on it
Accepting that anxiety is just as much a part of my condition as any other symptoms
Staying in the moment - avoid dwelling on future 'what if's'
Not Helpful
No therapy has been helpful
Counselling
Acupuncture
Meditation
Mindfulness
Breathing exercises (exacerbate tremors)
CBT – wasn't specific enough, therapist would need to understand PD
CBT
CBT – no long-term benefit
Tai Chi – no long-term benefit

Table 5

Therapies and Anxiety Management

Therapies
Massage – no long-term benefit
Not Attempted
I have not tried any therapy
Therapy is not needed
I avoid therapies
Access Challenges
Can't access psychological therapy
No funding for long term counselling
Waiting list for counselling too long
Tai chi was too expensive
Counselling was too expensive
Mobility impacts ability to access therapy engagement
No therapy has been offered to me
Complementary Therapies
Reiki
Bowen therapy
Massage
Reflexology
Chiropractic
Acupuncture
Hypnotherapy
Autogenic therapy
Conductive education

Anxiety Management Discussion

In the first survey of this thesis portfolio, 205 PwP responded to questions regarding their methods of anxiety management. To our knowledge, this is the first survey to use open ended questions to characterise anxiety management in PwP. Whilst participant responses were analysed and transformed into representative statements for rating in a second survey, no further stages of research or analysis followed. It is therefore acknowledged that conclusions are limited. However,

tentative reflections are made on some of the broad themes that are present and consideration given to areas that future research may wish to take forwards.

The participant responses highlight the perceived value of engaging in exercise and physical activity. There is a growing evidence base for the value of physical exercise in Parkinson's disease (for a review see Lauzé, Daneault, & Duval, 2016). However, the focus of these studies has been on the physical gains, with the few that focused on mental health benefits focussing on depression. Future research should investigate the potential anxiety benefits of exercise for PwP, especially given the growing evidence advocating the benefits of exercise to mental health in the general population (Mikkelsen, Stojanovska, Polenakovic, Bosevski, & Apostolopoulos, 2017). Similarly, many participants reported benefit from a range of established 'PwP only' group activities (not exclusive to physical activity). There is already some evidence that is indicative of a range of benefits associated with attendance of such groups (Sharma, Robbins, Wagner, & Colgrove, 2015). But again, their impact on anxiety has not yet been measured and future research is needed to clarify this. For many, being outside in natural surroundings was considered a way of reducing anxiety. This appears to align with existing research outside of Parkinson's relating to the reduction in anxiety associated with direct contact with nature (Kohlleppel, Bradley, & Jacob, 2002).

Various means of communication were identified as helpful. Many expressed the value of communicating with others with knowledge or experience of Parkinson's and/or anxiety. Meanwhile others did not find this helpful, preferring to communicate with 'non-experts'. Additionally, some people did not find any anxiety benefits from communicating. There were also a range of examples where participants did not feel able to communicate. These reasons included not wanting to burden others, not being able to initiate the conversation, or not knowing the channels to access support.

Participants listed a large array of 'therapies' as helpful. These included pharmacological, physical, psychological and complementary therapies as well as alternative medicines. As outlined in the empirical paper, some research studies have begun to view the efficacy of Cognitive Behavioural Therapy (CBT) interventions for anxiety among PwP, but this is not yet the case with the other psychological therapies. Given the range of psychological therapies listed by the survey

participants, consideration of the efficacy of these therapies for those with Parkinson's may be useful for future research. A significant number of physical therapies were listed. Whilst there is an evidence base for their physical benefit for PwP (Keus et al., 2007), studies are yet to explore the potential impact on anxiety. In light of our findings, this may be a valuable avenue for further research to explore. Finally, complementary therapies and alternative therapies were used by a number of participants. Whilst these are not evidence based, it this study provides a useful snapshot of the extent of their use among this population.

A range of access difficulties were cited in relation to psychological therapies. These stemmed from mobility issues, waiting lists and cost. In other chronic physical health conditions, efforts have been made to address this through the creation of specialist pathways within mental health services which prioritise timely treatment and flexibility to complete home visits (Clarke et al., 2018; National Collaborating Centre for Mental Health, 2018). These survey responses highlight that that such access is not present for those with PwP. In our population, many of those who did access therapies did not find them helpful. This was the case for a number of therapies, but for CBT some participants expanded on the reasons why it was not helpful. Firstly, it was critiqued for its lack of long-term benefit. It was said to lack specificity to Parkinson's and it was suggested that the therapist would require specific knowledge of Parkinson's. This appears to be supported by the findings of the empirical paper.

For many participants, methods that help them to manage life demands have a positive impact on anxiety. Examples include pacing, routine, self-care, relaxation and breaking tasks into smaller steps. Given the impairment in activities of daily living found stemming from motor and non-motor Parkinson's symptoms (Bhatia & Gupta, 2003), it is understandable that techniques for managing life demands are valued by many participants as a means of managing anxiety. Interestingly, whilst managing demands was important, many participants also highlighted the importance of keeping 'occupied'.

Participants raised the importance of sleep to the management of anxiety. Sleep disturbance is known to exacerbate anxiety symptom severity in the general population (Cox & Olatunji, 2016). It is also a common non-motor symptom of Parkinson's (Chaudhuri, Healy, & Schapira, 2006) with a known relationship with

anxiety (Borek, Kohn, & Friedman, 2006). Our findings indicate that, for many, effective sleep management contributed to reduction in anxiety. Similarly, many participants referred to dietary adjustments that reduce anxiety. Research into Nutrition and Parkinson's is in its infancy, but preliminary findings suggest that adjustments to diet can influence both motor and non-motor symptoms (Seidl, Santiago, Bilyk, & Potashkin, 2014).

Limitations

As previously stated, the second phase of the NGT was not completed with this data set. As a result, the findings of this part of the study are limited to the 'brainstorming' phase. Whilst this provides a broad overview of anxiety management techniques of our participants, at such a preliminary stage, the conclusions are limited.

Future Research

It is planned that this research team will build on these preliminary findings. The second phase of NGT should achieve insight into the extent to which participants identify with each technique as a useful anxiety management tool. This next phase should also aim to better understand the benefits of the approaches, considering: the time taken for the benefit to be felt, the longevity of the benefit, whether the benefit extended to other symptoms of Parkinson's, whether the approaches have been recommended by medical professionals.

Chapter Seven: Discussion and Critical Evaluation

Overview of Chapter

The final chapter summarises and integrates the findings from the systematic review (Chapter 2) and empirical research project (Chapters 4 and 6). A critical evaluation of each will be provided and the strengths and limitations discussed. The overall clinical implications are considered and recommendations for future research made. Reflections on the process of completing the thesis portfolio are also included. Finally, a conclusion from the whole portfolio is provided.

Main Findings

Systematic Review

The systematic review examined the evidence for the relationship between anxiety and quality of life in (PwP) by systematically identifying, selecting, synthesising and interpreting studies that investigated this relationship. Twenty-two research studies were included. From these, 17 correlation coefficients were extracted (directly or through conversion from standardised beta) and meta-analysed. The weighted pooled estimate effect size of the relationship between anxiety and quality of life was large ($r = 0.53$). The incorporation of a meta-analysis was beneficial as it pooled many studies and therefore offers a more precise estimate of the relationship. The systematic review also extracted regression data from 20 studies. The review of regression-based findings provided a useful summary of models that examined the extent to which anxiety predicts QOL in PwP. The regression models of 18 of these studies found that anxiety accounted for significant variance in QOL. Placed among other variables, such as disease stage, activities of daily living, disability and depression, it was consistently among the strongest predictors of QOL and in many cases accounted for unique variance in QOL.

Empirical Project

The aim of the empirical research project was to develop an in-depth characterisation of anxiety in Parkinson's from large surveys of PwP. The steering group, including two Patient and Public Involvement volunteers, sought to achieve this though two co-designed online surveys using a modified Nominal Group Technique. The first survey used open ended questions to collect qualitative accounts of the anxiety experiences of 205 PwP. These responses were analysed and

converted into representative statements that captured the experiences. These statements were then rated in a second online survey by 341 participants according to how much they identified with each experience. Quantitative analysis of the statement rankings produced a summary list of the anxiety experiences that were ranked according to the extent that participants identified with each experience. This study is the largest one worldwide to characterise anxiety in PwP. It identified that the anxiety experiences of this sample were wide ranging. Among these diverse experiences it was noticeable that some experiences were akin to common anxiety experiences that are well identified among those without Parkinson's. In contrast, the majority of the anxiety experiences related specifically to, or were aggravated by, challenges associated specifically with Parkinson's.

An additional component of the first brainstorming survey asked PwP how they managed their anxiety. This resulted in the identification of a very wide range of methods used by PwP. Given the number of methods identified, advice from PPI input was that including the items in the second survey would be too burdensome to complete. The decision was therefore taken not to include them in the second survey. Whilst conclusions drawn from this brainstorming phase are inevitably limited, it does provide a useful insight into the range of methods used among over 200 PwP who experience anxiety. Many methods were unconventional, but even the more conventional ones have a limited evidence base in this population. In line with previous findings (Deane et al., 2014), this data highlights the need for further research into anxiety management.

Synthesis of Main Findings

Both studies contribute to research evidence on anxiety in Parkinson's, therefore addressing one of the top three Parkinson's research priorities identified by those with direct and personal experience of Parkinson's (Deane et al., 2014). Taken together, these studies highlight the significance of anxiety among PwP, and provide much more information on its character.

Critical Evaluation

Systematic Review

The systematic review is the first to review existing evidence on the relationship between anxiety and QOL in PwP. A key strength is that the study not

only provides a quantitative synthesis of studies through meta-analysis of correlations, but extends the review to incorporate findings of multiple regression models.

We acknowledge that, to some extent, the findings of the current review are unsurprising. After all, it is well established that increased anxiety is related to poorer QOL (Mendlowicz & Stein, 2000). This is a finding that has been replicated across a number of physical health domains, with correlation and regression analyses investigated the anxiety-QOL relationship (Blakemore et al. 2014; Morris, Van Wijck, Joice, & Donaghy, 2013; Mosaku, Kolawole, Mume, & Ikem, 2008; Nekouei, Yousefy, Nekouei, & Sadeqhi, 2010). However, this review is the first to examine the relationship between anxiety and QOL for PWP.

It is evident from the review that a key approach to exploring the relationship between anxiety and QOL is to perform correlation and/or regression analyses on participant scores on anxiety and QOL measures. All 22 studies reviewed in this paper took this approach. Whilst this approach is common, we acknowledge that it is one that can be conceptually critiqued. The primary concern is that one of the domains captured by quality of life measures is 'psychological wellbeing'. For example, the PDQ-39 and PDQ-8 capture psychological wellbeing as one of eight domains of wellbeing, including mobility, social support, communication and activities of daily living. Of course, one component of 'psychological wellbeing' is anxiety. Thus, it is likely that even though QOL is a multifaceted construct, the extent to which the scores on the QOL and anxiety measures are related is inflated by the fact that they both measure anxiety to some extent. In future, this methodological issue may be addressed by the study teams exploring the effects of removing anxiety items from the QOL measures at point of analysis.

In consideration of this methodological issue, one approach considered in this review was to complete additional analyses where the 'psychological wellbeing' domain of QOL measures was removed from the analyses in order to review the anxiety-QOL relationship without the QOL items that directly explored anxiety. However, this was not possible as only three correlation studies and three regression studies reported the relationship between the anxiety measure and each of the subdomains of the QOL measures. Further, four of these six studies used the PDQ-39 as a QOL measure. In this measure, the questions that address anxiety are

distributed among a number of the sub-domains, rather than being clustered into one. Removing these sub-domains would remove other valuable 'non psychological' components of QOL and therefore undermine the analysis. The remaining two studies reported just two subdomains of the SF-36, physical and mental. Further analysis whereby the 'mental' questions were removed would be not be appropriate as only two of those 18 questions were anxiety focused. We therefore accept that the correlation and regression statistics may be inflated, but that this is a problem inherent with the methodology used by the studies reviewed.

It is acknowledged that confidence in the review findings would be increased if the screening, eligibility and inclusion processes of studies were entirely independently duplicated. However, the pragmatic approach whereby the principle investigator (DC) took any uncertainties for discussion with the project supervisor (KD) was deemed sufficiently thorough. The independent duplication of quality assessment by an additional author (CI) for 50% of articles was also adequate. It is acknowledged that exclusion of 'grey literature', additional literature and articles that were not written in English increase the risk of publication bias. However, a focus on peer-reviewed research facilitated a systematic and transparent review process and was an appropriately pragmatic approach in the context of a thesis portfolio.

It is important to consider that the rate of heterogeneity in the meta-analysis was substantial according to Higgins and Green's (2011) interpretation. This heterogeneity was likely influenced by differences in methodologies, assessment methods and demographic differences among participants (Huedo-Medina, Sanchez-Meca, Marin-Martinez, & Botella 2006). This is well exemplified by the variation in how the studies assessed both anxiety and QOL, with six measures of anxiety and four measures of QOL used. Whilst such heterogeneity is common in meta-analyses (Higgins, 2008), this inconsistency must be held in mind when interpreting the findings (Higgins, Thompson, Deeks & Altman, 2003). Despite the heterogeneity reducing when studies that estimated r from standardised beta were removed in the sensitivity analysis, the decision was taken not to remove them from the overall meta-analysis. This decision increases heterogeneity, but did not inflate the effect size estimate and enabled the inclusion of five additional studies.

Overall, the quality of the included studies was good and methodologies robust. However, in the majority of studies, this quality was limited by the omission of sample size justification. This raised concerns that the studies may be underpowered, particularly for the multiple regressions. An effort to address this was made in this review by comparing study sample sizes of studies including multiple regressions against well-established sample size criteria. Additionally, studies' acknowledgment and management of collinearity was also considered. In doing so it was highlighted that five studies met the sample size and collinearity criteria and therefore invited more confidence in their findings. The high consistency with which anxiety significantly predicted QOL among those studies that met the criteria and those that did not was noted. It is also notable that some of the multiple regression studies reported unstandardised beta values, rather than the standardised beta values reported by the majority. Whilst unstandardised values enable interpretation of whether anxiety is a significant predictor of QOL, it does not allow the comparison of predictive ability across variables. This therefore restricted conclusions for these studies.

Empirical Project

The empirical project is the largest existing study examining the nature of anxiety in Parkinson's. It has generated a valuable data set with unique findings and significant potential for future analyses.

The presence of PPI input for the entirety of the project is a significant strength. The benefits of this are reviewed in detail in Chapter Three, but PPI involvement was particularly valuable for designing accessible surveys and analysing participant responses to the first survey. The support during the design phase likely increased the accessibility and acceptability of the survey, a notion supported by participant feedback. In the analysis of open-ended survey responses, researcher coding decisions are known to threaten the reliability and validity of findings (Seidel & Kelle, 1995). Having PPI input to the steering group that reviewed all such decisions significantly increases confidence in the reliability and validity of our findings.

The use of modified NGT research methodology was a strength. It facilitated the recruitment of large participant numbers and brought the benefits of both

qualitative and quantitative methodologies, offering relatively detailed and nuanced participant description as well as quantitative rating of anxiety experiences. Thus, it enabled the research project to achieve its aim to capture the broad range of anxiety experiences among PwP and to gain understanding of the extent to which these are experienced.

Whilst NGT was chosen following careful consideration of potential research methodologies, the approach is not without weakness. As with thematic analysis, relative to some other methodologies it enables rich analysis of participant responses but without follow-up and clarification. Yet, approaches such as extended semi-structured interviews would likely invite richer participant responses and also give the research interviewers the opportunity to seek clarification through follow up questions. It is also important to acknowledge that the online format of the methodology likely biases the population. Low socioeconomic status and older age are both associated with lower rates of access to the internet (OFCOM, 2019; Tirado-Morueta, Aguaded-Gómez, & Hernando-Gómez, 2018). It is therefore probable that our approach underrepresented these groups. The online approach also did not support accessibility for those with dementia.

The study provides a broad description of common experiences of anxiety in PWP, offering an important overview of participant experiences. In doing so, it addresses a significant gap in the literature. However, as outlined in Chapter One, it is known that neither Parkinson's or anxiety are experienced in a uniform way. It may therefore be the case that sub-populations among these participants have quite different experiences of anxiety when compared to each other. The research team has plans for further analyses to examine these issues.

Participant anxiety responses were ranked according to their median values. The decision was taken not to use mean values. This was in accordance with the argument that means should not be used to represent ordinal data from Likert scales (Jamieson, 2004). Whilst this decision is justified, it must be acknowledged that the use of medians restricts the sensitivity with which the items are ranked, with many items sharing the same median score.

Implications of Current Findings

Theoretical Implications

The theoretical implications of the rich characterisation of anxiety in PWP provided by the empirical study, were considered with respect to the augmented CBT model by Egan and colleagues (2015). In particular, we considered which aspects of the augmented CBT model were supported by our findings, which aspects could be developed further and which aspects we were unable to comment on. This reflection is achieved narratively but is also illustrated in Figure 1.

There are some elements of the Egan et al. augmented CBT model that fall outside the scope of the current study. For example, our study does not incorporate depression, the factors that maintain it, or its relationship with anxiety. Further, the survey methodology focussed on the maintenance of anxiety in PWP, rather than the more deep-rooted longitudinal factors such as core beliefs, cohort beliefs or illness beliefs, cited in the Egan et al. model. Their model also uses arrows to represent causal links between components. As our findings are predominantly qualitative and focus on the experience of anxiety in PWP, it is not possible to comment on causality. We make this distinction in our diagrammatic representation by using lines to link these components, rather than arrow heads.

