Doctoral Thesis

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Factors Influencing Wellbeing in Carers of People with Huntington's Disease.

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Word Count

Thesis Section	Main Text	Appendices (including tables, figures, and references)	Total
Thesis Abstract	294	-	294
Literature Review	7,436	10,996	18,432
Research Paper	7,931	7,495	15,426
Critical Appraisal	3,936	1,564	5,500
Ethics	4,385	2,494	6,879
Total	23,982	22,549	46,531

Thesis Abstract

This thesis explores factors associated with wellbeing in carers of people with Huntington's disease (HD). Section one presents a systematic literature review examining factors associated with psychological outcomes in HD carers. Six databases were searched (CINAHL, EMBASE, MEDLINE, PsycINFO, Scopus, and Web of Science), resulting in 24 included papers. Caring for someone with more advanced HD, greater functional impairment, and more severe behavioural/psychological difficulties was associated with higher carer burden and carer depression. Indicators of providing higher amounts of care were associated with higher carer burden and lower quality of life. Evidence for other relationships was inconclusive. The findings additionally highlighted the need for further theoretically informed research.

Section two describes a cross-sectional quantitative study examining whether satisfaction with family relationships and friendships predicted positive wellbeing and negative feelings in HD carers. It further examined whether these relationship satisfaction variables moderated the relationships between person with HD functional capacity and behavioural/psychological difficulties and carer wellbeing outcomes. The study analysed secondary data from 880 people with HD and their carers participating in Enroll-HD, an international observational cohort study. Hierarchical multiple regression models found that satisfaction with family relationships and friendships were independent predictors of higher positive wellbeing and lower negative feelings in HD carers, after controlling for carer demographics, caring intensity, and person with HD motor and cognitive difficulties, functional capacity, and behavioural/psychological difficulties. These findings were consistent across sub-group analyses for spousal carers, adults caring for their parent, and main carers. However, moderation analyses were non-significant. The importance of

relationship satisfaction for wellbeing in HD carers suggests interventions to support this group would benefit from considering both individual and systemic factors.

Section three presents a critical appraisal of these projects, including a discussion of their strengths, limitations, and personal reflections on the research process.

Declaration

This thesis was undertaken between January 2022 and June 2024 as part requirement of the Lancaster University Doctorate in Clinical Psychology. The work documented here is my own, except where due reference has been made in the text. This thesis has not been submitted for an award of a higher degree elsewhere.

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Date: 28th June 2024

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Section One: Systematic Literature Review

A Systematic Review of Factors Associated with Psychological Outcomes in Carers of People with Huntington's Disease.

Word count: 7,436

(Excluding title page, references, figures, tables, and appendix)

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Abstract

This systematic review is the first to collate and synthesise the findings from published quantitative empirical studies on factors associated with psychological outcomes in carers of people with Huntington's disease (HD). Six databases (CINAHL, Embase, Medline, PsycINFO, Scopus, and Web of Science) were searched using search terms related to HD, carers, and psychological outcomes. Twenty-four studies were included. Results were summarised using narrative synthesis, grouped by conceptually similar outcomes. The most frequently measured outcome was quality of life, although a wider variety of potential associated factors were studied for carer burden. Examined variables differed but included carer demographics, caring environment characteristics, HD-related difficulties, and social support. Caring for someone with more advanced HD with greater functional impairment and more severe behavioural/psychological difficulties was associated with higher carer burden and carer depression, although with less evidence for depression. Indicators of greater caring intensity, such as longer time spent caring and being the main carer, were associated with higher burden and lower quality of life. Evidence for other relationships was inconclusive and studies rarely used psychological theory. Results indicate the need for further research using larger samples, longitudinal methods, and theoretically informed analyses to strengthen the evidence base and inform carer support interventions.

Keywords: Huntington's disease, caregivers, caregiver burden, quality of life, psychological wellbeing

A Systematic Review of Factors Associated with Psychological Outcomes in Carers of People with Huntington's Disease.

Internationally, the demand for long-term care is rising due to factors such as population ageing and increases in long-term health conditions [1,2]. This demand is predominantly met by "informal" carers, who provide unpaid care to family or friends requiring support due to ill health or disability [3]. While caring for a loved one can be rewarding, it can also present challenges, including difficult and/or physically demanding tasks, financial pressures, social isolation, and physical health problems [4,5]. Psychological difficulties are also common, including perceived burden, anxiety, depression, and stress [6–8]. Moreover, as well as being problematic in their own right, psychological difficulties in carers are associated with carer burnout and care breakdown [7,9], highlighting the importance of understanding and attending to carers' emotional health. However, in many countries, carers' needs are overlooked or poorly understood in healthcare policy and practice, with poor provision of formal support [10,11].

The Experience of HD Carers

Evidence suggests that carers of people with rare conditions such as Huntington's disease (HD) are at risk of experiencing unmet practical and psychological needs [12]. HD is a genetic neurodegenerative condition which affects approximately 4.8 persons per 100,000 globally [13]. It develops due to an expansion in the cytosine-adenine-guanine (CAG) repeat and causes progressive motor impairment and cognitive problems; behavioural and psychological difficulties are also common [14]. There is no cure and limited treatments for symptoms. Formal diagnosis ("manifest HD") is made when unequivocal motor symptoms are present, typically in middle age [15]. The term 'premanifest' is used to describe

individuals who carry the genetic expansion, confirmed by genetic testing, but have not yet developed motor symptoms. Similar to other long-term conditions, the care needs of people with HD (pwHD) are predominantly met by family or friends [16].

Although carers of pwHD face similar difficulties to other carers, HD presents some additional unique challenges. Its progressive nature requires carers to adapt continually, and features of HD, such as unpredictable and aggressive behaviour, irritability, and perseveration (difficulty switching ideas or stopping behaviours), can be challenging to manage [17–19]. Caring is often juggled with childcare and employment as HD presents in middle age, and financial difficulties are common due to the impact on work for carers and pwHD [20]. Carers have reported experiencing prolonged grief and loss related to changes in their relationship with their loved one and previous roles and identities [21]. The genetic nature of HD means that carers may be at risk of or have children at risk of HD, have witnessed HD progression in family members, or provide care to multiple pwHD [20]. Carers of pwHD also report isolation, loss of social connections, lack of understanding and appropriate support from professionals, and stigma and discrimination [21–23]. Within this challenging context, carers of pwHD report lower quality of life (QoL) and higher psychological distress and mood problems than carers of people with other neurological conditions [24–26].

Theoretical Approaches to Carer Wellbeing

Stress process/stress coping models [27,28] are frequently employed to understand how caring impacts positive and negative indicators of wellbeing [29–31]. In these models, elements of caring, such as caring environment characteristics, care recipient clinical factors, and the strain caring can place on other roles, relationships, and self-identity, are viewed as stressors. While stressors can directly influence wellbeing, their impact is highly contingent on the resources available to carers to manage their role, including psychosocial resources

such as coping skills, beliefs, and social support, and carers' appraisals of their resources and ability to cope.

While these models have found empirical support in carers of people with neurological conditions [32–35], they have been criticised for framing caring solely as a stressful experience, driving a focus on negative concepts such as carer burden or strain and emotional distress in research which provides an unbalanced understanding of their experiences (Molyneaux et al., 2011; Purkis & Ceci, 2015; Quinn & Toms, 2019). More recently, positive psychology approaches have highlighted that carers of people with neurological conditions also report positive psychological outcomes, such as a sense of achievement or self-efficacy, increased closeness with family, spiritual growth, acceptance, and positive appraisals of caring [39–41].

The Current Review

The link between caring for someone with HD and significant impacts on psychological health and wellbeing highlights the importance of understanding factors which increase the risk of psychological distress or promote wellbeing in carers of pwHD. Consequently, this paper aims to synthesise evidence regarding factors associated with psychological outcomes (e.g., QoL, carer burden, depression, etc.) in carers of pwHD. The review takes a broad focus to enable the inclusion of positive psychological outcomes; including only negative experiences is likely to provide a skewed picture and hinder attempts to develop theory and practice regarding the facilitators of wellbeing in carers of pwHD [38,42]. The results of this review could contribute to the wellbeing of carers of pwHD by supporting the identification of those at risk of negative outcomes, informing the development of effective psychological interventions, and influencing healthcare policy and service development to meet the needs of carers of pwHD. Efforts to support carer

psychological health and wellbeing may also have positive implications for pwHD, as poorer carer mental health and carer burden are associated with worse health outcomes in care recipients [43–45].

This review builds on three existing reviews about the psychological experiences of carers of pwHD [20,21,46], although these had different review questions. Additional papers may have been published since Domaradzki's [20] review of quantitative and qualitative papers about the experiences of family caregivers of people with manifest HD. Additionally, this review may have excluded relevant literature due to date limits on searches, and it did not search multiple databases or conduct a quality appraisal, limitations which are addressed in this review. The focus on quantitative literature in the present review could complement findings from a meta-synthesis of qualitative studies about the experiences of carers of pwHD [46]. More recently, a mixed methods review created a taxonomy of experiences of spiritual suffering, grief/loss, and coping in carers of pwHD [21]. In contrast, the present review summarises factors quantitatively associated with any psychological outcome in carers of pwHD. Therefore, the current review aimed to synthesise and evaluate the existing quantitative evidence regarding factors associated with carer psychological outcomes to provide an up-to-date understanding of these factors, which is currently lacking, and identify potential gaps in the literature for future research. The research question was "What are the factors associated with psychological outcomes in carers of people with premanifest or manifest HD?".

Materials and Methods

This review aimed to identify, evaluate, and synthesise existing quantitative evidence on factors associated with psychological outcomes in carers of people with premanifest or manifest HD. The review protocol was pre-registered on the prospective register of

systematic reviews (PROSPERO; ID number: CRD42023430991) and conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [47].

Searches

Informal scoping searches were completed using PsycINFO to identify possible search terms and assess topic suitability. Formal searches were then completed using CINAHL, EMBASE, Medline, PsycINFO, Scopus, and Web of Science in May 2023, combining terms for caregivers, Huntington's disease, and psychological outcomes (see Table 1.1 for search strategy example). Databases were selected to provide coverage of psychological and medical journals where relevant literature was likely to be published. The search strategy was developed with an academic librarian. No filters or date limits were used and, therefore, papers would be included back to the earliest papers each database included.

[Insert Table 1.1]

Inclusion Criteria

Studies were included if they:

- Were available in English
- Were peer-reviewed empirical papers (the author checked that publishing journals employed peer review)
- Included participants who were informal (e.g., not paid) carers of at least one individual with HD (premanifest and/or manifest)
- Used a quantitative design to identify statistical relationships between carer psychological outcomes and at least one other variable (e.g., demographics, clinical

variables, or other psychological variables). Any statistical design was included (e.g., correlations, t-tests, regression, etc.)

- Studies involving carers of other conditions were included if HD carer results were reported separately
- The inclusion criteria, pre-registered on PROSPERO, indicated that participants should be carers of people with genetically confirmed HD. However, many papers did not clearly report the genetic status of pwHD. Therefore, studies where participants were described as carers of pwHD were included.

Studies were excluded if they:

- Used qualitative methodology only
- Reported on formal (paid) carers
- Were not published in a peer-reviewed journal, e.g., theses, dissertations etc.
- Were intervention studies which reported the only intervention effects (i.e. no baseline cross-sectional data were included indicating a relationship between variables)

Selection

Searches returned 8,195 results. Mendeley [48] was used to manage references and Rayyan.ai [33] was used for screening. Initially, 4,320 duplicates were removed. Title and abstract screening according to the inclusion criteria resulted in 3,771 exclusions. Full texts of the remaining 126 articles were assessed for eligibility. Of these, 24 were included (see Figure 1). Several articles were excluded because it was unclear whether participants were carers. For example, some studies included spouses of pwHD who may have been carers, but this was not mentioned [e.g., 49]. Another paper using secondary data described gene-negative and family control groups as carers, but it was unclear from reporting or measures

used whether they provided care [50]. Following discussion with the supervisory team, it was agreed that articles would be included if participants were identified as carers, demographic information demonstrated most participants provided care, or carer-specific measures were used. One study was excluded as its outcome measure related to a specific HD symptom (fear of choking and dysphagia) rather than an indicator of general psychological health or wellbeing [51]. A second researcher assessed the eligibility of 12 articles (10%) at full-text stage blinded to the initial decision, finding no discrepancies. Reference lists of included papers were hand searched, identifying no new papers.

[Insert Figure 1]

Data Extraction and Synthesis

The following data were extracted into a Microsoft Excel worksheet: author, year, country of origin, sample size and recruitment setting, demographics, and caregiving context variables (e.g., relationship with pwHD, main carer), methodology, variables investigated including measures used, findings and related statistical outputs (including measures of effect where present), and theoretical models used. Where appropriate data were available, Pearson's *r* was calculated as a measure of effect for the reported associations. A narrative synthesis was conducted following guidance from Popay et al.[52]. The diversity of examined variables, and statistical approaches for particular variables, meant there were only a very small number of directly comparable analyses across the findings. Thus, the data were unsuitable for meta-analysis due to substantial methodological and statistical heterogeneity [53]. While it may be possible to conduct a meta-synthesis with a small number of studies, a number of limitations have been raised. For example, findings may not be robust, may lack generalisability, and may be influenced by bias and outliers [54,55]. Moreover, narrative

synthesis has been argued to be preferable when studies are heterogeneous, outcomes are measured differently, or the quality is variable [56,57]. Narrative synthesis has been argued to emphasise flexibility and depth, allowing for a nuanced interpretation that acknowledges study differences and broader contextual insights [57,58]. In this context, narrative synthesis was considered better suited to the current evidence base and scope of the review.

Findings across the studies were grouped by conceptually similar outcomes. Tabulation was used to preliminarily synthesise paper characteristics and results, identifying reported variables and patterns in their associations with carer outcomes. Relationships within and between studies were examined, with consideration of the quality assessment, methods, and other potential moderating factors. Finally, the robustness of the synthesis was considered through critical reflection and the PRISMA checklist.

Quality Assessment

Kmet et al.'s (2004) 14-item quality assessment tool was used to evaluate the methodological quality of included papers. Areas assessed include appropriateness of methods, processes undertaken to limit bias in sampling and analyses, and quality of reporting. It was chosen because it was designed for use with varied study designs and has been used in reviews about psychological outcomes in carers [59,60]. Further, its instructions aid reproducibility, with most questions demonstrating acceptable to excellent inter-rater reliability [61]. Items can be scored as yes = 2, partial = 1, no = 0, or not applicable. Summary scores are calculated by dividing the total score by the number of eligible questions (e.g., excluding N/A questions) and multiplying by 100. A second researcher appraised 25% (n = 6) of papers independently. Discrepancies generally related to criteria interpretation and were resolved via discussion.

Results

Study Characteristics

The 24 studies were published between 2002 and 2023. Seventeen studies used a cross-sectional design. Five studies included longitudinal analyses over two time points. Two studies used experimental designs. Studies were conducted in the following countries: United States (*n* = 9), Poland (*n* = 3), The Netherlands (*n* = 3), France (*n* = 2), United Kingdom (*n* = 2), Australia (*n* = 2), international cohorts (*n* = 2), and Canada (*n* = 1).

Sample sizes ranged from 17 - 1,726 (*M* = 145), with a total of 3,489 participants included in this review. Of the 17 studies which reported gender breakdowns, seven samples were relatively equally split between men and women (45-59%), and ten had predominantly female samples (60-88%). Twenty studies reported age data; most carers were middle-aged (*M* range = 43-60 years). Of the 14 studies that reported the relationship between carer and pwHD, 13 identified spouses/partners as the largest group (48-100%). Ten studies reported that 47.0-100% of carers lived with the pwHD, while 14 papers reported no co-habitation information or reported it qualitatively. Five studies reported whether the participant was the main carer, ranging from 48-90%. Twelve studies included carers of people with manifest HD. Twelve studies either did not report HD status or reported it ambiguously, for example, referring to genetic status (Modrzejewska-Zielonka et al., 2022; Tanigaki et al., 2020), parents with HD (Kavanaugh, 2014), or carers of pwHD.

Studies reported the following psychological outcomes: QoL or life satisfaction (*n* = 13*)*; carer burden (*n* = 11); mood (depression (*n* = 5*)*; anxiety (*n* = 1); and psychological distress (*n* = 1)); and perceived benefits of caring (*n* = 2*)*. See Table 1.2 for study characteristics.

[Insert Table 1.2]

Quality Appraisal

Quality appraisal scores ranged from 53.8-90.9%. Studies dropped points for using sampling approaches which may have introduced bias and use of small samples. Several papers also dropped points due to unclear or lack of reporting of information necessary to answer questions. Full scores are given in Table 1.3.

[Insert Table 1.3]

Outcome Measures

Carer Burden

Four validated measures of subjective carer burden were used, which assess negative perceptions about the impact of caring on areas including psychosocial function, emotional health, and practical aspects of life like finances. Four studies used the Zarit Burden Inventory [62,63], three studies used the Caregiver Strain Index [64], three studies used the 24-item Caregiver Burden Inventory [65], and two studies used the subjective burden sub-scale from the Caregiver Appraisal Scale [66].

Quality of Life/Life Satisfaction

Five validated measures of QoL/life satisfaction were used. Three studies measured health-related QoL (HR-QoL), a subjective assessment of functioning in areas of life directly or indirectly impacted by health, illness, or injury [67], using the 36-item Short-Form Health Survey [SF-36; 68] or the 136-item Sickness Impact Profile [SIP; 69], which assess the impact of illness on physical, social, and emotional functioning.

In contrast, eight papers used more holistic measures of QoL/life satisfaction, which include QoL factors beyond the impact of illness on functioning [70]. Six papers used either the 38-item or 15-item Huntington's Disease QoL Questionnaire for Carers (HDQoL-C) [71], which was developed with carers of pwHD. Its three subscales assess satisfaction with life, positive wellbeing, and negative feelings. One study used the 26-item World Health Organisation (WHO) QoL measure (WHOQoL-BREF Group, 1994), which examines mental and physical health, social relationships, and satisfaction with one's environment. One study measured general life satisfaction with the 13-item Life Satisfaction Index-Z [73]. Additionally, two studies used an unvalidated single item to assess overall QoL [70,74]. This was the only measure of QoL used Ready et al. (2008).

Benefits of Caring

Two validated measures to assess perceived benefits of caring were used, one developed for carers of people with cardiovascular disease [75] and one adapted from a scale developed for breast cancer patients [76]. Validation information for the adapted scale was not provided [77].

Mood

Four validated mood measures designed for general populations were used. One study used the 27-item Child Depression Inventory to assess depressive symptoms experienced in the last two weeks in adolescent participants [78]. One study used the 20-item Centre of Epidemiological Studies Depression Scale [79]. One study used the Hospital Anxiety and Depression scale [80]. One study measured the intensity of psychological distress using the 53-item Brief Symptom Inventory [81]. The latter measures assess symptoms experienced in the last week.

With the exception of the HDQoL-C, all measures used in the included studies were either generic or developed with different populations.

Study Results

Key findings are summarised below, grouped by outcome, with a section on carer burden, QoL/life satisfaction, mood, and benefits of caring. The following terms are used to refer to results: correlation/correlate was used when referring to findings from a correlation analysis (e.g., Pearson's or Spearman's correlation). Predictor was used when a finding is from a multivariate analysis which controls for the influence of other variables (e.g., multiple regression). Association was used as a general term to refer to a statistically significant relationship between two variables regardless of the statistical analysis used.

Carer Burden

Ten studies examined carer burden; see Table 1.4 for results summary.

[Insert Table 1.4]

Care/Carer Characteristics. Five studies examined relationships between carer demographics or care environment characteristics and carer burden. Two studies examined carer gender and age, one finding no association [82] and the other finding female gender and younger age were moderately correlated with higher burden, with younger age remaining a predictor in multivariate modelling [83]. Therefore, it is challenging to draw conclusions on the relationship between these variables and burden. All four studies including one or more variables indicative of higher caring intensity (e.g., being the main carer, higher time spent caring, cohabiting with pwHD, caring for more than one person), found that at least one was

associated with higher burden (small-moderate effect where reported) [82,84–86]. Higher caring intensity, therefore, appears associated with higher carer burden.

PwHD Characteristics. Ten studies examined associations between pwHD characteristics and carer burden. All three studies found that caring for someone in a more advanced stage of HD was associated with higher carer burden (moderate effect where reported/calculable) [85,87,88]. Of the four studies that examined duration of HD (in years), two found a non-significant relationship with carer burden (small effect where reported/calculable) [82,89], one found longer duration of HD was associated with lower carer burden (effect size not reported/calculable) [90], and one found longer HD duration predicted higher carer burden in multivariate modelling [86]. The lack of a clear association could relate to individuality in HD progression over time. No reliable conclusion could be drawn from the two studies examining associations between CAG repeat length and burden [89,90].

Seven papers examined relationships between motor symptoms and carer burden. Two studies found that more severe motor symptoms were correlated with higher carer burden (moderate effect where reported) [83,85] while another found no association (very small effect) [82]. The latter study used a dichotomised (rather than continuous) motor difficulties variable, with a small number of participants with no motor difficulties (n = 5), which may explain this difference. In multivariate regression models including other HD symptoms, three studies found no association [83,91,92] and one found that higher motor symptoms predicted higher carer burden [89]. This difference may relate to the other studies including measures of functional and cognitive capacity in their models.

Six studies found that measures of pwHD functioning (e.g., total functional capacity or independence) were associated with carer burden cross-sectionally [82,85,86,89,91] and longitudinal increases in burden [91] (moderate to large effect where reported/calculable).

Two of four studies found pwHD functioning remained a significant predictor in multivariate models [91,92]. Non-significant findings may relate to differences in included regression variables [86,89]. One study also found that lower functional capacity was indirectly associated with higher carer burden, predominantly mediated through variables indicative of HD severity [90]. These findings suggest that lower pwHD functional capacity was associated with higher carer burden.

Five of seven studies found that more severe behavioural/psychological difficulties, including total behavioural difficulties, apathy, irritability/aggression, depression, and behavioural executive dysfunction, were associated with (moderate-large effect where reported) [83,84,88] or predicted higher carer burden in multivariate models including other HD related difficulties [83,86,89,91,92]. Contrastingly, one study found that in carers of those with more advanced HD, higher apathy was associated with lower carer burden [88]. The study finding no association reported a very small effect, perhaps due to dichotomising the variable and having a very small group with no behavioural difficulties (n = 2) [82]. Thus, pwHD behavioural/psychological difficulties generally appear related to higher carer burden.

Two of three studies found indicators of lower cognitive function (including anosognosia: a lack of insight/awareness) were associated with higher carer burden with a large effect [83,92]. Multiple regression findings were equivocal, with two studies finding better cognitive function predicted lower burden [83,92] and two finding no relationship [89,91]. This suggests further research is needed to draw reliable conclusions.

Finally, four of five studies found that pwHD age was not directly associated with [83,84,90] or did not predict carer burden in multivariate modelling [89], suggesting a lack of a direct relationship between these variables.

Time. Two studies looked at whether levels of carer burden changed over time, with one finding increases when follow-up was 12 months or more (data to calculate effect not

reported) [85,91] and one finding no change, likely due to the short follow-up (8 weeks, data to calculate effect not reported) [85].

Income. No reliable conclusion could be drawn on income, with one study finding higher family income predicted lower carer burden in multivariate modelling [86] and the other finding no association [82], although it was underpowered to detect the small effect reported.

Social Support. One study found that higher social support, using a measure incorporating objective and subjective elements of social support, predicted lower carer burden in a multivariate model including HD clinical variables, caring environment characteristics, and family income [86].

QoL/Life Satisfaction

Eleven studies examined QoL or life satisfaction. Results are summarised in Table 1.5.

[Insert Table 1.5]

Care/Carer Characteristics. Five studies examined relationships between carer demographic or care environment characteristics and QoL/life satisfaction. One study found a small association between higher carer age and lower physical QoL [93]. One study found that spousal carers and carers of parents with HD reported lower emotional QoL compared to carers with other relationships (small effect) [94]. Two studies examined QoL differences in carers with children at risk of HD, with one finding emotional QoL was lower compared to carers without children at risk (small effect) [94], but both found no differences in overall QoL (very small effects) [82]. Similar findings regarding overall (non-significant very small

effect) and emotional quality of life (significant small effect) were observed for carers who lived with the pwHD compared to those who did not in one study [86]. Being the main carer was not associated with QoL in one study, although it was underpowered to detect the small effect reported [74]. The lack of replication of these findings suggests a need for further research examining associations between the relationship between carer and pwHD and QoL. Two of three studies found greater time spent caring (e.g., years or hours spent caring) had small-moderate associations with lower QoL [74,94], suggesting spending more time caring may be linked to lower QoL in HD carers.

Carer Psychological and Health Factors. Two of three studies found that higher depression/low mood correlated with (large effect) [93] or predicted lower QoL in multivariate analysis [25]. The third study found no correlation between depressive symptoms or perceived stressfulness and life satisfaction; however, it was underpowered (n = 17) to detect the small-moderate effects reported [95]. Thus, higher depression may be related to lower QoL. Further studies would be needed to establish the link between stress and QoL. Two studies also found that QoL was moderately associated with better perceived health status [71,95].

Roscoe et al. [95] examined several positive psychological constructs, finding that greater perceived benefits of caring, greater spirituality, and a higher sense of mastery in life had moderate to strong correlations with higher life satisfaction. Helder et al. [96] examined carers' illness appraisals and coping styles, finding that, after controlling for carer demographics and HD-related factors, greater attribution of pwHD difficulties to HD and active and restraint (waiting to act) coping predicted lower physical and emotional QoL, while more planning predicted higher physical QoL. However, more studies would be necessary to confirm the links identified in these papers.

PwHD Characteristics. Two out of five studies found that indicators of symptom severity, including higher overall symptoms, and lower motor function, cognitive function, and functional capacity in the pwHD, were associated with lower QoL (moderate effect where reported) [70,97], although non-significant findings came from studies which were underpowered to detect reported small-moderate effects found reliably [74,82,95]. Total behavioural difficulties were not associated with QoL in two studies (small effects) [70,82], although, when behaviours were examined individually, disruptive/aggressive behaviour had a strong negative correlation with QoL [70]. One study found that higher HD-related difficulties strongly correlated with higher QoL when carers' appraisals of caring and their capabilities were controlled [95]. This study's focus on late-stage HD may have meant more pwHD in the sample received care outside the home (53% residential care) than in other studies, which could reduce the impact of HD-related difficulties on carers. Thus, reliable conclusions about the relationship between pwHD characteristics and carer QoL cannot be drawn.

Time. Two studies examined change in QoL over time, finding no significant changes at six or 12-month follow-up [25,70]. Although the studies were underpowered, the small effect (where reported/calculable) suggests a lack of clinically significant change.

Social Support. Three studies examined relationships between social support and QoL/life satisfaction, finding that the amount of social contact [87] and measures of satisfaction with social support focused on emotional support correlated with (moderate effect) [95] or predicted higher QoL in multivariate modelling [25].