The Egan et al. model was developed in response to the argument that a CBT model for PWP would need to be augmented to incorporate Parkinson's specific components. Given that such a high proportion of the anxiety experiences identified in our study were influenced by Parkinsonian elements, our findings support this fundamental principle of the model. It is also important to reflect that there was a distinct proportion of the anxiety experiences that did not seem to be 'Parkinson's specific', but which were nevertheless, consistent with CBT for anxiety. The Egan et al. model is grounded in second wave CBT. Consistent with this, our findings suggest that for a proportion of experiences of anxiety in PWP, formulation within second wave CBT approaches for anxiety would be appropriate.

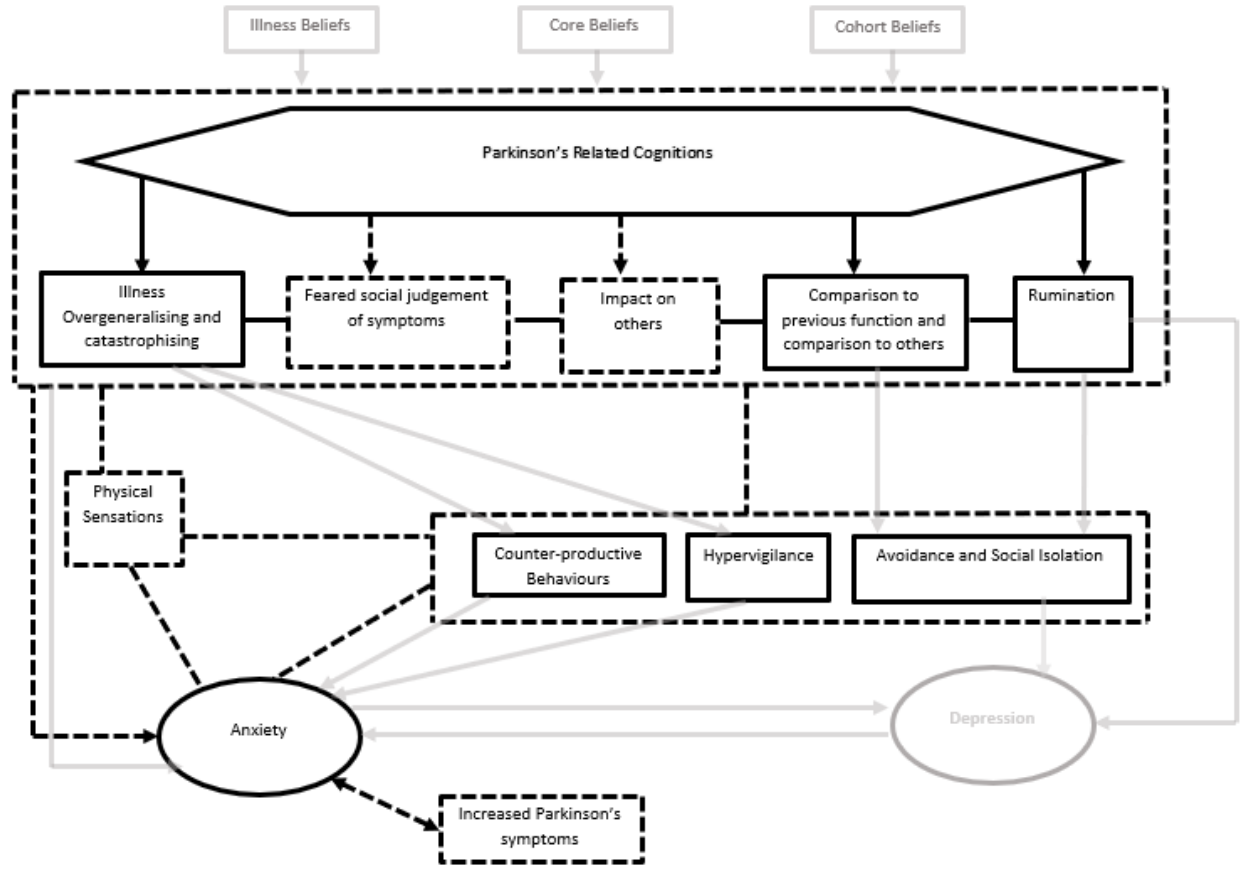
'Parkinson's related cognitions' have a central role in the Egan et al. (2015) model. It proposes that anxiety is associated in particular with 'illness overgeneralising and catastrophising.' Our results support this, but suggest that additional Parkinson's related cognitions are also present. Firstly, while Egan et al. (2015) suggest 'rumination' and 'comparison to previous function and comparison to others' contribute to depression, our findings suggest they are also a feature of the anxiety experience. Our study also identifies two further types of Parkinson's related

cognitions, namely 'feared social judgement of symptoms' (e.g. 'I worry how others will perceive my Parkinson's symptoms and that they will judge me negatively) and 'feared impact on others' (e.g. 'I worry about upsetting those close to me and making things difficult for them').

Behavioural responses to anxiety are a key part of the Egan et al. model and in particular, 'Counter-productive behaviours' (safety behaviours) and 'hypervigilance' as factors maintaining anxiety in PWP. The presence of these behavioural responses is supported by our findings. Further, our findings suggest that 'avoidance and social isolation', a factor which the existing model links to depression, can also form part of the anxiety experience.

The physical sensations associated with the anxiety experience are not addressed in the Egan et al. model. Our current findings suggest that these are a significant part of the anxiety experience in this population. The physical symptoms reported, whilst common across anxiety, are notable in that many could also be Parkinsonian in nature. For example, increased fatigue, sweating, muscle tension and urinary and faecal urgency are also known symptoms of Parkinson's (Chaudhuri et al., 2005).

Finally, the Egan et al. model places an emphasis on the way that Parkinsonian symptoms and an individual's cognitive and behavioural responses to them contribute to the anxiety experience. The findings of our study highlight that for many people in this population, the experience of anxiety can additionally contribute to an exacerbation of other Parkinsonian symptoms (e.g. 'anxiety has made my Parkinson symptom's worse'). This is not currently captured by the Egan et al. model.



Greyed out = Part of existing model, but unable to comment on these areas as not addressed by this study.

= Part of the existing model that is supported by the present study.

= Added to the model following based on the present study.

Figure 1. A visual representation of the theoretical implications of the current study with respect to the Egan et al. (2015) augmented CBT model of depression and anxiety in Parkinson's.

Clinical Implications

The systematic review brings the significance of the relationship between anxiety and QOL to the fore. As well as consistently highlighting a strong relationship between the two constructs it demonstrates that anxiety was frequently among the variables predicting the greatest, and sometimes unique, variance in QOL. Crucially, the relationship between anxiety and QOL appears comparable to other long-term health conditions (Mosaku, Kolawole, Mume, & Ikem, 2008) where patients have greater access to psychological interventions than PwP do (Clarke, Furmaniak, & Pilling, 2018). Given that untreated mental health in physical health

patients is associated with significant detriment to the patient and the healthcare system (Naylor et al., 2012), it is important that this review was conducted.

The existing evidence base for the use of psychological therapy for anxiety in PwP is in its infancy. With an unpublished randomised control trial (RCT) for Cognitive Behavioural Therapy (CBT) underway in this population (Mulders et al., 2018), the evidence is currently limited to case studies, pilots studies and single case experimental designs (Calleo et al., 2015; Dissanayaka et al., 2017; Feeney, Egan, & Gasson, 2005; Kraepelien, Svenningsson, Lindefors, & Kaldo, 2015; Mohlman et al., 2010; Troeung, Egan, & Gasson, 2014). This empirical project demonstrates that some of the participant population experience some similar anxiety experiences to people without Parkinson's. This may offer some promise that some components of existing mainstream CBT formulation and practices may be applicable to PwP.

The findings also invite reflection on the degree of specialist knowledge of Parkinson's symptoms that may be required by psychological therapists in order to effectively treat anxiety co-occurring in this disease. Further, this study highlighted that anxiety symptoms can be triggered by other Parkinson's symptoms. Therefore, the indirect role that optimal control of other Parkinson's symptoms (e.g. by optimising medications) might have on anxiety, should be considered. Additionally, it may be possible to draw on existing research into managing anxiety in chronic disease. For example, managing the anxieties of adjusting to a diagnosis or about the feared progression of disease (De Ridder, Geenan, Kuijer, & van Middendorp, 2008; Herschbach et al., 2010).

The empirical project also highlights that, for PwP, people close to them are regularly implicated in their anxiety experience. Research exploring psychological therapy that incorporates PwP as well as their wider support network has indicated that this more systemic approach can bring benefit to PwP and those around them (Dissanayaka et al., 2017). It is hoped that the present study further presents the potential benefit to be gained from incorporating the system around the individual into onward assessment, formation and intervention.

Areas for Future Development

The strong association found between anxiety and quality of life for PwP, provides some support for the existing notion that researchers and clinicians should

place greater emphasis on seeking to improve the assessment, conceptualisation and intervention for anxiety in Parkinson's. The findings in the empirical project have provided a useful foundation regarding the unique character of anxiety is Parkinson's. It is hoped that other research will build on these findings. It would be interesting to better characterise methods used by PwP to manage their anxiety and then rank their efficacy and acceptability. This would inform the design of therapeutic packages which might be wider than a singular intervention.

This research provides the first two surveys of a programme of research designed to better conceptualise the anxiety experience of PwP. The next stage, which is already underway, is to use exploratory factor analysis of the data collected to develop a psychometric scale that captures the anxiety experience of PwP. The only existing anxiety measure for PwP, is the Parkinson's Anxiety Scale (PAS) (Leentjens et al., 2014). The PAS is limited to 12 items across the domains of persistent anxiety, episodic anxiety and avoidance behaviours. Given the range of anxiety experiences identified in this empirical project, and the large number of themes that fall outside of the persistent, episodic and avoidance categories, the generation of our new anxiety scale from a rich data set should be a valuable additional resource.

In acknowledgment of the fact that neither Parkinson's or anxiety are experienced uniformly by every individual, the data we have collected will then be analysed to establish whether the anxiety experience changes according to variables associated with Parkinsonian presentation. Initially, this will be achieved by comparing PAS anxiety scores among different subgroups (e.g. time since diagnosis, Parkinson's phenotype) of Parkinsonian presentation. Then, Structural Equation Modelling (SEM) will be used to model the associations between the ranked anxiety items described in this study – allowing us to test the hypothesis that the model changes according to Parkinsonian presentation.

Having then developed a more comprehensive characterisation and assessment of Parkinsonian anxiety, ultimately the research team aim to use this to inform the development of a psychological intervention for anxiety in PwP. It is important to acknowledge however, that there is currently significant distance between the findings of the current study and the actual implementation of any tangible changes to future clinical practice. It is well documented that translating

research findings to changes to healthcare practice is a challenging process, especially if the changes are complex or require re-organisation of care or better collaborations between disciplines (Wensing, Grol, & Grimshaw, 2020). If this "evidence to practice gap" (Woolf, 2008) is to be bridged, it is important to reflect on the challenges. A framework of these challenges (Wensing et al., 2020), will now be discussed.

The first factor identified is the credibility of the proposed changes themselves. We recognise therefore, that the current findings are in their infancy. There is significant scope for extending the findings further. This may include validation of the model, development of a related intervention, a feasibility randomised control trial (RCT) and if appropriate, a full RCT. It is likely that this more extensive body of research would hold more credibility and likelihood of translation into clinical practice.

The attitudes, opinions and values of the targeted professionals and 'opinion leaders' is another of the identified factors. With this in mind it would be useful to consult these professionals throughout the process of developing changes. In this field, it would be particularly useful to liaise with opinion leaders such as the recently established Parkinson's UK Excellence Network Mental Health Hub, a group comprised of expert researchers and clinicians with the aim of developing best practice. It is important to ensure professionals see the value in identifying the "additional" complexity of anxiety identified by this project. If they see it as an additional burden of learning without value then it is unlikely to be implemented.

Another important factor to consider is the needs, attitudes and preferences of the patient group. Given that these elements are intrinsically embedded within this project, there is hope that this will facilitate the translation process. The economic and organisational context in which the translation sits is also a consideration. It is well established that the National Health Service can be a challenging environment for the adoption of innovation and change (Department of Health and Social Care, 2016). Looking to examples of where such translations have successfully occurred with health psychology in the NHS may provide useful direction.

Finally, the methods and strategies for dissemination and implementation are considered important. It is hoped that widespread dissemination of our findings not

only though peer reviewed articles and international movement disorders conferences but also in lay reports for members of Parkinson's UK and in distribution to the Parkinson's UK Excellence Network Mental Health Hub will support this. Providing appropriate training in the delivery of the intervention is also important.

Reflections on the Process of Completing the Thesis Portfolio

My primary reflection is on the extent to which I believe the project benefitted from the PPI involvement. From the outset of the involvement of the two PPI volunteers (BC and JM), my motivation for the project increased significantly. Listening to first-hand accounts of their experiences and their reasons why the project had potential to add significant value was powerful. It gave me an increased sense of the project's value and the importance of maximising its potential. In terms of their direct contribution, their recommendations for making the participant facing content more user friendly was vital. Whilst this took a number of iterations, the benefits to accessibility were notable. It was particularly pleasing to receive a letter of praise from a participant regarding the clarity of our first survey compared to his previous experiences as a research participant. The PPI expertise added to an already wide range of expertise of colleagues in the steering group; KD (researcher with over 20 years expertise in Parkinson's as well as a disabled person and wheelchair user with experience of a functional movement disorder), CF (Clinical Psychologist), CIC (CBT Therapist). I valued this range of perspectives hugely.

The recruitment of large participant numbers from across the UK added significant value to the empirical project. Given that participants were required to have a diagnosis of Parkinson's and have experienced anxiety to an extent that impacts quality of life, there was the potential for recruitment to be a challenge. Fundamental to successful recruitment was the support of Parkinson's UK. This taught me the value of maintaining good relationships with key gatekeepers, in this case the Research Participation Lead at Parkinson's UK.

Overall Conclusions

Anxiety occurs at a high rate in people with Parkinson's. The systematic review showed that there is a strong correlation between anxiety and QOL. In fact, anxiety consistently predicts significant, and sometimes unique variance in QOL.

Despite this high negative impact there is little existing evidence for interventions for anxiety in PwP.

The empirical project better characterised the nature of anxiety in PwP. This showed that there were aspects of their anxiety experiences that were akin to anxiety in the general population. However, there were a substantial set of characteristics that were specific to Parkinson's or had the potential to be aggravated by Parkinsonian symptoms. This suggests that, whilst some mainstream anxiety interventions may also be effective for PwP, researchers and therapists are likely to need knowledge of Parkinson's-specific context in order to develop and deliver relevant and holistic assessments and therapeutic interventions.

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Appendices

Appendix A: Symptoms of Parkinson's

Adapted from Jankovic, (2008) and Chaudhuri, Yates and Martinez-Martin, (2005).

Motor Symptoms	**Non-Motor Symptoms**
Tremor (shaking)	**Cognitive**
Bradykinesia (slowness of movement)	Cognitive impairment
Rigidity (muscle stiffness)	Bradyphrenia (slowness of thought, slower information processing)
Postural instability (difficulty maintaining balance)	Word finding difficulties
Hypomimia (Reduced facial expression)	Attention deficit
Dysarthria (speech difficulty)	**Neuropsychiatric**
Dysphagia (difficulty swallowing)	Depression
Sialorrhea (excessive salivation or drooling)	Apathy
Decreased arm swing	Anxiety
Shuffling gait	Anhedonia (reduced motivation pleasure)
Altered gait	Hallucinations
Difficulty rising from chair or turning in bed	Delusions
Micrographia (abnormally small handwriting)	Dementia
Difficulty cutting food	Repetitive behaviour
Difficulty eating	Confusion
Difficulty maintaining hygiene	Delirium (could be drug induced)
Slow activities of daily living	Obsessional behaviour (usually drug induced)
Glabellar reflex (limited inhibition of blink reflex)	**Sensory**
Blepharospasm (twitch of the eye lid)	Ageusia (taste disturbance/loss)
Dystonia (muscle spasms and contractions)	Pain (shoulder, back)
Striatal deformity (abnormal postures of hands/feet)	Paraesthesia (tingling sensation)
Scoliosis (twisting of the spine)	Smell disturbance/loss
Camptocormia (forward bending of the spine)	**Autonomic Nervous System**
	Constipation
	Bladder disturbance
	Urinary and sexual dysfunction
	Abnormal sweating
	Seborrhoea (excessive secretion of sebum)

	Weight loss
	Dry eyes
	Orthostatic hypotension (falling blood pressure when standing or sitting)
	Falls related to orthostatic hypotension
	Coat hanger pain (neck and shoulder) related to orthostatic hypotension
	Hypersexuality (likely to be drug induced)
	Sleep Disorders
	Insomnia
	REM behaviour disorder
	Non-REM-sleep related movement disorders
	Vivid dreams
	Daytime drowsiness
	Sleep fragmentation
	Restless legs syndrome
	Sleep disordered breathing
	Gastrointestinal Symptoms (overlap with Autonomic Symptoms)
	Dribbling of saliva
	Ageusia (loss of taste)
	Dysphagia (choking)
	Difficulty swallowing
	Reflux
	Vomiting
	Nausea
	Constipation
	Unsatisfactory voiding of bowel
	Faecal incontinence
	Other
	Fatigue
	Diplopia
	Blurred vision
	Weight loss
	Weight gain (possibly drug induced)

Appendix B: Movement Disorder Journal Author Guidelines

Author Guidelines

Editorial Office Information

A. Jon Stoessl, CM, MD, FRCPC, FCAHS
Editor-in-Chief
University of British Columbia
Vancouver, British Columbia, Canada
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Submission of MDS commissioned articles.

Prior to writing for a Task Force, Evidence Based Medicine (EBM) Reviews Guidelines, etc, the Chief Editor of *Movement Disorders(MD)* must be advised of the intent by the chair of the Task Force, EMB and PG groups. If the topic is agreed to be appropriate for MD, the task force may submit the final manuscript for peer review and editor decision regarding publication. If the topic is deemed to be better suited for Movement Disorders Clinical Practice (MDCP), this will be transmitted to author and chairperson.