Income. Two studies found no association between household income or economic pressure and QoL [25,82], although they were underpowered to reliably detect the small-moderate effects reported for these variables.

Mood

Five studies examined factors associated with mood-related variables. Results are presented in Table 1.6.

[Insert Table 1.6]

Carer Characteristics. Three studies examined the relationship between carer demographics and carer depression, finding no significant correlations for gender, ethnicity, education level, relationship to pwHD, marital status, and indicators of caring intensity (e.g., time spent caring, number of care tasks performed) [84,95,98]. However, these studies were underpowered to reliably detect the small effects reported (where reported/calculable).

Carer Psychological and Health Factors. Two studies examined carer psychological factors and depression. Moderate to large correlations were found between a higher sense of control over problem-solving (Pickett et al., 2007), sense of mastery, spirituality, and lower perceived stressfulness [95] and lower depression. Indicators of poorer carer health were strongly correlated with higher depression, including lower carer perceived health status [95] and higher daytime sleep problems [99]. However, the lack of replication of these findings precludes drawing firm conclusions about links between carer psychological/health factors and depression.

PwHD Characteristics. Two of three studies that examined pwHD behavioural/psychological factors found that higher pwHD depression and being difficult to get on with had small correlations with higher carer depression [84,98]. Pickett et al. [84] also found that lower pwHD physical functioning was indirectly (but not directly) associated with higher carer depression via caregiver burden.

Time. One study found no significant difference in carer mood between baseline and 12-month follow-up (data to calculate effect size not reported) [25]**.**

Psychosocial. One study of adolescent carers found that school problems were moderately correlated with higher depressive symptoms [98]. No significant correlations between satisfaction with emotional, tangible, and informational social support and carer depression were found in carers of people with late-stage HD, although it was underpowered to reliably detect the moderate effect sizes reported [95].

Perceived Benefits of Caring

Two studies examined perceived benefits of caring. An experimental study found that carers shown reminders of their own mortality reported significantly lower benefits of caring compared to controls (large effect), even after controlling for carer demographics, HD stage and life satisfaction [77]. Further, carers of people with less time since HD diagnosis shown mortality reminders reported lower benefit finding than controls, whilst those caring for someone with greater time since diagnosis reported similar levels of benefit finding to controls. Another study found that benefit finding was strongly correlated with higher life satisfaction, HR-QoL, and spirituality [95].

Discussion

The present review included 24 studies and provides a systematic evaluation of the evidence regarding factors associated with psychological outcomes in carers of pwHD. The most frequently measured outcomes were QoL and carer burden. Just five studies examined mood outcomes, and only two examined perceived benefits of caring. Relationships were examined between psychological outcomes and factors including carer demographics and psychological factors, caring environment characteristics, HD-related difficulties, pwHD

behavioural/psychological difficulties, and social support. The most frequently measured outcome was quality of life, although a wider variety of potential associated factors were studied for carer burden. Findings suggested that higher carer burden and lower QoL were associated with indicators of higher caring intensity, such as more time spent caring and being the main carer. More advanced HD, lower functional capacity, and more severe pwHD behavioural/psychological difficulties were also associated with higher carer burden. However, overall, it was challenging to draw confident conclusions about the nature of the relationships examined due to the small number of studies, contradictory findings, and methodological issues. The following sections will discuss findings with stronger evidence and theoretical implications before examining methodological limitations in more detail.

Caring Context

The reviewed studies found that indicators of higher caring intensity (e.g., greater time spent caring, caring for more than one person, being the main carer) were associated with higher burden and lower QoL in HD carers, with small-moderate effects. It is noted, however, that findings for specific variables were not always consistent across the studies. For example, Yu et al. (2019) reported non-significant relationships between years spent caring and carer burden and QoL, with very small effects reported compared to the moderate associations found for burden [84] and QoL [74]. Reviews of evidence for carers of people with other neurological conditions have similarly found that associations between caring intensity and carer burden and QoL are inconsistent across studies [9,100–102]. The differences in the reviewed studies may relate to measurement differences in carer burden or sample differences, although it is difficult to make comparisons due to differences in reported sample characteristics. It has also been argued that measures such as years spent caring are open to interpretation of what constitutes caring [100], which may contribute to variance.

PwHD Characteristics

The evidence suggests that more advanced HD disease stage, lower functional capacity, and greater behavioural/psychological difficulties in pwHD were associated with higher carer burden. Most studies found that poorer motor function was associated with but did not predict burden in multivariate modelling, which is similar to the findings of a review conducted on carers of people with Parkinson's [100]. Similarly, studies found that cognitive difficulties were associated with higher burden, but findings were mixed as to whether they were a predictor of burden in multivariate analysis. This may suggest that the functional and behavioural/psychological impacts of motor and cognitive symptoms are more taxing for carers of pwHD to manage than these symptoms per se. Regression models where behavioural and functional outcomes remained significant predictors, but motor and cognitive difficulties were non-significant, may support this hypothesis [83,91,92], although this was not seen universally. The links between behavioural difficulties and burden are consistent with qualitative findings suggesting that carers of pwHD find behaviours such as irritability and aggression upsetting, demanding, and embarrassing at times [20].

Theoretical Implications

The findings above are consistent with stress process models [103], which view care recipient difficulties and caring intensity as stressors that can directly affect carer wellbeing. However, these models also argue that the impact of stressors is also highly contingent on the resources available to carers to manage their role, including psychosocial resources such as coping skills, beliefs, and social support, and carers' appraisals of their resources and ability to cope. Such factors were almost wholly unexplored in the reviewed studies. While there were some preliminary findings that perceived benefits of caring, attributing pwHD

difficulties to HD, and belief in one's problem-solving ability were associated with higher QoL and lower depression [84,96], these came from single studies so their generalisability remains untested. Similarly, while personal resources, such as coping styles, sense of mastery, and carer's spirituality, were associated with QoL, these findings also came from single studies [95,96]. Furthermore, it remains unclear whether the hypothesised mechanisms through which these factors influence carer wellbeing are relevant to HD carers as they were not tested in the reviewed studies.

Theoretical models also suggest that social support plays an important role in maintaining wellbeing, either directly or by moderating the impact of stressful life events on wellbeing outcomes [103,104]. Social support has been found to predict lower carer burden, higher wellbeing, and lower psychological difficulties [105–107] and buffer carers against the negative impacts of caring stress and negative appraisals [108,109] in carers of people with other neurological conditions, suggesting support for direct and moderating effects. Preliminary evidence from carers of pwHD suggests that more social contact and higher emotional social support are associated with higher QoL/life satisfaction and carer burden, with two studies providing evidence that social support remains a predictor of QoL and carer burden in multivariate modelling [25,74,86,95]. However, whether social support is an independent predictor of other wellbeing outcomes when controlling for other factors or moderates the relationship between stressors and wellbeing remains unclear as this was not tested in the reviewed studies.

Despite their relevance to the findings of this review, stress process approaches have been critiqued for driving research on concepts such as burden and strain while overlooking positive aspects of caring due to underlying assumptions that caring is a negative experience [42]. A key finding of this review is that this negative framing predominates the quantitative literature about caring for pwHD, with most studies examining burden, indicators of poor

mental health, or factors likely to negatively impact QoL. Just six papers examined perceived benefits of caring and/or protective factors, with protective factors framed as reducing the negative impact of caring. This negative focus disconnects carers from their full range of experience, generating a skewed understanding which may hinder the development of theory and practice regarding carer adaptation and wellbeing [38,42]. Furthermore, this focus has failed to stimulate the development of effective interventions for carer wellbeing in other carer groups [37]. A review of evidence from dementia carers identified that positive aspects of caring, including finding meaning, self-efficacy, mastery, and emotional rewards in the role and caring tasks, were associated with lower symptoms of depression and burden and higher QoL and self-efficacy [36]. While one small-scale study did find that a higher sense of mastery and spirituality were associated with life satisfaction [95], positive aspects of caring and the mechanisms through which they support carer wellbeing remain underexplored in carers of pwHD.

Literature Limitations

It was often difficult to draw conclusions about the nature of relationships examined in the literature. In some cases this related to a lack of evidence, particularly for QoL and mood outcomes where it was common for an association to be examined in one or two studies only. However, methodological limitations which contributed to this difficulty and limited the generalisability of findings were also identified.

Just one study included *a priori* justification for their sample size [25] and 12 studies identified sample size as a limitation post hoc. Non-significant small-moderate effects were often found in studies insufficiently powered to reliably detect them, contributing to finding heterogeneity. Additionally, many studies reported insufficient detail to determine effect size or did not report details of non-significant effects, making it difficult to determine whether

appropriate statistical power had been reached. Recruitment methods may also have introduced bias. For example, recruitment from medical clinics facilitates alignment between the sampling frame and target population but excludes those not accessing professional support, whereas recruitment from HD associations makes it challenging to determine whether selection bias is present in the sample. However, this reflects the challenge of recruiting large representative samples in rare conditions research [110].

Several studies reported limited demographic information and/or caregiving context variables which may have influenced the impact of providing care on participants. Providing this kind of information could help identify whether certain groups of carers are underrepresented in the current evidence base and identify the contributions that these factors may make to psychological outcomes in carers of pwHD. Furthermore, ethnicity was rarely reported, and, in papers where it was reported, samples were predominantly white, potentially limiting the extent to which these findings can be generalised to other populations.

Most papers used cross-sectional, correlational designs, limiting the ability to draw conclusions on the direction of relationships and causality. Furthermore, the majority of studies (n = 15) used analysis methods that did not account for interdependency between variables. Differences in the conceptualisation and measurement of outcome and explanatory variables between papers and the variation in covariates in regression models made it difficult to compare findings directly to draw conclusions. Furthermore, most studies (n = 18) used measures developed with other populations, and the psychometric properties in carers of pwHD remain unclear as they were rarely reported in the reviewed studies.

The lack of explicit theoretical grounding for the analyses in many of the papers is likely to have contributed to these design issues. Out of 24 studies, only six used theory-driven analyses [25,77,84,95,96,98], mostly incorporating stress process models [27,111,112]. Clearer integration of existing theoretical frameworks related to carer

adaptation, such as stress process models or positive aspects of caring approaches, may have also encouraged examination of the hypothesised psychological mechanisms underlying associations between stressors and carer outcomes.

The limitations identified in the literature are similar to those noted in systematic reviews for carers of people with other neurological conditions [100,113] and indicate the need for further high-quality research to understand the needs of carers of pwHD.

Review Strengths and Limitations

To my knowledge, this is the first systematic review of the quantitative evidence regarding factors associated with psychological outcomes in carers of pwHD, and so it makes a unique contribution to the evidence base. It has several strengths, including a rigorous search strategy, inclusion of findings from a range of countries, and the use of a validated quality appraisal tool suited to appraising literature using various quantitative methods. It also extends the findings of the previous review about the experience of carers of pwHD which included quantitative papers [20] by reviewing 11 additional papers published since its publication.

However, no study is without limitations. Although a second-rater quality appraised a selection of papers to limit risk of bias, most papers were assessed by a single researcher, which could have introduced bias. Furthermore, grey literature and doctoral theses were excluded due to resource and time constraints, which may have exposed this review to publication bias, although it was observed that several studies did report non-significant findings. Nonetheless, reviews comparing results from unpublished and published research could improve understandings of factors associated with psychological outcomes in carers of pwHD. Finally, findings from non-English speaking researchers may have been excluded as only English language papers were included. Although studies were drawn from several

countries, they share cultural similarities (e.g., westernised, individualistic, industrialised). This may limit the generalisability of the findings to other cultures, given that caring is heavily influenced by society and culture [10].

Clinical Implications

The consistent finding that factors linked to caring for someone with HD were associated with higher carer burden and psychological distress, and lower QoL suggests that carers of pwHD may benefit from additional support to manage their role. However, the lack of established causality and uncertainty about the underlying psychological processes through which caring influences psychological outcomes makes it challenging to provide clinical recommendations, particularly for individual-level psychologically informed interventions, because the modifiable factors they should target are unclear. There is some evidence to indicate interventions for pwHD behavioural/psychological difficulties may reduce carer burden. This could include the use of a formulation framework developed for pwHD [114] to understand triggers and functions of behaviour and develop positive behaviour support plans, as well as to support pwHD's psychological wellbeing, which is frequently overlooked in HD treatment [115]. Preliminary evidence from a psychoeducation intervention for male HD carers appears to support this approach, as information about how carers could respond to psychological and behavioural aspects of HD was seen as particularly beneficial [116].

While individual-level interventions may benefit carers, there is also a need to consider carers' social and cultural context as this heavily influences their experience [10]. Changes to public policy are a key way to create a more supportive environment for carers [117]. Policy recommendations to achieve this include the provision of social protection (e.g., carer benefits), formal services, including formal care and services for carers, training and support to carers, labour market reforms that allow carers to work flexibility, and ensuring

that carers' voices are represented in the design and delivery of health and social care systems [3,5].

Future Research

Further research using adequately powered samples would aid the robustness and generalisability of findings. The use of longitudinal designs and more complex modelling approaches could develop understandings of directionality, causality, and the mechanisms through which caring influences psychological outcomes. Theory-driven research would also strengthen the evidence base and encourage the exploration of modifiable processes which could be the targets of interventions. Future research should also consider positive aspects of caregiving to provide a more holistic understanding of carers' needs and experiences and identify factors which support or boost wellbeing.

The evidence base would also be strengthened by widening its current focus on individual-level factors which influence carer wellbeing to consider the impact of their wider social and cultural contexts. The relationship between carer and the pwHD is a social context factor which may benefit from further investigation given preliminary findings that this is associated with QoL differences in carers of pwHD ([94], alongside evidence from carers of people with other conditions which suggests that this relationship can influence carers' motivations, needs, and experiences [118–120]. Further research on adolescent carers of pwHD would also be beneficial as qualitative evidence suggests they have unique experiences [46].

Furthermore, social determinants of health such as socioeconomic status, education level, and gender are understudied in carers of pwHD but have been linked to psychological health in carers of people with other conditions [121], suggesting the need for further exploration in this population, including consideration of the impact of intersectionality.

Evidence that carers of pwHD report experiencing discrimination and a lack of appropriate support and information from professionals [22,23], indicates that considering cultural norms and the impact of social policy on carers' psychological wellbeing may also be of value. Finally, building evidence from more varied country contexts would help build cross-cultural understandings of the psychological impacts of caring for someone with HD.

Conclusion

This review synthesised evidence regarding factors associated with psychological outcomes in carers of pwHD. Evidence suggests that caring for someone with more advanced HD, greater functional impairment, and more severe behavioural/psychological difficulties was associated with higher carer burden and carer depression. Indicators of caring intensity, such as higher time spent caring and being the main carer, were also associated with higher burden and lower QoL. Carers of pwHD may benefit from additional support to manage the demands of caring, particularly as HD progresses. Psychological approaches to supporting carers and pwHD with psychological and behavioural problems may also be beneficial. This review also highlights the need for further research, particularly theory-driven research, longitudinal research, and research looking at factors which promote positive wellbeing, to develop our understanding of which factors influence psychological outcomes in carers of pwHD.

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Tables

Table 1.1

Example Search Strategy (Medline)

Search Number	Search Type	Terms
S1: HD	MeSH	(MH "Huntington Disease")
	Keywords	TI (Huntington* N3 (disease* OR chorea*)) OR AB (Huntington* N3 (disease* OR chorea*))
S2: Carers	MeSH	(MH "Caregivers") OR (MH "Psychosocial Support Systems") OR (MH "Family Support") OR (MH "Family+")
	Keywords	(“psychosocial support” OR carer OR caregiver OR famil* OR spouse* OR sibling* OR child OR partner OR dyad OR son OR daughter OR mother OR father OR husband OR wife OR relative)
S3: Psychological outcomes	MeSH	(MH "Psychological Distress+") OR (MH "Stress, Physiological+") OR (MH "Depression") OR (MH "Depressive Disorder, Major") OR (MH "Depressive Disorder+") OR (MH "Anxiety+") OR (MH "Anxiety Disorders+") OR (MH "Grief+") OR (MH "Loneliness") OR (MH "Fear+") OR (MH "Sadness") OR (MH "Caregiver Burden") OR (MH "Mental Health") OR (MH "Adaptation, Psychological+") OR (MH "Guilt+") OR (MH "Anger+") OR (MH "Shame+") OR (MH "Optimism") OR (MH "Quality of Life") OR

	(MH "Suicide") OR (MH "Suicidal Ideation") OR (MH "Suicide, Completed") OR (MH "Suicide, Attempted") OR (MH "Social Support+")
Keywords	((Anxiet* OR anxious* OR phobi* OR fear) OR (angry OR anger) OR (burden*) OR (Depress* OR dysthymi* OR sad) Or (mood N3 disorder) OR (Affective N3 disorder) OR (distress* OR (emotional N3 distress) OR (psycholog* N3 distress)) OR ((psyc* OR neuropsyc*) N3 sympt*) OR ((psyc* OR neuropsyc*) N3 outcome*) OR (psych* N3 adjust*) OR (grief OR griev*) OR (happ*) OR (“Quality of life” OR qol OR “Health related quality of life” OR hrqol OR hrql OR “life quality” OR Wellbeing OR well-being OR “life satisfaction” OR welfare) OR (lone* OR isolat*) OR (“self esteem” OR “self-esteem”) OR ((personal OR perceived) N3 autonom*) OR (blame OR cop* OR guilt OR hope OR loss OR mastery OR optimis* OR shame OR stress OR suicid*) OR (positive N5 (experienc* OR view* OR perception* OR apprais*)) OR (“relationship quality” OR “relationship satisfaction”) OR (“social support” OR “psychosocial support”)) OR AB ((Anxiet* OR anxious* OR phobi* OR fear) OR (angry OR anger) OR (burden*) OR (Depress* OR dysthymi* OR sad) Or (mood N3 disorder) OR (Affective N3 disorder) OR (distress* OR (emotional N3 distress) OR (psycholog* N3 distress)) OR ((psyc* OR neuropsyc*) N3 sympt*) OR ((psyc* OR neuropsyc*) N3 outcome*) OR (psych* N3 adjust*) OR (grief OR griev*) OR (happ*) OR (“Quality of life” OR qol OR “Health related quality of life” OR hrqol OR hrql OR “life

	quality” OR Wellbeing OR well-being OR “life satisfaction” OR welfare) OR (lone* OR isolat*) OR (“self esteem” OR “self-esteem”) OR ((personal OR perceived) N3 autonom*) OR (blame OR cop* OR guilt OR hope OR loss OR mastery OR optimis* OR shame OR stress OR suicid*) OR (positive N5 (experienc* OR view* OR perception* OR apprais*)) OR (“relationship quality” OR “relationship satisfaction”) OR (“social support” OR “psychosocial support”))
Total Medline (S1 AND S2 AND S3): 1,232	

Table 1.2

Study Characteristics

Study Country	Sample (*n*)	Recruitment Setting	Demographics	Design and analysis	Theory	Measures Psychological outcome(s)	Correlate(s)
Aubeeluck et al., 2019 Enroll-HD - Argentina, Australia, Canada, Denmark, France, Germany, Italy, New Zealand, Netherlands,	1,716	International Observational Cohort	Mean age (SD): 52.8 (13.1) Gender: 59.9% female	Cross-sectional, t-tests	None mentioned	Huntington's Disease Quality of Life Carer's Questionnaire (HDQoL-C) (short form)	From HDQoL-C: Relationship to pwHD Child at risk Duration of caring

Poland, Spain, UK, USA							
Aubeeluck et al., 2013 Euro-HDB - Italy, France	301	European Observational Cohort	Mean age (SD): 58.1 (13.2) Gender: 60% female Relationship: 64% partner Main carer: 81%	Cross-sectional, t-tests	None mentioned	HDQoL-C	Huntington Clinical Self-report Instrument Unified Huntington's Disease Rating Scale (UHDRS) - Independence Scale
Aubeeluck and Buchanan, 2007 UK	87	National HD association	Mean age (SD): men 59.6 (12.7); women 57.2 (15.1)	Cross-sectional, correlation	None mentioned	HDQoL-C	Visual Analogue Scale - Perceived health status

			Gender: 62.1% Relationship: 100% spouse Hours spent caring: All spent 40hrs + caring				
Banaszkiewicz et al., 2012 Poland	80	Outpatient clinic	Not reported	Cross-sectional, simple linear regression and forward stepwise regression	None mentioned	Caregiver Burden Inventory (CBI)	UHDRS - Total motor score (TMS), cognitive, behaviour total, apathy, psychotic symptoms, anxiety, irritability, aggression, total function capacity (TFC) Hamilton Depression

							Scale PWHD characteristics: Duration of HD; # CAG repeats; age; gender; age at onset, years of education
Bayen e al., 2023 France	80	Outpatient clinic	Mean age (SD): 57.2 (12.9) Gender: 60% female Age: 57.2 (12.9; 20-80) Relationship: Spouse 67.5% Caring multiple	Cross-sectional, t-tests, multiple regression (and stepwise multiple regression?)	None mentioned	Zarit Burden Inventory (ZBI)	UHDRS - TMS, cognitive, behaviour total, TFC, independence Oslo Social Support Scale Caring environment: Caring for additional relatives with HD or

			pwHD: 19% Mean hours of informal care provided: 7.3 Employed: 46%				another difficulty, in receipt of formal care PwHD characteristics: HD duration Income
Cox, 2012 USA	31	Support groups	Age range: 25-76 Gender: 67.7% female Relationship: 77.4% spouse Main carer: 87.1% Education: 33.3% high school diploma	Cross-sectional, correlation	None mentioned	HDQoL-C	Carer age Caring environment: Years HD known in family, years of caring, # family members in HH, hours spent caring Income Hours of paid employment

			Previously cared for a pwHD: 32.3% At risk/symptomatic children: 80.6% Carer with disability: 45.2%				Hours of childcare # instances of socialising
Helder et al., 2002 The Netherlands	90	Outpatient clinic	Mean age (SD): 53.0 (10.0) Gender: 46.6% female Relationship: 100% spouse Employed: 55.6%	Cross-sectional, hierarchical regression	Self-Regulatory Model (Leventhal, 2016)	Short-Form Health Survey (SF-36)	Illness Perception Questionnaire Coping Orientation to Problems Experienced Inventory

			Caring at home: 72.2%/27.8% cared for in a nursing home				
Hergert and Cimino, 2021 USA	50	Outpatient clinic	Mean age (SD): 52.2 (14.4) Gender: 46.4% female Relationship: 56% spouse Education (years), mean (SD)): 14.2 (2.7)	Cross-sectional, correlation and multiple regression	None mentioned	Caregiver Appraisal Scale (CAS) (subjective burden sub-scale)	Frontal Systems Behavioural Scale UHDRS -TMS, cognitive, memory, executive function Cognitive composite for pwHD: Stroop Test, Trail Making Test (TMT), Hopkins Verbal Learning Test, Neuropsychological

							Assessment Battery PwHD demographic: Age, education(years), sex Carer demographics: Age, education(years), sex
Ho et al., 2004 UK	56	Outpatient clinic	Mean age (SD): 54.7 (11.4) Gender: 59% female Employed: 51.8% Average age left education (Years (SD)): 19.7 (8.9)	Cross-sectional, correlation	None mentioned	SF-36 Sickness Impact Profile	Telephone Interview of Cognitive Status Beck Depression Inventory Carer Demographics: Age

			Daily contact with pwHD: 89%				
Kalkers et al., 2022 The Netherlands	158	Nursing homes	Not reported	Cross-sectional, t-test	None mentioned	Swallowing QoL Questionnaire Fear sub-scale Single item about fear of pwHD choking	Care Dependency Scale
Kavanaugh, 2014 USA	40	National and state HD associations	Mean age (SD): 17 (2.6) Gender: 77% female Relationship: 100% children PwHD gender:	Cross-sectional, correlation	Stress Process Model (Pearlin, 1990)	Child Depression Inventory	Affected Individual Questionnaire Multidimensional Assessment of Caregiving Activities Conflict Behaviour Questionnaire

			61% female Duration of caregiving (years (SD)): 4.8 (3.2) Education: 40% in college, 40% in high school, 15% in middle school, 5% not in education				School Problems composite Carer Demographics: Age, gender, duration of caring
Luszczynska at al., 2014 Poland, Australia, New Zealand, USA, UK	50	National HD associations	Mean age (SD): 43.2 (14.5) Gender: 68% female Relationship: 47.9% spouse	Experimental, correlation, ANOVA, hierarchical regression	Anxiety Buffer Disruption Theory (Pyszczynski	Benefit Finding Scale	HDQoL-C PwHD disease stage Carer demographics: Age Experimental

			Gene negative: 64% Years since patient diagnosis (SD): 10.1 (6.4) Years caregiving (SD): 8.7 (6.9) PwHD disease stage: 49.0% middle		& Kesebir, 2011)		Condition; Mortality reminder
Maibach et al., 2022 USA	106	Outpatient clinic	PwHD lives in same household: 82%	Randomised Control Trial, correlation, ANOVA, and regression	None mentioned	CBI	UHDRS - TFC, TMS, independence, disease stage Caring environment: Lives with pwHD Unclear which

							demographic characteristics were included in analyses
Modrzejewska-Zielonka et al., 2022 Poland	144	Unclear	Not reported	Cross-sectional and longitudinal, linear, multiple, and stepwise regression	None mentioned	CBI	UHDRS - TMS, behaviour, cognitive, functional assessment, independence, TFC PwHD characteristics: Age, gender, time since onset
O'Connor and McCabe, 2011 Australia	43	National HD association	Mean age (SD): 60 (9.7)	Longitudinal, t-test and multiple regression	Stress Coping Model (Lazarus and	World Health Organisation Quality of Life Questionnaire	Relationship Assessment Scale Profile of Mood States

					Folkman, 1984)		Social Support Questionnaire (satisfaction subscale) Economic Pressure Scale Income
Pickett et al., 2007 USA	62	Outpatient clinic	Mean age (SD): 55.4 (10.8) Gender: 58.1% female Ethnicity: 91.9% European American Relationship: 71.0% spouse	Cross-sectional, correlation, multiple regression, path analysis and Sobel test	Two-factor Model of Caregiver Appraisal (Lawton et al., 1991)	Brief Symptom Inventory (BSI)	UHDRS 0 TFC Problem-Solving Inventory CAS BSI (pwHD) Carer demographics: Age, race, gender, education level, employment, marital

	Living in same household: 83.9% Employed (yes): 75.8% Education: 54.8% College degree or higher	status, relationship to pwHD, living arrangement with pwHD, year of caring, hours of caring per day PwHD demographics. Age, race, gender, education level, employment, marital status, years since diagnosis

Ready et al., 2008 USA	22	Outpatient clinic	Mean age (SD): 50.2 (12.6) Gender: 86.4% female Ethnicity: 90.0% Caucasian Relationship: 59.1% spouse Live in same house hold: 72.2% Education (years (SD)): 14.3 (2.4)	Longitudinal, t-test and correlation	None mentioned	Single item for QoL	UHDRS - Behavioural Time (6-month follow-up)

Roscoe et al., 2009 USA	17	Outpatient clinics	Mean age: 54 Gender: 88% female Ethnicity: 94% white Relationship: 71% spouse Living in same HH: 47% Employed: 60% Education (years): 14 Mean duration of caring (years): 9 Mean hours of informal care	Cross-sectional, correlation	Stress Process Model (Pearlin, 1990)	Life Satisfaction Index-Z CESD SF-36	Katz Index of Independence in Daily Living Perceived Benefits of Caregiving Mastery Scale Spiritual Involvement and Beliefs Scale-revised Social support Scale Duration of caregiving in hours and months Single item for perceived

			(per week) :45 Caring for more than one pwHD: 41%				stressfulness in last 90 days
Schumacher-Kuper et al., 2021 The Netherlands	80	Outpatient clinic	Gender: 51.5% female	Cross-sectional, network analysis	None mentioned	Centre for Epidemiological Studies Depression Scale SF-36	UHDRS - TMS Montreal Cognitive Assessment Carer characteristics: gender, relationship to pwHD PwHD characteristics: Age, years of education,

							year since diagnosis, gender, psychotropic drug use, CAG repeat length, comorbidities
Shaw et al., 2022 Canada	48	National HD associations	Mean age (SD): 58.1 (13.9) Gender: 75.6% female Relationship: 61.0% spouse Main carer: 85.4% Duration of care (mean years (SD)): 10.2 (8.7) Previously carer	Cross-sectional, t-test	None mentioned	HDQoL CSI	PwHD Motor Transition Status

			for a pwHD: 22.0% Employed: 46.3%				
Tanigaki et al., 2020 USA	22	Outpatient clinic	Mean age (SD): 54.8 (13.8) Gender 54.5% female	Cross-sectional, correlation	None mentioned	Hospital Anxiety and Depression Scale	Pittsburgh Sleep Quality Index
Wibawa et al., 2020 Australia	38	Outpatient clinic	Mean age (SD): 55.8 (12.8) Gender: 55.3% female Relationship: 60.5% spouse	Cross-sectional, t-test, best subsets regression,	None mentioned	ZBI	UHDRS - TMS, TFC, functional assessment, independence Rating of Anosognosia Scale

	and general linear model	Problem Behaviour Assessment-Short Mini-mental State Exam Symbol Digit Modalities Stroop Interference Verbal Fluency (Letter and Category) TMT CAG Disease Burden Score

Youssov et al., 2022 France	148	Outpatient clinic	Mean age (SD): 56.8 (14.2) Gender: 64.8% female Relationship: 67.6% spouse Main carer: 48.5% Mean years of caring (SD): 6.7(5) Median weekly hours of care: 154	Longitudinal, ANOVA, t-test, Chi-square, Fisher's exact test.	None mentioned	ZBI	UHDRS - Disease stage

Yu et al., 2019 USA	20	Outpatient clinic]	Mean age (SD):48.9 (13.7) Gender: 60.0% female Main carer: 90.0% Children at risk: 80.0% Mean year of caring (SD): 8.8 (9.1) Mean weekly hours of care (SD): 42.7 (59.1)	Cross-sectional, correlation and t-test	None mentioned	MCSI HDQoL-C	UHDRS - TMS, TFC, independence, cognitive, behavioural Characteristics of carer: Age, gender, married, child at risk Caring Environment: Main carer, prior experience of caring, suitable home, family support, duration of HD in family, HH size, employment, unpaid childcare, hours for hobbies,

					hours spent caring, financial problems

Table 1.3

Quality Appraisal

Study	1. Question / objective sufficiently described?	2. Study design evident and appropriate?	3. Method of subject/comparison group selection or source of information/input variables described and appropriate?	4 Subject (and comparison group, if applicable) characteristics sufficiently described?	5. If interventional and random allocation was possible, was it described?	6. If interventional and blinding of investigators was possible, was it reported?	7. If interventional and blinding of subjects was possible, was it reported?	8. Outcome and (if applicable) exposure measure(s) well defined and robust to measurement / misclassification bias?	9. Sample size appropriate?	10. Analytic methods described/justified and appropriate?	11. Some estimate of variance is reported for the main results?	12. Controlled for confounding?	13.Results reported in sufficient detail?	14. Conclusions supported by the results?	Total score	Total possible sum	Summary score
Aubeeluck and Buchanan (2007)	2	2	1	1	N/A	N/A	N/A	2	1	2	2	N/A	2	2	17	20	85

Aubeeluck et al. (2013)	1	2	1	2	N/A	N/A	N/A	2	2	2	0	N/A	1	2	15	20	75
Aubeeluck et al. (2019)	2	2	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	18	20	90
Banaszkiewicz et al. (2012)	1	2	1	0	N/A	N/A	N/A	2	1	2	2	1	2	2	16	22	73
Bayen et al. (2023)	2	2	2	2	N/A	N/A	N/A	1	2	2	1	1	1	2	18	22	82
Cox (2012)	2	1	1	2	N/A	N/A	N/A	2	1	2	1	N/A	1	2	15	20	75
Helder et al. (2002)	2	2	1	2	N/A	N/A	N/A	1	2	2	2	1	1	2	18	22	82
Hergert and Cimino (2021)	2	2	1	1	N/A	N/A	N/A	2	2	2	2	1	2	2	19	22	86
Ho et al. (2004)	1	2	1	2	N/A	N/A	N/A	2	1	2	2	N/A	2	2	17	20	85
Kalkers et al. (2022)	2	2	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	18	20	90

Kavanaugh (2014)	2	2	1	2	N/A	N/A	N/A	2	1	2	2	N/A	2	2	18	20	90
Luszczynska et al. (2014)	2	2	1	2	1	N/A	1	2	1	2	1	2	2	2	21	26	81
Maibach et al. (2022)	1	2	1	1	1	2	2	1	1	2	0	N/A	0	1	15	26	58
Modrzejewska-Zielonka et al. (2022)	1	2	1	1	N/A	N/A	N/A	2	1	1	0	0	2	2	13	22	59
O'Connor and McCabe (2011)	2	2	1	2	N/A	N/A	N/A	2	0	2	2	N/A	2	2	17	20	85
Pickett et al. (2007)	2	2	1	2	N/A	N/A	N/A	2	0	1	1	N/A	2	2	15	20	75
Ready et al. (2008)	2	2	1	2	N/A	N/A	N/A	2	0	2	1	N/A	2	2	16	20	80
Roscoe et al. (2009)	2	2	1	2	N/A	N/A	N/A	2	0	2	2	N/A	2	2	17	20	85

Schumacher-Kuper et al. (2021)	2	2	1	1	N/A	N/A	N/A	2	1	2	0	N/A	1	2	14	20	70
Shaw et al. (2022)	1	2	1	2	N/A	N/A	N/A	2	0	2	0	N/A	0	1	11	20	55
Tanigaki et al. (2020)	1	1	1	1	N/A	N/A	N/A	2	0	2	2	N/A	2	1	13	20	65
Wibawa et al. (2020)	2	2	1	1	N/A	N/A	N/A	2	1	2	2	N/A	2	2	17	20	85
Youssov et al. (2022)	1	2	1	2	N/A	N/A	N/A	1	1	1	2	N/A	2	2	15	20	75
Yu et al. (2019)	1	2	1	2	N/A	N/A	N/A	2	0	2	1	N/A	2	2	15	20	75

NB: Papers were scored according to how carer results were reported.

Scoring guidance: Yes = 2, Partial = 1, No = 0

Table 1.4

Carer Burden Results

Author	Design and analysis	Result	Non-significant results
Banaszkiewicz et al., 2012†	Simple linear regression and forward stepwise regression	In linear regression, pwHD motor score R^2=0.32/***r* = *0.58***, p=0.003, depressive symptoms R^2=0.21/***r* = 0.47**, p=0.003, and function capacity score R^2=0.30/***r* = 0.56**, p=0.003 were significant predictors. In multiple regression, pwHD motor score β= 0.45 [CI: 0.24, 0.67], p= <0.001 and depressive symptoms β= 0.33 [CI: 0.12, 0.55], p= 0.003 remained significant predictors.	Linear regression: PwHD age R^2=0.01/***r* = 0.01**, gender R^2=0.02/***r* = 0.02**, years of education R^2=0.03/***r* = 0.21**, age at onset R^2=0.03/***r* = -0.07**, duration of HD R^2=0.01/***r* = 0.11,** cognitive function R^2=0.11/***r* = -0.35**, total behavioural difficulties R^2=0.10/***r* = 0.34**, apathy R^2=0.07***/r* = 0.30**, psychotic symptoms R^2=0.01/***r* = -0.08**, anxiety R^2=0.02/***r* = 0.19**, irritability R^2=0.01/***r* = 0.14**, and aggression R^2=0.03/***r* = 0.21.**

			Multiple regression: Functional capacity, β= not reported.
Bayen e al., 2023	T-tests, correlation, stepwise multiple regression	Carers caring for more than one person with HD had significantly higher care burden scores than those caring for one pwHD (mean = 42.2 vs 32.5, *p*=0.04). Data to calculate effect size not reported. Carer burden was moderately correlated with time spent caring (***r* = 0.47**, p=<0.001) In stepwise regression duration of HD (years) β= 1.5 [CI: 0.7, 2.4; standardised β 0.39], p= <0.001, pwHD aggression	PwHD total functional capacity, carer caring for more than one person with HD, carer employment, and receipt of formal carer were not predictors in the stepwise regression, β= not reported.

β= 10.6 [CI: 2.8, 18.3; standardised β 0.26], p= 0.008, family income β= -0.002 [CI: -0.003, -0.000; standardised β -0.21], p= 0.027, and carer social support β= -1.8 [CI: -3.4, -0.2; standardised β -0.26], p= 0.0025 were significant predictors.

Hergert and Cimino, 2021	Correlation and multiple regression	Carer burden was correlated with pwHD motor symptoms (***r* = 0.35**, p=<0.05), cognitive symptoms (***r* = -0.51**, p=<0.001), memory difficulties (***r* = -0.46**, p=<0.01), executive functioning (***r* = -0.50**, p=<0.001), total behavioural difficulties (pwHD rated: ***r* = 0.37**, p=<0.01; carer rated: ***r* = 0.68**, p=<0.001), apathy (pwHD rated: ***r* = 0.29**, p=<0.05; carer rated: ***r* = 0.61**, p=<0.001), disinhibition (carer rated: ***r* = 0.49**, p=<0.001), and behavioural executive dysfunction (pwHD rated: ***r* = 0.42**, p=<0.01; carer rated**: *r* = 0.65**, p=<0.001), and carer age (***r* = -0.41**, p=<0.01:) and sex (***r* = 0.35**, p=<0.05). In multiple regression, carer age (β= -0.34, p =<0.01) and pwHD cognitive symptoms (β=-0.37, p =<0.01), and behavioural executive dysfunctions (carer rated: β= 0.35, p =<0.01) remained significant predictors. The model	Correlations between pwHD age, education level, sex, HD duration, CAG repeat length, CAG age-product and pwHD rated disinhibition, and carer education level (*r* not reported). Carer sex, pwHD motor symptoms and pwHD reported behavioural executive dysfunction were not significant predictors in the multiple regression, β= not reported.

accounted for 63% of the variance in carer burden scores (adj R^2=0.63, p =<0.001).

An exploratory multiple regression model including memory and executive function difficulties was significant (adj R^2=0.23, p =<0.001), but individual predictors were not, β= not reported=).

Maibach et al., 2022	Correlation, ANOVA, and regression	Carer burden was positively correlated lower pwHD functional capacity, motor function, and independence (*r* not reported). Carers who lived with the pwHD and of people with stage three HD (requiring support most of the day) reported significantly higher burden than those in early HD stages (1 and 2; no data reported). Carer burden did not change between baseline and 12-week follow-up.	Does not report the variables included in the analyses nor the data for non-significant results.
Modrzejewska-Zielonka et al., 2022	Linear, multiple and stepwise regression	At baseline pwHD behavioural difficulties (β= 0.2, p =<0.001), independence (β=-0.3, p =<0.05), and age (β=-0.1, p =<0.05) predicted carer burden. Between baseline and follow-up (up to 8 years) increases in carer burden related to help with basic function and not having a break were predicted by pwHD functional assessment (basic function: β=-0.39, p =<0.01; no break: β=-0.43, p =<0.01) and independence (basic function: β=-0.52, p =<0.01; no break: β=-0.51, p =<0.01).	At baseline, pwHD cognitive function, functional capacity, time from onset and gender did not predict carer burden score or scores on individual items. Increases in carer burden between baseline and follow-up were not predicted by pwHD motor or cognitive symptoms or total functional assessment, β= not reported.

		12 individual carer burden items were significantly correlated with change in disease burden score (a calculation of lifetime exposure to the HD genetic mutation) between baseline and follow-up (data to calculate effect not reported).	Carer burden was not predicted by time in a multiple regression model including pwHD HD symptoms and age (Only *p* value reported).
Pickett et al., 2007	Correlation	Carer burden was correlated with pwHD functioning (***r* = 0.40**, p=<0.001), caregiver depression (***r* = 0.29**, p=<0.05), number years since HD diagnosis (pwHD reported: ***r* = -0.26**, p=<0.05; carer reported: ***r* = -0.28**, p=<0.05), and longer time caring (***r* = -0.48**, p=<0.001)	Not associated with carer age, pwHD, ethnicity, gender, education level, employment status, marital status, relationship to pwHD, and cohabitation status (*r* not reported). Not correlated with carer problem-solving appraisal (***r***

			= **-0.24**) and pwHD depression (***r*** **= -0.17**), *p* values not reported.
Schumacher-Kuper et al., 2021	Network analysis	Conditional on the other variables, higher carer burden was associated with longer CAG repeat length, higher psychotropic drug use, and fewer years since diagnosis. An indirect/marginal relationship between pwHD cognitive function and carer burden was predominantly mediated by the following paths: cognitive function>years since diagnosis>carer burden and cognitive function>CAG repeat length>carer burden. An indirect/marginal relationship between pwHD function capacity and carer burden was predominantly mediated by two pathways: functional capacity>CAG repeat length>carer burden and functional	Carer and pwHD gender were not related to carer burden. Data to calculate effect size not reported.

		capacity>psychotropic drug use> carer burden. An indirect/marginal relationship between pwHD age and carer burden was predominantly mediated via CAG repeat length. An indirect/marginal relationship between pwHD education level and carer burden was mediated via years since diagnosis. Data to calculate effect size not reported.	
Shaw et al., 2022	T-test	Significant difference in carer burden related to "some behaviour is upsetting" between carers of people with premanifest and manifest HD. no data reported.	No significant difference between carers of people with manifest compared to premanifest HD in overall carer burden, no data reported.

Wibawa et al., 2020†	T-test, best subsets regression, and general linear model	Significant differences between pwHD no anosognosia and anosognosia group of both measures of carer burden (ZBI: *d* = 1.34 /***r* = 0.56**, p = <0.001; and CBI: d = 1.34 /***r* = 0.56**, p = <0.001). In best subsets regression a model including pwHD Stroop interference score and PBA best predicted ZBI scores (R^2 = 40.1%, Cp = -0.4, S = 11.4) and a model including Stroop Interference and functional capacity best predicted CBI scores (R^2 = 44.7%, Cp = 0.0, S = 13.0). When analysed in a general linear model including the Stroop Interference, total functional capacity and behavioural difficulties, only the Stroop Interference remained significant for the ZBI (β = -0.40, *p* = <0.05, overall fit R2 = 0.45, *p* = <0.01) and CBI (β = -0.35, *p* = <0.05, overall fit R2 = 0.49, p = <0.01).	Total functional capacity (ZBI: β = 0.21, CBI: β = 0.16, *p* values not reported) and behavioural difficulties (ZBI: β = 0.21, =, CBI: β = 1.64, *p* values not reported) did not significantly predict carer burden in the general linear model.

Youssov et al., 2022†	ANOVA, t-test, Chi-square. Fisher's exact test	When split by HD disease stage, carer burden was significantly different between the four groups (difference between stage I and IV ***r* = 0.86**, p = <0.001). Using clustering analysis participants were grouped into four clusters (A-D) according to similarities in pwHD difficulties and carer burden. Clusters A and B comprised of people with more advanced HD symptoms and clusters C and D had less advanced symptoms. Carer burden was significantly different between the clusters at baseline, as were changes at follow-up (p = <0.001).

Yu et al., 2019††	Correlation and t-test	Carer burden scores were significantly different between main carers and non-main carers (***r* = 0.22**, $p = 0.04$) and significantly correlated to pwHD total functional capacity (***r* = -0.46**, $p = 0.04$).	Carer gender ($r = 0.05$, $p = 0.5$), age (***r* = 0.05,** $p = 0.85$), marital status (***r* = 0.05,** $p = 0.88$); duration of HD in family (***r* = 0.21**, $p = 0.38$), duration of caring (***r* = -0.05**, $p = 0.83$), prior experience of caring (***r* = -0.01**, $p = 0.88$; child at risk (***r* = 0.08**, $p = 0.$); household size (***r* = -0.06**, $p = 0.79$), living in a suitable home (***r* = -0.18**, $p = 0.11$); presence of family support (***r* = -0.18,** $p = 0.1$), hours of paid work weekly (carer) (***r* = -0.12**, $p = 0.61$), hours of childcare performed (***r* = 0.11**, $p = 0.66$), hours of weekly HD care provided (***r* = -0.02**, $p = 0.95$); hours for hobbies (***r* = 0.27**, $p = 0.26$); total family

	income (***r* = -0.20**, p = 0.43), financial difficulties (***r* = <001**, p = 0.85); and pwHD independence (***r* = -0.23,** p = 0.34), presence of pwHD motor difficulties (***r* = -0.06**, p = 0.61), cognitive impairment (insufficient data reported), and behavioural issues. (***r* = 0.05,** p = 0.66)

NB: Cp = Mallow's Cp; S = standard error of regression

Comparable effect sizes (i.e. Pearson's r) are indicated in bold.

† Pearson's *r* calculated by the author

†† Pearson's *r* calculated by the author for t-tests but not correlations

Table 1.5

Quality of Life/Life Satisfaction Results

Author	Design and analysis	Results	Non-significant findings

Aubeeluck et al., 2019†	T-tests, correlation	*Spousal carers compared to other carers pooled group (carer for parent, carer for child)* Total score feelings about living with HD Z = -2.729 (N1= 509, N2 = 1093) p=0.006 (spousal carers: median =110, IQR = 42; pooled group median (114, IQR=43), ***r* = 0.07**. Positive feelings subscale: z=-2.729 (n1=519, N2=1109), p<0.001 (spousal carers: median 44, IQR = 20; other carers median = 48, IQR = 18), ***r* = -0.07**. *Carers of parents compared to pooled group* Total score feelings about living with HD: Z = −3.087 (N1 = 176, N2 = 1426), p = 0.002 (carers of parents: median = 116.3, IQR = 41.0; pooled group: median = 109.96, IQR = 42.0) , ***r* = -0.08** Negative feelings subscale: Z = 3.180 (N1 = 178, N2 = 1496), p = 0.001 (carers for parents: median = 53.14, IQR =	*Spousal carers compared to other carers pooled group (carer for parent, carer for child)* Overall satisfaction with life: Z = −0.493 (N1 = 520, N2 = 1123), , *p* = 0.62, ***r* = -0.01**; negative feelings subscale (data not reported). *Carers of parents compared to pooled group* Overall satisfaction with life: Z = −0.499 (N1 = 175, N2 = 1468) , *p* = 0.62, ***r* = -0.1**, positive feelings subscale (data not reported). *Carers of children compared to pooled*

28.0; pooled group: median = 48.12, IQR = 28.0), ***r* = 0.08**

Carers of children compared to pooled group

Total score feelings about living with HD: Z = −3.995 (N1 = 201, N2 = 1401), p < 0.001 (carers for children: median = 103.35, IQR = 43.0; pooled group: median = 111.72, IQR = 40.0), ***r* = -0.10**

Negative feelings subscale: Z = 6.260 (N1 = 206, N2 = 1468), p < 0.001 (carers for children: median = 41.31, IQR = 26.0; pooled group: median = 49.72, IQR = 27.0), ***r* = 0.15**

Carers living with pwHD compared to those not

Total score feelings about living with HD: Z = −4.504 (N1 = 339, N2 = 1260), p < 0.001. (living with HD patient: median = 109, IQR = 43.0; not living with HD patient: median = 116, IQR = 39.0), ***r* = -0.11**

group

Overall satisfaction with life: Z = −2.02 (N1 = 205, N2 = 1438) , *p* = 0.04 – non-significant due to *p* value set for multiple comparisons**, *r* = -0.01**, positive feelings subscale (data not reported).

Carers living with pwHD compared to those not

Overall satisfaction with life: Z = −1.572 (N1 = 346, N2 = 1294), ***r* = -0.05**

Carers with children at risk/gene carrier/symptomatic compared to not

Negative feelings subscale: (p = 0.006, living with HD patient: median = 49.0, IQR = 28.75; not living with HD patient: median = 54, IQR = 25.0) (Z and *n* not reported)

Positive feelings subscale: (p < 0.001, living with HD patient: median = 45, IQR = 20.0; not living with HD patient: median = 48, IQR = 18.0) (Z and *n* not reported)

Carers with children at risk/gene carrier/symptomatic compared to not

Total score feelings about living with HD: Z = −4.514 (N1 = 635, N2 = 956), p < 0.001 (children who are at risk/carrier/symptomatic: median = 108, IQR = 43.0; no children who are at risk/carrier/symptomatic: median = 117, IQR = 42.0), ***r* = -0.11**

Negative feelings subscale: p < 0.001 (children who are at risk/carrier/symptomatic: median = 47.0, IQR = 28.0; no

Overall satisfaction with life: Z = −4.504 (N1 = 339, N2 = 1260) , *p* = 0.953, ***r* = -0.11** positive feelings (data not reported).

Duration of caring

Satisfaction with professional support (*rs* not reported)

Positive feelings subscale (*rs* not reported)

children who are at risk/carrier/symptomatic: median = 54.0, IQR = 26.0) (Z and *n* not reported)

Duration of caring

Weak, negative correlations with

Total life satisfaction (*rs* = −0.066, N = 1563, p = 0.009)

Personal life satisfaction (*rs* = −0.076, N = 1609, p = 0.002)

Total feelings about living with HD (*rs* = −0.072, N = 1602, p = 0.005)

Negative feelings subscale (*rs* = −0.132, N = 1583, p < 0.001)

Aubeeluck et al., 2013	T-tests	When pwHD were split into groups according to high, medium, and low symptom severity and compared to the other two groups combined, carers of pwHD with low dependence (*p = <0.001)*, low motor symptoms (p = <0.05), and low overall clinical severity (p = <0.05) reported significantly higher QoL. Carers of people with high dependence scored reported significant lower QoL (p = <0.05). Data to calculate the magnitude of effect not reported.	No significant differences for moderate group in any analysis. No significant differences for the high motor symptom and high overall clinical severity analyses. No data reported.
Aubeeluck and Buchanan, 2007	Correlation	Moderate correlations between perceived health status and overall satisfaction with life (***r* = 0.34**, p=<0.01) for satisfaction with life and total feelings about living with HD (***r* = 0.43**, p<0.01)	

Cox, 2012	Correlation	Hours spent caring had a moderate negative correlation with feelings about living with HD (***r*=- 0.43**, p=<0.05) Number of times socialised in the last month was moderately correlated with overall satisfaction with life (***r*= 0.48**, p=<0.05) and feelings about living with HD (***r*= 0.47**, p=<0.05)	Carer age, years of known HD in family, years spent caring, number of people in the household, household income, hours of paid work and hours of unpaid childcare (*r* not reported).
Helder et al., 2002	Hierarchical regression	Perceived duration of HD was weakly correlated with physical health QoL (***r*= 0.27**, p=<0.01). Active coping contributed negatively predicted role functioning limitations related to physical health (β = –0.67, p < .001) and planning coping positively predicted role functioning limitations related to physical health (β = 0.51, p <.01). Spouses' perceptions of symptoms associated with HD (β = –0.51, p <0.01) and restraint coping (β = –0.36, p <0.01) negatively predicted limitations in role function related to emotion health. The final model including	Coping styles and other illness perceptions were not correlated with QoL (*r* not reported). In the final model, illness perceptions and coping styles did not predict the following HR-QoL subscales: physical functioning, role-functioning limitations related to physical problems, bodily pain, general health, vitality, or social functioning. β not reported.

demographics, HD symptoms, illness perceptions, and carer coping styles significantly predicted role functioning limitations related to emotional difficulties (R^2=0.29, p=0.01) and mental health (R^2=0.30, p=0.01)

Ho et al., 2004	Correlation	For the SF-36 measure of HR-QOL, carer age was correlated with physical health summary score (***r* = -0.30**, p=<0.05), physical functioning (***r* = -0.43**, p=<0.01), physical role limitations (***r* = -0.28**, p=<0.05), emotional role limitations (***r* = -0.30**, p=<0.05), and pain (***r*= -0.28**, p=<0.05). Depressive symptoms were correlated with total QoL score (***r* = -0.57**, p=<0.01), physical health summary score (***r* = -0.71**, p=<0.01), mental health summary score (***r* = -0.77**, p=<0.01), physical functioning (***r* = -0.42**, p=<0.01), physical role limitations (***r* = -0.59**, p=<0.01), mental health (***r* = -0.77**, p=<0.01), emotional role limitations (***r* = -0.50**, p=<0.01), vitality (***r* = -0.66**, p=<0.01), pain (***r* = -0.48**, p=<0.01), and general health perceptions (***r* = -0.62**, p=<0.01). For the SIP measure of HR-QoL, carer age was correlated with eating (***r* = 0.29**, p=<0.05). Depressive symptoms were	Care age not correlated with SF-36 subscales: mental health (***r* = -0.14**), vitality (***r* = -0.21**), general health perceptions (***r* = -0.03**), mental health summary score (***r* = -0.25**)and overall QoL score (***r* = -0.19**). Carer age not correlated with SIP subscales, sleep and rest (***r* = 0.13**), work (***r* = 0.06**), home management **(*r* = 0.13),** recreation (***r* = 0.24),** ambulation **(*r* = 0.12),** mobility **(*r* = 0.19**), body care/movement (***r* = 0.09**), social interactions (***r* = 0.15**), emotional behaviour (***r* = 0.06**), communication (***r* = 0.31**), physical QoL summary score (***r* = 0.20**), psychosocial QoL summary score (***r* =**

correlated with total QoL score (***r*= 0.74**, p=<0.01), physical QoL summary score (***r* = 0.41**, p=<0.01), psychosocial QoL summary score (***r* = 0.66**, p=<0.01), sleep and rest (***r* = 0.63**, p=<0.01), work (*r*= 0.37, p=<0.01), home management (***r*= 0.53**, p=<0.01), recreation (*r*= 0.62, p=<0.01), mobility (***r*= 0.34**, p=<0.05), body care/movement (***r* = 0.36**, p=<0.01), social interaction (***r* = 0.61**, p=<0.01), alertness (***r* = 0.55**, p=<0.01), and emotional behaviour (***r* = 0.51**, p=<0.01).