The final manuscript needs to conform to the following criteria:

1. ***Quality of manuscript***- The manuscript must be clearly written, thinking in the readership and scientific community, to be published in the printed version. For figure/table limits, please see the "Scope" section, as the limit will depend on the type of manuscript you submit. Additional data may be presented as supplemental data available online.

2. ***Length***- *7000 words* maximum.

3. ***Authors***- The first 8 will be shown in the top page after the article. All other involved authors will be listed as part of the Study Task Force/Group, etc.

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3) Submission of work from other sources that was not done by the author and is presented as a new and original (plagiarism);
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Give a brief description of the background and relevance of the scientific contribution.

(4) Methods

Describe the methodology of the study. For experimental investigation of human or animal subjects, please state in this section that an appropriate institutional review board approved the project. For those investigators who do not have formal ethics review committees, the principles outlined in the “Declaration of Helsinki” should be followed. For investigations in human subjects, state in this section the manner in which informed consent was obtained from the subjects. A letter of consent must accompany all photographs, patient descriptions, and pedigrees in which a possibility of identification exists. The authors are responsible for ensuring anonymity.

(5) Results

No specific regulations.

(6) Discussion

No specific regulations.

(7) Acknowledgment

No specific regulations. These may be published on line at the discretion of the editor.

(8) Authors' Roles

List all authors along with their specific roles in the project and preparation of the manuscript.

These may include but are not restricted to:

1) Research project: A. Conception, B. Organization, C. Execution;

2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique;

3) Manuscript: A. Writing of the first draft, B. Review and Critique.

(9) Financial Disclosures of all authors (for the preceding 12 months)

Full Financial Disclosures of all Authors for the Past Year: Information concerning all sources of financial support and funding for the preceding twelve months, regardless of relationship to current manuscript, must be submitted with the following categories suggested.

List sources or “none”.

Stock Ownership in medically-related fields

Intellectual Property Rights

Consultancies

Expert Testimony

Advisory Boards

Employment

Partnerships

Contracts

Honoraria

Royalties

Grants

Other

(10) References

See "Details of Style" below for the proper formatting of citations and References.

(11) Video Legend

No specific regulations but should be concise and reflect the sequence of observations on the video

(12) Figures

Figures and Illustrations: Adapt any figures to an appropriate size of art and letters to make them readable in the printed version. Illustrations in full color are accepted at additional charge from the publisher. In the case of review articles or in special circumstances, color articles may be included at no charge with the permission of the Chief Editor. Any illustration or figure from another publication must be acknowledged in the figure legend, and the copyright holder's written permission to reprint in print and online edition of *Movement* Disorders must be submitted to the editors.

In addition, figures to illustrate concepts are welcome particularly in review articles, and may be enhanced by a professional artist at no cost to author at the discretion of the Editors.

(13) Tables

Tables should be typed neatly, each on a separate page, with a title above and any notes below. Explain all abbreviations. Do not repeat the same information in tables and figures that is present in text. Tables and figures should be uploaded as individual files and not part of the manuscript text. (You do not need to mail hard copies of your manuscript).

***Tables and Figure Legends**

Double-space legends of fewer than 40 words for tables and figures. For photomicrographs, include the type of specimen, original magnification, and stain type. Include internal scale-markers on photomicrographs when appropriate. Where applicable, indicate the method used to digitally enhance images.

Copyright and Disclosure Forms

The corresponding author should upload one PDF file that includes copyright and disclosure forms for all authors to the Movement Disorders submission site with the revised version of the paper. These forms also can be emailed to mdjedoffice@movementdisorders.org.

Digital Artwork Preparation

For best reproduction, electronic artwork files must be in TIFF or EPS format, at a resolution of 600 dpi or higher, sized to print. *Movement* Disorders offers Rapid Inspector™ to help ensure that your electronic graphics files are suitable for print purposes. This free, stand-alone software application will help you to inspect and verify illustrations right on your computer. Go to http://rapidinspector.cadmus.com/wi/index.jsp and create a new account. JPG files are of low resolution and will not be acceptable for publication.

Details of Style

No patient identifiers (e.g., patient initials) are to be included in the manuscript or video (e.g., case reports, tables, figures, etc.).

Units of measure: Conventional units of measure according to the Systeme International (SI) are preferred. The metric system is preferred for length, area, mass, and volume. Express temperature in degrees Celsius.

Drug Names: Use generic names only in referring to drugs, followed in parentheses after first mention by any commonly used generic variant.

Abbreviations: Follow the list of abbreviations given in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (see section on References). For additional abbreviations, consult the CBE Style Manual (available from the Council of Biology Editors, 9650 Rockville Pike, Bethesda, Maryland 20814, USA) or other standard sources. We encourage authors to minimize the use of abbreviations except where they are routinely employed and the full term would be cumbersome (eg MPTP).

Spelling: American spelling is used throughout the Journal.

References *Movement* Disorders complies with the reference style given in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals". (See Annals of Internal Medicine 1982;96:766-771, or British Medical Journal 1982:284:1766-1770.) References are to be cited in the text by number, and in the list of References they are to be numbered in the order in which they are cited.

The reference section should be double-spaced at the end of the text, following the sample formats given below.

Provide all authors' names when fewer than seven; when seven or more, list the first three and add et al.

Provide article titles and inclusive pages.

Accuracy of reference data is the responsibility of the author.

For abbreviations of journal names, refer to List of Journals Indexed in Index Medicus (available from the Superintendent of Documents, U.S. Government Printing Office, Washington DC 20402, USA, DHEW Publication No. (NIH) 83-267; ISSN 0093-3821).

Sample References

• Journal article: 1. Krack P, Benzzzouz A, Pollak P, et al. Treatment of tremor in Parkinson’s disease by Subthalamic nucleus stiumulation. Mov Disord 1998; 13: 907-914.

• Book: 2.Fahn S, Jankovic J, editors. Principles and Practice of Movement Disorders, Philadelphia, Churchill Livingstone, 2010, pp 96.

• Chapter in a book: 3. Olanow CW. Hpyerkinetic Movement Disorders. In: Fauci A, Braunwald E, Kasper D, Hauser S, Longo D, Jameson JL, Loscalzo J. Eds. Harrison’s Textbook of Medicine 17th edition. 2008; p2560-2565.

Accepted Articles:

Materials Required for Publication

After acceptance, please check to be sure that you have submitted your signed copyright transfer and author consent form as well as permissions forms (if applicable).

Authors using images of their patients, whether in artwork or video format, must submit a copy (signed by the corresponding author) of the copyright transfer and author consent form. A sample form is available to authors on Manuscript Central.

Proofs

Proofs must be returned within two days of receipt; late return may cause a delay in publication of an article.

Please check text, tables, legends, and references carefully. To expedite publication, page proofs rather than galleys will be sent electronically to the author, and it may be necessary to charge for alterations other than correction of printing errors.

E-mail proof pages to: MDS Production Editor, Movement Disorders. E-mail: mdsprod@wiley.com.

For Video Clips or Pictures of Patients (U.S. Contributors Only)

The United States Health Insurance Portability and Accountability Act of 1996 ("HIPAA") According to HIPAA, the following core elements must be included in the consent form:

1. A specific and meaningful description of the information to be used

2. The name of the Physician and/or Hospital allowed to disclose the information

3. That the video clip and/or photograph will be submitted for publication in a peer-reviewed medical journal

4. That the video clip and/or photograph will eventually be used by the readers of a peer-reviewed medical journal for educational purposes

5. An expiration date that relates to the individual or the purpose of the use or disclosure

6. The individual's signature and the date the authorization is signed.

In addition, the patient's consent form should include the following:

1. A statement that the Patient has the right to revoke his or her consent in writing

2. A statement regarding whether the Physician has the ability to condition medical treatment on the Patient's giving such consent

3. A statement that information, once disclosed, may be subject to further disclosure by the recipient journal, in which case confidentiality would no longer be assured. The consenting party must understand, additionally, that in some cases the video might be re-presented elsewhere because the journal has policies that allow permissions and/or use copyrighted materials with other educational organizations. The consenting party must understand that in such a case the signed author's consent form may be shared with this third party and the consenting party consents to this sharing of information for educational purposes.

Reporting Guidelines

Data reporting should follow appropriate checklists and guidelines (e.g., STROBE for observational trials; CONSORT for clinical trials), and other checklists should be consulted for other reports including diagnostic accuracy (STARD) or meta-analyses (PRISMA).

Additional guidance on checklists and guidelines can be found here: **http://www.equator-network.org/**

Checklists can be downloaded from the following:

STROBE: **http://strobe-statement.org**

CONSORT: **http://www.consort-statement.org/consortstatement/**

STARD: **http://www.stard-statement.org/**

PRISMA: **http://www.prisma-statement.org/**

OnlineOpen

OnlineOpen is available to authors of primary research articles who wish to make their article available to non-subscribers on publication, or whose funding agency requires grantees to archive the final version of their article.

With OnlineOpen, the author, the author's funding agency, or the author's institution pays a fee to ensure that the article is made available to non-subscribers upon publication via Wiley Online Library, as well as deposited in the funding agency's preferred archive. For the full list of terms and conditions, see http://wileyonlinelibrary.com/onlineopen#OnlineOpen_Terms.

Any authors wishing to send their paper OnlineOpen will be required to complete the payment form available from our website at: https://onlinelibrary.wiley.com/onlineOpenOrder. Prior to acceptance there is no requirement to inform an Editorial Office that you intend to publish your paper OnlineOpen if you do not wish to.

All OnlineOpen articles are treated in the same way as any other article. They go through the journal's standard peer-review process and will be accepted or rejected based on their own merit.

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All figures accepted in color will be reproduced in full color in the online edition of the journal at no cost to authors. Authors are required to pay the cost of reproducing color figures in print unless color charges are waived by the editors. The charge for printing figures in color is $700 per figure. Color agreement forms will be sent in conjunction with the PDF proofs.

Authors are not required to pay for printed pages, except in the cases of errata. For errata due to publisher error, there is no page charge. For errata due to author error, the charge to the author is $150 per printed page.

Appendix C: Details of Systematic Review Searches

Database	Search term 1	And/or	Search term 2	And/or	Search term 3	And/or	Search term 4
CINAHL	MJ Parkinson Disease	And	MJ Quality of life	And	TX stress	Or	TX anxiety
MEDLINE	MeSH Parkinson's Disease	And	MeSH Quality of life	And	TX stress	Or	TX anxiety
PsycINFO	MA Parkinson's Disease	And	MA Quality of life	And	TX stress	Or	TX anxiety

Note. MJ = Word in Major Subject Heading, MESH = Medical Subject Headings (MeSH), MA = MeSH Subject Headings, TX = All text.

Appendix D: National Heart, Lung and Blood Institute Quality Assessment Tool for Observational, Cohort and Cross-Sectional Studies.

NIH NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Study Quality Assessment Tools

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			

Criteria	Yes	No	Other (CD, NR, NA)*
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			

Criteria	Yes	No	Other (CD, NR, NA)*
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

The guidance document below is organized by question number from the tool for quality assessment of observational cohort and cross-sectional studies.

Question 1. Research question

Did the authors describe their goal in conducting this research? Is it easy to understand what they were looking to find? This issue is important for any scientific paper of any type. Higher quality scientific research explicitly defines a research question.

Questions 2 and 3. Study population

Did the authors describe the group of people from which the study participants were selected or recruited, using demographics, location, and time period? If you were to conduct this study again, would you know who to recruit, from where, and from what time period? Is the cohort population free of the outcomes of interest at the time they were recruited?

An example would be men over 40 years old with type 2 diabetes who began seeking medical care at Phoenix Good Samaritan Hospital between January 1, 1990 and December 31, 1994. In this example, the population is clearly described as: (1) who (men over 40 years old with type 2 diabetes); (2) where (Phoenix Good Samaritan Hospital); and (3) when (between January 1, 1990 and December 31, 1994). Another

example is women ages 34 to 59 years of age in 1980 who were in the nursing profession and had no known coronary disease, stroke, cancer, hypercholesterolemia, or diabetes, and were recruited from the 11 most populous States, with contact information obtained from State nursing boards.

In cohort studies, it is crucial that the population at baseline is free of the outcome of interest. For example, the nurses' population above would be an appropriate group in which to study incident coronary disease. This information is usually found either in descriptions of population recruitment, definitions of variables, or inclusion/exclusion criteria.

You may need to look at prior papers on methods in order to make the assessment for this question. Those papers are usually in the reference list.

If fewer than 50% of eligible persons participated in the study, then there is concern that the study population does not adequately represent the target population. This increases the risk of bias.

Question 4. Groups recruited from the same population and uniform eligibility criteria

Were the inclusion and exclusion criteria developed prior to recruitment or selection of the study population? Were the same underlying criteria used for all of the subjects involved? This issue is related to the description of the study population, above, and you may find the information for both of these questions in the same section of the paper.

Most cohort studies begin with the selection of the cohort; participants in this cohort are then measured or evaluated to determine their exposure status. However, some cohort studies may recruit or select exposed participants in a different time or place than unexposed participants, especially retrospective cohort studies–which is when data are obtained from the past (retrospectively), but the analysis examines exposures prior to outcomes. For example, one research question could be whether diabetic men with clinical depression are at higher risk for cardiovascular disease than those without clinical depression. So, diabetic men with depression might be selected from a mental health clinic, while diabetic men without depression might be selected from an internal medicine or endocrinology clinic. This study recruits groups from different clinic populations, so this example would get a "no."

However, the women nurses described in the question above were selected based on the same inclusion/exclusion criteria, so that example would get a "yes."

Question 5. Sample size justification

Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Do they note or discuss the statistical power of the study? This question is about whether or not the study had enough participants to detect an association if one truly existed.

A paragraph in the methods section of the article may explain the sample size needed to detect a hypothesized difference in outcomes. You may also find a discussion of power in the discussion section (such as the study had 85 percent power to detect a 20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05). Sometimes estimates of variance and/or estimates of effect size are given, instead of sample size calculations. In any of these cases, the answer would be "yes."

However, observational cohort studies often do not report anything about power or sample sizes because the analyses are exploratory in nature. In this case, the answer would be "no." This is not a "fatal flaw." It just may indicate that attention was not paid to whether the study was sufficiently sized to answer a prespecified question– i.e., it may have been an exploratory, hypothesis-generating study.

Question 6. Exposure assessed prior to outcome measurement

This question is important because, in order to determine whether an exposure causes an outcome, the exposure must come before the outcome.

For some prospective cohort studies, the investigator enrolls the cohort and then determines the exposure status of various members of the cohort (large epidemiological studies like Framingham used this approach). However, for other cohort studies, the cohort is selected based on its exposure status, as in the example above of depressed diabetic men (the exposure being depression). Other examples include a cohort identified by its exposure to fluoridated drinking water and then compared to a cohort living in an area without fluoridated water, or a cohort of military personnel exposed to combat in the Gulf War compared to a cohort of military personnel not deployed in a combat zone.

With either of these types of cohort studies, the cohort is followed forward in time (i.e., prospectively) to assess the outcomes that occurred in the exposed members compared to nonexposed members of the cohort. Therefore, you begin the study in the present by looking at groups that were exposed (or not) to some biological or behavioral factor, intervention, etc., and then you follow them forward in time to examine outcomes. If a cohort study is conducted properly, the answer to this question should be "yes," since the exposure status of members of the cohort was determined at the beginning of the study before the outcomes occurred.

For retrospective cohort studies, the same principal applies. The difference is that, rather than identifying a cohort in the present and following them forward in time, the investigators go back in time (i.e., retrospectively) and select a cohort based on their exposure status in the past and then follow them forward to assess the outcomes that occurred in the exposed and nonexposed cohort members. Because in retrospective cohort studies the exposure and outcomes may have already occurred (it depends on how long they follow the cohort), it is important to make sure that the exposure preceded the outcome.

Sometimes cross-sectional studies are conducted (or cross-sectional analyses of cohort-study data), where the exposures and outcomes are measured during the same timeframe. As a result, cross-sectional analyses provide weaker evidence than

regular cohort studies regarding a potential causal relationship between exposures and outcomes. For cross-sectional analyses, the answer to Question 6 should be "no."

Question 7. Sufficient timeframe to see an effect

Did the study allow enough time for a sufficient number of outcomes to occur or be observed, or enough time for an exposure to have a biological effect on an outcome? In the examples given above, if clinical depression has a biological effect on increasing risk for CVD, such an effect may take years. In the other example, if higher dietary sodium increases BP, a short timeframe may be sufficient to assess its association with BP, but a longer timeframe would be needed to examine its association with heart attacks.

The issue of timeframe is important to enable meaningful analysis of the relationships between exposures and outcomes to be conducted. This often requires at least several years, especially when looking at health outcomes, but it depends on the research question and outcomes being examined.

Cross-sectional analyses allow no time to see an effect, since the exposures and outcomes are assessed at the same time, so those would get a "no" response.

Question 8. Different levels of the exposure of interest

If the exposure can be defined as a range (examples: drug dosage, amount of physical activity, amount of sodium consumed), were multiple categories of that exposure assessed? (for example, for drugs: not on the medication, on a low dose, medium dose, high dose; for dietary sodium, higher than average U.S. consumption, lower than recommended consumption, between the two). Sometimes discrete categories of exposure are not used, but instead exposures are measured as continuous variables (for example, mg/day of dietary sodium or BP values).

In any case, studying different levels of exposure (where possible) enables investigators to assess trends or dose-response relationships between exposures and outcomes–e.g., the higher the exposure, the greater the rate of the health outcome. The presence of trends or dose-response relationships lends credibility to the hypothesis of causality between exposure and outcome.

For some exposures, however, this question may not be applicable (e.g., the exposure may be a dichotomous variable like living in a rural setting versus an urban setting, or vaccinated/not vaccinated with a one-time vaccine). If there are only two possible exposures (yes/no), then this question should be given an "NA," and it should not count negatively towards the quality rating.

Question 9. Exposure measures and assessment

Were the exposure measures defined in detail? Were the tools or methods used to measure exposure accurate and reliable–for example, have they been validated or are they objective? This issue is important as it influences confidence in the reported exposures. When exposures are measured with less accuracy or validity, it is harder to see an association between exposure and outcome even if one exists. Also as

important is whether the exposures were assessed in the same manner within groups and between groups; if not, bias may result.

For example, retrospective self-report of dietary salt intake is not as valid and reliable as prospectively using a standardized dietary log plus testing participants' urine for sodium content. Another example is measurement of BP, where there may be quite a difference between usual care, where clinicians measure BP however it is done in their practice setting (which can vary considerably), and use of trained BP assessors using standardized equipment (e.g., the same BP device which has been tested and calibrated) and a standardized protocol (e.g., patient is seated for 5 minutes with feet flat on the floor, BP is taken twice in each arm, and all four measurements are averaged). In each of these cases, the former would get a "no" and the latter a "yes."

Here is a final example that illustrates the point about why it is important to assess exposures consistently across all groups: If people with higher BP (exposed cohort) are seen by their providers more frequently than those without elevated BP (nonexposed group), it also increases the chances of detecting and documenting changes in health outcomes, including CVD-related events. Therefore, it may lead to the conclusion that higher BP leads to more CVD events. This may be true, but it could also be due to the fact that the subjects with higher BP were seen more often; thus, more CVD-related events were detected and documented simply because they had more encounters with the health care system. Thus, it could bias the results and lead to an erroneous conclusion.

Question 10. Repeated exposure assessment

Was the exposure for each person measured more than once during the course of the study period? Multiple measurements with the same result increase our confidence that the exposure status was correctly classified. Also, multiple measurements enable investigators to look at changes in exposure over time, for example, people who ate high dietary sodium throughout the followup period, compared to those who started out high then reduced their intake, compared to those who ate low sodium throughout. Once again, this may not be applicable in all cases. In many older studies, exposure was measured only at baseline. However, multiple exposure measurements do result in a stronger study design.

Question 11. Outcome measures

Were the outcomes defined in detail? Were the tools or methods for measuring outcomes accurate and reliable–for example, have they been validated or are they objective? This issue is important because it influences confidence in the validity of study results. Also important is whether the outcomes were assessed in the same manner within groups and between groups.

An example of an outcome measure that is objective, accurate, and reliable is death–the outcome measured with more accuracy than any other. But even with a measure as objective as death, there can be differences in the accuracy and reliability of how death was assessed by the investigators. Did they base it on an autopsy report, death certificate, death registry, or report from a family member? Another example is a

study of whether dietary fat intake is related to blood cholesterol level (cholesterol level being the outcome), and the cholesterol level is measured from fasting blood samples that are all sent to the same laboratory. These examples would get a "yes." An example of a "no" would be self-report by subjects that they had a heart attack, or self-report of how much they weigh (if body weight is the outcome of interest).

Similar to the example in Question 9, results may be biased if one group (e.g., people with high BP) is seen more frequently than another group (people with normal BP) because more frequent encounters with the health care system increases the chances of outcomes being detected and documented.

Question 12. Blinding of outcome assessors

Blinding means that outcome assessors did not know whether the participant was exposed or unexposed. It is also sometimes called "masking." The objective is to look for evidence in the article that the person(s) assessing the outcome(s) for the study (for example, examining medical records to determine the outcomes that occurred in the exposed and comparison groups) is masked to the exposure status of the participant. Sometimes the person measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome assessor would most likely not be blinded to exposure status because they also took measurements of exposures. If so, make a note of that in the comments section.

As you assess this criterion, think about whether it is likely that the person(s) doing the outcome assessment would know (or be able to figure out) the exposure status of the study participants. If the answer is no, then blinding is adequate. An example of adequate blinding of the outcome assessors is to create a separate committee, whose members were not involved in the care of the patient and had no information about the study participants' exposure status. The committee would then be provided with copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information. The committee would then review the records for prespecified outcomes according to the study protocol. If blinding was not possible, which is sometimes the case, mark "NA" and explain the potential for bias.

Question 13. Followup rate

Higher overall followup rates are always better than lower followup rates, even though higher rates are expected in shorter studies, whereas lower overall followup rates are often seen in studies of longer duration. Usually, an acceptable overall followup rate is considered 80 percent or more of participants whose exposures were measured at baseline. However, this is just a general guideline. For example, a 6-month cohort study examining the relationship between dietary sodium intake and BP level may have over 90 percent followup, but a 20-year cohort study examining effects of sodium intake on stroke may have only a 65 percent followup rate.

Question 14. Statistical analyses

Were key potential confounding variables measured and adjusted for, such as by statistical adjustment for baseline differences? Logistic regression or other regression methods are often used to account for the influence of variables not of interest.

This is a key issue in cohort studies, because statistical analyses need to control for potential confounders, in contrast to an RCT, where the randomization process controls for potential confounders. All key factors that may be associated both with the exposure of interest and the outcome–that are not of interest to the research question–should be controlled for in the analyses.

For example, in a study of the relationship between cardiorespiratory fitness and CVD events (heart attacks and strokes), the study should control for age, BP, blood cholesterol, and body weight, because all of these factors are associated both with low fitness and with CVD events. Well-done cohort studies control for multiple potential confounders.

Some general guidance for determining the overall quality rating of observational cohort and cross-sectional studies

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of quality.

Internal validity for cohort studies is the extent to which the results reported in the study can truly be attributed to the exposure being evaluated and not to flaws in the design or conduct of the study–in other words, the ability of the study to draw associative conclusions about the effects of the exposures being studied on outcomes. Any such flaws can increase the risk of bias.

Critical appraisal involves considering the risk of potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues throughout the questions above. High risk of bias translates to a rating of poor quality. Low risk of bias translates to a rating of good quality. (Thus, the greater the risk of bias, the lower the quality rating of the study.)

In addition, the more attention in the study design to issues that can help determine whether there is a causal relationship between the exposure and outcome, the higher quality the study. These include exposures occurring prior to outcomes, evaluation of a dose-response gradient, accuracy of measurement of both exposure and outcome, sufficient timeframe to see an effect, and appropriate control for confounding–all concepts reflected in the tool.

Generally, when you evaluate a study, you will not see a "fatal flaw," but you will find some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no" you should ask, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, does this factor cause you to doubt the results that are reported

in the study or doubt the ability of the study to accurately assess an association between exposure and outcome?

The best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal. Examples of studies rated good, fair, and poor are useful, but each study must be assessed on its own based on the details that are reported and consideration of the concepts for minimizing bias.

Appendix E: Quality Ratings

Principle Author (DC) Quality Ratings:

Article	Population clearly defined	Participation rate at least 50%	Subject recruited from same or similar populations. Were inclusion and exclusion criteria pre specified and applied uniformly to all participants?	Was sample size justification, power description, or variance and effect estimates provided.	Were measures clearly defined, valid, reliable and implemented consistently across all study participants?	Notes
Chrischilles et al., 2002	*					*Limited detail on recruitment
Carod Artal et al., 2007		*				*Does not report participation rate
Carod-Artal et al., 2008		*				*Does not report participation rate
McKinlay et al., 2008	*	**	***		****	*Limited detail on recruitment **115 invited, 49 took part *** did not report where recruited from ****only 42 of 49 participants completed anxiety measure
Rahman et al., 2008	*		**			*No diagnostic criteria ** inclusion criteria lacked clarity
Quelhas & Costa, 2009		*				* Does not report participation rate
Gallagher et al., 2010	*	**				*insufficient detail on recruitment selection ** Does not report

						participation rate
Haviklova et al., 2011						
Hinnell et al., 2012		*				*Does not report participation rate
Dubayova et al., 2012		*				*participation rate below 50%
Hanna & Cronin Golomb, 2012	*	**				*Limited detail on recruitment **Does not report participation rate
Skorvanek et al., 2013	*	**				*Excludes age<65 **Does not report participation rate
Fereshtehnejad et al., 2014		*				*Does not report participation rate
Baig et al. 2015	*					*Includes only those < 3.5 years since diagnosis
Fereshtehnejad et al., 2015		*				*Does not report participation rate
Jones et al., 2015		*				*Does not report participation rate
Walton et al., 2015		*				*Does not report participation rate
Wu et al., 2015		**				* Includes only those < 5 years since diagnosis **Does not report

						participation rate
Fan et al., 2016	*	**				*Limited detail on recruitment **Does not report participation rate
D'Iorio et al., 2017		*				*Does not report participation rate
Yoon et al., 2017	*	**				* Includes only those < 2 years since diagnosis **Does not report participation rate
Prisnie et al., 2018						

Note. Green = criterion met; Red = criterion not met, Amber = unclear whether criterion was met.

Additional Author (CI) Quality Ratings:

Article	Population clearly defined	Participation rate at least 50%	Subject recruited from same or similar populations. Were inclusion and exclusion criteria pre specified and applied uniformly to all participants?	Was sample size justification, power description, or variance and effect estimates provided.	Were measures clearly defined, valid, reliable and implemented consistently across all study participants?	Notes
Chrischilles et al., 2002	*					*did not adequately detail how the participants were recruited
Carod Artal et al., 2007		*				* not reported
Carod-Artal et al., 2008		*				* not reported
McKinlay et al., 2008	*	**	***		****	* did not adequately detail how the participants were recruited ** 49 participants from total of 115 *** did not report from where participants were recruited **** not all participants completed the anxiety measure
Rahman et al., 2008	*		**			* did not adequately detail how the participants were recruited ** inclusion and exclusion criteria were not outlined
Quelhas & Costa, 2009		*				* not reported
Gallagher et al., 2010	*	**				* did not adequately detail how the

						participants were recruited ** not reported
Haviklova et al., 2011						
Hinnell et al., 2012		*				*not reported
Dubayova et al., 2012		*				*only 31.3%
Hanna & Cronin Golomb, 2012	*	**				* did not adequately detail how the participants were recruited **not reported

Note. Green = criterion met; Red = criterion not met, Amber = unclear whether criterion was met.

Appendix F: Articles Reviewed at Full-Text Screening

Paper	Reason for Exclusion	Exclusion Code
"<Ru Lai et al. - 2018 - Clinical Factors Associated with the Quality Of Life in Patients with Parkinson's disease.pdf>."	No reference to anxiety. No validated measure of anxiety used.	2
Aarsland, D., Marsh, L., & Schrag, A. (2009). Neuropsychiatric symptoms in Parkinson's disease. *Movement disorders: official journal of the Movement Disorder Society*, *24*(15), 2175-2186.	Just a general review of psychology in Parkinson's. No measures.	3
Aarsland, D., Taylor, J. P., & Weintraub, D. (2014). Psychiatric issues in cognitive impairment. *Movement Disorders*, *29*(5), 651-662.	Just a review of psych in Parkinson's. no measures or actually study.	3
Akanova, A. A., Kamenova, S. U., Yeshmanova, A. K., Beltenova, A. G., & Kondybayeva, A. M. (2015). The evaluation of cognitive skills and the quality of life between Parkinson Disease patients and healthy aged people above 60 years old. *Advances in Gerontology*, *28*(4), 741-748.	In Russian – unable to access.	1
Anderson, K. E., Gruber-Baldini, A. L., Vaughan, C. G., Reich, S. G., Fishman, P. S., Weiner, W. J., & Shulman, L. M. (2007). Impact of psychogenic movement disorders versus Parkinson's on disability, quality of life, and psychopathology. *Movement disorders: official journal of the Movement Disorder Society*, *22*(15), 2204-2209.	Compares Parkinson's to another illness across a number of domains, (QOL and anxiety included). But does not look at link between anxiety and QOL in Parkinson's.	4
Backer, J. H. (2006). "The symptom experience of patients with Parkinson's disease." Journal of Neuroscience Nursing 38(1): 51-57.	No measures	2

Balestrino, R., & Martinez-Martin, P. (2017). Reprint of "Neuropsychiatric symptoms, behavioural disorders, and quality of life in Parkinson's disease". *Journal of the Neurological Sciences, 374*, 3-8.	A narrative review of studies that look at psychiatric symptoms and QOL.	3
Barone, P., Antonini, A., Colosimo, C., Marconi, R., Morgante, L., Avarello, T. P., ... & Cicarelli, G. (2009). The PRIAMO study: a multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. *Movement disorders: official journal of the Movement Disorder Society*, *24*(11), 1641-1649.	impact of anxiety alone was not able to be determined as A & D combined for correlation	2
Bucks, R. S., Cruise, K. E., Skinner, T. C., Loftus, A. M., Barker, R. A., & Thomas, M. G. (2011). Coping processes and health-related quality of life in Parkinson's disease. *International Journal of Geriatric Psychiatry*, *26*(3), 247-255.	No validated measure of anxiety used.	2
Bugalho, P., Lampreia, T., Miguel, R., Mendonça, M. D., Caetano, A., & Barbosa, R. (2016). Non-Motor symptoms in Portuguese Parkinson's Disease patients: correlation and impact on Quality of Life and Activities of Daily Living. *Scientific reports*, *6*, 32267.	combining anxiety with insomnia before correlating it with QOL etc.	2
Cubí-Mollá, P., De Vries, J., & Devlin, N. (2014). A study of the relationship between health and subjective well-being in Parkinson's disease patients. *Value in Health*, *17*(4), 372-379.	No validated measure of anxiety used.	2
Chaudhuri, K. R., Sauerbier, A., Rojo, J. M., Sethi, K., Schapira, A. H. V., Brown, R. G., ... & Tsuboi, Y. (2015). The burden of non-motor symptoms in Parkinson's disease using a self-completed non-motor questionnaire: a simple grading system. *Parkinsonism & related disorders*, *21*(3), 287-291.	they don't directly correlate anxiety with QOL	4

Diaz, A. P., Freitas, F. C., de Oliveira Thais, M. E., da Silva Areas, F. Z., Schwarzbold, M. L., Debona, R., ... & Shukla, A. W. (2016). Variables associated with physical health-related quality of life in Parkinson's disease patients presenting for deep brain stimulation. *Neurological Sciences*, *37*(11), 1831-1837.	Reports HADS overall score in the regression (ie grouping anxiety and depression together). Therefore does not isolate the anxiety.	2
Dissanayaka, N. N., White, E., O'Sullivan, J. D., Marsh, R., Pachana, N. A., & Byrne, G. J. (2014). The clinical spectrum of anxiety in Parkinson's disease. *Movement Disorders*, *29*(8), 967-975.	This is a descriptive overview of anxiety in Parkinson's. No measures.	3
Dissanayaka, N. N., Sellbach, A., Silburn, P. A., O'Sullivan, J. D., Marsh, R., & Mellick, G. D. (2011). Factors associated with depression in Parkinson's disease. *Journal of affective disorders*, *132*(1-2), 82-88.	Explores factors associated with depression. (anxiety being one of them) – it does not explore anxiety and QOL.	4
Dowding, C. H., Shenton, C. L., & Salek, S. S. (2006). A review of the health-related quality of life and economic impact of Parkinson's disease. *Drugs & aging*, *23*(9), 693-721.	A comprehensive review of: QOL in Parkinson's disease specific QOL costs, burden components (not inc anxiety).	3
Fereshtehnejad, S. M., Ghazi, L., Shafieesabet, M., Shahidi, G. A., Delbari, A., & Lökk, J. (2014). Motor, psychiatric and fatigue features associated with nutritional status and its effects on quality of life in Parkinson's disease patients. *PLoS One*, *9*(3), e91153.	This is about nutrition status and factors that impact it (anxiety being one) - with a view that nutrition status impacts QOL – speculative link.	4
Forjaz, M. J., Frades-Payo, B., & Martinez-Martin, P. (2009). The current state of the art concerning quality of life in Parkinson's disease: II. Determining and associated factors. *Revista de neurologia*, *49*(12), 655-660.	In Spanish – not able to access.	1

Frazier, L. D. (2000). Coping with disease-related stressors in Parkinson's disease. *The Gerontologist*.	rejected because it looks at the factors that predict stress and factors that predict QOL - but doesn't look at stress predicting QOL.	4
Gison, A., Dall'Armi, V., Donati, V., Rizza, F., & Giaquinto, S. (2014). Dispositional optimism, depression, disability and quality of life in Parkinson's disease. *Functional neurology*, *29*(2), 113.	About optimism - not about anxiety and QOL.	4
Gison, A., Rizza, F., Bonassi, S., Dall'Armi, V., Lisi, S., & Giaquinto, S. (2014). The sense-of-coherence predicts health-related quality of life and emotional distress but not disability in Parkinson's disease. *BMC neurology*, *14*(1), 193.	About sense of coherence - not about anxiety and QOL.	4
Gison, A., Rizza, F., Bonassi, S., Donati, V., & Giaquinto, S. (2015). Effects of dispositional optimism on quality of life, emotional distress and disability in Parkinson's disease outpatients under rehabilitation. *Functional neurology*, *30*(2), 105.	About dispositional optimism - not about anxiety and QOL.	4
Gökçal, E., Veysel Eren, G. Ü. R., Selvitop, R., YILDIZ, G. B., & Talip, A. S. İ. L. (2017). Motor and non-motor symptoms in Parkinson's disease: effects on quality of life. *Archives of Neuropsychiatry*, *54*(2), 143.	No reference to anxiety.	2
Goldsworthy, B., & Knowles, S. (2008). Caregiving for Parkinson's disease patients: an exploration of a stress-appraisal model for quality of life and burden. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *63*(6), P372-P376.	About the burden and quality of life of Parkinson's disease caregivers based on a stress-appraisal model. Not about anxiety and QOL.	6
Ghorbani Saeedian, R., Nagyova, I., Krokavcova, M., Skorvanek, M., Rosenberger, J., Gdovinova, Z., ... & van Dijk, J. P. (2014). The role of social support	Looks at role of social support in anxiety and	4

in anxiety and depression among Parkinson's disease patients. *Disability and rehabilitation*, *36*(24), 2044-2049.	depression in Parkinson's. Not on topic.	
Greene, T., & Camicioli, R. (2007). Depressive symptoms and cognitive status affect health-related quality of life in older patients with Parkinson's disease. *Journal of the American Geriatrics Society*, *55*(11), 1888-1890.	No validated measure of anxiety used.	2
Grün, D., Pieri, V., Vaillant, M., & Diederich, N. J. (2016). Contributory factors to caregiver burden in Parkinson disease. *Journal of the American Medical Directors Association*, *17*(7), 626-632.	No validated measure of anxiety used.	2
Handley, J. (1999). "Psychological aspects of Parkinson's diseases." Elderly Care 11(4): 34-36.	No measures validated	2
Havlikova, E., Rosenberger, J., Nagyova, I., Middel, B., Dubayova, T., Gdovinova, Z., ... & van Dijk, J. P. (2008). Clinical and psychosocial factors associated with fatigue in patients with Parkinson's disease. *Parkinsonism & related disorders*, *14*(3), 187-192.	No direct correlation of anxiety with QOL	4
Hill, M. S. (2016). "Physical Activity Behavior and Health-Related Quality of Life in Parkinson's Disease Patients: Role of Social Cognitive Variables." Physical Activity Behavior & Health-related Quality of Life in Parkinson's Disease Patients: Role of Social Cognitive Variables: 1-1.	Anxiety not explored /measured	7
Hurt, C. S., Burn, D. J., Hindle, J., Samuel, M., Wilson, K., & Brown, R. G. (2014). Thinking positively about chronic illness: An exploration of optimism, illness perceptions and well-being in patients with P arkinson's disease. *British Journal of Health Psychology*, *19*(2), 363-379.	No validated measure of anxiety used (merges anxiety and depression with overall HADS score).	2