0.14), and overall QoL (***r* = 0.24**). Carer depressive symptoms not correlated with SIP subscales: ambulation (***r* = 0.27**) and communication (***r* = 0.14**). Carer cognitive function not correlated with either measure (SF-36 ***r* = 0.01 to 0.20**, SIP ***r* = -.03- to -0.18**).No *p* values reported for non-significant results.

O'Connor and McCabe, 2011	T-test and multiple regression	In multiple regression carer mood (β = -0.36, p= 0.05, sr^2 = 0.09) and social support (β = 0.47, p= 0.01, sr^2 = 0.15) predicted QoL (overall model: F (5, 26) = 4.24, p= <0.01, R^2=0.45)	QoL and mood did not change between baseline and 12-month follow-up, no data reported.
Ready et al., 2008††	T-test and correlation	Carer QoL was correlated with pwHD cognitive function (***r* = 0.47**, p=<0.05) at time one and functional capacity (***r* = 0.49,** p=<0.05) and disruptive/aggressive behaviour (***r* = -0.50,** p=<0.05) at time two. Retrospective ratings of QoL collected at time two were significantly correlated with pwHD functional capacity (***r* = 0.55**, p=<0.05), suicidal thoughts (***r* = -0.58**, p=<0.05), disruptive/aggressive behaviour (r = -0.58, p=<0.05), and cognitive function (***r* = 0.60**, p=<0.05).	Carer QoL was not correlated with pwHD motor (T1 ***r* = -0.14**, T2 ***r* = 0.10),** or overall behavioural/psychological difficulties (T1 ***r* = -0.17**, T2 ***r* = -0.17**) at any time point or with pwHD functional capacity at time one (***r* = 0.26**). or cognitive function at time two (***r* = 0.41**).No p values reported for these results. . No significant difference between carer QoL at time one and time two (t(17) = 0.29, p = 0.70), ***r* = -0.11** or between

		time one and their retrospective time one QoL ratings (t(17)= -1.14, *p* = 0.25), ***r* = -0.01**.
Roscoe et al., 2009	Correlation	Life satisfaction was correlated with HR-QoL (***r* = 0.58**, p=<0.05), perceived benefits of caring (***r* = 0.62**, p=<0.05), sense of mastery (**r = 0.57**, p=<0.05), spirituality (*r* = 0.98, p=<0.05), and satisfaction with emotional social support (***r* = 0.52**, p=<0.05). HR-QoL was associated with carer depressive symptoms (***r* = -0.49**, p=<0.05), perceived benefits of caregiving (***r* = 0.83**, p=<0.001) and spirituality (r = 0.70, p=<0.05). Life satisfaction was not correlated with pwHD functional status (***r* = 0.40**), involvement in caring (***r* = -0.07**), carer depressive symptoms (***r* = -0.43**), the perceived stressfulness of caring (***r* = -0.28**), satisfaction with tangible (***r* = <0.001),** information (***r* = 0.13**), and overall social support (***r* = 0.20**) . HR-QoL was not correlated with pwHD functional status (***r* = 0.20**),

			involvement in caring (***r* = 0.10**), the perceived stressfulness of caring (***r* = 0.11**), sense of mastery (***r* = 0.34),** satisfaction with tangible (***r* = 0.06**), information (***r* = -0.16**), emotional (***r* = 0.27**), and overall social support (***r* = -0.11**) . No *p* values reported.
Shaw et al., 2022	T-test	No significant results.	Motor transition status not associated with QoL, no data reported.

Yu et al., 2019††	Correlation and t-test	No significant results.	QoL was not associated with carer gender (***r* = 0.12**, $p = 0.85$), age (***r* = 0.17,** $p = 0.48$), marital status (***r* = 0.20**, $p = 0.85$); duration of HD in family (***r* = 0.09**, $p = 0.72$), duration of caring (***r* = 0.05**, $p = 0.84$), prior experience of caring (***r* = 0.23**, $p = 0.85$); child at risk (***r* = -0.09**, $p = 0.85$); household size (***r* = -0.32**, $p = 0.18$), living in a suitable home (***r* = 0.23**, $p = 0.85$); presence of family support (***r* = 0.07**, $p = 0.85$), hours of paid work weekly (carer) (***r* = -0.34**, $p = 0.14$), hours of childcare performed (***r* = -0.29**, $p = 0.22$), hours of weekly HD care provided (***r* = 0.02**, $p = 0.95$); hours for hobbies (***r* = 0.42**, p

= 0.07); total family income (***r* = 0.04**, *p* = 0.88), financial difficulties (***r* = -0.01**, *p* = 0.85); and pwHD independence (***r* = 0.30**, *p* = 0.20), pwHD total functional capacity (***r* = 0.002**, *p* = 0.99), and presence of pwHD motor difficulties (***r* = 0.05**, *p* = 0.85), cognitive impairment (insufficient data reported), and behavioural issues (***r* = -0.19**, *p* = 0.85).

Comparable effect sizes (i.e. Pearson's *r)* are indicated in bold.

† Pearson's *r* calculated by the author

†† Pearson's *r* calculated by the author for t-tests but not correlations

Table 1.6

Mood Results

Author	Design and analysis	Results	Non-significant results
Kavanaugh, 2014	Correlation	Depressive symptoms had a small correlation with school problems (***r* = 0.44**, p = <0.01)	Carer age (***r* = 0.03**), gender (***r* = 0.27**), duration of caring (***r* = 0.06**), total parent symptoms (***r* = 0.12**), amount of caring tasks (***r* = 0.17**), and parent/child conflict (***r* = 0.22**) .

Luszczynska at al., 2014†	Correlation, ANOVA, hierarchical regression	A main effect of being exposed to mortality reminder on finding benefits of caring ($F(1, 49) = 5.92$, $p = 0.001$, $\eta 2 = 0.11$); carers reminded of their mortality reported lower levels of benefit finding compared to controls ($d = 0.66$ / $\mathbf{r = 0.31}$). The main effect remained significant cater controlling for carer age, gender, life satisfaction and HD stage ($F(1, 45) = 4.26$, $p = 0.05$, $\eta 2 = 0.09$). The interaction between being shown mortality reminders and time since HD diagnosis was significant $\beta = 0.36$, $p=0.04$, $R^2=0.08$). Carers with less time since HD diagnosis shown mortality reminder reported significantly lower benefit finding than controls, but those with longer time since HD shown mortality reminders reported similar benefit finding to controls. Moderator values ≤ -1.18 SD	No correlation between level of benefit finding and HD stage, carer life satisfaction or carer age (*r* not reported). The interaction between carers carrying the HD gene and being shown mortality reminders was not significant $F(1, 47) = 0.32$, $p = 0.578$, $\eta 2 = 0.008$..

in time since HD diagnosis were the region of moderator significance, equivalent to 2.59 years since HD diagnosis.

Pickett et al., 2007	Correlation, multiple regression, mediation analysis, Sobel test	Carer depression was correlated with carer burden (***r* = 0.29,** p = <0.05), pwHD depression (***r* = 0.30**, p = <0.05), and subjective caregiver problem-solving ability (***r* = 0.27**, p = <0.05). PwHD physical function indirectly predicted carer depression via carer burden (z = -2.21, p = <0.05)	Carer depression was not correlated with pwHD physical function (***r* = <0.01**) , year since HD diagnosis; age, race, gender, education level, employment status, and marital status of the pwHD or carer; the carer relationship to the pwHD; carer living with pwHD; greater length of time caring (years), and amount of time spent caring per day (hours) (r not reported, except for pwHD physical function). Carer burden did not mediate the relationships between pwHD physical function, pwHD

depression, and carer problem-solving and carer depression, no data reported.

Length of time caring ($z = 1.90$, $>p = .05$) and years since HD diagnosis ($z = 1.58$, $>p = .05$) did not indirectly predict carer depression via carer burden.

Roscoe et al., 2009	Correlation	Depressive symptoms were correlated with HR-QoL (***r* = -0.50,** p = <0.001), perceived stressful of caring (***r* = 0.43**, p = <0.05), sense of mastery (***r* = -0.69**, p = <0.05), and spirituality (***r* = -0.54**, p = <0.05). Benefits of caring were correlated with life satisfaction (***r* = -0.62**, p = <0.05), HR-QoL (***r* = -0.69**, p = <0.05), and spirituality (***r* = -0.66**, p = <0.05).	Depressive symptoms were not correlated with pwHD functional status (***r* = -0.08**), involvement in caring (***r* = 0.08**), the perceived benefits of caring (***r* = -0.52**), sense of mastery (***r* = 0.34**), and satisfaction with tangible (***r* = 0.06**), information (***r* = -0.16**), emotional (***r* = 0.27),** and overall social support (***r* = -0.11**). Benefits of caring were not correlated with pwHD functional status (***r* = -0.14**), involvement in caring (***r* = 0.13**), carer depressive symptoms (***r* = -0.52**), sense of

			mastery (***r* = 0.35**), and satisfaction with tangible (***r* = -0.05**), information (***r* = -0.22**), emotional (***r* = -0.04**), and overall social support (***r* = -0.38**), no *p* values reported..
Tanigaki et al., 2020	Correlation	Carer disruptive daytime sleepiness was correlated with depressive symptoms (***r* = 0.78**, p = <0.001)	Depressive symptoms were not correlated with subjective sleep quality (***r* = 0.20**, p = 0.42), sleep latency (***r* = 0.08**, p = 0.72), sleep duration (***r* = 0.30**, p = 0.19), sleep efficiency (***r* = 0.13**, p = 0.57), sleep

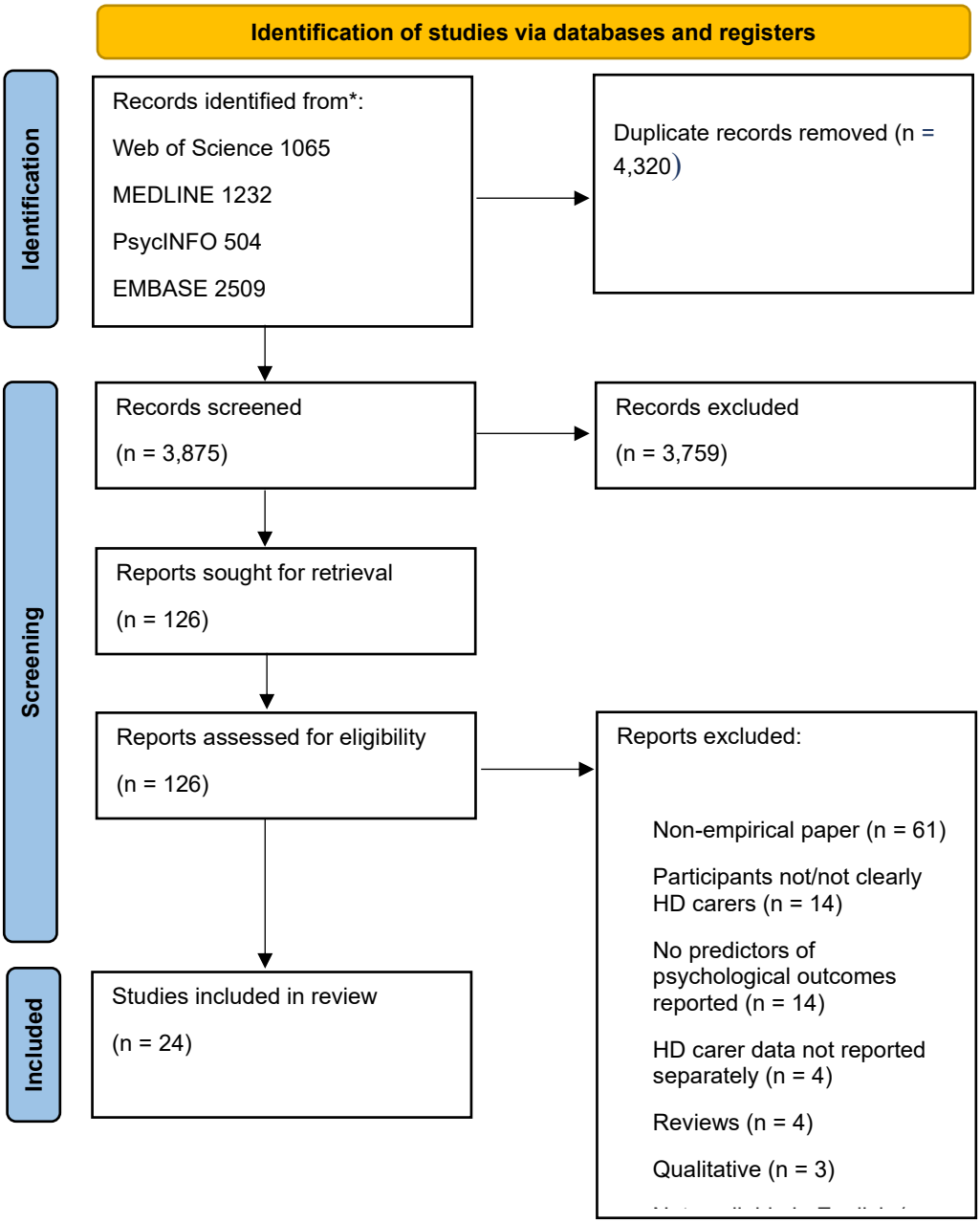
			disturbances (***r* = -0.03**, p = 0.89), and use of sleep medications (***r* = -0.18**, p = 0.44) . Anxiety was not correlated with subjective sleep quality (***r* = 0.08**, p = 0.76), sleep latency (***r* = 0.18,** p = 0.43), sleep duration (***r* = 0.08**, p = 0.74), sleep efficiency (***r* = 0.33**, p = 0.15), sleep disturbances (***r* = 0.26**, p = 0.26), use of sleep medications (***r* = 0.22**, p = 0.35), and disruptive daytime sleepiness(***r* = 0.37**, p = 0.10) .

Comparable effect sizes (i.e Pearon's *r)* are indicated in bold.

† Pearson's r calculated by the author

Figures

Figure 1: PRISMA Flow Diagram



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372: n71. Doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Appendices

Appendix 1-A

Health Psychology Review Author Guidelines

Aims and Scope

Health Psychology Review (HPR) contributes to the advancement of the discipline of health psychology and strengthens its relationship to the field of psychology as a whole, as well as to other related academic and professional arenas. *HPR* is dedicated to theoretical and conceptual work, as well as evaluative, integrative, meta-analytic and systematic reviews and interpretations of substantive issues in the general domain of health psychology. The journal particularly favours theory-based reviews of empirical contributions that afford integrative theoretical formulations of work in a given area of health psychology and reviews of developments that develop connections between areas of research within the general domain of health psychology as well as with other disciplines (ranging from biology to policy-oriented research domains). Papers that consider the cross-cultural and cross-national relevance and appropriateness of theories and key concepts are also welcomed. Articles focusing on methodological issues and problems of design and measurement will be considered if they make a direct and substantial contribution to theory.

Preparing Your Paper

Manuscripts must be written in English. American or British spelling and punctuation are acceptable, provided authors apply the style consistently throughout the manuscript.

Manuscript Length

The editorial team acknowledge that review articles are usually longer than articles reporting findings of primary research. Health psychology review does not impose any length restrictions on submitted articles. However, it is also recognised that articles should be

appropriately concise and pithy so that the main focus is not lost and the argument is not encumbered by unnecessary detail.

Meta-analyses and systematic reviews

In order to comply with international standards and for academic transparency, authors of meta-analyses and systematic reviews submitted to Health Psychology Review are required to include a statement in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (http://www.prisma-statement.org/) as a supplemental file for review (the final document will be included as online supplemental material). From January 1, 2021 all reviews with empirical content (e.g., systematic reviews, meta-analyses) will be required to be pre-registered on an appropriate independent, institutional registry such as Prospero https://www.crd.york.ac.uk/prospero/, the Open Science Framework https://osf.io/ or other registry (e.g., http://clinicaltrials.gov/, http://socialscienceregistry.org/, http://egap.org/designregistration/, http://ridie.3ieimpact.org/)

Structure

Your paper should be compiled in the following order: title page; abstract; keywords; main text introduction, materials and methods, results, discussion; acknowledgments; declaration of interest statement; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figures; figure captions (as a list).

Format-Free Submission

Authors may submit their paper in any scholarly format or layout. There are no strict formatting requirements, but all manuscripts must contain the essential elements needed to evaluate a manuscript: abstract, author affiliation, figures, tables, funder information, and references. Further details may be requested upon acceptance.

References can be in any style or format, so long as a consistent scholarly citation format is applied. Author name(s), journal or book title, article or chapter title, year of publication, volume and issue (where appropriate) and page numbers are essential. All bibliographic entries must contain a corresponding in-text citation. The addition of DOI (Digital Object Identifier) numbers is recommended but not essential.

The journal reference style will be applied to the paper post-acceptance by Taylor & Francis.

Section Two: Research Paper

Do Family Relationship and Friendship Satisfaction Predict Wellbeing in Carers of People with Huntington's Disease?

Word count: 7,931

(Excluding title page, references, figures, tables, and appendix)

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Abstract

Background: Caring for someone with Huntington's disease (HD) can be challenging, and studies indicate it can impact carers' wellbeing. Theoretical models suggest that satisfying social relationships may directly predict and/or buffer carers against the wellbeing impacts of caring-related stressors, such as functional and behavioural/psychological difficulties associated with HD. However, this has been underexplored in HD carers.

Objective: To examine whether satisfaction with family relationships and friendships predicted positive wellbeing and negative feelings in HD carers. To examine whether these relationship satisfaction variables moderated relationships between functional capacity and behavioural/psychological difficulties in the person with HD and carer positive wellbeing and negative feelings.

Methods: A quantitative, cross-sectional design was used. Participants were 880 HD carers, drawn from Enroll-HD, an international observational cohort of people with HD and their carers. Data were analysed using hierarchical multiple regression (including sub-group regression analyses for spousal carers, adults caring for a parent, main carers, and non-main carers) and moderation analyses.

Results: Family relationship and friendship satisfaction predicted positive wellbeing and negative feelings in HD carers after controlling for carer demographics, caring intensity, and HD-related difficulties. These findings were consistent across sub-group analyses for spousal carers, adults caring for a parent, and main carers. The moderation analyses were non-significant.

Conclusions: This study demonstrates that satisfaction with family relationships and friendships are important predictors of higher positive wellbeing and lower negative feelings for HD carers. The importance of interpersonal factors for wellbeing in HD carers suggests supportive interventions would benefit from considering both individual and systemic factors.

Keywords: Huntington's disease, caregivers, psychological wellbeing, interpersonal relationships

Introduction

Huntington's disease (HD) is a life-limiting genetic neurodegenerative condition caused by an expansion of the cytosine-adenine-guanine trinucleotide repeat in the huntingtin allele, which causes progressive motor impairment and cognitive decline [1]. Behavioural and psychological difficulties, including depression, anxiety, apathy, and irritability, are also common in people with HD (pwHD) [2]. As symptoms progress, pwHD often require additional support, which is frequently provided by friends and family [3]. Such carers are often called informal (e.g., unpaid) carers. However, this term is contested as "informal" carers often provide intensive support and perform similar tasks to paid carers [4]. With this in mind, this paper uses "carers" to refer to people who provide unpaid support to pwHD.

HD is challenging for pwHD and their carers. The range of symptoms and progressive nature of HD means carers must adapt to complex and changing care needs. Carers often lack appropriate information and support from professionals to manage their role [5]. HD-related difficulties can contribute to strain in family relationships, and carers report grief and loss of their loved one and their past self [6,7]. Caring can also create strain in other roles, such as childcare and employment, and contribute to financial difficulties [8]. The genetic nature of HD also presents unique challenges, as carers may have seen HD progression in other family members, be at risk of HD themselves, or have children at risk of HD [7,8]. Perhaps unsurprisingly, caring for someone with HD has been associated with higher carer burden (negative perceptions about the impact of caring on psychosocial function, emotional and physical health, and practical aspects of life [9]), mental health difficulties, and lower quality of life compared to carers of those with other neurological conditions [10–12].

The challenges faced by HD carers and their potential psychological impacts suggest that identifying factors which could maintain wellbeing may be of value for this group. There is a lack of consensus on how to define wellbeing; however, conceptualisations highlight that

it is a complex, multidimensional construct relating to optimal psychological functioning, happiness, life satisfaction, and achieving one's potential [13,14]. Conceptual understandings of wellbeing have been influenced by hedonic and eudemonic traditions. Hedonic wellbeing relates to happiness and life satisfaction and is referred to as subjective wellbeing [15,16]. Furthermore, although wellbeing is a positive psychology construct, negative emotions (their relative absence or balance with positive feelings) are a component of hedonic wellbeing [17]. Eudemonic wellbeing relates to human potential, flourishing, and meaning and is referred to as psychological wellbeing [15,16]. Despite conceptual differences, evidence suggests that both kinds of wellbeing are related concepts that contribute to an overall general factor of wellbeing [15,17,18]. The terms wellbeing, psychological wellbeing, and subjective wellbeing are often used interchangeably in research and have all been used to refer to conceptualisations of wellbeing which draw together eudemonic and hedonic traditions [16,19], indicating a lack of conceptual clarity around these terms. This paper uses the term "positive wellbeing" to refer to positive indicators of wellbeing identified in hedonic and eudemonic conceptualisations and "wellbeing" as an umbrella term encompassing positive wellbeing and negative emotions.

Theoretical models based on the stress process model [20,21] have been applied to understanding how caring for someone with a neurological condition impacts wellbeing [22–27]. Briefly, wellbeing is directly influenced by care recipient difficulties, called primary stressors. Care-related strain in other roles and activities and carers' sense of self (called secondary stressors) can also directly influence wellbeing [20,21]. However, the impact of stressors is also influenced by how carers make sense of their situation and the internal and external resources they have to manage or cope with stressors [20,21]. This includes factors such as personal appraisals, coping styles, beliefs, values, and social relationships. Additionally, carer background and contextual variables, such as gender, socioeconomic

status, and caring intensity, can influence carers' experiences of stressors and their access to coping resources, influencing wellbeing outcomes [20,21].

Several empirical studies with HD carers have examined the influence of factors theorised to be important for wellbeing, with a focus on caring contextual factors and primary stressors. For example, contextual factors such as higher caring intensity (indicated by providing higher amounts/levels of care) have been associated with lower quality of life and higher carer burden [28–33]. With regards to stressors, more severe HD-related difficulties, including behavioural/psychological difficulties, functional impairment, and cognitive difficulties, have been associated with higher carer burden, carer depressive symptoms, and lower quality of life [30,34–37]. Although these findings align with the stress process model, one notable limitation is that, with the exception of the results for carer burden, studies have not examined whether these factors predict carer wellbeing outcomes when accounting for the influence of other factors. Furthermore, less is known about what factors predict positive wellbeing outcomes in HD carers. This is important as reviews of evidence from carers of people with other conditions have highlighted that carers frequently report positive psychological impacts alongside negative experiences [38,39]. Additionally, as noted above, conceptualisations of wellbeing emphasise the presence of positive psychological outcomes rather than merely the absence of negative ones. Therefore, understanding predictors of positive and negative wellbeing outcomes is important.

Furthermore, few quantitative studies have examined the direct or indirect effects of resources theorised to support HD carer wellbeing, such as the impact of social relationships. With regards to direct effects, it has been suggested that higher quality social relationships contribute to greater wellbeing by fulfilling social needs and supporting affect regulation through everyday interactions [40,41]. While the stress process model acknowledges these direct effects, it also proposes that in times of stress, social relationships are a resource which

can buffer the carers against the negative impact of care-related stressors on their wellbeing by facilitating coping behaviours [21].

Relational approaches to studying the impact of social relationships on health and wellbeing highlight the importance of examining the qualities of the different relationships people have available to them [42]. The present study examines satisfaction with relationships, an indicator of relationship quality based on the subjective evaluation of thoughts, emotions, and behaviours associated with the relationship [43]. Satisfaction with relationships, including with partners, family, and friends, has been found to directly predict wellbeing and mental health outcomes in general adult populations [44–48]. Although relationship satisfaction appears less well studied in carers, higher levels of relationship satisfaction from carer to care recipient have been associated with lower carer burden and lower carer depression in dementia carers [49–52]. However, whether satisfaction with social relationships directly predicts wellbeing in HD carers remains untested.

Evidence examining whether relationship satisfaction can buffer people against the negative impacts of stress on wellbeing remains sparse. However, satisfaction with friendships has been found to buffer against the impact of stress on wellbeing in a general population [53] and marital relationship satisfaction has been found to moderate the impact of infertility stress on life satisfaction in couples [54]. For carers, studies have focused on the moderating role of social support rather than relationship qualities, finding that social support moderated the relationship between care stressors and psychological distress and quality of life [55–57]. Although separate constructs, social support is seen as a core interpersonal process that contributes to relationship satisfaction [42]. Therefore, taken together, the evidence indicates that satisfaction with social relationships has the potential to moderate the relationship between care stressors and wellbeing outcomes. However, this has not yet been examined in HD carers.

Consequently, the current study aimed to test the direct effects theory of social relationships by investigating whether satisfaction with family relationships and friendships predicted carer positive wellbeing and negative feelings when controlling for carer demographics, caring intensity, and pwHD motor and cognitive symptoms, functional impairment, and behavioural/psychological difficulties. Family relationships and friendships were considered as separate variables as studies have found differences in their effect on wellbeing outcomes in samples of adults and older adults [58–63]. Furthermore, the study aimed to test whether this relationship satisfaction buffered (i.e. moderated) the negative effects of pwHD's functional and behavioural/psychological difficulties (i.e. primary stressors) on carer wellbeing outcomes as suggested by the stress process model.

Specifically, the hypotheses were:

- Carer demographics, higher caring intensity, more severe pwHD difficulties (i.e. motor and cognitive symptoms, functional capacity, and behavioural/psychological difficulties), and lower satisfaction with family relationships and friendships would be positively correlated with negative feelings and negatively correlated with positive wellbeing in carers.
- Both relationship satisfaction variables would be independent predictors of higher positive wellbeing and lower negative feelings when demographics, caring intensity, and pwHD difficulties were controlled for.
- Both relationship satisfaction variables would moderate the relationships between pwHD functional capacity and behavioural/psychological difficulties and carer positive wellbeing and negative feelings.

Materials and Methods

Design

This study employed a quantitative, cross-sectional design using data from Enroll-HD, a worldwide prospective observational study of pwHD and their families. Participants were drawn from Enroll-HD to obtain an adequately powered sample for the proposed analyses, as recruitment can be challenging in rare conditions research [64]. Enroll-HD was chosen over other available datasets [e.g., 65] due to its global reach and larger sample of HD carers.