Hurt, C. S., Landau, S., Burn, D. J., Hindle, J. V., Samuel, M., Wilson, K., & Brown, R. G. (2012). Cognition, coping, and outcome in Parkinson's disease. *International Psychogeriatrics*, *24*(10), 1656-1663.	Does not refer to anxiety or QOL.	4
Isais-Millán, S., Piña-Fuentes, D., Guzmán-Astorga, C., Cervantes-Arriaga, A., & Rodríguez-Violante, M. (2016). Prevalence of neuropsychiatric disorders in drug-naive subjects with Parkinson's disease (PD). *Gac Med Mex*, *152*(3), 357-363.	In Spanish – not able to access. From abstract, doesn't look at QOL - just reports prevalence of neuropsychiatric disorders in PD.	1
Kadastik-Eerme, L., Muldmaa, M., Lilles, S., Rosenthal, M., Taba, N., & Taba, P. (2016). Nonmotor features in Parkinson's disease: what are the most important associated factors?. *Parkinson's Disease*, *2016*.	No validated measure of anxiety used. - only mental state - not broken down as sub-item in regression either	2
Karlsen, K. H., Tandberg, E., Årsland, D., & Larsen, J. P. (2000). Health related quality of life in Parkinson's disease: a prospective longitudinal study. *Journal of Neurology, Neurosurgery & Psychiatry*, *69*(5), 584-589.	No reference to anxiety.	7
Kasten, M., Hagenah, J., Graf, J., Lorwin, A., Vollstedt, E. J., Peters, E., ... & Klein, C. (2012). Cohort Profile: a population-based cohort to study non-motor symptoms in parkinsonism (EPIPARK). *International journal of epidemiology*, *42*(1), 128-128k.	Descriptive study. Not looking at QOL and anxiety	3
Kasten, M., Kertelge, L., Brüggemann, N., van der Vegt, J., Schmidt, A., Tadic, V., ... & Binkofski, F. (2010). Nonmotor symptoms in genetic Parkinson disease. *Archives of neurology*, *67*(6), 670-676.	Descriptive. Not related to anxiety and QOL.	3
Lee, S. M., Kim, M., Lee, H. M., Kwon, K. Y., & Koh, S. B. (2015). Nonmotor symptoms in essential tremor: Comparison with Parkinson's disease and normal	Compares prevalence of non-motor symptoms between essential tremor and Parkinson's patients.	8

control. *Journal of the neurological sciences*, *349*(1-2), 168-173.		
Leroi, I., Ahearn, D. J., Andrews, M., McDonald, K. R., Byrne, E. J., & Burns, A. (2011). Behavioural disorders, disability and quality of life in Parkinson's disease. *Age and ageing*, *40*(5), 614-621.	Recruits those with apathy and impulse control difficulties – too selective	8
Lutz, S. G., Holmes, J. D., Ready, E. A., Jenkins, M. E., & Johnson, A. M. (2016). Clinical presentation of anxiety in parkinson's disease: a scoping review. *OTJR: occupation, participation and health*, *36*(3), 134-147.	Descriptive review of anxiety in Parkinson's.	3
Lyons, K. E., & Pahwa, R. (2011). The impact and management of nonmotor symptoms of Parkinson's disease. *The American journal of managed care*, *17*, S308-14.	Descriptive article on non-motor symptoms in Parkinson's. No validated measures of anxiety.	3
Martínez-Martin, P., Carod-Artal, F. J., da Silveira Ribeiro, L., Ziomkowski, S., Vargas, A. P., Kummer, W., & Mesquita, H. M. (2008). Longitudinal psychometric attributes, responsiveness, and importance of change: An approach using the SCOPA-Psychosocial questionnaire. *Movement disorders: official journal of the Movement Disorder Society*, *23*(11), 1516-1523.	This is about how well a measure can track change.	4
Martinez-Martin, P., Rodriguez-Blazquez, C., Forjaz, M. J., Frades-Payo, B., Agüera-Ortiz, L., Weintraub, D., ... & Chaudhuri, K. R. (2015). Neuropsychiatric symptoms and caregiver's burden in Parkinson's disease. *Parkinsonism & related disorders*, *21*(6), 629-634.	a. It's about caregiver burden b. No validated measure of anxiety used (depression and anxiety merged)	6
Martinez-Martin, P. (2011). The importance of non-motor disturbances to quality of life in Parkinson's disease. *Journal of the neurological sciences*, *310*(1-2), 12-16.	Review of non-motor symptoms and QOL. No measures used.	3

	Chicago	
Matsui, K., Tachibana, H., Yamanishi, T., Oguru, M., Toda, K., Okuda, B., & Oka, N. (2013). Clinical correlates of anhedonia in patients with Parkinson's disease. *Clinical neurology and neurosurgery*, *115*(12), 2524-2527.	Used measures of anxiety and qol. However, the conclusion is: Anxiety is correlated to ability to feel pleasure. Ability to feel pleasure is correlated to qol.	4
McAuliffe, M. J., Baylor, C. R., & Yorkston, K. M. (2017). Variables associated with communicative participation in Parkinson's disease and its relationship to measures of health-related quality-of-life. *International Journal of Speech-Language Pathology*, *19*(4), 407-417.	Not anxiety focussed.	7
McCabe, M. P., Firth, L., & O'Connor, E. (2009). A comparison of mood and quality of life among people with progressive neurological illnesses and their caregivers. *Journal of clinical psychology in medical settings*, *16*(4), 355-362.	No validated measure of anxiety used. Compares neurological disease for their rate of mood disturbance and QOl.	2
Muslimović, D., Post, B., Speelman, J. D., Schmand, B., & de Haan, R. J. (2008). Determinants of disability and quality of life in mild to moderate Parkinson disease. *Neurology*, *70*(23), 2241-2247.	Report overall HADS, not HADS-A separately.	2
Obeso, I., Casabona, E., Rodríguez-Rojas, R., Bringas, M. L., Macías, R., Pavón, N., ... & Jahanshahi, M. (2017). Unilateral subthalamotomy in Parkinson's disease: Cognitive, psychiatric and neuroimaging changes. *Cortex*, *94*, 39-48.	Exploration of whether surgical intervention can bring about changes in movement, psychiatric and QOL status.	4
O'Connor, E. J., & McCabe, M. P. (2011). Predictors of quality of life in carers for people with a progressive neurological	About carers in different neuro diseases	6

illness: a longitudinal study. *Quality of Life Research*, *20*(5), 703-711.		
Ozdilek, B., & Gunal, D. I. (2012). Motor and non-motor symptoms in Turkish patients with Parkinson's disease affecting family caregiver burden and quality of life. *The Journal of neuropsychiatry and clinical neurosciences*, *24*(4), 478-483.	Only correlates patient's anxiety with its impact on the carer's QOL	6
Non-motor symptoms and quality of life in subjects with mild parkinsonian signs	Compares Parksinon's to other diseases in prevalence of anxiety etc	4
Perez-Lloret, S., Negre-Pages, L., Damier, P., Delval, A., Derkinderen, P., Destée, A., ... & Rascol, O. (2014). Prevalence, determinants, and effect on quality of life of freezing of gait in Parkinson disease. JAMA neurology, 71(7), 884-890.	Explores freezing of gait and QOL. Not anxiety focused.	7
Rieu, I., et al. (2016). "Impact of Mood and Behavioral Disorders on Quality of Life in Parkinson's disease." Journal of Parkinsons Disease Print 6(1): 267-277.	No Anxiety scale	2
Rizos, A., Martinez-Martin, P., Odin, P., Antonini, A., Kessel, B., Kozul, T. K., ... & Dietrichs, E. (2014). Characterizing motor and non-motor aspects of early-morning off periods in Parkinson's disease: an international multicenter study. *Parkinsonism & related disorders*, *20*(11), 1231-1235.	Characterising symptoms – no impact/QOL measure.	4
Rizza, F., Gison, A., Bonassi, S., Dall'Armi, V., Tonto, F., & Giaquinto, S. (2017). 'Locus of control', health-related quality of life, emotional distress and disability in Parkinson's disease. *Journal of health psychology*, *22*(7), 844-852.	Does not separate out anxiety in QOL regression	2
Rodríguez-Violante, M., Cervantes-Arriaga, A., Corona, T., Martínez-Ramírez, D., Morales-Briceño, H., & Martínez-Martín, P.	No validated measure of anxiety used.	2

(2013). Clinical determinants of health-related quality of life in Mexican patients with Parkinson's disease. *Archives of medical research*, *44*(2), 110-114.		
Robottom, B. J., Gruber-Baldini, A. L., Anderson, K. E., Reich, S. G., Fishman, P. S., Weiner, W. J., & Shulman, L. M. (2012). What determines resilience in patients with Parkinson's disease?. *Parkinsonism & related disorders*, *18*(2), 174-177.	Focus on resilience and factors it correlates, with. One of which being anxiety. Does not fit remit of anxiety and impact.	4
Santos-García, D., & de la Fuente-Fernández, R. (2013). Impact of non-motor symptoms on health-related and perceived quality of life in Parkinson's disease. *Journal of the neurological sciences*, *332*(1-2), 136-140.	No validated measure of anxiety used.	2
Santos-García, D., & De la Fuente-Fernández, R. (2015). Factors contributing to caregivers' stress and burden in Parkinson's disease. *Acta Neurologica Scandinavica*, *131*(4), 203-210.	About caregiver. Patient anxiety not explored	6
Sauerbier, A., & Chaudhuri, K. R. (2014). Non-motor symptoms: the core of multi-morbid Parkinson's disease. *British Journal of Hospital Medicine*, *75*(1), 18-24.	Review of non-motor symptoms in QOL.	3
Schiavolin, S., Raggi, A., Quintas, R., Cerniauskaite, M., Giovannetti, A. M., Covelli, V., ... & Leonardi, M. (2017). Psychosocial difficulties in patients with Parkinson's disease. *International Journal of Rehabilitation Research*, *40*(2), 112-118.	No validated measure of anxiety used. Regression just groups anxiety into Psychosocial difficulties'.	2
Schiehser, D. M., Han, S. D., Lessig, S., Song, D. D., Zizak, V., & Filoteo, J. V. (2009). Predictors of health status in nondepressed and nondemented individuals with Parkinson's disease. *Archives of Clinical Neuropsychology*, *24*(7), 699-709.	No validated measure of anxiety used. Used a subsection of the geriatric depression scale to measure anxiety.	2

Schreurs, K. M., De Ridder, D. T., & Bensing, J. M. (2000). A one year study of coping, social support and quality of life in parkinson's disease. *Psychology and Health*, *15*(1), 109-121.	Explores social support and coping - impact on QOL. Not anxiety focused.	7
Soh, S. E., McGinley, J. L., Watts, J. J., Iansek, R., & Morris, M. E. (2012). Health-related quality of life of Australians with Parkinson disease: A comparison with international studies. *Physiotherapy Canada*, *64*(4), 338-346.	No reference to anxiety,	7
Soh, S. E., McGinley, J. L., Watts, J. J., Iansek, R., Murphy, A. T., Menz, H. B., ... & Morris, M. E. (2013). Determinants of health-related quality of life in people with Parkinson's disease: a path analysis. *Quality of life research*, *22*(7), 1543-1553.	No reference to anxiety.	7
Solla, P., Cannas, A., Mulas, C. S., Perra, S., Corona, A., Bassareo, P. P., & Marrosu, F. (2014). Association between fatigue and other motor and non-motor symptoms in Parkinson's disease patients. *Journal of neurology*, *261*(2), 382-391.	No validated measure of anxiety used.	2
Song, W., Guo, X., Chen, K., Chen, X., Cao, B., Wei, Q., ... & Shang, H. F. (2014). The impact of non-motor symptoms on the Health-Related Quality of Life of Parkinson's disease patients from Southwest China. *Parkinsonism & related disorders*, *20*(2), 149-152.	No validated measure of anxiety used. Just used on' 'scale of non-motor symptoms' and did correlation to QOL.	2
Sproesser, E., Viana, M. A., Quagliato, E. M., & de Souza, E. A. P. (2010). The effect of psychotherapy in patients with PD: a controlled study. *Parkinsonism & related disorders*, *16*(4), 298-300.	Therapeutic intervention with QOL and anxiety used as outcome measures.	5
Takahashi, K., Kamide, N., Suzuki, M., & Fukuda, M. (2016). Quality of life in people with Parkinson's disease: the relevance of	About social relationship and being heard and how it	7

social relationships and communication. *Journal of physical therapy science*, *28*(2), 541-546.	impacts QOL. Not related to anxiety.	
Veazey, C., Cook, K. F., Stanley, M., Lai, E. C., & Kunik, M. E. (2009). Telephone-administered cognitive behavioral therapy: a case study of anxiety and depression in Parkinson's disease. *Journal of clinical psychology in medical settings*, *16*(3), 243-253.	Explored feasibility of telephone CBT for those with Parkinson's.	5
Visser, M., Verbaan, D., Van Rooden, S., Marinus, J., Van Hilten, J., & Stiggelbout, A. (2009). A longitudinal evaluation of health-related quality of life of patients with Parkinson's disease. *Value in Health*, *12*(2), 392-396.	No reference to anxiety.	7
Walker, R. W., Dunn, J. R., & Gray, W. K. (2011). Self-reported dysphagia and its correlates within a prevalent population of people with Parkinson's disease. *Dysphagia*, *26*(1), 92-96.	About dysphagia in Parkinson's and impact on QOL. No validated measure of anxiety used (uses total HADS score).	7
Winter, Y., von Campenhausen, S., Arend, M., Longo, K., Boetzel, K., Eggert, K., ... & Barone, P. (2011). Health-related quality of life and its determinants in Parkinson's disease: results of an Italian cohort study. *Parkinsonism & related disorders*, *17*(4), 265-269.	No validated measure of anxiety used.	2
Winter, Y., von Campenhausen, S., Gasser, J., Seppi, K., Reese, J. P., Pfeiffer, K. P., ... & Poewe, W. (2010). Social and clinical determinants of quality of life in Parkinson's disease in Austria: a cohort study. *Journal of neurology*, *257*(4), 638-645.	No validated measure of anxiety used.	2
Zhu, K., van Hilten, J. J., & Marinus, J. (2017). Onset and evolution of anxiety in	Factors associated with anxiety changes over time.	4

Parkinson's disease. *European journal of neurology*, *24*(2), 404-411.	Not related to impact/quality of Life.	
Duncan, G. W., et al. (2014). "Health-related quality of life in early Parkinson's disease: the impact of nonmotor symptoms." Movement Disorders **29**(2): 195-202.	No validated measure of anxiety, just an element of the non motor questionnaire.	2
Gomez-Esteban, J. C., et al. (2011). "Impact of psychiatric symptoms and sleep disorders on the quality of life of patients with Parkinson's disease." Journal of Neurology **258**(3): 494-499.	No validated measure of anxiety, just an element of Neuropsychiatric inventory	2
Simpson, J., et al. (2014). "Predictors of quality of life in people with Parkinson's disease: evidence for both domain specific and general relationships." Disability & Rehabilitation **36**(23): 1964-1970.	Anxiety only reported as part of depression and stress scale – not sure that the anxiety bit is validated. Also doesn't report PDQ score as a whole – just the sub dimensions.	2
Skorvanek, M., et al. (2015). "Relationship between the non-motor items of the MDS-UPDRS and Quality of Life in patients with Parkinson's disease." J Neurol Sci **353**(1-2): 87-91.	No validated measure of anxiety	2
Zhong, M., et al. (2016). "The relationship between specific cognitive defects and burden of care in Parkinson's disease." International Psychogeriatrics 28(2): 275-281.	Re care givers	6
Zheng, K. S., Dorfman, B. J., Christos, P. J., Khadem, N. R., Henchcliffe, C., Piboolnurak, P., & Nirenberg, M. J. (2012). Clinical characteristics of exacerbations in Parkinson disease. *The neurologist*, *18*(3), 120.	Correlates anxiety with exacerbations of PD symptoms – not QOL	4

Note. 1 = Not in English; 2 = No validated measure of anxiety; 3 = review article; 4 = QOL-anxiety relationship not explored; 5 = intervention methodology; 6 = Care giver focus; 7 = Anxiety not measured at all; 8 = Comparison methodology.

Appendix G: Survey One Advertisement

Advertisement

Page 1: Page 1

University of East Anglia

Volunteers needed to help us to better understand anxiety in Parkinson's

We are a research team at the University of East Anglia. We need volunteers to take part in the first phase of a research project looking at anxiety in Parkinson's. If you choose to take part, you will be asked to complete a survey. This will help us to learn from you about what your anxiety is/was like and also about anything that you have found useful to manage or reduce the anxiety.

To take part, you must meet the following criteria:

- Have a diagnosis of Parkinson's

- Be 18+ years old

- Can read and write in English

- Since your Parkinson's diagnosis, have experienced stress, worry or anxiety to an extent that has reduced your quality of life or sense of wellbeing.

- Must **not** have a diagnosis of dementia or difficulties that would make it challenging to complete the survey independently

Interested?

If so, please click 'finish' to find a link to further information about the project and the option to take part.

Page 2: Final page

University of East Anglia

Please click the link below for further information about the project and the option to take part:

https://uea.onlinesurveys.ac.uk/information-sheet

If you are unable to complete an online version, we can send you a postal copy. Please contact Daniel.curran@uea.ac.uk to request this.

Appendix H: Survey One Information sheet

Information sheet

Page 1: Page 1

The experience of anxiety in

Parkinson's Can you help?

We wish to invite you to take part in our research project. Before you decide whether to take part or not, it is important for you to understand what the project is about and what it would involve. Please take time to read through this information carefully and discuss it with family or friends if you wish. Ask us if there is anything that is not clear. Our contact details are given at the end of these pages.

This information sheet is also available as a paper copy from the project lead Daniel Curran (contact details listed below).

The research project:

This research team at the University of East Anglia would like to better understand the anxiety that people with Parkinson's can experience.

Why we are carrying out this piece of research

We know that many people with Parkinson's experience worry, stress and anxiety, but we do not know very much about the details of this experience. We think that it is important that we find out more about it so that we can then find better ways of helping people who experience it. We think that asking people who have experienced it is the best way to improve our

understanding.

Who do we need to take part?

To take part in the study you must meet the following criteria:

- Have a diagnosis of Parkinson's

- Have experienced stress, worry or anxiety since your Parkinson's diagnosis, to an extent that has reduced your quality of life and sense of wellbeing

- Be 18+ years old

- Be able to read and write in English

- Must **not** have a diagnosis of dementia or difficulties that would make it challenging to complete the survey independently.

If you do not meet all of these criteria then please do not continue.

What do you need to do?

We would like you to complete an online survey. It should take approximately 30-40 minutes to complete in total. However, it does not have to be completed all at once as you can save it at any time and return to finish it at a later time.

If you are unable to complete it online, we encourage you to get in touch with us at Daniel.curran@uea.ac.uk so that we can send a paper copy to you.

Who is organising and funding this consultation?

This consultation is funded by the University of East Anglia. It is led by Daniel Curran, who is a Trainee Clinical Psychologist in the Medical School at the University of East Anglia. From his time working for the NHS he has developed a particular interest in anxiety and the ways that it may be experienced by people with long term physical health conditions. The project is supervised by Dr Katherine Deane and Dr Catherine Ford of the University of East Anglia. Bob Chalmers and Jackie Malyon, who have experienced anxiety since being diagnosed with Parkinson's, have also helped us to design this piece of research.

How will I benefit from taking part in the study?

Taking part in the study will not bring any direct benefit to you. However, by taking part you will be making a significant contribution to our understanding of anxiety in Parkinson's. Better understanding may enable future studies to develop better treatments for anxiety in Parkinson's.

If you choose to provide us with your contact details then we will keep you up to date with the findings of our research.

Has the research been approved on ethical grounds?

This piece of research has been assessed by an independent group of people, called the University of East Anglia's University Research Ethics Committee, which protects your safety, rights, wellbeing and dignity. This research has been reviewed and approved by them.

What will happen to the information recorded in the consultation?

The answers that you provide to our survey questions will be anonymised and analysed. These answers will tell us what triggers the anxiety and how people manage it for themselves. The next phase of the research will put those answers into priority order.

Eventually this information will be presented in a number of written reports, including; a thesis project, a peer reviewed journal article, a report for Parkinson's UK and possibly presentations at Parkinson's conferences. Your anonymised responses may also be used to support future research within the university.

Data Security

All results and documents associated with this research are strictly confidential. Your responses will not be identifiable by name and will be stored securely and privately on a secure University of East Anglia computer server which is password protected in line with General Data Protection Regulation (2018).

If you choose to provide us with your contact details, this information will be separate from your survey responses but still stored securely and privately on a secure University of East Anglia computer server which is password protected. These details will only be used to send you information about the next phase of our research or for a report on the project. We will keep your details for one year and then destroy them securely.

If you have any questions about how your data is used in this research, in the first instance please contact the project lead Daniel Curran Daniel.curran@uea.ac.uk.

If you have any further questions or complaints about how your data was used you can contact Professor William Fraser who is the Dean of the School of Medicine at the University of East Anglia (tel: +44 (0)1603 59 3971, email: W.Fraser@uea.ac.uk) or the
University's data protection team (tel: +44 (0)1603 59 2431, email: dataprotection@uea.ac.uk). If you are dissatisfied in how this team handle your data complaint you can complain to the Information Commissioner's Office. Information on how to do this can be found at https://ico.org.uk/make-a-complaint/your-personal- information-concerns/personal-information-concerns/ or via their live chat service ico.org.uk/livechat, or call their helpline on 0303 123 1113.

What would happen if I said I wanted to take part but then changed my mind?

Up until the point that you submit your responses to the survey, you are free to withdraw from the study without consequence. However, once you have submitted the survey it is no longer possible to withdraw. This is because your name is not attached to your response, so we are not able to identify individual responses to remove them.

What if I have a complaint?

In the unlikely event that you have a complaint about this research project, you may complain directly to Professor William Fraser who is the Dean of the School of Medicine at the University of East Anglia (tel: +44 (0)1603 59 3971, email: W.Fraser@uea.ac.uk).

The University of East Anglia have appropriate Public Liability and

Negligence Insurance cover for this research project.

Page 2: Final page

Yes, I would like to take part in the research – what do I need to do now?

To take part in the research simply click the following link to access the survey:

https://uea.onlinesurveys.ac.uk/anxiety

I am not sure about taking part – where can I get further information?

We would be very happy to answer any questions you may have. Please contact Daniel Curran, Daniel.curran@uea.ac.uk.

No, I do not wish to take part in the consultation – what do I need to do now?

Nothing more. We will not contact you again directly, however we will be advertising this consultation via a number of routes so you may hear about it from another route.

How to contact us

You can contact Daniel Curran (chief investigator) daniel.curran@uea.ac.uk or Dr Katherine Deane (project supervisor) k.deane@uea.ac.uk

Appendix I: Survey One

Survey - Anxiety in Parkinson's

Page 1: Page 1

University of East Anglia

CONSENT FORM

Name of Lead Researcher: Daniel Curran

Title of Project: The experience of anxiety in Parkinson's

1. Please read each of the statements below and click in each box if you agree with the statement.

	Required
	I agree
I confirm that I have read the information sheet provided for the anxiety study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐

I understand that my participation is voluntary, and that at any point up until I submit my survey responses I am free to withdraw from the study without any impact on my care. However, I also understand once I have submitted my response I am not able to withdraw from the study as there is no way for the researchers to know which response was mine.	☐
I understand that if I decide to share my contact details, they will be kept by the research team for a year.	☐
I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐
I understand that my data will be stored confidentially and securely by the research team at the University of East Anglia	☐
I understand that the findings from this research will be published	☐
I agree to take part in this study.	☐

If you have selected each of the above boxes and wish to proceed to the online survey please click 'next' below.

Page 2: survey

2. **Gender** Are you: *Required*

- male
- female
- transgender
- other
- prefer not to say

3. **Age** How old are you? *Required*

- 18-30
- 31-50
- 51-64
- 65-80
- 81+
- Prefer not to say

4. **Sexual Orientation** How would you describe your sexual orientation? *Required*

- Heterosexual / Straight
- Bisexual
- Homosexual Other
- Prefer not to say

5. **Ethnicity** How would you describe your ethnic origin? (Please select one box only) *Required*

- White
- Black or Black British Asian
- or Asian British
- Mixed/multiple ethnic groups Other
- Prefer not to say

6. **Living Arrangements** What are your living arrangements? *Required*

- I live in my own home
- I live in supported accommodation / care home Other

6.a. If you ticked to say that you live in your own home, which of the following applies:

- I live with my partner and/or family but I do not receive care from them or from external carers
- I live with my partner and/or family and I do receive care from them or from external carers
- I live alone and do not receive care from anybody
- I live alone with some support from paid carers or partner or family etc Other
- Prefer not to say

7. **Health** How long is it since you were diagnosed with Parkinson's? *Required*

8. Have you fallen in the last 12 months? *Required*

- Yes No
-

9. Have you experienced freezing of gait (when walking, do you suddenly stop or freeze as if your feet are stuck to the floor) in the past month? *Required*

- Yes
- No

10. Over the past week, have you usually had shaking or tremor? *Required*

- Not at all OR I do have some but it does not cause problems with any activities Yes
- tremor causes problems with some or all activities

11. Over the past week have you had difficulty with repetitious movements eg. difficulty with typing or buttoning a shirt or does your handwriting progressively get smaller? *Required*

- Yes
- No

12. Do you have any other physical health conditions in addition to Parkinson's? *Required*

- Yes
- No

12.a. If so, please list them below:

13. Have you received an anxiety diagnosis from a medical professional? *Required*

- Yes
- No

14. Have you received any psychological support for your anxiety? *Required*

- Yes
- No

14.a. If so, did you find it helpful?

15. Have you received any other mental health diagnoses? *Required*

- Yes
- No

15.a. If so, please list them below:

16. Are you prescribed any medication to support you with anxiety *Required*

- Yes
- No

16.a. If so, please list youranxiety medications below:

Page 3: Parkinson's Disease Quality of Life Questionnaire (PDQ-8)

17. *Due to having Parkinson's disease, how often **during the last month** have you:*

	Never	Occasionally	Sometimes	Often	Always - or cannot do at all
Had difficulty getting around in public?	☐	☐	☐	☐	☐
Had difficulty dressing yourself?	☐	☐	☐	☐	☐
Felt depressed?	☐	☐	☐	☐	☐
Had problems with your close personal relationships?	☐	☐	☐	☐	☐
Had problems with your concentration, e.g. when reading or watching TV?	☐	☐	☐	☐	☐
Felt unable to communicate with people properly?	☐	☐	☐	☐	☐
Had painful muscle cramps or spasms?	☐	☐	☐	☐	☐
Felt embarrassed in public due to having Parkinson's disease?	☐	☐	☐	☐	☐

Please check that you have selected **one** response option per question

have asserted their moral rights.

Page 4: Anxiety

Anxiety

18. In the past four weeks, to what extent did you experience the following symptoms? *Required*

Please don't select more than 1 answer(s) per row. Please

select at least 5 answer(s).

	Not at all, or never	Very mild, or rarely	Mild, or sometimes	Moderate, or often	Severe, or (nearly) always
Feeling anxious or nervous	☐	☐	☐	☐	☐
Feeling tense or stressed	☐	☐	☐	☐	☐
Being unable to relax	☐	☐	☐	☐	☐
Excessive worrying about everyday matters	☐	☐	☐	☐	☐
Fear of something bad, or even the worst, happening	☐	☐	☐	☐	☐

19. In the past four weeks, did you experience episodes of the following symptoms? *Required*

Please don't select more than 1 answer(s) per row. Please

select at least 4 answer(s).

	Never	Rarely	Sometimes	Often	Nearly always

Panic or intense fear	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐
Heart palpitations and heart beating fast (not related to physical effort or activity)	☐	☐	☐	☐	☐
Fear of losing control	☐	☐	☐	☐	☐

20. In the past four weeks, to what extent did you fear or avoid the following situations?
Required

Please don't select more than 1 answer(s) per row. Please

select at least 3 answer(s).

	Never	Rarely	Sometimes	Often	Nearly always
Social situations (where one may be observed, or evaluated by others, such as speaking in public, or talking to unknown people)	☐	☐	☐	☐	☐

Public settings (situations from which it may be difficult or embarrassing to escape, such as queues or lines, crowds, bridges, or public transportation)	☐	☐	☐	☐	☐
Specific objects or situations (such as flying, heights, spiders or other animals, needles or blood)	☐	☐	☐	☐	☐

Page 5: More detail on your anxiety

We understand that people experience anxiety in all sorts of different ways and that the questions that you have just answered about anxiety may not have covered everything. So we would really like for you to share with us **your** individual experience of anxiety since your Parkinson's diagnosis. There is no right or wrong answer – anything you think of is valuable to us.

We have left several text boxes below for you to tell us more about your anxiety. There are some questions at the top of each box that might help you to think about your anxiety, but please do not feel that you have to stick only to the questions. Please be as detailed as you can.

21. How would you describe your anxiety?

22. What runs through your mind when you are anxious? Are there things or that you particularly worry or think about? Do you notice the anxiety in your body (physical symptoms), if so in what way?

23. Is the anxiety constant? If not, how long does it last for (e.g. minutes, hours, days, weeks, months, years)? Do you find that there are particular things or environments that set the anxiety off or make itworse?

24. How does the anxiety impact on your life? Does the anxiety change your behaviour at all, if so, how? Are there things that you avoid because they make you anxious, what is it about those situations?

25. If you take medication for Parkinson's, do you think this has any effect on your anxiety?

26. Is there anything else that you would like to tell us about your anxiety that you have not already mentioned?

Page 6: What are the things that you find helpful?

We also recognise that people are likely have all different sorts of ways to try to manage their anxiety. However, we don't know very much about what these methods are. We are really curious to know about things **you** have tried and found helpful to manage or reduce the anxiety. Again, there is no right or wrong answer, please be as specific as possible.

We have left space below for you to tell us more. We have also left some examples but please do not feel that you have to stick to them – they are only suggestions. Only you know what has worked for you. Please be as detailed as you can.

27. **Communication**. Have you found talking about your experiences helpful to manage or reduce your anxiety? For example: support groups, speaking to friends/family, speaking with others who have anxiety, speaking with others who have Parkinson's, or any other form of communicating?

28. **Types of therapies.** Have you found any 'therapies' helpful to reduced or manage your anxiety? For example: any psychological talking therapy (such as counselling or cognitive behaviour therapy), relaxation techniques, medication, complementary therapies (such as yoga, tai chi, massage, acupuncture), meditation, or any other forms of therapy.

29. **Lifestyle.** Are there parts of your lifestyle that you have found helpful to reduce or manage your anxiety? For example: exercise, travel, hobbies, dietary changes, sleep routines, or any other parts of your lifestyle.

30. **Anything else you find helpful.** Are there any other things that you find helpful to reduce or manage your anxiety?

Page 7: submission of survey

The survey is nearly complete.

Remember for queries related to the survey, you can contact Daniel Curran (chief investigator) daniel.curran@uea.ac.uk or Dr Katherine Deane (project supervisor) k.deane@uea.ac.uk

We would like you to know that more information about anxiety in Parkinson's can be found on the Parkinson's UK website https://www.parkinsons.org.uk/information-and-support/anxiety

We would also like to make you aware that there are free and confidential helplines that you can contact for advice and support, see below:

- Call Samaritans for free any time on 116 123. They offer a confidential listening service. See also https://www.samaritans.org/
- Call Parkinson's UK on Free* confidential helpline 0808 800 0303 Monday to Friday 9am–8pm
- Call SANEline on 0300 304 7000 between 4.30pm and 10.30pm each evening.
- You may also wish to speak to your GP if you feel you need further support with coping with your anxiety.

To submit your responses please click 'finish' below. Please remember that clicking 'finish' will confirm that your consent to participate in this survey.

Page 8: Final page

Thank you very much for taking the time to complete this survey. We really value your contribution.

Remember, you can contact Daniel Curran (chief investigator) daniel.curran@uea.ac.uk or Dr Katherine Deane (project supervisor) k.deane@uea.ac.uk

We would like to remind you that more information about anxiety in Parkinson's can be found on the Parkinson's UK website https://www.parkinsons.org.uk/information-and-support/anxiety

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- Call Parkinson's UK on Free* confidential helpline 0808 800 0303 Monday to Friday 9am–8pm
- Call SANEline on 0300 304 7000 between 4.30pm and 10.30pm each evening.
- It may also be advisable to contact your GP

What's next?

You now have the option to provide us with your contact email. Please do this if you would like either or both of the following:

- For us to contact you to tell you more about the second phase of our research. Once again, your involvement would be greatly appreciated.
- For us to provide you with a brief report of our research findings when the project is complete.

If either option interests you, please click on the following link.
https://uea.onlinesurveys.ac.uk/contact-details

Appendix J: Survey Two Advertisement

Advertisement

Page 1: Page 1

University of East Anglia

Volunteers needed to help us to better understand anxiety in Parkinson's

We are a research team at the University of East Anglia. We need volunteers to take part in the second phase of a study looking at anxiety in Parkinson's.

If you choose to take part, you will be asked to answer some survey questions about things our previous participants (who have experienced anxiety since being diagnosed with Parkinson's) have said about their anxiety. Specifically, we would like to know how much you relate to their experiences about what the anxiety is like.

Please note, you **can** take part in this survey regardless of whether or not you took part in our previous research.

To take part, you must meet the following criteria:

- Have a diagnosis of Parkinson's

- Be 18+ years old

- Can read and write in English

- Since your Parkinson's diagnosis, have experienced stress, worry or anxiety to an extent that has reduced your quality of life or sense of wellbeing.

- Must **not** have a diagnosis of dementia or difficulties that would make it challenging to complete the survey independently

Interested?