Correlations were conducted to examine relationships between the main variables (hypothesis one). Hierarchical regression was used to examine hypothesis two, with a model based on the stress process model [20] in which carer demographics and caregiving environment characteristics (i.e., carer context and background variables) were entered in block one, followed by pwHD motor and cognitive symptoms, functional capacity, and behavioural/psychological difficulties (i.e. primary stressors) in block two, and satisfaction with family relationships and friendships (i.e. resources) in block three to examine whether these predicted carer positive wellbeing and negative feelings. Carer age, gender, and education level were included in block one as they have been previously associated with carer psychological outcomes [66–69]. Whether the participant was the main carer of the pwHD was also included in block one as factors indicative of caring intensity have been associated with carer burden and quality of life in HD carers [28,32,33]. More severe motor and cognitive symptoms, functional impairment, and behavioural/psychological difficulties in pwHD have been linked to carer outcomes, including carer burden, quality of life, and depression (34,38,66,67), and these variables were, therefore, entered at step two. Moderation analysis was used to examine hypothesis three, whether satisfaction with friendships and family relationships buffered (i.e. moderated) the impact of functional capacity and

behavioural/psychological difficulties associated with HD on carers' positive wellbeing and negative feelings. Where sample sizes allowed for adequately powered analysis, subgroup analyses were conducted to examine the findings in different types of carers (e.g., spouse, child, parent, etc.) and in those who were the main carer versus those who were not.

The study design was developed in consultation with a clinician working with pwHD and their carers and four experts by experience (UK-based). The researcher discussed (via videocall) experiences of caring and sought feedback on which variables in the Enroll-HD dataset the experts by experience felt may influence wellbeing to inform model selection. In line with the feedback, pwHD behavioural difficulties, particularly irritability and aggression, were included in the analysis and sub-group analyses for different carer groups were conducted.

Participants

Currently 21,116 participants are in Enroll-HD, drawn from North America, Latin America, Europe, Asia, and Australasia. Participants are recruited through 179 specialist HD clinics and word of mouth and include carriers of the HD gene expansion, family members without the gene expansion, and community controls with no HD-affected relatives.

Participants were included in the present study if they were adults (aged 18 and over) caring for someone with manifest HD. Carer baseline data (i.e. the first visit where carer data were available) were used to provide the largest sample. Data were available for 1,051 participants. Participants with complete data for the variables of interest were selected for analysis, resulting in a sample of 880. *A priori* power analyses were conducted using G*power [72], indicating that a sample of 865 would be required to detect a small effect (f^2 = 0.01) with 80% power ($p \leq .05$) for the hierarchical regression. For moderation analysis, it has been suggested that 0.005, 0.01, and 0.025 constitute small, medium, and large effect

sizes, respectively [73]. Therefore, a sample of 967 would be required to detect a moderate effect or 389 for a large effect with 80% power ($p \leq .05$) in this study. The data were received in October 2023; no data collected after this were included in the study.

Procedure

Participants are invited to take part in Enroll-HD annually during routine clinical appointments. To obtain informed consent (including for secondary data analysis), participant information is provided in oral and written form (documentation varies by country), following which participants are asked to sign a consent form. Participants can withdraw from the study at any time without reason. Demographic data are collected alongside clinical assessments, including pwHD motor function, cognitive function, psychological and behavioural difficulties, and a carer quality of life/wellbeing measure. See Landwehrmeyer [74] for the full Enroll-HD study protocol. Data for the relevant carer are stored together with the pwHD's data, making it possible to link pwHD and their carers.

To access the dataset, an application using the dataset request form was reviewed and agreed by Enroll-HD's Scientific Review Committee. The dataset was provided in an anonymised form to protect participant confidentiality and was transferred via secure file transfer. The researchers signed agreements to process the data per General Data Protection Regulation and Data Protection Act (2018) principles to ensure data security and protect participant confidentiality. The data were stored on password-protected Lancaster University cloud storage accessible only to the researchers.

Ethics and Regulatory Approval

This study was granted ethical approval by Lancaster University Faculty of Health and Medicine Research Ethics Committee. For Enroll-HD, ethical approval has been obtained

for each research site via Institutional Review Boards or Independent Ethics Committees according to local regulations.

Carer Measures

Huntington Disease Quality of Life for Carers-Short Form (HDQoL-C; 28)

The HDQoL–C is a 23-item self-report quality of life measure designed with HD carers. It has demonstrated good internal consistency and reliability in the Enroll-HD sample [28]. The measure has three sections. Section one captures demographics and caregiving environment characteristics. This study used carer gender (male/female), age (years), education level (years), and whether the carer was the main carer of the pwHD (yes/no) from this section.

Items in section two relate to satisfaction with various aspects of life, scored from 0 = *dissatisfied* to 10 = *satisfied*. Two items which rate satisfaction with family relationships and friendships were selected. It has been suggested that satisfaction with relationships implies a global evaluation of the relationship as a whole and, therefore, may be amenable to measurement as a unitary construct [75]. Single-item measures of intimate partner relationship satisfaction have been found to have good test-retest reliability and convergent validity compared to multi-item measures [75,76], supporting this approach.

Items in section three assess the frequency with which respondents experience various practical and emotional aspects of caregiving, rated from 0 = *never* to 10 = *always*. The negative and positive feelings sub-scales from section three were selected as outcome variables. The negative feelings sub-scale has eight items related to exhaustion and feelings of distress, such as sadness/depression, grief, loss, and stress. Total scores range from 0-80. The positive feelings sub-scale has seven items related to both hedonic and eudemonic wellbeing concepts such as hope, safety, ability to cope, role reward, feeling supported, and

quality of life. Given this mix of items, it is referred to as the positive wellbeing sub-scale in this paper, as this was felt to represent its content more clearly. Total scores range from 0-70. Higher scores indicate more positive wellbeing or negative feelings. A validation study using the Enroll-HD sample reported excellent internal consistency for the negative feelings and positive wellbeing subscales (Cronbach alpha = 0.90 and 0.81, respectively) [28].

PwHD Measures

Unified Huntington's Disease Rating Scale (UHDRS; 77)

This is a clinician-rated assessment tool developed to assess functioning in the core domains affected by HD. The total motor function score (TMS) and total functional capacity score (TFC) were used in this study. The TMS is the sum of 31 items related to motor features of HD scored from 0 = *normal* to 4 = *unable to complete*, with higher scores indicating more severe motor symptoms (range = 0 - 124). The TFC score is a sum of five items about the ability to complete daily functional activities scored from 0 = *unable* to 2 or 3 = *normal*, depending on the item. Higher scores indicate higher functional capacity (range: 0 -13). The TMS and TFC have excellent internal consistency in pwHD (Cronbach alpha = .95 for both scales) [77].

Symbol Digit Modalities Test (SDMT; 78)

A measure of processing speed, participants match as many symbols as possible with numbers according to a reference key in 90 seconds. The test can be administered in written or oral format for those with motor difficulties. More correct responses indicate better performance (maximum score = 110). It was chosen as a cognitive function measure for this study as it has been found to be particularly sensitive to HD-related cognitive change, including in early HD, compared to other cognitive tests included in the Enroll-HD dataset

[79–84]. This test also requires minimal adjustment for different languages, unlike other sensitive tests such as the Stroop Word, which is beneficial in this international sample [80].

Problem Behaviours Assessment-Short Form (PBA-S; 79)

This is an 11-item semi-structured clinical interview which assesses behavioural and psychological difficulties associated with HD. The scores for the severity and frequency of each behaviour (scored from 0-4) are multiplied to create an overall behaviour score, with higher scores indicating more severe difficulties. It is a valid and reliable measure of behavioural/psychological difficulties in pwHD [85]. This study used the apathy, affect, and irritability sub-scales identified in Callaghan et al.'s [92] factor analysis, which have been used in past research [86], although Cronbach alphas have not been previously reported. The apathy scale includes items for apathy, perseveration, and disorientated behaviour, and the affect scale includes items for depression, anxiety, and suicidality. Scores in these sub-scales range from 0-48. The irritability scale includes items for irritability and aggression, with scores ranging from 0-36.

Statistical Analysis

Visual inspection via histograms and Q-Q plots indicated that all continuous variables were not normally distributed. Therefore, two-tailed Spearman's *rs* correlation coefficients were conducted to explore relationships between study variables. Hierarchical regressions with theoretically determined blocks were then conducted to test whether satisfaction with family relationships and friendships predicted positive wellbeing and negative feelings after controlling for carer demographics, caring intensity, and pwHD difficulties. Linearity, homoscedasticity, and normality of residuals were examined using scatterplots. Before

performing subgroup analyses, sample sizes were checked and where samples were adequately powered, the regressions were repeated for the appropriate sub-groups.

Data were analysed using SPSS 29 [87], with moderation analyses conducted using Hayes PROCESS Tool (model two) [88], with the statistical threshold set to $p = \leq 0.05$. Correlation coefficients were interpreted as: 0.1 = small, 0.3 = moderate, and 0.5 = strong [89]. Cronbach's alpha was calculated for all scales. Opinions vary about acceptable alpha values [90,91]; however, ≥ .70 is generally considered acceptable [92].

Missing Data

Missing data were handled via listwise deletion. The SMDT had the most missing data ($n = 108$). Listwise deletion has been found to be robust against potential bias in regression models even when violations of missingness completely at random occur, as long as missingness is not dependent on the dependent variable [93].

The data for excluded participants were analysed to examine differences with the included sample using Wilcoxon-Rank sum for continuous variables and Chi-squared tests for categorical variables. Excluded participants cared for pwHD with significantly lower functional capacity Z = -6.48 ($N1 = 880$, $N2 = 170$), $p < 0.001$, more severe motor difficulties Z = -6.80 ($N1 = 880$, $N2 = 163$), higher apathy Z = -3.43 ($N1 = 880$, $N2 = 149$), $p < 0.01$, and lower irritability Z = -2.33 ($N1 = 880$, $N2 = 167$), $p = 0.02$. Differences for carer age, education level, gender, main carer, pwHD SDMT and affect scores, and carer negative feelings and positive wellbeing were non-significant.

Results

Descriptive Statistics

The sample (n = 880) is described in Table 2.1. Participants were predominantly women (78.2%), consistent with evidence that informal care is largely provided by women and girls [94]. The mean age of the sample was 52.0 (SD = 13.5). Most participants were the main carer of the pwHD (82.4%), and the mean number of years providing care was 7.0 (SD = 8.02). Most participants were married (79.7%), and the most common relationship to pwHD was spouse/partner (58.2%). Mean years in education was 13.9 (SD = 4.20), and most participants were employed (full or part-time) (88.5%). The mean age and education level were similar to those found in other studies of HD carers [30,33,70,95].

[Insert Table 2.1]

Means and standard deviations of predictor and outcome variables are presented in Table 2.2. Internal consistency was acceptable to excellent for all scales, except the PBA-S irritability ($\alpha = 0.61$) and apathy ($\alpha = 0.54$) sub-scales. Mean values for negative feelings (M = 34.0, SD = 13.98) and positive wellbeing (M = 46.35, SD = 12.63) fell in the middle of the score range for the scales. Satisfaction with friendships (M = 8.14, SD = 1.91) and family relationships (M = 7.97, SD = 2.08) was high. PwHD mean scores for irritability, apathy, and affect were comparable to those reported by Gunn et al. [86]. TFC scores suggested most pwHD were in the early-middle stages of HD (stage I, 31.4%, stage II, 40.3%), with the mean score consistent with stage II/V [96]. PwHD mean SDMT and TMS scores were consistent with those found for participants in early-middle stages of HD in another study [95].

[Insert Table 2.2]

Correlations

Non-parametric bivariate correlations were used to examine relationships between key variables to investigate hypothesis one, that carer positive wellbeing and negative feelings would be associated with carer demographics, caring intensity, and pwHD difficulties (see Table 2.3). Higher negative feelings were significantly correlated with being a female carer, being the main carer, lower pwHD functional capacity, cognitive function, and higher apathy and irritability with small-moderate effects, and lower satisfaction with family relationships and friendships with moderate effects. Higher positive wellbeing was significantly correlated with higher carer age and education, lower pwHD apathy, affect, and irritability with small-moderate effects, and higher satisfaction with family relationships and friendships with moderate-large effects. Negative feelings and positive wellbeing had a moderate-large association.

[Insert Table 2.3]

Regressions

Hierarchical multiple regression analyses were conducted to investigate hypothesis two: that, in line with the direct effects theory of how social relationships influence wellbeing, satisfaction with family relationships and friendships would significantly predict carers' negative feelings and positive wellbeing when controlling for demographics, caring intensity, and pwHD difficulties. Variables were entered into the models in the following blocks: 1. Carer demographic variables and caring intensity (age, gender, education, main carer); 2. pwHD difficulties (TMS, TFC, SDMT score, apathy, affect, and irritability); 3.

satisfaction with family relationships and friendships. The outcome variables were negative feelings in model one and positive wellbeing in model two. See Table 2.4 for results.

[Insert Table 2.4]

Model One: Negative Feelings

In support of hypothesis two, satisfaction with family relationships and friendships were significant independent predictors of carer negative feelings after controlling for carer demographics, caring intensity, and pwHD difficulties. The overall model was significant ($F(2,867) = 48.48$, $R^2 = .18$, $R^2\_adj = .17$, $p < .001$), as was each step of the model ($p < .001$). At step 3, carer gender ($\beta = .20$, $p < .001$), being the main carer ($\beta = .08$, $p = .01$), pwHD irritability ($\beta = .09$, $p = .01$), satisfaction with family relationships ($\beta = -.16$, $p < .001$) and satisfaction with friendships ($\beta = -.20$, $p < .001$) were significant independent predictors of negative feelings. PwHD apathy ($\beta = .07$, $p = .07$) approached significance. The addition of satisfaction with family relationships and friendships at step 3 accounted for an additional 9.1% of model variance. As can be seen in Table 2.4, a relatively small amount of variance was explained in blocks 1 (5%) and 2 (4%).

Model Two: Positive Wellbeing

In support of hypothesis two, satisfaction with family relationships and friendships were significant independent predictors of carer positive wellbeing after controlling for carer demographics, caring intensity, and pwHD difficulties. The overall model was significant ($F(2,867) = 127.89$, $R^2 = .30$, $R^2\_adj = .29$, $p < .001$), as was each step of the model ($p < .001$). At step 3, carer age ($\beta = .07$, $p = .02$), carer education level ($\beta = .14$, $p < .001$), pwHD apathy ($\beta = -.20$, $p < .001$), satisfaction with family relationships ($\beta = .26$, $p < .001$) and

satisfaction with friendships (β = .28, $p < .001$) were significant independent predictors of positive wellbeing. The addition of satisfaction with family relationships and friendships at step 3 accounted for an additional 21% of model variance. As can be seen in Table 2.4, a relatively small amount of variance was explained in blocks 1 (4%) and 2 (5%).

Exploratory Sub-group Regressions

An *a priori* power analysis indicated a sample of 90 was required to reliably detect the moderate effects found in the main regression analyses ($f^2 = 0.22$ in the negative feelings model). Therefore, sub-group analyses for spousal carers ($n = 512$), adult children caring for a parent with HD ($n = 130$), main carers ($n = 725$), and non-main carers ($n = 155$) were possible. The same predictors were included as for the main models except that the main/non-main carer variable was omitted for the main/non-main carer subgroups.

Details for the subgroup analyses are given in Appendix 2-B. For all four groups, the overall negative feelings ($R^2\_adj = .17$-$.25$) and positive wellbeing models ($R^2\_adj = .28$-$.42$) remained significant. The addition of satisfaction with family relationships and friendships at step 3 continued to predict significant additional variance in the outcomes (negative feelings 7-10%; positive wellbeing 17-26%). Satisfaction with family relationships and friendships also remained significant independent predictors at step 3 in all models except the non-main carer model for negative feelings where they both approached significance ($p = 0.06$).

Carer demographics and caring intensity accounted for between 3-5% of variance in the final models, with the exception of the negative feelings model for carers of parents where they accounted for 11% of variance. PwHD characteristics accounted for between 5-15% of the variance in the final models, with the largest amount explained in the non-main carer positive wellbeing model (15%). See Tables 2.5 to 2.8.

[Insert Tables 2.5 to 2.8]

Moderation Analyses

Moderation analysis was used to test hypothesis three, that both satisfaction with family relationships and friendships would moderate the relationship between pwHDs' functional capacity and behavioural/psychological difficulties and carer positive wellbeing and negative feelings. This was in line with the stress process model prediction of the buffering impact of social relationships on the relationship between primary stressors and wellbeing. All eight moderation analyses had satisfaction with family relationships and satisfaction with friendships as the two moderators. Outcomes were negative feelings (models 1, 3, 5, and 7) and positive wellbeing (models 2, 4, 6, and 8). Predictors were TFC score (models 1 and 2), pwHD apathy (models 3 and 4), pwHD affect (models 5 and 6), and pwHD irritability (models 7 and 8). See Figure 2.1.

[Insert Figure 2.1]

The moderation analyses were repeated, controlling for carer age, education level, and gender. No change in significance/non-significance was found. Therefore, non-controlled models are presented in Table 2.9. Contrary to hypothesis three, satisfaction with family relationships and friendships did not significantly moderate the relationships between pwHD functional capacity and behavioural/psychological difficulties and carer wellbeing in any of the models.

[Insert Table 2.9]

Power analysis indicated that a sample size of 2,412 would be required to reliably detect the largest effect found in the main moderation analyses ($f^2 = 0.004$). Therefore, sub-group moderation analyses were not conducted as no sub-group sample sizes met this threshold.

Discussion

This cross-sectional study examined the relationships between carer stressors, satisfaction with family relationships and friendships, and positive wellbeing and negative feelings in HD carers. Hypothesis one was partially supported as higher negative feelings (distress and exhaustion) in HD carers were correlated with being the main carer; more severe pwHD motor and cognitive symptoms, functional impairment, and behavioural/psychological difficulties; and lower satisfaction with family relationships and friendships. Higher positive wellbeing was correlated with lower caring intensity; less severe pwHD motor and cognitive symptoms, functional impairment, and behavioural/psychological difficulties; and higher satisfaction with family relationships and friendships. In support of hypothesis two, satisfaction with family relationships and friendships predicted lower negative feelings and higher positive wellbeing after controlling for carer demographics, caring intensity, and pwHD difficulties, providing support for the direct effect model of how social relationships influence wellbeing. Satisfaction with family relationships and friends provided a significant contribution to the amount of explained variance in carer positive wellbeing and negative feelings, above that explained by carer demographics, caring intensity, and pwHD difficulties. Similar findings were seen across sub-group analyses for spousal carers, adults caring for their parent, and main and non-main carers. Furthermore, satisfaction with family relationships and friendships were significant independent predictors of the wellbeing outcomes in all models, except the negative feelings model for non-main carers. Contrary to

hypothesis three, satisfaction with family relationships and friendships did not significantly moderate the relationships between pwHD functional capacity and behavioural/psychological difficulties and carer positive wellbeing and negative feelings, respectively. This is contrary to the stress process model prediction that social relationships buffer carers against the negative impacts of caring stressors on wellbeing.

Correlation and Regression Findings

Hypothesis one, regarding correlations between carer demographics, caring intensity, pwHD difficulties (i.e. motor and cognitive symptoms, functional capacity, and behavioural/psychological difficulties), and satisfaction with relationships, was partially supported. Higher carer negative feelings were associated with being female and the main carer, and pwHD higher functional impairment, cognitive difficulties, apathy, and irritability, with small-moderate effects. Similar associations have been found between higher caring intensity and pwHD difficulties and higher carer burden, although several studies also found associations between higher motor symptoms and higher carer burden [30,32–34,70], which the current study did not. This may be because carer burden measures include negative perceptions about the impact of care needs/tasks on the carer (86–88) and, thus, may be more impacted by HD motor symptoms than the measure in the current study, which was predominantly related to distressed emotions.

Higher positive wellbeing was associated with higher carer age and years of education and lower pwHD apathy, affective difficulties, and irritability with small-moderate effects. These findings extend previous evidence that higher carer quality of life was associated with less severe global HD symptoms and lower functional, cognitive, and behavioural/psychological difficulties in pwHD with moderate-large effects [71,97] by linking these factors to other indicators of positive wellbeing. Furthermore, satisfaction with

family relationships and friendships was associated with lower negative feelings and higher positive wellbeing with a moderate-large effect, indicating the relative importance of satisfying social relationships for wellbeing in this sample.

In support of hypothesis two, satisfaction with family relationships and friendships were independent predictors of higher positive wellbeing and lower negative feelings in HD carers after controlling for carer demographics, caring intensity, and pwHD motor and cognitive symptoms, functional impairment, and behavioural/psychological difficulties. This effect was seen for negative feelings in spousal and adult carers of parents with HD, and main carers and across all carer types for positive wellbeing. Furthermore, the relationship satisfaction variables added significant additional variance in predicting both wellbeing outcomes in all groups. This indicates that these variables are important wellbeing predictors for various kinds of HD carers.

Previous studies have found that higher social support, a function of satisfying social relationships, predicted lower carer burden in HD carers [30]; the current study extends these findings by establishing a relationship between satisfaction with social relationships and a more general negative psychological outcome measure. With regards to positive psychological outcomes, higher social support has also been found to independently predict higher carer quality of life [11], demonstrating the importance of social factors for promoting positive wellbeing in HD carers, as well as reducing potential negative emotional impacts. These findings provide support for the direct effects theory of social relationships in HD carers, which argues that social relationships have a direct positive impact on wellbeing regardless of stress via everyday, quality social interactions that support affect regulation and meet social needs [40,98].

This study also extends previous findings by establishing the importance of satisfying relationships with both family and friends as predictors of positive wellbeing and negative

feelings in HD carers. This aligns with qualitative research, which has highlighted that HD carers value support from family and friends to manage their role [99,100]. Furthermore, these two relationship satisfaction variables accounted for a significant proportion of variance in the models over and above that which was explained by caring intensity and pwHD difficulties. The impact on the positive wellbeing was especially high, accounting for an additional 16-26% of explained variance in the final models. Taken together, findings suggest that helping HD carers to establish and/or maintain satisfying relationships with family and friends may support their wellbeing, with particular benefit for promoting positive aspects of wellbeing. This may be especially relevant to HD carers, given that they report strain in interpersonal relationships [99–101] and are at greater risk of losing social connections compared to carers of people with other neurological conditions [12].

Generally, carer demographic and caring context variables explained a comparatively small amount of variance (3-5%) compared to satisfaction with social relationships. However, for adult children caring for a parent these variables accounted for 11% of variance in the negative feelings model. Qualitative studies have identified that daughters report feeling that they have no choice in providing care or feel obliged due to societal norms [102,103]. In contrast, sons describe fulfilling a sense of duty and spouses report viewing caring as a natural part of their relationship [102–104]. It may be that these different motivations account for the gender differences seen in negative feelings for parental carers. However, this would need to be tested in future research, particularly as the identified difference comes from a relatively small sample. The stress process model also highlights that other contextual factors, such as socioeconomic status, access to health and social care services, and other life difficulties, are also likely to influence the impact of caring on wellbeing [21]. However, whether these factors predict wellbeing remains underexplored in HD carers.

Much previous research has aimed to identify which HD-related difficulties are predictive of HD carer wellbeing, with varied results for the HD-related difficulties included in this study (see Chapter 1). Although there were similarities in the overall variance explained in the models by HD-related difficulties, there was some variation in individual predictors (See Appendix 2-B for further details). This suggests that the impact of specific HD-related difficulties may vary according to carer type, potentially explaining the variation in previous findings as studies have often used mixed carer samples. Additionally, HD-related difficulties explained a similar amount of variance in positive wellbeing for non-main carers as the relationship satisfaction variables (15% and 16%, respectively). This suggests that pwHD difficulties have a larger impact on the positive wellbeing of non-main carers than the other groups examined. This appears surprising as one might expect HD-related difficulties to be more taxing on those providing higher levels of care (e.g., main carers). It may be that non-main carers are less used to or adapted to their loved one's difficulties than those providing higher levels of care leading to a larger negative impact on positive wellbeing. However, further research would be required to confirm this, particularly as there were a relatively small number of participants per variable in this model which may have impacted the stability of the regression model, and thus limit the generalisability of findings [105].

Moderation Findings

Contrary to hypothesis three, satisfaction with family relationships and friendships did not moderate the relationship between pwHD functional capacity, affect, apathy, or irritability and positive wellbeing and negative feelings. These findings are inconsistent with the stress process model which suggests that social relationships act as a protective buffer against the impact of care-related stressors on wellbeing [21]. In this study, the effects of satisfying social relationships appear more consistent with the direct effects model, which argues that

social relationships are beneficial for supporting wellbeing irrespective of stress levels [98]. However, studies with carers of people with other conditions have found support for the buffering effect of social relationships on relationships between care recipient difficulties and carer psychological outcomes [56,106]. As such, consideration of why this study did not produce the expected moderation effects is warranted.

One reason may be that this study was inadequately powered to detect moderate effects in double moderation models. However, all models reported effect sizes indicative of a small effect in moderation analysis (e.g., $f^2 = <0.005$) [73]. The largest effects were reported for the moderation of the relationship between pwHD affect and carer negative feelings ($f^2 = 0.004$) and pwHD apathy and positive wellbeing ($f^2 = .003$). Post-hoc analysis indicated that samples of 2,412 and 3,215 would have been required to reliably detect these effects, respectively. However, the very small-small effects found in the models calls into question their clinical meaningfulness at an individual psychological level, although there is a lack of clear consensus regarding what effect size should be considered clinically meaningful [107].

Another reason for the null findings may have been an overlap between satisfaction with family relationships and the other predictors, as carers were predominantly family members of the pwHD. Carers of pwHD report that family relationships can be negatively affected by the impact of HD [8,108] and may experience prolonged grief and loss of their loved one [6]. Thus, satisfaction with family relationships may have been affected by pwHD difficulties. This overlap may also have contributed to satisfaction with family relationships being a weaker predictor in the regression models.

Furthermore, previous studies with carers have examined social support as a moderator, rather than satisfaction with relationships. It may be that social support moderates the relationships between functional capacity and behavioural/psychological difficulties in pwHD and HD carer wellbeing outcomes, although this remains untested. However, the

relationships between these pwHD factors and positive wellbeing and negative feelings were also weak, so while other social relationship measures may moderate these relationships, the overall effect on wellbeing is likely to be small.

Strengths and Limitations

To my knowledge, this is the first study to test whether satisfaction with family relationships and friendships moderates the relationship between primary stressors and carer wellbeing outcomes and to examine predictors of positive wellbeing in HD carers. The use of a large international cohort of pwHD and carers to test theoretically informed models controlling for a range of factors is also a strength of this study. Regarding limitations, as this study was cross-sectional it is not possible to draw conclusions about causality. Most carers were caring for someone in the early-middle stages of HD, and the sample was predominantly female, so findings may be less applicable to carers of people with more advanced HD and male carers. Additionally, the fact that participants excluded due to missing data were caring for pwHD with more severe functional difficulties and behavioural/psychological difficulties may limit the generalisability of the results. [86]

While the use of secondary data enabled a large enough sample to conduct well-powered statistical modelling [109], the lack of control over how concepts were operationalised and measured presents limitations. For example, only single-item, unvalidated measures of relationship satisfaction and caring intensity were available. It is also noted that other characteristics of social relationships considered to be important for wellbeing, such as social support, social network size, and other indicators of relationship quality such as intimacy and trust, are not available in Enroll-HD and may have different relationships to wellbeing in HD carers. It has also been highlighted that subjective measures of caring intensity, such as those included in the HDQoL-C, may be vulnerable to bias [26].

Furthermore, the Cronbach's alpha for the PBA-S apathy and irritability subscales were low, which may call into question the reliability of these measures, and as such, some caution should be exercised when interpreting the importance of specific behavioural/psychological difficulties. This may reflect the incorporation of related but distinct behaviours (e.g., apathy, disorientation, and perseveration, and irritability and aggression), in the sub-scales. While these subscales have been used in previous research [86], the Cronbach alphas have not been previously reported.

Caring is a contextualised process that is influenced by the social and cultural context in which carers operate [109]. However, the HDQoL-C does not collect carer ethnicity, and country-level data are not routinely available to researchers to protect participant anonymity. Therefore, these factors were not included in this study limiting the ability to assess the role of these factors in carer wellbeing. Furthermore, the sample may be unrepresentative of the countries represented, and it is known that certain regions (Latin America and Asia) are less well-represented in the Enroll-HD sample, potentially limiting the cross-cultural applicability of these findings. Additionally, Enroll-HD does not collect data on carer secondary stressors, such as strain in relationships or other roles, or some important psychosocial resources that are theorised to influence the impact of stressors on carer wellbeing outcomes, such as coping styles. The ability to include such variables may have increased the explanatory power of the regression models and contributed to more theoretically informed understandings of wellbeing in HD carers. [111]

Clinical Implications

The finding that satisfaction with friendships and family relationships were predictors of lower negative feelings and higher positive wellbeing in HD carers suggests that efforts to promote and sustain satisfying connections with family and friends may support their

wellbeing. Currently, a lack of evidence exists regarding the acceptability and efficacy of peer support interventions in HD carers. However, reviews of peer support interventions in carers of people with dementia and Parkinson's have found that they can improve mental health [110,111], suggesting they may have promise for HD carers. However, overall it is challenging to make clinical recommendations at the individual psychological level as psychological understandings of wellbeing in HD carers remain in their infancy.

The relative importance of satisfying social relationships for predicting carer wellbeing suggests that it is important to consider the influence of the carers' wider systemic context. For example, HD carers report challenges in accessing adequate and appropriate healthcare for their loved one due to a lack of knowledge among professionals [5,112]. Consistent with this, it has been argued that improvements to health and social care systems for people with long-term conditions or disability are more likely to positively improve the lives of carers and the people they support than individual-level psychological interventions aimed at carers [113]. Furthermore, many countries do not provide an enabling environment for carers and that reform to labour laws, social welfare systems, and health and social care are needed to support carer wellbeing [94,114].

Future Research

The lack of quantitative research into the wellbeing of HD carers explicitly grounded in psychological theory is problematic. Stress process models would indicate a need to move away from the current focus on linking HD clinical factors and carer wellbeing towards examining the role of psychosocial influences. The findings that relationship satisfaction often explained a relatively large amount of variance in carer wellbeing compared to pwHD difficulties in the examined models suggests this approach could support the development of more holistic understandings of wellbeing in this group. Factors that remain underexplored in

HD carers but have been found to predict wellbeing in other carer groups include coping styles, motivation, sense of mastery over one's life, and formal support [38,115–117]. Qualitative studies have also found that HD carers report secondary stressors such as role and intrapsychic strains, including changes in self-concept or feelings of role captivity related to caring [6,8], which may warrant further exploration in quantitative research. Additionally, studies examining different facets of positive wellbeing would be beneficial given its multifaceted and contested nature. Furthermore, studies examining whether other characteristics of social relationships, such as social support, moderate relationships between stressors and wellbeing would also be indicated.

Future studies may benefit from considering sociocultural factors such as income, access to health and social care services for pwHD and carers, and discrimination, which have been highlighted as concerns by HD carers [8]. This could help evidence the need for systemic changes to support carer wellbeing. The evidence base would benefit from further studies examining protective factors and factors which contribute to positive indicators of wellbeing. Furthermore, future research validating the positive and negative wellbeing scales in different samples, or studies using more well-established measures of wellbeing, could provide further confidence in the findings, given that these scales have not been widely used in research to date.

The use of longitudinal designs to establish causal relationships between caring stressors, personal and social resources, and carer wellbeing would also make a significant contribution to the evidence base. Longitudinal designs could also be used to examine trajectories of carer wellbeing to identify patterns of adaptation over time and factors which contribute to or interfere with adaptation. This could identify interventional targets and whether there are particular times or circumstances in which interventions may be most needed.

Conclusion

This study demonstrates that satisfaction with family relationships and friendships are important predictors of higher positive wellbeing and lower negative feelings for HD carers after controlling for care demographics, caring intensity, and pwHD motor and cognitive symptoms, functional impairment, and behavioural/psychological difficulties. However, satisfaction with friendships and family relationships did not moderate the relationships between pwHD functional capacity and behavioural/psychological difficulties and carers' positive wellbeing and negative feelings. While further research would be needed to make strong clinical recommendations, the importance of the interpersonal context on carer wellbeing suggests interventions for carers of people with HD should consider individual and systemic factors.

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Tables

Table 2.1

Demographics

N = 880		N	%
Gender	Male	323	36.70
	Female	557	78.23
Main Carer	No	155	17.61
	Yes	725	82.39
Marital Status	Married/partner	701	79.66
	Single/separated/divorced	179	37.14
Employment	Unemployed	303	34.43
	Employed	577	88.50
Relationship to pwHD	Sibling	75	8.53
	Spouse	512	58.25
	Parent	130	14.79
	Child	81	9.22
	Other	30	3.41
	Multiple	51	5.80
PwHD Functional Capacity	I	276	31.4
Stage	II	355	40.3
	III	200	22.7
	IV	41	4.7
	V	8	0.9
	Mean	SD	Range
Carer Age	51.98	13.53	18-86

Carer Education (Years)	13.90	4.20	0-31
# Years Caring	7.01	8.02	0-53

Table 2.2

Descriptive Statistics

	Mean	SD	Range	Cronbach's α
SDMT Total	22.24	12.76	0-67	
Satisfaction Family Relationships	7.97	2.08	0-10	
Satisfaction Friendships	8.14	1.91	0-10	
Total Motor Score	36.00	18.44	0-95	.95
Total Functional Capacity	8.42	3.30	0-13	.84
PBA-s Apathy subscale	6.64	7.67	0-44	.54
PBA-s Affect subscale	5.18	6.33	0-48	.78
PBA-s Irritability subscale	3.64	5.35	0-32	.61
HDQoL-C Negative Feelings	34.00	13.89	7-70	.90
HDQoL-C Positive Feelings	46.35	12.63	4-70	.76

TMS: Total Motor Score; TFC: Total Functional Capacity; SDMT: Symbol Digit Modalities; PBA: Problem Behaviour Checklist; HDQoL-C: Huntington Disease Quality of Life Questionnaire for Carers.

Table 2.3

Spearman's Rho Correlation Coefficients

N = 880	Age	Gender	Education (Years)	Main Carer	TMS	TFC	SDMT Total	PBA Apathy	PBA Affect	PBA Irritability	Satisfaction Family	Satisfaction Friendships	HDQoL-C Negative
Gender	-0.02												
Education (Years)	-.07*	-0.02											
Main Carer	.23**	-0.01	-0.06										
TMS	0.05	-0.07*	-0.03	0.04									
TFC	-0.05	0.02	0.07*	-0.05	-0.64**								
SDMT Total	0.01	0.02	0.12**	-0.01	-0.71**	0.61**							
PBA Apathy	-.09**	0.003	-0.05	0.02	0.28**	-0.45**	-0.30**						
PBA Affect	-0.06	-0.10**	-0.04	-0.002	-0.01	-0.08*	0.01	0.42**					
PBA Irritability	-0.03	0.08*	0.01	0.02	0.02	-0.09**	0.02	0.34**	0.40**				
Satisfaction Family	0.12**	-0.002	-0.11**	-0.03	-0.05	0.05	0.03	-0.10**	-0.04	-.097**			
Satisfaction Friendships	0.07	0.06	-0.04	-0.08*	0.03	-0.002	-0.03	-0.08*	-0.09*	-.11**	0.60**		
HDQoL-C Negative	-0.003	.21**	-0.05	0.11**	0.04	-0.09**	-0.08*	0.15**	0.05	.15**	-0.26**	-0.27**	
HDQoL-C Positive	.13**	-0.06	.09**	-0.04	-0.03	0.06	0.07	-0.22**	-0.11**	-.14**	0.41**	0.42**	-0.44**

TMS: Total Motor Score; TFC: Total Functional Capacity; SDMT: Symbol Digit Modalities; PBA: Problem Behaviour Checklist; HDQoL-C: Huntington Disease Quality of Life Questionnaire for Carers.

* $p < 0.05$ level (2-tailed).

**p <0.01 level (2-tailed).

Table 2.4

Regression Analyses Predicting Negative Feelings and Positive Wellbeing

N = 880		Independent Variable	Unstandardised Coefficients *B*	*SE*	Standardised Coefficients Beta	*t*	*p*	R^2	Adjusted R^2	ΔR^2	F Change	Sig. F Change
Model One: Negative Feelings	Step 1							0.05	0.05	0.055	12.72	<0.001
		Age	-0.03	0.03	-0.03	-0.86	0.39					
		Gender	5.83	0.95	0.20	6.16	<0.001					
		Education (Years)	-0.11	0.11	-0.03	-1.01	0.31					
		Main Carer	4.12	1.23	0.11	3.34	<0.001					
	Step 2							0.09	0.08	0.037	5.86	<0.001
		Age	-0.01	0.03	-0.01	-0.34	0.73					
		Gender	5.38	0.95	0.19	5.66	<0.001					
		Education (Years)	-0.07	0.11	-0.02	-0.65	0.52					

	Main Carer	3.74	1.22	0.10	3.07	<0.001				
	TMS	-0.02	0.04	-0.03	-0.50	0.62				
	TFC	-0.20	0.21	-0.05	-0.97	0.33				
	SDMT	-0.03	0.05	-0.03	-0.55	0.58				
	PBA Affect	0.00	0.08	0.00	-0.03	0.97				
	PBA Irritability	0.31	0.10	0.12	3.21	<0.001				
	PBA Apathy	0.16	0.07	0.09	2.16	0.03				
Step 3							0.18	0.17	0.091	48.48	<0.001
	Age	0.02	0.03	0.02	0.59	0.56				
	Gender	5.73	0.91	0.20	6.33	<0.001				
	Education (Years)	-0.12	0.10	-0.04	-1.19	0.23				
	Main Carer	2.92	1.16	0.08	2.52	0.01				
	TMS	-0.02	0.04	-0.03	-0.59	0.56				
	TFC	-0.21	0.20	-0.05	-1.05	0.29				
	SDMT	-0.03	0.05	-0.03	-0.68	0.50				

		PBA Affect	-0.01	0.08	-0.01	-0.18	0.86				
		PBA Irritability	0.24	0.09	0.09	2.57	0.01				
		PBA Apathy	0.13	0.07	0.07	1.80	0.07				
		Satisfaction	-1.06	0.24	-0.16	-4.44	<0.001				
		Family									
		Satisfaction	-1.43	0.26	-0.20	-5.53	<0.001				
		Friendships									
Model	Step 1							0.04	0.03	0.04	8.34	<0.001
Two:		Age	0.13	0.03	0.14	4.19	<0.001				
Positive		Gender	-1.24	0.87	-0.05	-1.43	0.15				
Feelings		Education	0.36	0.10	0.12	3.59	<0.001				
		(Years)									
		Main Carer	-2.30	1.13	-0.07	-2.03	0.04				
	Step 2							0.09	0.08	0.05	8.07	<0.001
		Age	0.11	0.03	0.11	3.40	<0.001				
		Gender	-0.76	0.87	-0.03	-0.87	0.38				

	Education (Years)	0.33	0.10	0.11	3.35	<0.001				
	Main Carer	-1.93	1.11	-0.06	-1.74	0.08				
	TMS	0.02	0.03	0.02	0.48	0.63				
	TFC	-0.18	0.19	-0.05	-0.98	0.33				
	SDMT	0.03	0.05	0.03	0.65	0.51				
	PBA Affect	0.07	0.08	0.03	0.91	0.37				
	PBA Irritability	-0.18	0.09	-0.08	-2.02	0.04				
	PBA Apathy	-0.37	0.07	-0.22	-5.40	<0.001				
Step 3							0.30	0.29	0.21	127.89	<0.001
	Age	0.06	0.03	0.07	2.27	0.02				
	Gender	-1.21	0.76	-0.05	-1.58	0.11				
	Education (Years)	0.41	0.09	0.14	4.66	<0.001				
	Main Carer	-0.83	0.98	-0.02	-0.84	0.40				
	TMS	0.02	0.03	0.03	0.68	0.49				

TFC	-0.17	0.17	-0.05	-1.05	0.29
SDMT	0.04	0.04	0.04	0.90	0.37
PBA Affect	0.08	0.07	0.04	1.23	0.22
PBA Irritability	-0.08	0.08	-0.03	-1.00	0.32
PBA Apathy	-0.32	0.06	-0.20	-5.35	<0.001
Satisfaction	1.55	0.20	0.26	7.69	<0.001
Family					
Satisfaction	1.87	0.22	0.28	8.53	<0.001
Friendships					

TMS: Total Motor Score; TFC: Total Functional Capacity; SDMT: Symbol Digit Modalities; PBA: Problem Behaviour Checklist; HDQoL-C: Huntington Disease Quality of Life Questionnaire for Carers.

Table 2.5

Regression Analyses Predicting Negative Feelings and Positive Wellbeing in Spousal Carers

N = 512		Independent Variable	Unstandardised Coefficients *B*	Unstandardised Coefficients *SE*	Standardised Coefficients Beta	*t*	*p*	R^2	Adjusted R^2	ΔR^2	F Change	Sig. F Change
Model One: Negative Feelings	Step 1							0.050	0.040	0.050	7.040	<0.001
		Age	-0.13	0.05	-0.11	-2.45	0.01					
		Gender	5.14	1.22	0.18	4.22	<0.001					
		Education (Years)	-0.13	0.14	-0.04	-0.93	0.35					
		Main Carer	-1.11	2.81	-0.02	-0.40	0.69					
	Step 2							0.130	0.110	0.080	7.610	<0.001
		Age	-0.15	0.05	-0.13	-2.92	<0.01					
		Gender	4.56	1.23	0.16	3.71	<0.001					
		Education (Years)	0.00	0.14	0.00	0.02	0.98					
		Main Carer	-2.31	2.72	-0.04	-0.85	0.40					
		TMS	-0.01	0.05	-0.01	-0.14	0.89					
		TFC	-0.26	0.26	-0.06	-0.98	0.33					
		SDMT	-0.16	0.07	-0.15	-2.32	0.02					

		PBA Affect	0.05	0.11	0.02	0.45	0.65				
		PBA Irritability	0.34	0.13	0.13	2.66	0.01				
		PBA Apathy	0.15	0.10	0.08	1.47	0.14				
	Step 3							0.23	0.21	0.09	30.24	<0.001
		Age	-0.12	0.05	-0.10	-2.35	0.02				
		Gender	5.24	1.17	0.19	4.48	<0.001				
		Education (Years)	-0.04	0.13	-0.01	-0.27	0.79				
		Main Carer	-1.58	2.57	-0.02	-0.61	0.54				
		TMS	0.00	0.05	0.01	0.09	0.93				
		TFC	-0.29	0.25	-0.07	-1.17	0.24				
		SDMT	-0.14	0.07	-0.12	-2.09	0.04				
		PBA Affect	0.00	0.11	0.00	-0.02	0.98				
		PBA Irritability	0.27	0.12	0.10	2.22	0.03				
		PBA Apathy	0.12	0.10	0.06	1.22	0.22				
		Satisfaction Family	-0.99	0.32	-0.14	-3.07	<0.01				
		Satisfaction Friendships	-1.60	0.35	-0.22	-4.55	<0.001				
Model Two:	Step 1							0.04	0.03	0.04	5.26	<0.001
		Age	0.14	0.05	0.12	2.74	0.01				

Positive Feelings	Gender	-1.59	1.14	-0.06	-1.40	0.16					
	Education (Years)	0.40	0.13	0.13	3.00	<0.01					
	Main Carer	3.78	2.62	0.06	1.44	0.15					
	Step 2						0.10	0.08	0.06	5.49	<0.001
	Age	0.13	0.05	0.12	2.74	0.01					
	Gender	-1.48	1.16	-0.06	-1.27	0.20					
	Education (Years)	0.34	0.13	0.11	2.58	0.01					
	Main Carer	4.41	2.56	0.07	1.72	0.09					
	TMS	-0.04	0.05	-0.06	-0.96	0.34					
	TFC	-0.13	0.25	-0.03	-0.53	0.60					
	SDMT	0.00	0.07	0.00	0.03	0.97					
	PBA Affect	-0.02	0.11	-0.01	-0.23	0.82					
	PBA Irritability	-0.04	0.12	-0.02	-0.31	0.76					
	PBA Apathy	-0.39	0.09	-0.23	-4.09	<0.001					
	Step 3						0.28	0.26	0.18	62.64	<0.001
	Age	0.08	0.04	0.08	1.91	0.06					
	Gender	-2.19	1.04	-0.08	-2.10	0.04					
	Education (Years)	0.41	0.12	0.14	3.46	0.001					

Main Carer	3.29	2.30	0.05	1.43	0.15
TMS	-0.05	0.04	-0.07	-1.23	0.22
TFC	-0.11	0.22	-0.03	-0.49	0.63
SDMT	-0.02	0.06	-0.02	-0.41	0.68
PBA Affect	0.03	0.10	0.01	0.27	0.79
PBA Irritability	0.05	0.11	0.02	0.49	0.63
PBA Apathy	-0.36	0.09	-0.21	-4.22	<0.001
Satisfaction	1.78	0.29	0.28	6.20	<0.001
Family					
Satisfaction	1.51	0.31	0.22	4.80	<0.001
Friendships					

TMS: Total Motor Score; TFC: Total Functional Capacity; SDMT: Symbol Digit Modalities; PBA: Problem Behaviour Checklist; HDQoL-C: Huntington Disease Quality of Life Questionnaire for Carers.

Table 2.6

Regression Analyses Predicting Negative Feelings and Positive Wellbeing in Adult Carers of Parents with HD

N = 130		Independent Variable	Unstandardised Coefficients *B*	Unstandardised Coefficients *SE*	Standardised Coefficients Beta	*t*	*p*	R^2	Adjusted R^2	ΔR^2	F Change	Sig. F Change
Model One: Negative Feelings	Step 1							0.11	0.08	0.11	3.89	<0.01
		Age	-0.06	0.12	-0.04	-0.52	0.60					
		Gender	7.75	2.45	0.27	3.16	<0.01					
		Education (Years)	-0.07	0.28	-0.02	-0.24	0.81					
		Main Carer	6.24	2.43	0.22	2.56	0.01					
	Step 2							0.15	0.08	0.04	0.88	0.51
		Age	-0.09	0.13	-0.06	-0.69	0.49					
		Gender	8.40	2.62	0.29	3.21	<0.01					
		Education (Years)	0.02	0.28	0.01	0.09	0.93					
		Main Carer	6.60	2.50	0.23	2.63	0.01					
		TMS	0.07	0.11	0.10	0.67	0.51					
		TFC	-0.27	0.60	-0.06	-0.45	0.66					
		SDMT	-0.01	0.13	-0.01	-0.09	0.93					

		PBA Affect	0.30	0.21	0.13	1.42	0.16				
		PBA Irritability	-0.33	0.28	-0.11	-1.16	0.25				
		PBA Apathy	0.02	0.17	0.01	0.13	0.89				
	Step 3							0.25	0.18	0.10	8.18	<0.001
		Age	-0.04	0.13	-0.03	-0.32	0.75				
		Gender	8.90	2.53	0.31	3.51	<0.01				
		Education (Years)	-0.11	0.27	-0.03	-0.40	0.69				
		Main Carer	4.14	2.45	0.14	1.69	0.09				
		TMS	0.02	0.10	0.03	0.19	0.85				
		TFC	-0.22	0.57	-0.05	-0.38	0.70				
		SDMT	-0.07	0.13	-0.07	-0.59	0.56				
		PBA Affect	0.26	0.20	0.11	1.29	0.20				
		PBA Irritability	-0.43	0.27	-0.14	-1.59	0.11				
		PBA Apathy	0.01	0.16	0.00	0.04	0.97				
		Satisfaction Family	-1.13	0.56	-0.19	-2.01	0.05				
		Satisfaction Friendships	-1.46	0.65	-0.22	-2.25	0.03				
Model Two:	Step 1							0.04	0.01	0.04	1.45	0.22
		Age	0.14	0.11	0.11	1.24	0.22				

Positive Feelings	Gender	1.95	2.20	0.08	0.89	0.38					
	Education (Years)	0.17	0.25	0.06	0.70	0.49					
	Main Carer	-3.57	2.18	-0.14	-1.63	0.10					
	Step 2						0.15	0.08	0.11	2.51	0.02
	Age	0.12	0.12	0.10	1.03	0.30					
	Gender	0.93	2.26	0.04	0.41	0.68					
	Education (Years)	0.14	0.24	0.05	0.56	0.58					
	Main Carer	-3.84	2.16	-0.16	-1.77	0.08					
	TMS	-0.06	0.09	-0.10	-0.67	0.51					
	TFC	-0.64	0.52	-0.17	-1.24	0.22					
	SDMT	0.24	0.11	0.25	2.13	0.03					
	PBA Affect	-0.14	0.18	-0.07	-0.77	0.44					
	PBA Irritability	-0.03	0.24	-0.01	-0.13	0.90					
	PBA Apathy	-0.25	0.14	-0.18	-1.72	0.09					
	Step 3						0.42	0.36	0.26	26.39	<0.001
	Age	0.05	0.10	0.04	0.52	0.60					
	Gender	0.34	1.94	0.01	0.17	0.86					
	Education (Years)	0.31	0.21	0.11	1.52	0.13					

Main Carer	-0.49	1.88	-0.02	-0.26	0.79
TMS	0.01	0.08	0.02	0.12	0.90
TFC	-0.69	0.44	-0.18	-1.58	0.12
SDMT	0.32	0.10	0.34	3.38	<0.01
PBA Affect	-0.09	0.15	-0.04	-0.57	0.57
PBA Irritability	0.11	0.21	0.04	0.52	0.60
PBA Apathy	-0.22	0.12	-0.16	-1.79	0.08
Satisfaction	1.65	0.43	0.32	3.82	<0.001
Family					
Satisfaction	1.90	0.49	0.33	3.85	<0.001
Friendships					

TMS: Total Motor Score; TFC: Total Functional Capacity; SDMT: Symbol Digit Modalities; PBA: Problem Behaviour Checklist; HDQoL-C: Huntington Disease Quality of Life Questionnaire for Carers.

Table 2.7

Regression Analyses Predicting Negative Feelings and Positive Wellbeing in Main Carers

N = 715		Independent Variable	Unstandardised Coefficients *B*	Unstandardised Coefficients *SE*	Standardised Coefficients Beta	*t*	*p*	R^2	Adjusted R^2	ΔR^2	F Change	Sig. F Change
Model One: Negative Feelings	Step 1							0.05	0.05	0.05	13.01	<0.001
		Age	-0.05	0.04	-0.04	-1.19	0.23					
		Gender	6.05	1.04	0.21	5.80	<0.001					
		Education (Years)	-0.18	0.12	-0.06	-1.51	0.13					
	Step 2							0.10	0.09	0.05	6.93	<0.001
		Age	-0.04	0.04	-0.03	-0.97	0.33					
		Gender	5.64	1.05	0.20	5.40	<0.001					
		Education (Years)	-0.12	0.12	-0.04	-0.98	0.33					
		TMS	0.02	0.04	0.03	0.48	0.63					
		TFC	-0.35	0.22	-0.08	-1.57	0.12					
		SDMT	-0.01	0.06	-0.01	-0.17	0.86					
		PBA Affect	0.04	0.09	0.02	0.46	0.65					
		PBA Irritability	0.30	0.11	0.12	2.88	<0.01					

		PBA Apathy	0.14	0.08	0.08	1.66	0.10				
	Step 3							0.19	0.18	0.09	40.29	<0.001
		Age	0.01	0.04	0.01	0.15	0.88				
		Gender	6.08	1.00	0.21	6.11	<0.001				
		Education (Years)	-0.15	0.11	-0.05	-1.33	0.18				
		TMS	0.01	0.04	0.01	0.26	0.79				
		TFC	-0.36	0.21	-0.08	-1.69	0.09				
		SDMT	-0.01	0.05	-0.01	-0.23	0.82				
		PBA Affect	0.05	0.09	0.02	0.54	0.59				
		PBA Irritability	0.23	0.10	0.09	2.26	0.02				
		PBA Apathy	0.11	0.08	0.06	1.35	0.18				
		Satisfaction Family	-1.05	0.26	-0.16	-4.00	<0.001				
		Satisfaction Friendships	-1.42	0.28	-0.20	-5.05	<0.001				
Model Two: Positive Feelings	Step 1							0.04	0.03	0.04	9.39	<0.001
		Age	0.14	0.04	0.14	3.81	<0.001				
		Gender	-0.95	0.96	-0.04	-0.98	0.33				
		Education (Years)	0.41	0.11	0.14	3.69	<0.001				

Step 2						0.09	0.08	0.05	6.55	<0.001
	Age	0.12	0.04	0.13	3.49	<0.01				
	Gender	-0.61	0.97	-0.02	-0.63	0.53				
	Education (Years)	0.37	0.11	0.12	3.37	<0.01				
	TMS	-0.01	0.04	-0.02	-0.31	0.76				
	TFC	0.00	0.21	0.00	-0.01	0.99				
	SDMT	0.01	0.05	0.01	0.11	0.91				
	PBA Affect	0.01	0.09	0.01	0.14	0.89				
	PBA Irritability	-0.11	0.10	-0.05	-1.15	0.25				
	PBA Apathy	-0.33	0.08	-0.20	-4.36	<0.001				
Step 3						0.30	0.29	0.21	109.83	<0.001
	Age	0.06	0.03	0.06	2.00	0.05				
	Gender	-1.17	0.85	-0.04	-1.38	0.17				
	Education (Years)	0.43	0.10	0.14	4.40	<0.001				
	TMS	0.00	0.03	0.01	0.12	0.91				
	TFC	0.01	0.18	0.00	0.07	0.95				
	SDMT	0.01	0.05	0.01	0.19	0.85				
	PBA Affect	0.00	0.08	0.00	0.00	1.00				
	PBA Irritability	-0.01	0.09	0.00	-0.06	0.95				

PBA Apathy	-0.29	0.07	-0.17	-4.32	<0.001
Satisfaction	1.68	0.22	0.27	7.48	<0.001
Family Satisfaction	1.80	0.24	0.27	7.50	<0.001
Friendships					

TMS: Total Motor Score; TFC: Total Functional Capacity; SDMT: Symbol Digit Modalities; PBA: Problem Behaviour Checklist; HDQoL-C: Huntington Disease Quality of Life Questionnaire for Carers.