If so, please click 'finish' to find a link to further information about the project and the option to take part.

Page 2: Final page

Please click the link below for further information about the project and the option to take part:

https://uea.onlinesurveys.ac.uk/information-sheets

If you are unable to complete an online version, we can send you a postal copy. Please contact Daniel.curran@uea.ac.uk to request this.

Appendix K: Survey Two Information Sheet

Information sheet

Page 1: Page 1

University of East Anglia

The experience of anxiety in Parkinson's Can you

help?

We wish to invite you to take part in our research project. Before you decide whether to take part or not, it is important for you to understand what the project is about and what it would involve. Please take time to read through this information carefully and discuss it with family or friends if you wish. Ask us if there is anything that is not clear. Our contact details are given at the end of these pages.

This information sheet is also available as a paper copy from the project lead Daniel Curran (contact details listed below).

The research project

This research team at the University of East Anglia would like to better understand the anxiety that people with Parkinson's can experience.

Why we are carrying out this piece of research

Earlier in the year we asked many people with Parkinson's to tell us more about their experiences of anxiety. We have collected their responses and made a list of the main themes that this group raised. We now want to move into a second phase of research where we encourage people with Parkinson's to rate how much they can relate to each of these experiences that were identified. We feel that by doing this we will gain an even greater insight into the anxiety experience of people with Parkinson's.

Please note, you **can** take part in this survey regardless of whether or not you took part in our previous research.

Who do we need to take part?

To take part in the study you must meet the following criteria:

- Have a diagnosis of Parkinson's

- Have experienced stress, worry or anxiety since your Parkinson's diagnosis, to an extent that has reduced your quality of life and sense of wellbeing

- Be 18+ years old

- Be able to read and write in English

- Must **not** have a diagnosis of dementia or difficulties that would make it challenging to complete the survey independently.

If you do not meet all of these criteria then please do not continue.

What do you need to do?

We would like you to complete an online survey. It should take approximately 30-45 minutes to complete in total. However, it does not have to be completed all at once as you can save it at any time and return to finish it at a later time.

If you are unable to complete it online, we encourage you to get in touch with us at Daniel.curran@uea.ac.uk so that we can send a paper copy to you.

Who is organising and funding this consultation?

This consultation is funded by the University of East Anglia. It is led by Daniel Curran, who is a Trainee Clinical Psychologist in the Medical School at the University of East Anglia. From his time working for the NHS he has developed a particular interest in anxiety and the ways that it may be experienced by people with long term physical health conditions. The project is supervised by Dr Katherine Deane and Dr Catherine Ford of the University of East Anglia. Bob Chalmers and Jackie Malyon, who have experienced anxiety since being diagnosed with Parkinson's, have also helped us to design this piece of research.

How will I benefit from taking part in the study?

Taking part in the study will not bring any direct benefit to you. However, by taking part you will be making a significant contribution to our understanding of anxiety in Parkinson's. Better understanding may enable future studies to develop better treatments

for anxiety in Parkinson's.

If you choose to provide us with your contact details then we will keep you up to date with the findings of our research.

Has the research been approved on ethical grounds?

This piece of research has been assessed by an independent group of people, called the University of East Anglia's University Research Ethics Committee, which protects your safety, rights, wellbeing and dignity. This research has been reviewed and approved by them.

What will happen to the information recorded in the consultation?

The answers that you provide to our survey questions will be anonymised and analysed. The findings will be presented in a number of written reports, including; a thesis project, a peer reviewed journal article, a report for Parkinson's UK and possibly presentations at Parkinson's conferences. Your anonymised responses may also be used to support further research within the university.

Data Security

All results and documents associated with this research are strictly confidential. Your responses will not be identifiable by name and will be stored securely and privately on a secure University of East Anglia computer server which is password protected in line with General Data Protection Regulation (2018).

If you choose to provide us with your contact details, this information will be separate from your survey responses but still stored securely and privately on a secure University of East Anglia computer server which is password protected. These details will only be used to send you a report on the project. We will keep your details for one year and then destroy them securely.

If you have any questions about how your data is used in this research, in the first instance please contact the project lead Daniel Curran Daniel.curran@uea.ac.uk.

If you have any further questions or complaints about how your data was used you can contact Professor William Fraser who is the Dean of the School of Medicine at the University of East Anglia (tel: +44 (0)1603 59 3971, email: W.Fraser@uea.ac.uk) or the University's data protection team (tel: +44 (0)1603 59 2431, email:

dataprotection@uea.ac.uk). If you are dissatisfied in how this team handle your data complaint you can complain to the Information Commissioner's Office. Information on how to do this can be found at https://ico.org.uk/make-a-complaint/your-personal-information-concerns/personal-information-concerns/ or via their live chat service ico.org.uk/livechat, or call their helpline on 0303 123 1113.

What would happen if I said I wanted to take part but then changed my mind?

Up until the point that you submit your responses to the survey, you are free to withdraw from the study without consequence. However, once you have submitted the survey it is no longer possible to withdraw. This is because your name is not attached to your response, so we are not able to identify individual responses to remove them.

What if I have a complaint?

In the unlikely event that you have a complaint about this research project, you may complain directly to Professor William Fraser who is the Dean of the School of Medicine at the University of East Anglia (tel: +44 (0)1603 59 3971, email: W.Fraser@uea.ac.uk) .

The University of East Anglia have appropriate Public Liability and Negligence Insurance cover for this research project.

Page 2: Information sheet

University of East Anglia

Yes, I would like to take part in the research – what do I need to do now? To take part

in the research simply click the following link to access the survey:

https://uea.onlinesurveys.ac.uk/survey-anxiety--parkinsons

I am not sure about taking part – where can I get further information?

We would be very happy to answer any questions you may have. Please contact Daniel Curran, Daniel.curran@uea.ac.uk.

No, I do not wish to take part in the consultation – what do I need to do now?

Nothing more. We will not contact you again directly, however we will be advertising this consultation via a number of routes so you may hear about it from another route.

How to contact us

You can contact Daniel Curran (chief investigator) daniel.curran@uea.ac.uk or Dr Katherine Deane (project supervisor) k.deane@uea.ac.uk

THANK YOU FOR READING THIS INFORMATION SHEET

To take part in the research, please click 'finish' to access a link to our survey.

Page 3: Final page

To begin the survey, simply click on the following link:

https://uea.onlinesurveys.ac.uk/survey-anxiety--parkinsons

Appendix L: Survey Two

New survey - Anxiety in Parkinson's

Page 1: Page 1

CONSENT FORM

Name of lead researcher: Daniel Curran

Title of Project: The experience of anxiety in Parkinson’s

1. Please read each of the statements below and click in each box if you agree with the statement.

	Required
	I agree
I confirm that I have read the information sheet provided for the anxiety study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐

I understand that my participation is voluntary, and that at any point up until I submit my survey responses I am free to withdraw from the study without any impact on my care. However, I also understand once I have submitted my response I am not able to withdraw from the study as there is no way for the researchers to know which response was mine.	☐
I understand that if I decide to share my contact details, they will be kept by the research team for a year.	☐
I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐
I understand that my data will be stored confidentially and securely by the research team at the University of East Anglia	☐
I understand that the findings from this research will be published	☐
I agree to take part in this study.	☐

If you have selected each of the above boxes and wish to proceed to the online survey please click 'next' below.

Page 2: survey

2. How would you describe your gender? *Required*

- ○ Male Female
- ○ Transgender
- ○ Other
- ○ Prefer not to say

3. How old are you? *Optional*

4. How would you describe your sexual orientation? *Required*

- Heterosexual / Straight
- Bisexual
- Homosexual / Gay Other
- Prefer not to say

5. How would you describe your ethnic origin? (Please select one box only) *Required*

- White
- Black or Black British
- Asian or Asian British Mixed/multiple
- ethnic groups Other
- Prefer not to say

6. Earlier this year (March-April) we produced another survey about anxiety and Parkinson's. Did you take part in that survey too?

- Yes No

7. What are your living arrangements? *Required*

- I live in my own home
- I live in supported accommodation / care home Other
-

7.a. If you ticked to say that you live in your own home, which of the following applies:

- I live with my partner and/or family but I do not receive care from them or from external carers
- I live with my partner and/or family and I do receive care from them or from external carers
- I live alone and do not receive care from anybody
- I live alone with some support from paid carers or partner or family etc Other
- Prefer not to say
-

8. How long is it since you were diagnosed with Parkinson's? (in years) *Required*

9. Have you fallen in the last 12 months? *Required*

- Yes No

10. Have you experienced freezing of gait (when walking, do you suddenly stop or freeze as if your feet are stuck to the floor) in the past month? *Required*

- Yes No

11. Over the past week, have you usually had shaking or tremor? *Required*

- Yes shaking or tremor causes problems with some or all activities
- Not at all OR I do have some shaking or tremor but it does not cause problems with any activities

12. Over the past week have you had difficulty with repetitious movements eg. difficulty with typing or buttoning a shirt or does your handwriting progressively get smaller? *Required*

- Yes
- No

13. Do you have any other physical health conditions in addition to Parkinson's? *Required*

- Yes No
-

13.a. If so, please list them below:

14. When did you first experience anxiety that impacted your quality of life?

- Before I was diagnosed with Parkinson's After I
- was diagnosed with Parkinson's

14.a. If you experienced the anxiety before your Parkinson's diagnosis, what has been your experience of the anxiety since the diagnosis?

- Not applicable Anxiety
- is worse Anxiety is
- unchanged Anxiety is
- better

15. Overall, to what extent does the anxiety impact on your life?

- Not at all
- Mildly
- Moderately
- Severely

16. Please select from the following options the one that best describes how often you experience anxiety

- Everyday
- A few days per week A
- few days per month
- Less often

17. To what extent does your anxiety increase when your Parkinson's symptoms are bad?

- Never or almost never
- Rarely
- Sometimes
- Often
- Always or almost always

18. Have you received an anxiety diagnosis from a medical professional? *Required*

- Yes
- No

19. Have you received any psychological therapy for your anxiety (for example counselling or cognitive behavioural therapy)? *Required*

- Yes No

19.a. If so, did you find it helpful?

20. Have you received any other mental health diagnoses? *Required*

- Yes No

20.a. If so, please list them below:

21. Are you prescribed any medication to support you with anxiety? *Required*

- Yes No

21.a. If so, please list youranxiety medications below:

22. How would you describe the impact of your **Parkinson's** medication on the anxiety?

- Not applicable
- Makes my anxiety worse Has
- no effect of my anxiety Makes
- my anxiety better
- Makes my anxiety vary, i.e. as I go on/the medication works I get less anxiety, whereas when I go off/the medication stops working I get more anxiety

Page 3: Parkinson's Disease Quality of Life Questionnaire (PDQ-8)

23. *Due to having Parkinson's disease, how often **during the last month** have you:*

	Never	Occasionally	Sometimes	Often	Always - or cannot do at all
Had difficulty getting around in public?	☐	☐	☐	☐	☐
Had difficulty dressing yourself?	☐	☐	☐	☐	☐
Felt depressed?	☐	☐	☐	☐	☐
Had problems with your close personal relationships?	☐	☐	☐	☐	☐
Had problems with your concentration, e.g. when reading or watching TV?	☐	☐	☐	☐	☐
Felt unable to communicate with people properly?	☐	☐	☐	☐	☐
Had painful muscle cramps or spasms?	☐	☐	☐	☐	☐
Felt embarrassed in public due to having Parkinson's disease?	☐	☐	☐	☐	☐

Please check that you have selected **one** response option per question

Page 4: Anxiety

Anxiety

24. In the past four weeks, to what extent did you experience the following symptoms? *Required*

Please don't select more than 1 answer(s) per row. Please

select at least 5 answer(s).

	Not at all, or never	Very mild, or rarely	Mild, or sometimes	Moderate, or often	Severe, or (nearly) always
Feeling anxious or nervous	☐	☐	☐	☐	☐
Feeling tense or stressed	☐	☐	☐	☐	☐
Being unable to relax	☐	☐	☐	☐	☐
Excessive worrying about everyday matters	☐	☐	☐	☐	☐
Fear of something bad, or even the worst, happening	☐	☐	☐	☐	☐

25. In the past four weeks, did you experience episodes of the following symptoms? *Required*

Please don't select more than 1 answer(s) per row. Please

select at least 4 answer(s).

	Never	Rarely	Sometimes	Often	Nearly always

Panic or intense fear	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐
Heart palpitations and heart beating fast (not related to physical effort or activity)	☐	☐	☐	☐	☐
Fear of losing control	☐	☐	☐	☐	☐

26. In the past four weeks, to what extent did you fear or avoid the following situations?

Required

Please don't select more than 1 answer(s) per row. Please

select at least 3 answer(s).

	Never	Rarely	Sometimes	Often	Nearly always
Social situations (where one may be observed, or evaluated by others, such as speaking in public, or talking to unknown people)	☐	☐	☐	☐	☐

Public settings (situations from which it may be difficult or embarrassing to escape, such as queues or lines, crowds, bridges, or public transportation)	☐	☐	☐	☐	☐
Specific objects or situations (such as flying, heights, spiders or other animals, needles or blood)	☐	☐	☐	☐	☐

Page 5: More detail on your anxiety

The following pages of questions are based our earlier research where a large number of people with Parkinson's told us about their anxiety. We received a very wide range of descriptions of what anxiety felt like and was affected by. It is unlikely that any one person would experience all of the things described below. We now want to ask how typical each description is of the anxiety that you experience.

On each page the questions are grouped into small tables to make them easier to view. But if you would rather view each question individually you can do so by clicking 'view as separate questions instead?' (in blue).

Triggers

27. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When I am alone	☐	☐	☐	☐	☐
When I am not occupied/busy	☐	☐	☐	☐	☐
When I wake up	☐	☐	☐	☐	☐
At night	☐	☐	☐	☐	☐
When I am tired	☐	☐	☐	☐	☐
By specific seasons or extremes of weather	☐	☐	☐	☐	☐

28. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When I drink caffeine	☐	☐	☐	☐	☐
When I smell strong smells or odours	☐	☐	☐	☐	☐
When I have tremor	☐	☐	☐	☐	☐
When I have difficulty with movement or coordination	☐	☐	☐	☐	☐

29. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When I am at home	☐	☐	☐	☐	☐
By being outside my home	☐	☐	☐	☐	☐
When exercising	☐	☐	☐	☐	☐
When walking	☐	☐	☐	☐	☐

30. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When the ground looks slippery	☐	☐	☐	☐	☐
When in confined or enclosed spaces	☐	☐	☐	☐	☐
When in public settings	☐	☐	☐	☐	☐
When I am in crowded and/or noisy places	☐	☐	☐	☐	☐
If people are too close and I feel my movement is restricted	☐	☐	☐	☐	☐
When I am travelling	☐	☐	☐	☐	☐

31. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When I am in social situations (where one may be observed or evaluated by others, such as speaking in public or meeting new people)	☐	☐	☐	☐	☐

When I am ignored in social situations	☐	☐	☐	☐	☐
When I eat in public	☐	☐	☐	☐	☐
When I am unsure if I can reach a toilet in time	☐	☐	☐	☐	☐
When I feel time pressured (for example making it to an appointment in time or at a supermarket till where I have to coordinate tasks quickly)	☐	☐	☐	☐	☐
When others do not understand what I am experiencing	☐	☐	☐	☐	☐

32. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When loved ones get upset	☐	☐	☐	☐	☐
When I have disagreements with others or am criticised by others	☐	☐	☐	☐	☐

When I am stressed by life or work (e.g. when a number of tasks fall together)	☐	☐	☐	☐	☐
When I do not meet demands or expectations	☐	☐	☐	☐	☐
When I am not able to perform a task or role that I previously would have been able to	☐	☐	☐	☐	☐
When trying to organise myself and make decisions	☐	☐	☐	☐	☐

33. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When I am having a medical consultation/appointment	☐	☐	☐	☐	☐
When I am unhappy about the healthcare I am receiving	☐	☐	☐	☐	☐
When I see others at the later stage of Parkinson's	☐	☐	☐	☐	☐
When reading about Parkinson's	☐	☐	☐	☐	☐

I am not aware what the trigger is or why the anxiety occurs	☐	☐	☐	☐	☐

34. How typical is it that your anxiety is triggered or made worse by the items below?

Please don't select more than 1 answer(s) per row.