Table 2.8

Regression Analyses Predicting Negative Feelings and Positive Wellbeing in Non-Main Carers

N = 155		Independent Variable	Unstandardised Coefficients		Standardised Coefficients						F Change	Sig. F Change
			B	*SE*	Beta	*t*	*p*	R^2	Adjusted R^2	ΔR^2		
Model One: Negative Feelings	Step 1							0.03	0.01	0.03	1.52	0.21
		Age	0.03	0.08	0.03	0.40	0.69					
		Gender	4.18	2.30	0.15	1.82	0.07					
		Education (Years)	0.21	0.26	0.07	0.82	0.41					
	Step 2							0.09	0.03	0.06	1.64	0.14
		Age	0.08	0.08	0.08	0.91	0.36					
		Gender	3.22	2.32	0.11	1.39	0.17					
		Education (Years)	0.23	0.27	0.07	0.86	0.39					
		TMS	-0.18	0.10	-0.27	-1.78	0.08					
		TFC	0.40	0.54	0.11	0.74	0.46					
		SDMT	-0.11	0.12	-0.11	-0.92	0.36					
		PBA Affect	-0.24	0.19	-0.12	-1.30	0.19					
		PBA Irritability	0.19	0.25	0.07	0.76	0.45					

		PBA Apathy	0.40	0.19	0.23	2.16	0.03				
	Step 3							0.17	0.10	0.08	6.53	<0.01
		Age	0.07	0.08	0.07	0.83	0.41				
		Gender	3.53	2.23	0.12	1.58	0.12				
		Education (Years)	0.10	0.26	0.03	0.38	0.70				
		TMS	-0.15	0.10	-0.22	-1.50	0.14				
		TFC	0.45	0.53	0.12	0.85	0.40				
		SDMT	-0.12	0.12	-0.12	-1.05	0.30				
		PBA Affect	-0.29	0.18	-0.14	-1.60	0.11				
		PBA Irritability	0.13	0.25	0.04	0.52	0.61				
		PBA Apathy	0.32	0.18	0.18	1.74	0.08				
		Satisfaction Family	-1.07	0.57	-0.17	-1.88	0.06				
		Satisfaction Friendships	-1.30	0.68	-0.17	-1.90	0.06				
Model Two: Positive Feelings	Step 1							0.03	0.01	0.03	1.68	0.17
		Age	0.13	0.07	0.15	1.89	0.06				
		Gender	-2.31	2.05	-0.09	-1.13	0.26				
		Education (Years)	0.15	0.23	0.05	0.64	0.52				

Step 2						0.19	0.13	0.15	4.56	<0.001
	Age	0.04	0.07	0.05	0.57	0.57				
	Gender	-1.02	1.95	-0.04	-0.52	0.60				
	Education (Years)	0.18	0.22	0.06	0.79	0.43				
	TMS	0.14	0.09	0.24	1.69	0.09				
	TFC	-0.89	0.46	-0.26	-1.94	0.05				
	SDMT	0.15	0.10	0.17	1.46	0.15				
	PBA Affect	0.36	0.16	0.20	2.29	0.02				
	PBA Irritability	-0.46	0.21	-0.18	-2.15	0.03				
	PBA Apathy	-0.65	0.16	-0.42	-4.15	<0.001				
Step 3						0.35	0.30	0.16	17.55	<0.001
	Age	0.06	0.06	0.07	0.92	0.36				
	Gender	-1.47	1.76	-0.06	-0.83	0.41				
	Education (Years)	0.33	0.21	0.12	1.62	0.11				
	TMS	0.10	0.08	0.16	1.23	0.22				
	TFC	-0.96	0.41	-0.28	-2.32	0.02				
	SDMT	0.16	0.09	0.18	1.72	0.09				
	PBA Affect	0.42	0.14	0.23	2.98	<0.01				
	PBA Irritability	-0.37	0.19	-0.14	-1.92	0.06				

PBA Apathy	-0.56	0.14	-0.36	-3.89	<0.001
Satisfaction	0.98	0.45	0.17	2.18	0.03
Family Satisfaction	2.12	0.54	0.31	3.92	<0.001
Friendships					

TMS: Total Motor Score; TFC: Total Functional Capacity; SDMT: Symbol Digit Modalities; PBA: Problem Behaviour Checklist; HDQoL-C: Huntington Disease Quality of Life Questionnaire for Carers.

Table 2.9

Moderation Analysis Predicting Negative and Positive Feelings

N = 880		*b*	SE	*t*	ΔR^2	p
Model One - Negative Feelings	Constant	58.09	5.6	10.37		<.001
	TFC	-0.39	0.63	-0.62		0.053
	Family	-1.39	0.64	-2.18		0.03
	Friendships	-1.18	0.69	-1.71		0.09
	TFC x Family	0.035	0.07	0.48	0.0002	0.63
	TFC x Friendships	-0.036	0.08	-0.47	0.0002	0.64
Model Two - Positive Feelings	Constant	13.12	4.72	2.78		0.005
	TFC	0.57	0.53	1.07		0.28
	Family	1.35	0.54	2.51		0.01
	Friendships	2.52	0.58	4.36		<.001
	TFC x Family	0.03	0.06	0.5	0.0002	0.62
	TFC x Friendships	-0.07	0.06	-1.1	0.001	0.27
Model Three - Negative Feelings	Constant	54.24	2.82	19.22		<.001
	Apathy	-0.003	0.26	-0.01		0.99
	Family	-1.2	0.33	-3.61		<.001
	Friendships	-1.51	0.35	-4.34		<.001
	Apathy x Family	0.02	0.03	0.57	0.0003	0.57
	Apathy x Friendships	0.01	0.03	0.44	0.0002	0.66

Model Four - Positive Feelings	Constant	18.63	2.34	7.97		<.001
	Apathy	0.02	0.22	0.1		0.92
	Family	1.51	0.27	5.43		<.001
	Friendships	2.19	0.28	7.61		<.001
	Apathy x Family	0.003	0.025	0.13	<0.0001	0.89
	Apathy x Friendships	-0.04	0.03	-1.71	0.0025	0.09
Model Five - Negative Feelings	Constant	53.9	2.82	19.1		<.001
	Affect	0.12	0.33	0.36		0.72
	Family	-1.51	0.32	-4.67		<.001
	Friendships	-1.03	0.34	-3.01		0.003
	Affect x Family	0.06	0.04	1.58	0.0025	0.12
	Affect x Friendships	-0.06	0.03	-1.7	0.0031	0.08
Model Six - Positive Feelings	Constant	19.15	2.34	8.06		<.001
	Affect	-0.22	0.28	-0.78		<.001
	Family	1.52	0.27	5.61		<.001
	Friendships	1.93	0.29	6.69		<.001
	Affect x Family	0.02	0.03	0.58	0.0003	0.56
	Affect x Friendships	-0.01	0.03	-0.18	<0.0001	0.86
Model Seven - Negative Feelings	Constant	53.17	2.71	19.64		<.001
	Irritability	0.2	0.39	0.52		0.6
	Family	-1.17	0.31	-3.74		<.001

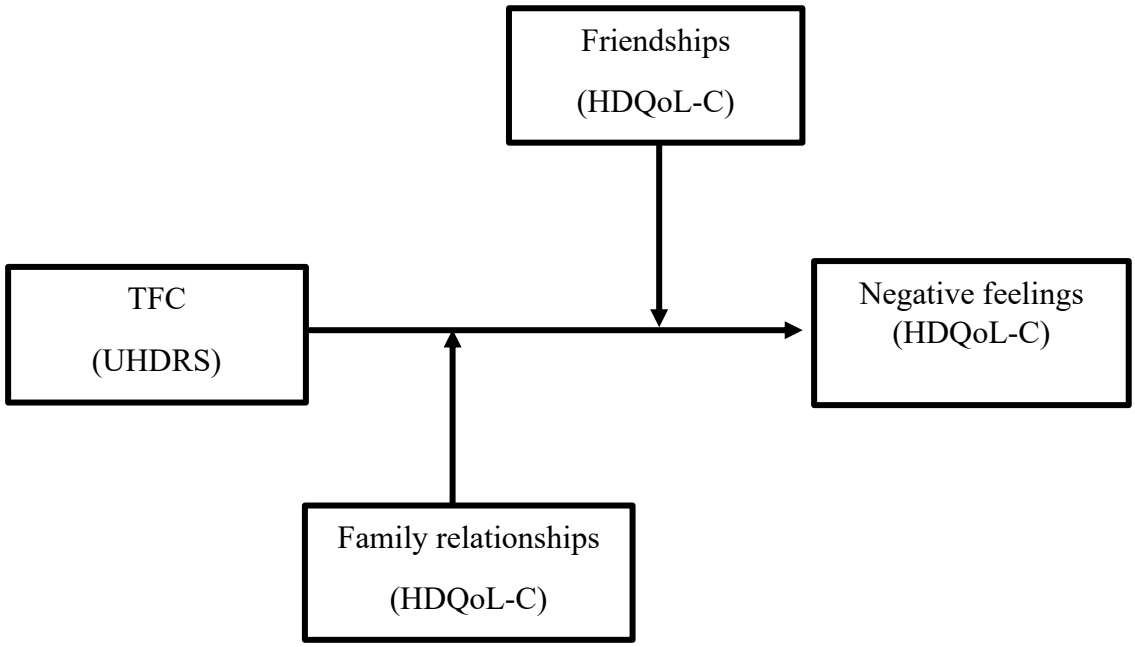
	Friendships	-1.38	0.34	-4.08		<.001
	Irritability x Family	0.02	0.04	0.36	0.0001	0.72
	Irritability x Friendships	0.01	0.05	0.12	<0.0001	0.9
Model Eight - Positive Feelings	Constant	19.12	2.29	8.34		<.001
	Irritability	-0.22	0.33	-0.66		0.51
	Family	1.44	0.26	5.45		<.001
	Friendships	2.02	0.29	7.08		<.001
	Irritability x Family	0.03	0.04	0.86	0.0006	0.39
	Irritability x Friendships	-0.03	0.04	-0.8	0.0006	0.43

TFC = Total Functional Capacity

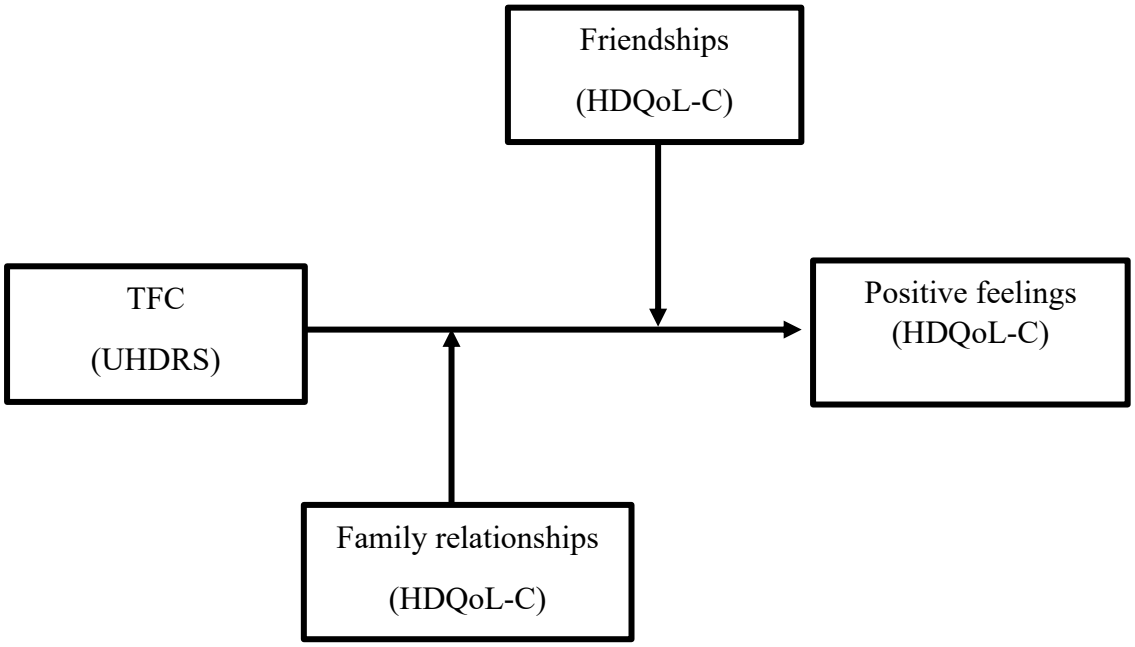
Figures

Figure 2.1

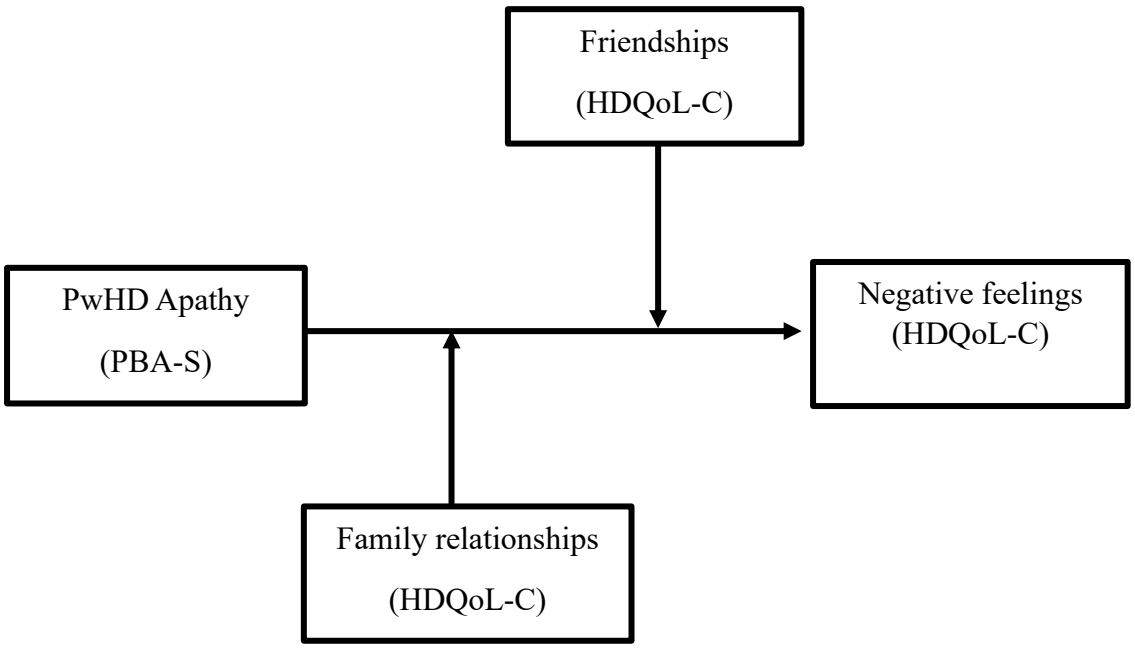
Moderation Model 1.



Moderation Model 2.



Moderation Model 3.



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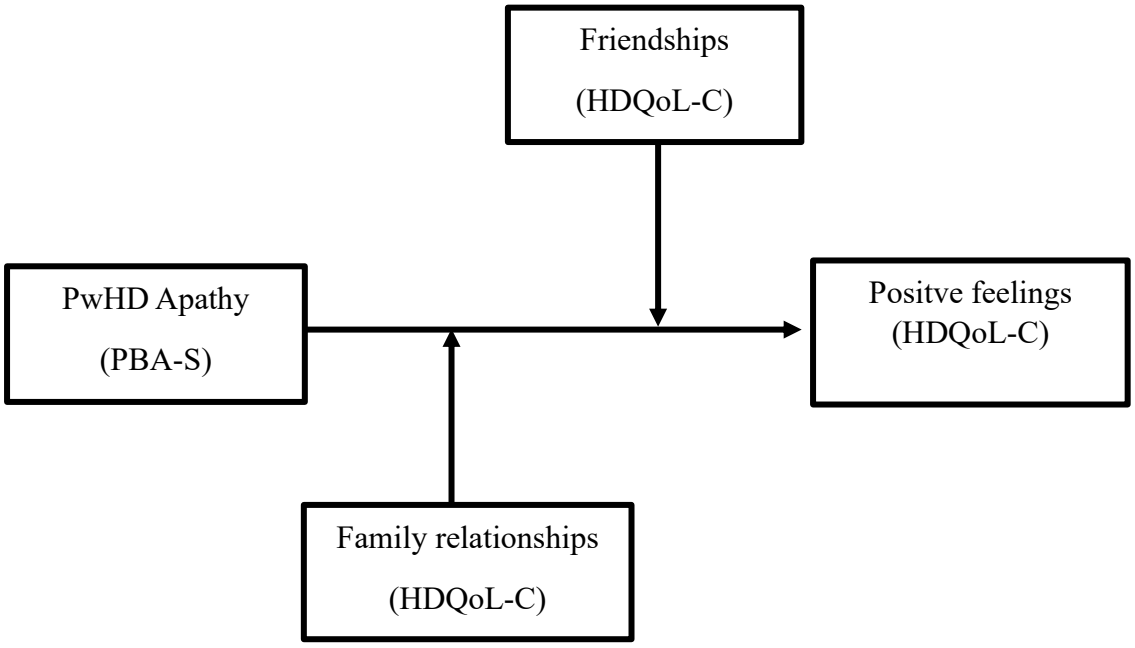
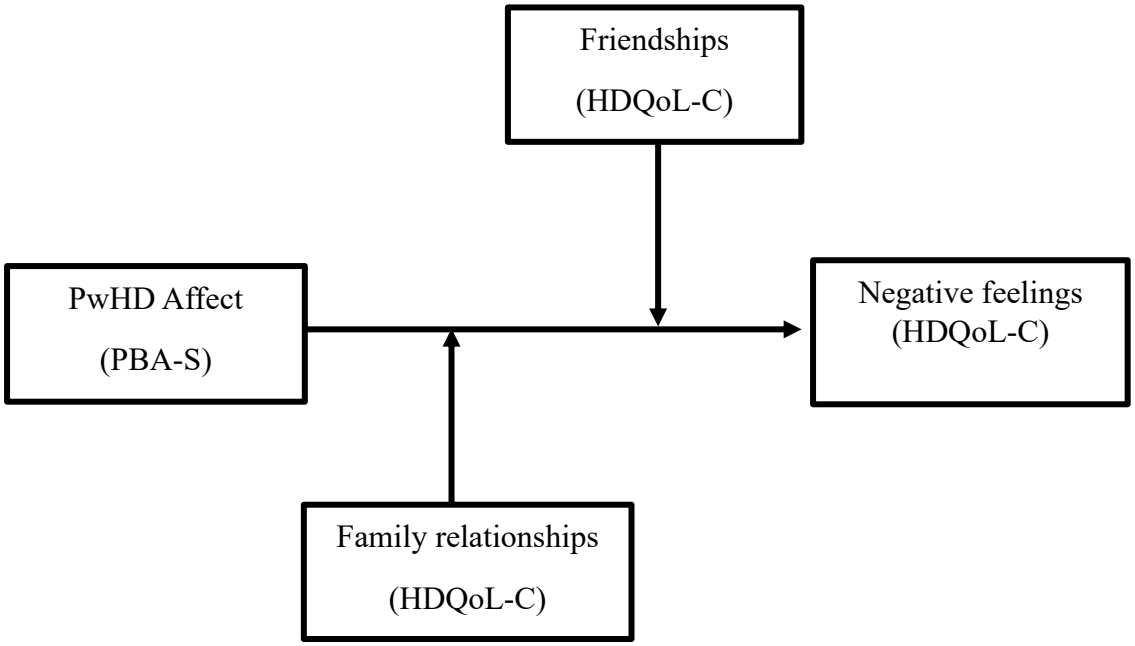


Moderation Model 5.



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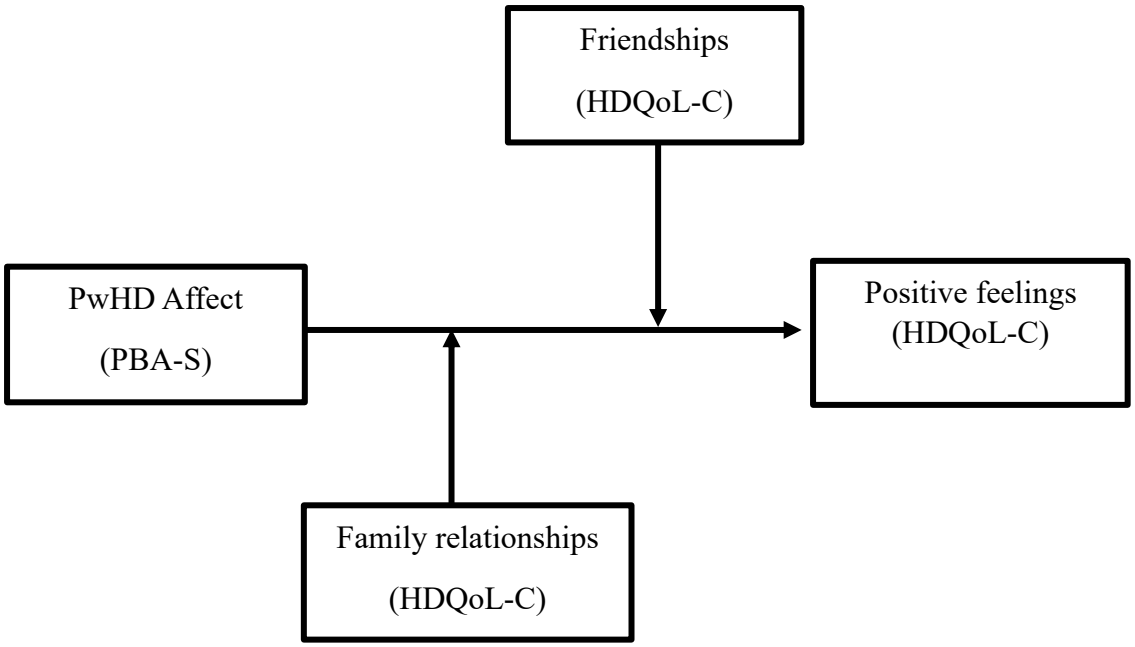

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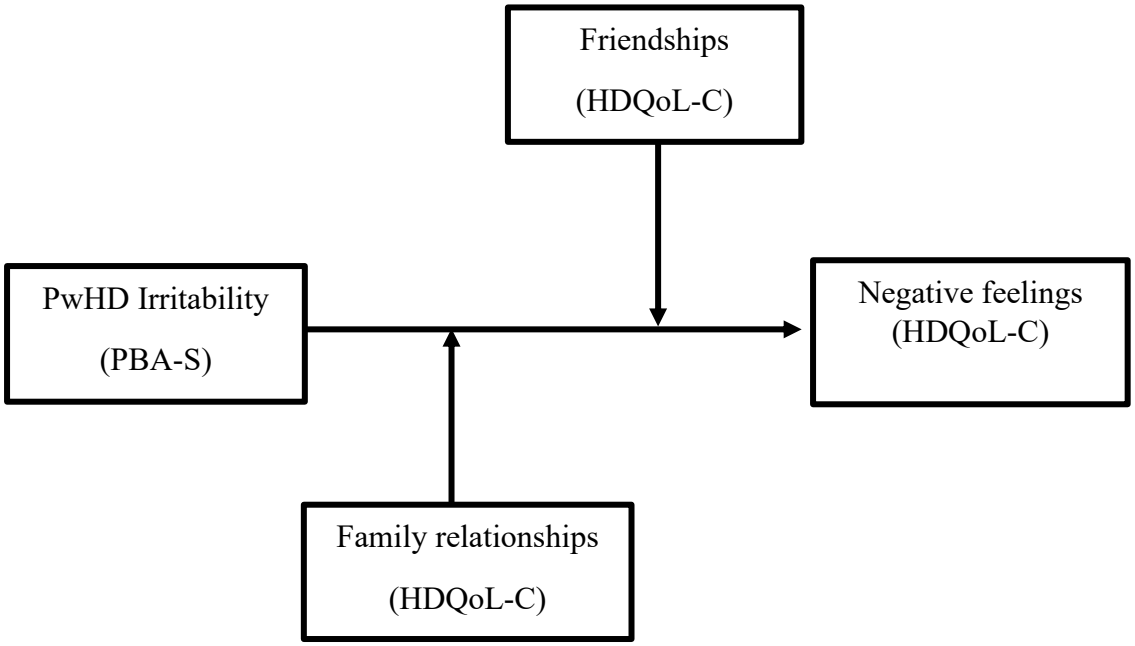
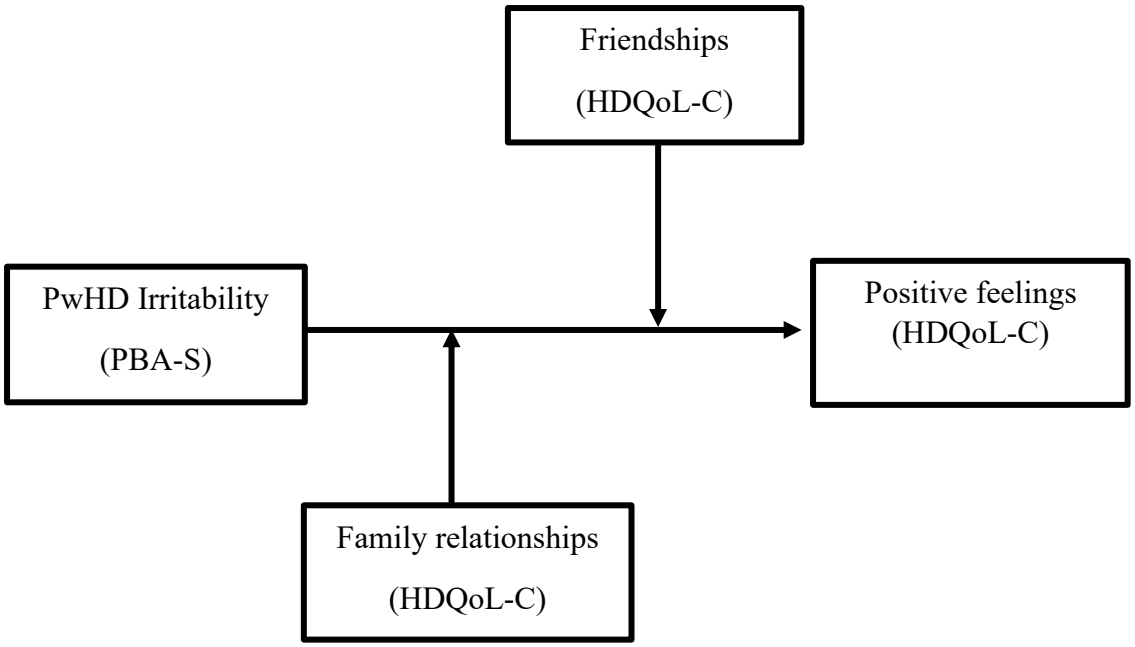


Moderation Model 8.