	Not applicable	Never or almost never	Rarely	Sometimes	Often	Always or almost always
When I have hallucinations	☐	☐	☐	☐	☐	☐
When I have difficulties with sexual performance	☐	☐	☐	☐	☐	☐
When I am in pain	☐	☐	☐	☐	☐	☐
Around menstruation	☐	☐	☐	☐	☐	☐

Page 6: More detail on your anxiety

Thoughts

35. How typical is it that you have thoughts on the following issues when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I compare my health status to those who are in better health	☐	☐	☐	☐	☐
I worry about the rate at which my Parkinson's symptoms progress and how I will cope at their worst	☐	☐	☐	☐	☐
I worry about falling and/or the consequences of falling	☐	☐	☐	☐	☐
I worry about my speech (e.g. not speaking clearly or being understood)	☐	☐	☐	☐	☐
I worry I will freeze (stop moving) in hazardous situations	☐	☐	☐	☐	☐
I worry I will get dementia	☐	☐	☐	☐	☐

36. How typical is it that you have thoughts on the following issues when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I worry about my employability	☐	☐	☐	☐	☐
I worry about money and my ability to maintain financial security	☐	☐	☐	☐	☐
I worry that I am not able to contribute and will let others down or become a burden	☐	☐	☐	☐	☐
I fear being left alone because others are not able to cope with my symptoms	☐	☐	☐	☐	☐
I worry about the impact of my Parkinson's on my family and how they will cope	☐	☐	☐	☐	☐
I am worried that others are embarrassed to be with me	☐	☐	☐	☐	☐

37. How typical is it that you have thoughts on the following issues when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I worry about my death	☐	☐	☐	☐	☐
I focus too much on my medication (e.g. when its due, side effects, whether it's working)	☐	☐	☐	☐	☐
I worry I will lose control and won't be able to do my everyday tasks	☐	☐	☐	☐	☐
I worry I will lose my identity	☐	☐	☐	☐	☐
I worry about my future ability to be an effective parent or carer for those who need my support	☐	☐	☐	☐	☐
I worry about having to go into a care home and the quality of the care I would receive there	☐	☐	☐	☐	☐

38. How typical is it that you have thoughts on the following issues when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always

I worry about upsetting those close to me or making things difficult for them	☐	☐	☐	☐	☐
I worry how others will perceive my Parkinson's symptoms and that they will judge me negatively	☐	☐	☐	☐	☐
I worry that someone will knock me over in busy places	☐	☐	☐	☐	☐
I worry about eating in public and that others will judge me negatively	☐	☐	☐	☐	☐
I worry about dribbling and that others will judge me negatively	☐	☐	☐	☐	☐
I am embarrassed by the frequency and urgency with which I need to urinate	☐	☐	☐	☐	☐

39. How typical is it that you have thoughts on the following issues when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I worry about the embarrassment of having a toileting accident (being incontinent)	☐	☐	☐	☐	☐
I worry that I will be not be able to function properly in public situations (e.g. on escalators, in supermarkets, in pubs)	☐	☐	☐	☐	☐
I worry that I stand out as different	☐	☐	☐	☐	☐
I compare my current abilities to my past abilities	☐	☐	☐	☐	☐
I worry about feeling anxious; how long it will last for, whether it will impact on my health, or how I will cope with it	☐	☐	☐	☐	☐

When experiencing physical symptoms of anxiety, I worry that they mean something more catastrophic (for example that I will stop breathing, pass out, have a stroke or a heart attack)	☐	☐	☐	☐	☐

40. How typical is it that you have thoughts on the following issues when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I worry about what is causing my anxiety	☐	☐	☐	☐	☐
I worry that others will notice I'm anxious	☐	☐	☐	☐	☐
I think about past events over and over again	☐	☐	☐	☐	☐
I worry about the possibility of failing or making a mistake	☐	☐	☐	☐	☐
I worry about the possibility of being late to appointments	☐	☐	☐	☐	☐
I worry about the welfare of others	☐	☐	☐	☐	☐

Page 7: More detail on your anxiety

Physical symptoms

41. How typical is it that you experience the following physical symptoms when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
Changes to body temperature	☐	☐	☐	☐	☐
Increased sweating	☐	☐	☐	☐	☐
Increased heart rate	☐	☐	☐	☐	☐
Headache	☐	☐	☐	☐	☐
Muscle tension	☐	☐	☐	☐	☐
Chest discomfort	☐	☐	☐	☐	☐

42. How typical is it that you experience the following physical symptoms when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
Fatigue or tiredness	☐	☐	☐	☐	☐
Stomach discomfort (churning/butterflies)	☐	☐	☐	☐	☐

I need to use the toilet	☐	☐	☐	☐	☐
Nausea	☐	☐	☐	☐	☐
Feeling disorientated or dizzy	☐	☐	☐	☐	☐
Restlessness	☐	☐	☐	☐	☐
Difficulty breathing	☐	☐	☐	☐	☐
Feeling very alert and focused	☐	☐	☐	☐	☐

Page 8: More detail on your anxiety

Emotions

43. How typical is it that you experience each of the following emotions when anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
Feeling overwhelmed	☐	☐	☐	☐	☐
Feeling of dread	☐	☐	☐	☐	☐
Feeling nervous	☐	☐	☐	☐	☐
Feeling panicked	☐	☐	☐	☐	☐
Feeling frightened/scared/terrified	☐	☐	☐	☐	☐
Feeling upset	☐	☐	☐	☐	☐
Feeling irritated	☐	☐	☐	☐	☐
Feeling angry	☐	☐	☐	☐	☐

Page 9: More detail on your anxiety

Behavioural changes

44. How typical is it that you behave in each of the following ways when anxious or to avoid becoming anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I am more argumentative or short tempered	☐	☐	☐	☐	☐
I try to disguise my anxiety	☐	☐	☐	☐	☐
I try to distract myself from the anxiety	☐	☐	☐	☐	☐
I drink alcohol to try to reduce my anxiety and/or Parkinson's symptoms	☐	☐	☐	☐	☐
I physically harm myself when anxious	☐	☐	☐	☐	☐

I plan things in great detail, including how to get out of a situation/location quickly (e.g. sit near the exit or toilet)	☐	☐	☐	☐	☐

When I enter an anxiety provoking situation I try to get in and out of the situation as quickly as possible	☐	☐	☐	☐	☐

45. How typical is it that you behave in each of the following ways when anxious or to avoid becoming anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I prefer to be accompanied by someone familiar when going into new places/situations	☐	☐	☐	☐	☐
I withdraw and isolate myself	☐	☐	☐	☐	☐
I avoid giving an opinion or disagreeing with others	☐	☐	☐	☐	☐
I avoid decision making and/or positions of responsibility	☐	☐	☐	☐	☐
I avoid social interactions	☐	☐	☐	☐	☐
I avoid leaving home	☐	☐	☐	☐	☐

I over-analyse or check over things more than I need to	☐	☐	☐	☐	☐

46. How typical is it that you behave in each of the following ways when anxious or to avoid becoming anxious?

Please don't select more than 1 answer(s) per row.

	Never or almost never	Rarely	Sometimes	Often	Always or almost always
I avoid public situations	☐	☐	☐	☐	☐
In public, I select food or drink that is easier to manage or I avoid eating or drinking altogether	☐	☐	☐	☐	☐
I avoid busy or crowded places	☐	☐	☐	☐	☐
I avoid confined spaces or places that are not easy to escape from	☐	☐	☐	☐	☐
I avoid driving	☐	☐	☐	☐	☐
I avoid some methods of travel (e.g. public transport, car travel, plane travel, etc.)	☐	☐	☐	☐	☐

Page 10: More detail on your anxiety

Impact

47. In each of the areas below, to what extent does your anxiety impact you?

Please don't select more than 1 answer(s) per row.

	Not at all	Rarely	Sometimes	Often	Always
Has impacted my confidence	☐	☐	☐	☐	☐
Has restricted me and impacted my freedom and independence	☐	☐	☐	☐	☐
Has made my Parkinson's symptoms worse	☐	☐	☐	☐	☐
Has impacted my sleep	☐	☐	☐	☐	☐

48. In each of the areas below, to what extent does your anxiety impact you?

Please don't select more than 1 answer(s) per row.

	Not at all	Rarely	Sometimes	Often	Always
Has impacted my relationships	☐	☐	☐	☐	☐
Has made me more isolated	☐	☐	☐	☐	☐
Has made it harder to complete daily tasks	☐	☐	☐	☐	☐

Has made it hard to think clearly	☐	☐	☐	☐	☐
Has made it hard to express myself	☐	☐	☐	☐	☐

49. In each of the areas below, to what extent does your anxiety impact you?

Please don't select more than 1 answer(s) per row.

	Not applicable	Not at all	Rarely	Sometimes	Often	Always
Has impacted my ability to work	☐	☐	☐	☐	☐	☐
Has impacted my ability to be an effective parent or carer for those who need my support	☐	☐	☐	☐	☐	☐

Page 11: More detail on your anxiety

50. How much do you agree with the following statements about your anxiety?

Please don't select more than 1 answer(s) per row.

	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree

I view my anxiety as a proportionate and rational response to the difficulties I experience with Parkinson’s	☐	☐	☐	☐	☐
I view my anxiety as largely irrational and out of proportion	☐	☐	☐	☐	☐
My anxiety was triggered or made worse in the period just after my diagnosis of Parkinson’s	☐	☐	☐	☐	☐
There is no fixed focus to my worry; I worry about anything, including irrational things, things I have no control over	☐	☐	☐	☐	☐
I feel out of control with my worry and find it hard to stop	☐	☐	☐	☐	☐
I worry about small things that never used to bother me as much	☐	☐	☐	☐	☐
I blow things out of proportion and make mountains out of molehills	☐	☐	☐	☐	☐

Page 12: submission of survey

The survey is nearly complete.

Remember for queries related to the survey, you can contact Daniel Curran (chief investigator) daniel.curran@uea.ac.uk or Dr Katherine Deane (project supervisor) k.deane@uea.ac.uk

We would like you to know that more information about anxiety in Parkinson's can be found on the Parkinson's UK website https://www.parkinsons.org.uk/information-and- support/anxiety

We would also like to make you aware that there are free and confidential helplines that you can contact for advice and support, see below:

Call Samaritans for free any time on 116 123. They offer a confidential listening service. See also https://www.samaritans.org/
Call Parkinson's UK on Free* confidential helpline 0808 800 0303 Monday to Friday 9am–8pm
Call SANEline on 0300 304 7000 between 4.30pm and 10.30pm each evening. You may also wish to speak to your GP if you feel you need further support with coping with your anxiety.

To submit your responses please click 'finish' below. Please remember that clicking 'finish' will confirm that your consent to participate in this survey.

Page 13: Final page

Thank you very much for taking the time to complete this survey. We

really value your contribution.

Remember, you can contact Daniel Curran (chief investigator) daniel.curran@uea.ac.uk or Dr Katherine Deane (project supervisor) k.deane@uea.ac.uk

We would like to remind you that more information about anxiety in Parkinson's can be found on the Parkinson's UK website https://www.parkinsons.org.uk/information-and- support/anxiety

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Call Parkinson's UK on Free* confidential helpline 0808 800 0303 Monday to Friday 9am–8pm
Call SANEline on 0300 304 7000 between 4.30pm and 10.30pm each evening. It may also be advisable to contact your GP

What's next?

You now have the option to provide us with your contact email. Please do this if you would like us to provide you with a brief report of our research findings when the project is complete.

If this interests you, please click on the following link:

https://uea.onlinesurveys.ac.uk/contact-details

Appendix M: Ethical Approval from Faculty of Medicine and Health Sciences Ethics Committee

Faculty of Medicine and Health Sciences Research Ethics Committee

Daniel Curren
MED

Research & Innovation Services
Floor 1, The Registry
University of East Anglia
Norwich Research Park
Norwich, NR4 7TJ

Email: fmh.ethics@uea.ac.uk

Web: www.uea.ac.uk/researchandenterprise

10 January 2019

Dear Daniel

Title: **Anxiety in Parkinson's: A mixed methods investigation**

Reference: 201819 - 046

Your submission (above) was considered by the Faculty Research Ethics Committee at their meeting on 13 December 2018, and following subsequent review of some minor amendments, I confirm that your proposal has been approved.

Please could you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance and also that any adverse events which occur during your project are reported to the Committee. Please could you also arrange to send us a report once your project is completed.

Approval by the FMH Research Committee should not be taken as evidence that your study is compliant with GDPR and the Data Protection Act 2018. If you need guidance on how to make your study GDPR compliant, please contact your institution's Data Protection Officer.

Yours sincerely

Professor M J Wilkinson
Chair
FMH Research Ethics Committee

Appendix N: List of Codes Identified for the Nominal Group Technique Analysis in the Empirical Paper

Trigger	Thought	Behaviour	Emotion	Physical	Impact
TR1 = Unknown	TH1 = Various focal points	B1 = Safety seeking behaviours	E1 = Upset	P1 = Fight or flight	I1 = Verbal expression
TR2 = Social situations	TH2 = Future PD progression /impact	B2 = Alcohol	E2 = Scared	P2 = Fatigue	I2 = Cognition
TR3 = Out of home / in public	TH3 = Family	B3 = Checking	E3 = Dread	P3 = Headache	I3 = Work
TR4 = Busy / crowded / environments	TH4 = Finances /employment	B4 = Isolative	E4 = Angry		I4 = Confidence
TR5 = Night / Sleep/Tired	TH5 = Catastrophic misinterpretation of physical anxiety symptom	B5 = Escape	E5 = Irritated		I5 = Independence
TR6 = Parkinson's Symptoms	TH6 = Social evaluation	B6 = Behavioural expression of difficult emotion	E6 = Nervous		I6 = Increase Parkinson's symptoms
TR7 = Time pressure / Demand / Organisation	TH7 = Process of worry	B7 = Avoid social situations	E7 = Overwhelmed		I7 = Sleep
TR8 = Interpersonal/ relationship	TH8 = Meta-worry	B8 = Avoid busy places	E8 = Stressed		I8 = Relationships
TR9 = Confined Spaces	TH9 = Irrational	B9 = Avoid leaving home			I9 = Daily tasks
TR10 = Travel	TH10 = Something catastrophic	B10 = Avoid travel			
TR11 = Meeting life demands / expectations	TH11 = Going out alone	B11 = Avoid new places / activities			
TR12 = Toilet related	TH12 = Crowds	B12 = Avoid decision making / responsibility			

Trigger	Thought	Behaviour	Emotion	Physical	Impact
TR13 = New scenarios / out of comfort zone	TH13 = Toilet	B13 = Attempt to disguise anxiety			
TR14 = Being unoccupied	TH14 = Falling	B14 = Attempt to Distract from anxiety			
TR15 = Chemicals	TH15 = Being alone	B15 = Self-harm			
TR16 = Exercise	TH16 = Past				
TR17 = Season / time of day	TH17 = Compare to others / past				
TR18 = Menstruation	TH18 = Speech				
TR19 = Isolation	TH19 = Fear of failure				
TR20 = Medical/PD contact	TH20 = Future Dementia				

Appendix O: Items for Online Appendix for Movement Disorders (Empirical Project)

Table 1: Items with medians below the cut off for inclusion in main paper

Triggers	**N**	**Median**	**Theme**
When I am at home	334	2	N
When exercising	332	2	EP
When walking	333	2	EP
When I am unhappy about the healthcare I am receiving	336	2	EP
When I wake up	334	2	EP
By specific seasons or extremes of weather	333	2	EP
When I have hallucinations	75	2	P
Around menstruation	6	1.5	N
When I drink caffeine	337	1	N
When I smell strong smells or odours	334	1	N
Thoughts			
When experiencing physical symptoms of anxiety, I worry that they mean something more catastrophic (for example that I will stop breathing, pass out, have a stroke or a heart attack)	332	2	N
I worry that I stand out as different	338	2	EP
I worry about dribbling and that others will judge me negatively	338	2	P
I worry that someone will knock me over in busy places	340	2	EP
I focus too much on my medication (e.g. when its due, side effects, whether it's working)	334	2	EP
I am worried that others are embarrassed to be with me	338	2	EP
I fear being left alone because others are not able to cope with my symptoms	336	2	EP
I worry about money and my ability to maintain financial security	339	2	EP
I worry I will freeze (stop moving) in hazardous	337	2	P

situations			
I worry about my employability	333	1	EP
Behaviours			
I avoid driving	328	2	EP
I avoid some methods of travel (e.g. public transport, car travel, plane travel, etc.)	337	2	EP
I avoid leaving home	333	2	EP
I drink alcohol to try to reduce my anxiety and/or Parkinson's symptoms	337	1	EP
I physically harm myself when anxious	336	1	N
Physical Symptoms			
Difficulty breathing	336	2	N
Feeling very alert and focused	226	2	EP
Headache	332	2	EP
Feeling disorientated or dizzy	337	2	N
Nausea	336	2	EP
Chest discomfort	332	2	N

Note. P = directly related to Parkinson's; N = normal for anxiety outside of Parkinson's EP = common anxiety experience but likely exacerbated by Parkinson's. Likert Scale: 1 = Not at all, 2 = Rarely, 3 = Sometimes, 4= Often, 5 = Always.

Table 2. Full list of participant demographic and clinical information

Variable	Survey one percentage (%) of participant sample (n = 205)	Survey two percentage (%) of participant sample (n = 341)
Sexual Orientation		
Heterosexual	95.60	96.50
Homosexual	1.50	0.30
Bisexual	2.00	2.00
Prefer not to say	1.00	0.30
Other	0	0.90
Living Arrangements		
Live in own home	94.60	95.60
Live in supported accommodation	1.50	0.30
Other	3.90	4.10
Care arrangements		
Live with family, but do not require support from them or others	57.70	58.30
Live with family and require support from them or others	27.80	26.10
Live alone and require no additional care	11.30	11.00
Live alone and require support from family or others	1.50	3.40
Other	1.00	0.30
Prefer not to say	0.50	0.90
Additional physical health condition	56.60	57.50
Anxiety diagnosis from medical professional	40.50	33.70
Overall impact of anxiety on your life	*Not asked*	
Not at all		2.10
Mildly		35.90
Moderate		49.10
Severe		12.60
Frequency of anxiety	*Not asked*	

Everyday		31.90
A few days per week		41.30
A few days per month		21.50
Less often		5.30
Extent to which anxiety increases when Parkinson's symptoms are bad	*Not asked*	
Never or almost never		5.30
Rarely		10.90
Sometimes		31.80
Often		35.90
Always		16.20
Years since diagnosis	5.08 (4.56)	5.69 (4.64)

Appendix P: List of codes identified for the Nominal Group Technique Analysis in the Additional Results and Discussion Chapter

Communication	Lifestyle	Therapies
C1 = General	L1 = Managing Demands	T1 = Psychological Therapies
C2 = Social Network	L2 = Diet	T2 = Physical Therapies
C3 = Professionals	L3 = Sleep	T3 = Mindfulness
C4 = Parkinson's specific	L4 = Connection	T4 = Medication
C5 = Not helpful	L5 = Staying Occupied	T5 = Alternative Medicine
C6 = Do not talk	L6 = Hobbies/Leisure	T6 = Other
	L7 = Exercise	T7 = Not helpful
	L8 = Mind body-exercise	T8 = Not attempted
	L9 = Being Outdoors	T9 = Access Challenges
	L10 = Relaxation	T10 = Complementary therapies
	L11 = Other	