Appendices

Appendix 2-A

Journal of Huntington's Disease Author Guidelines

Aims and scope

The *Journal of Huntington's Disease* is an international multidisciplinary journal to facilitate progress in understanding the genetics, molecular correlates, pathogenesis, pharmacology, diagnosis and treatment of Huntington's disease and related disorders. The journal publishes research reports, reviews, short communications, letters-to-the-editor, and will consider research that has negative findings. The journal is dedicated to providing an open forum for original research in basic science, translational research and clinical medicine that will expedite our fundamental understanding and improve treatment of Huntington's disease and related disorders.

Preparing Your Paper

1. Manuscripts must be written in English.
2. Manuscripts should be double-spaced throughout with wide margins (2.5cm or 1in), including the abstract and references. Every page of the manuscript, including the title page, references, tables, etc., should include a page number centered at the bottom.
3. Title page should include:
    a. Title (should be clear, descriptive and concise).
    b. Full name(s) of author(s).
    c. Full affiliation(s). Delineate affiliations with lowercase letters.
    d. Present address of author(s), if different from affiliation.
    e. Running title (45 characters or less, including spaces).
    f. Complete correspondence address, including telephone number and email address.

g. Leave the author information blank if double-blind peer review is wished for, but do include the information in the cover letter.

4. The abstract for research papers should follow the "structured abstract" format:

   BACKGROUND:

   OBJECTIVE:

   METHODS:

   RESULTS:

   CONCLUSIONS:

   The abstract should try to be no longer than 250 words. Include a list of 4-10 keywords. These keywords should be terms from the MeSH database.

5. Manuscripts should be organized in the following order with headings and subheadings typed on a separate line, without indentation: Introduction, Materials and Methods, Results, Discussion, References**.**

6. References: Authors are requested to use the Vancouver citation style. Place citations as numbers in square brackets in the text. All publications cited in the text should be presented in a list of references at the end of the manuscript. List the references in the order in which they appear in the text. Only articles published or accepted for publication should be listed in the reference list. We discourage textual references to unpublished and unavailable data. With permission, the author can reference a personal communication with name in the discussion section. If an article has a DOI, this should be provided after the page number details. The number is added after the letters 'doi'. Manuscripts will not be considered if they do not conform to the Vancouver citation guidelines.

7. Tables

a. Number according to their sequence in the text. The text should include references to all tables.
b. Provide each table on a separate page of the manuscript after the references.
c. Include a brief and self-explanatory title with any explanations essential to the understanding of the table given in footnotes at the bottom of the table.
d. Vertical lines should not be used to separate columns. Leave some extra space between the columns instead.

8. Figures
    a. Number the figures according to their sequence in the text. The text should include references to all figures.
    b. Figures should preferably be formatted in TIF or EPS format. JPG is also acceptable.
    c. A description of the statistical treatment of error analysis should be included in the figure or legend. We discourage the use of bar graphs where possible.
    d. Each illustration should have a brief self-explanatory legend that should be typed separately from the figure in the section of the manuscript following the tables.

Appendix 2-B

Sub-group Analysis Regressions

Hierarchical multiple regression analyses to investigate whether satisfaction with family relationships and friendships were predictors of negative feelings and positive wellbeing were investigated in the following groups: spousal carers, adult children caring for a parent with HD, main carers, and non-main carers. Variables were entered into the models in the following blocks: 1. Carer demographic variables and caring intensity (age, gender, education, main carer [excluded in main carer and non-main carer models]); 2. pwHD difficulties (TMS, TFC, SDMT score, apathy, affect, and irritability); 3. satisfaction with family relationships and friendships. The outcome variables were negative feelings and positive wellbeing (see Tables 2.5-2.8).

Model 1: Negative feelings

For negative feelings, the overall model was significant for all four subgroups: spouses ($F(2,499) = 30.24$, $R^2 = .23$, $R^2\_adj = .21$, $p < .001$), adult children ($F(2,117) = 8.18$, $R^2 = .25$, $R^2\_adj = .18$, $p < .001$), main carers ($F(2,713) = 40.29$, $R^2 = .19$, $R^2\_adj = .18$, $p < .001$), and non-main carers ($F(2,143) = 6.53$, $R^2 = .17$, $R^2\_adj = .10$, $p < .01$). The addition of satisfaction with family relationships and friendships also predicted significant additional variance in all four models (spouses: $\Delta R^2 = 0.09$, $p < 0.001$, adult children $\Delta R^2 = 0.10$, $p < 0.001$, main carers $\Delta R^2 = 0.09$, $p < 0.001$, and non-main carers $\Delta R^2 = 0.08$, $p < 0.01$). These variables accounted for an additional 8-10% of the variance in the models.

Each step of the model was significant for the models with larger samples: spousal and main carers ($p < .001$). For the models with smaller samples, some steps were not significant: step 1 was non-significant for non-main carers and step 2 was non-significant for

both adult children and non-main carers. Block 1 explained 3-11% of variance and block 2 explained 5-8%.

Considering the individual predictors at step 3, age was a significant predictor for spouses (β = -.10 *p* .02) and gender was a significant predictor for spouses (β = .19, *p* < .001) and adult children (β = .31, *p* < .01). The SDMT score was a significant predictor for spouses (β = -.12, *p* <.04) and irritability was a significant predictor for spouses (β = .10, *p* .03) and main carers (β = -.16, *p* < .001). Satisfaction with family relationships and friendships were significant predictors for spouses (β = -.22, *p* < .01, β = -.22, *p* < .001), adult children (β = -.19, *p* .05, β = -.16, *p* .03), and main carers (β = -.16, *p* < .001, β = -.20, *p* < .001), and approached significance for non-main carers (β = -.17, *p* .06, β = -.17, *p* = .06).

Model 2: Positive Wellbeing

For positive wellbeing, the overall model was significant for spouses ($F(2,499) = 62.64$, $R^2 = .28$, $R^2\_adj = .26$, $p < .001$), adult children ($F(2,117) = 26.39$, $R^2 = .42$, $R^2\_adj = .36$, $p < .001$), main carers ($F(2,713) = 109.83$, $R^2 = .30$, $R^2\_adj = .29$, $p < .001$), and non-main carers ($F(2,143) = 17.55$, $R^2 = .35$, $R^2\_adj = .30$, $p < .001$). The addition of satisfaction with relationships and satisfaction with friendships predicted significant additional variance in all four models (spouses: $\Delta R^2 = 0.18$, p <0.001, adult children $\Delta R^2 = 0.26$, p <0.001, main carers $\Delta R^2 = 0.21$, p <0.001, and non-main carers $\Delta R^2 = 0.16$, p <0.01). These variables accounted for an additional 16-26% of the variance in the models.

Each step of the model was significant for the models with larger samples: spousal and main carers ($p < .001$). For the models with smaller samples (adult children and non-main carers) step 1 was non-significant for adult children and non-main carers, but step 2 was significant for both groups.

Considering the individual predictors, at step 3, gender was a significant predictor for spouses (β = -.08, *p* .04), and education was a significant predictor for spouses (β = .14, *p* = .001). The TFC was a significant predictor for non-main carers (β = -.28, *p* = .02). The SDMT score was a significant predictor for adult children (β = .34, *p* < .01). Apathy was a significant predictor for spouses (β = -.21, *p* < .001), main carers (β = -.17, *p* < .001), non-main carers (β = -.36, *p* = 0.08), and approached significance for adult children (β = -.16, *p* =.08). Affect was a significant predictor for non-main carers (β = .23, *p* <0.01). Irritability also approached significance for non-main carers (β = -.14, *p* = 0.06). Satisfaction with family relationships and friendships were significant predictors for spouses (β = .28, *p* < .001, β = .22, *p* < .001), adult children (β = .32, *p* < .001, β = .33, *p* < .001), main carers (β = .27, *p* < .001, β = .27, *p* < .001), and non-main carers (β = .17, *p* .03, β = .31, *p* < .001). Block 1 explained 3-11% of the variance, and block 2 explained 5-15% of the variance.

Moderation Analyses

Power analysis indicated that a sample size of 2,412 would be required to reliably detect the largest effect found in the main moderation analyses (f^2 = 0.004). Therefore, the sample for spouses (*n* = 512), carers of parents (*n* = 130), main carers (*n* = 715), and non-main carers (*n* = 155), were not adequately powered to conduct sub-group moderation analysis.

Section Three: Critical Appraisal

Word count: 3,936

(Excluding title page, references, figures, tables, and appendix)

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Critical Appraisal

This paper aims to provide a critical reflection on the research process, with consideration of the strengths and limitations of the study. The main findings of the systematic literature review and research paper will be summarised. Some of the key decisions taken during the research process will be considered, along with personal reflections, and recommendations for future research. Finally, clinical recommendations will be considered.

Main Findings

The systematic literature review aimed to examine factors associated with psychological outcomes in carers of people with Huntington's disease (pwHD). A systematic search of six databases was conducted, resulting in 24 included papers. Examined psychological outcomes included perceived carer burden, quality of life, and mood. Relationships between these outcomes and several different factors were explored, with an emphasis on HD clinical characteristics and pwHD behavioural/psychological difficulties. Other factors including carer demographics, indicators of caring intensity, and social support, were also considered. Although quality of life was the most frequently measured outcome, carer burden was examined with a greater range of factors. It was frequently difficult to draw conclusions about the nature of the examined relationships due to the small number of studies, contradictory findings, and methodological limitations. However, evidence suggested that indicators of higher caring intensity, such as greater time spent caring or being the main carer, were associated with higher carer burden and lower quality of life. HD-related difficulties, including greater overall HD difficulties, lower functional capacity, and more behavioural/psychological difficulties, were also associated with higher carer burden. The results indicated that future research would benefit from using larger samples, integrating

theory into design and analysis, and examining positive psychological outcomes and protective factors.

The research study aimed to investigate whether satisfaction with family relationships and friendships predicted wellbeing outcomes (positive wellbeing and negative feelings) in carers of pwHD. Further, it aimed to investigate whether satisfaction with these relationships moderated the relationship between pwHD functional capacity and behavioural/psychological difficulties and carer wellbeing outcomes, in line with the stress process model which suggests that social relationships can buffer people against the impact of stressors, such as difficulties associated with providing care to a loved one, on wellbeing [1]. A total of 880 carers and pwHD participating in Enroll-HD, an international observational cohort study, were included in the study. Data were analysed using hierarchical multiple regression to examine whether satisfaction with family relationships and friendships predicted carer self-reported positive wellbeing and negative feelings, after controlling for carer demographics (age, gender, education), caring intensity (being the main carer), and pwHD motor symptoms, cognitive difficulties, functional capacity, and behavioural/psychological difficulties. Sub-group regression analyses were also conducted for spouses, adults caring for their parents, main carers, and non-main carers. Moderation analysis was used to examine whether the relationship satisfaction variables moderated the relationships between pwHD functional capacity and behavioural/psychological difficulties and carer wellbeing outcomes.

The results demonstrated that the addition of satisfaction with family relationships and friendships made a significant contribution to the positive wellbeing and negative feelings models for all groups, after controlling for carer demographics, caring intensity, and pwHD characteristics, contributing an additional 8-10% and 16-26% of the variance in the negative feelings and positive wellbeing models, respectively. Both variables also remained significant independent predictors of higher positive wellbeing and lower negative feelings

for all groups, with the exception of the negative feelings model for non-main carers in which these variables approached significance as independent predictors ($p = 0.06$). However, the moderation analyses were non-significant. Results aligned with the main effects model of how social relationships impact health and wellbeing, which suggests that social relationships directly influence wellbeing regardless of stress levels [2].

Methodology Choices

The aim of my research was to identify patterns in and processes underlying relationships between caregiving stressors (e.g., care recipient characteristics and caring intensity), satisfaction with social relationships, and wellbeing. Therefore, a quantitative approach was suitable for meeting these aims. The ability to detect trends in experiences shared across groups makes quantitative approaches useful for developing theory and informing policy and practice.

I chose to use secondary data to obtain a large international sample, addressing a weakness identified in the literature review that many existing findings were based on small samples from a limited range of countries. This choice was made partly due to an expectation that it would be challenging to recruit a large enough sample for my study in the available timeframe given that recruitment is a challenge in rare-condition research [3]. Furthermore, as HD is a rare condition, the same small pool of people are repeatedly asked to participate in research, which could lead to harm associated with perceived research burden [4]. I also felt there was an ethical imperative to use Enroll-HD data, given that participants had given their time with the hopes that it would be used by researchers to produce findings that may benefit their lives. Enroll-HD was chosen over other possible databases as it provided access to a larger sample of carers than other available datasets such as HD burden of illness study (HDBOI) [5].

The use of recruitment approaches that may introduce bias, for example using outpatient clinic lists or convenience samples, was observed in the literature review. The Enroll-HD sample benefits from being recruited from a variety of settings, including clinical centres, national HD associations, and word of mouth, with the aim of obtaining the most representative sample possible. I hoped that this would reduce potential recruitment bias. Furthermore, the international nature of the Enroll-HD sample, recruiting from 23 countries including those in Latin America, Asia, and Australasia, provided the study with the possibility of identifying cross-cultural patterns in carer wellbeing, aiding the generalisability of the findings. These factors also provided benefits over other available datasets which recruited solely from healthcare settings (e.g., HDBOI) and a fewer range of countries (e.g., HDBOI, Euro HD Disease Burden study) [5,6]. However, it is noted that fewer carers participate in the study than pwHD. This may be because data collection happens in person, and carers may not have time to attend. Some carers have also been found to reject or not identify with the label carer [7] and, therefore, may have chosen not to complete the questionnaire. These factors may reduce the generalisability of the findings but are hard to mitigate in secondary data research.

One limitation of using secondary data is the lack of control over what variables are selected and how they are conceptualised and measured, restricting the kinds of questions that can be examined. For example, originally, I had hoped to conduct research that could help to develop psychological understandings of depression and anxiety in pwHD, as there is a relative lack of psychologically informed evidence about psychological distress in this group [8]. However, this was not possible, as while Enroll-HD does collect measures of depression and anxiety in pwHD, there is a lack of other psychological data which would enable the exploration of underlying psychological processes which may lead to distress. In contrast, a large range of biomedical variables are collected. This reflects the predominance of

attempting to understand all difficulties associated with HD according to a biomedical framework [8], exemplified by the focus in research on trying to link psychological and behavioural difficulties seen in pwHD to HD disease processes [9]. In contrast, the outcome measures collected with carers provided more scope for psychologically focused research.

However, one challenge of the carer outcome measure was considering what underlying concepts the sub-scales I used reflected. The complete measure is presented as a measure of quality of life. Quality of life is a broad, multifaceted concept, and contentions remain regarding its definition [10]. However, definitions often encompass someone's subjective appraisal of their position in aspects of life, including physical health, psychosocial functioning, and their environment, compared to their goals, values, and expectations, which are influenced by their sociocultural context [10,11]. While the overall total score of the measure does encompass many of these facets, the items in the positive and negative feelings subscales used in the research paper seemed focused on psychological functioning and thus felt more consistent with conceptualisations of wellbeing [12] than the broader conceptualisation of quality of life.

An alternative conceptualisation could be mental health. Again, there is a lack of consensus regarding the definition of mental health, with many conceptualisations referring to wellbeing or being closely aligned with definitions of wellbeing (e.g., encompassing positive and negative experiences, emotion and function, and ideas about flourishing and potential) [13]. However, attempts to distinguish mental health from wellbeing suggest that mental health relates to abilities to think, feel, and act in ways that facilitate participation in an enjoyable and value-aligned life [14], concepts which felt less clearly captured by the outcome measure. Within the challenges posed by the overlap between these terms and lack of conceptual clarity, I considered the measure more aligned with definitions of wellbeing

and aimed to aid reader clarity by providing definitions of the terms positive wellbeing and wellbeing used in the research paper.

A strength of the scale was that it was developed with carers of pwHD [15], so the aspects of wellbeing captured may be particularly salient for this group. A further strength is that it enabled the examination of a positive psychological outcome, as well as a negative outcome. This allowed the study to address a weakness identified in the literature review regarding the lack of studies examining positive outcomes in HD carers, presenting a one-sided, deficit-focused perspective on their mental health and wellbeing. As well as being more consistent with some theoretical understandings of mental health and wellbeing [16], this also aligned with my own values around psychological health being more than the absence of distress and interest in positive psychology concepts. However, it is acknowledged that definitions of wellbeing remain varied and contested [12]. Thus, while the inclusion of positive wellbeing and negative feelings in the research study provides an examination of important facets of the concept, they are not a holistic representation. In particular, although the measure of positive wellbeing captured some items that could be understood as sitting within eudemonic wellbeing traditions (e.g., role as rewarding and ability to cope, which could reflect a sense of environmental mastery), on balance the outcomes captured more hedonic elements of wellbeing. Therefore, future research examining other factors considered part of eudemonic wellbeing in this population could be useful, particularly as eudemonic wellbeing is known to influence hedonic wellbeing [12].

I chose to use items related to social relationships from the carer outcome measure because I wanted to examine a factor that might promote wellbeing, rather than focus solely on factors likely to negatively impact wellbeing which was identified as a weakness of the evidence base in the literature review. Furthermore, it felt important to consider systemic influences on carer wellbeing given that the context within which carers operate is considered

to be highly important for wellbeing [17,18]. I was also concerned that a focus on individual coping approaches could inadvertently blame carers for struggling to adapt to a highly challenging situation by locating the responsibility for wellbeing within a model of individual resilience [19].

Initially, I had hoped to use a measure of perceived social support as a large body of evidence has demonstrated the importance of perceived social support for wellbeing outcomes across a wide range of different populations [1,2]. This includes support for its role as a moderator of relationships between stressors and wellbeing/mental health outcomes, aligning with the stress process model which I planned to test in my study. However, the only available variables relating to social relationships in the Enroll-HD dataset were satisfaction with friendships and family relationships. As noted in the paper, one drawback of these variables was that they are not a validated measure, potentially reducing their reliability compared to a validated measure of social support. Furthermore, social support measures often measure different types of support (e.g., emotional, practical, etc.), and the ability to identify whether particular kinds of social support are important for carer wellbeing could have contributed to clinical recommendations regarding peer support.

Nonetheless, the measures of relationship satisfaction also had strengths. Firstly, relationship satisfaction is an important characteristic of relationships which has been linked to wellbeing in other groups, including as a moderator of relationships between stressors and wellbeing indicators [20,21], but has not previously been explored in HD carers. The focus on social support in evidence examining how social relationships influence health and wellbeing has also been criticised for focusing on function at the expense of understanding the role of the relational context in which support occurs [22]. This is important as relational characteristics, such as relationship satisfaction, intimacy, and perceived similarity, influence whether received support is perceived positively [23,24]. Furthermore, there appear to be

gender and cultural differences in what kinds of social support functions are sought out and their impact on wellbeing [25,26]. It was hoped that the measurement of perceived satisfaction with relationships would have relevance across the international sample as it could accommodate culturally mediated ideas about what makes relationships satisfying, including beliefs about social support [27].

Although the Problem Behaviours Assessment [28] is considered a reliable and valid measure of behavioural/psychological difficulties related to HD and is frequently used in research, a limitation of this study was the low internal consistency scores of the apathy and irritability sub-scales. These sub-scales were selected because they had been validated in another international sample (16) and other validation studies have also found a similar three-factor structure for the measure [29]. Recently, a Rasch analysis validation of the PBA in the Enroll-HD sample recommended using a total severity rating score, excluding items related to behaviour frequency due to problems with establishing reliability for these items [30]. However, as previous studies have found that different pwHD behavioural/psychological difficulties have different effects on carer wellbeing outcomes [31,32], it felt important to use the sub-scales rather than a total score to provide a more granular understanding of the impact of behavioural/psychological difficulties in this sample. Nonetheless, it may be beneficial for future validation studies that aim to establish a more reliable factor structure for the Enroll-HD sample or for future research to consider alternative measures.

Including the Voices of HD Carers

One strength of the research study was the choice to consult with four experts by experience in the early stages of the project to help inform the study design. Involving experts by experience is considered a valuable way to help research studies be more responsive to the needs and experiences of participants [33,34]. During discussions with the experts by

experience the incredibly challenging nature of caring for someone with HD was repeatedly highlighted. The difficulties of certain kinds of behaviour, particularly verbal and physical aggression, were noted, emphasising the need to consider different categories of behaviour rather than using a composite measure and, thus, I used the PBA-S subscales despite their noted limitations rather than a composite measure. Each expert by experience also emphasised the importance of social connections for wellbeing. This reassured me that examining the role of social relationships for carers of pwHD could be valuable. I was struck by a sense that the people with whom I spoke felt their experiences were largely overlooked and that they valued the potential contribution the study could make to HD carers regardless of its exact design.

The experts by experience suggested it would be helpful to consider carers with different relationships to the pwHD separately (e.g., spouses, children, etc.), as although there were many commonalities in experiences, the nature of the relationship with the person with HD was felt to lead to different challenges. This perspective is supported by research with carers of pwHD which found differences in quality of life between spousal carers and those caring for their parent with HD [35]. Sub-group analyses for the regressions for spouses, adults caring for their parents, main carers, and non-main carers were performed separately. These analyses indicated that social relationships remained important contributors to positive wellbeing and negative feelings for these groups. However, the samples were not adequately powered to conduct regressions for parents caring for a child with HD and carers for their siblings or sub-group moderation analyses. Therefore, future research may benefit from examining whether there are differences in predictors of wellbeing or differences in moderation effects observed in this study for these groups.

Theory Integration

The literature review identified a lack of theory-driven research in the existing evidence base regarding wellbeing in HD carers. This reflects wider concerns that psychology is facing a "theory crisis" which has led to a focus on finding and reproducing effects rather than seeking to explain these phenomena in empirical studies [36,37]. Integrating theory into research helps guide clear and testable research questions, guide methodology, and encourage the investigation of modifiable mechanisms which can provide practical steps to solve real-world problems [38,39]. Therefore, the integration of theories which seek to explain the underlying mechanisms between the variables of interest is a strength of the research study.

The stress process model was chosen because it has been usefully applied to carers of people with various neurological conditions, including HD [40–45]. Furthermore, the data collected by Enroll-HD lent itself to testing the assumptions of this theory. However, the theory has been critiqued for driving an unhelpful focus on negative carer outcomes, such as carer burden or mood problems [18,46,47]. Although the model was initially developed to consider depression, the underlying psychological processes it proposes have also been applied to positive wellbeing indicators [41,44]. It could also be argued that the focus on the impact of stressors is problematic as it assumes caring for someone is a stressful, challenging experience. However, theorising regarding positive aspects of caregiving is also rooted in an acknowledgement that the caring role is challenging [47,48]. Furthermore, the challenging nature of caring for someone with HD is clearly communicated in qualitative research [49,50] and the views obtained from experts by experience. Therefore, while I was conscious of the usefulness of considering a more holistic representation of wellbeing in this group, I did not want to lose sight of this reality.

Future HD carer research may also benefit from testing whether the theoretical assumptions of psychological therapies which have been found to be effective in carers of

people with other conditions, such as compassion-focused therapy and acceptance and commitment therapy [51,52], are supported in this group. Such research could help guide the development of therapeutic interventions for carers of pwHD. Furthermore, expanding models to include broader factors known to be associated with mental health difficulties, such as experiences of trauma [53] or the cumulative effects of stressors beyond caring, could develop our understanding of the circumstances in which HD carers may be most likely to benefit from interventions to support their wellbeing.

Premanifest Versus Manifest HD Participants

A decision was made to focus on the experiences of carers of people with manifest HD (i.e., those who are showing unequivocal motor symptoms) in the research paper rather than premanifest HD (i.e., individuals who carry the genetic expansion but have not yet received a manifest HD diagnosis). This was because it was expected that the experiences of these groups of carers were likely to be different due to the differing needs of the pwHD, and, therefore, these groups should be considered separately. It might be assumed that people with premanifest HD would be unlikely to need additional support from carers as HD symptoms are not present. However, subtle changes in functioning, particularly cognitive functioning, have been noted in people with premanifest HD [54]. Psychological difficulties such as depression and anxiety are also common in this group [55,56]. Loved ones may, therefore, provide people with premanifest HD with additional support, although the context and content of this support is likely to produce different caring experiences. For this reason, I sought to include the experiences of premanifest HD carers in my literature review, although no relevant studies were identified. Therefore, future research examining factors that influence psychological wellbeing in premanifest carers would be beneficial.

Clinical Implications

Both papers identified that factors associated with caring for someone with HD were associated with negative impacts on positive and negative indicators of wellbeing, suggesting that carers of pwHD may benefit from additional practical and emotional support to manage their role. Several papers, including the current research study, have now identified characteristics of social relationships, including satisfaction with social relationships and perceived social support, as independent predictors of different positive and negative indicators of wellbeing. Therefore, interventions focused on building and maintaining satisfying and supportive social relationships may be beneficial for wellbeing in HD carers, although as noted in the research paper, further research into their acceptability and efficacy in this group would be needed.

Evidence from both papers also indicates that interventions for behavioural/psychological difficulties associated with HD may also have a positive impact on carer wellbeing. International HD treatment guidelines highlight the need to consider environmental contributors to irritability and apathy [57], which were identified as independent predictors of carer wellbeing in several of the regression analyses in the research paper. Furthermore, they recommend considering whether apathy and irritability could be related to depression and consider appropriate treatments for this if so. These are areas where the expertise provided by a clinical psychologist and/or the specialist knowledge provided by a neuropsychologist to untangle whether these behaviours are manifestations of underlying cognitive changes or mental health difficulties (or both) is likely to be helpful. This could include the utilisation of a formulation framework developed for use with pwHD which incorporates a biopsychosocial approach to understanding distress and behaviour in this group [58]. However, it is noted the HD clinical characteristics explained a relatively small amount of variance in the regression models in the research paper. This suggests these kinds

of interventions would be most helpful as part of a wider, more holistic offer to support carer wellbeing.

The relative importance of satisfying social relationships for predicting carer wellbeing indicates the need to consider the influence of the wider sociocultural context in which carers are situated. This is supported by previous research, which has highlighted that wider contextual factors serve to make carers' roles more challenging [17]. International organisations identify that social protection and labour policy, as well as the provision of (or lack of) appropriate health and social care, have the power to support carers' wellbeing [59,60]. Within the UK context, while various kinds of government and third sector support are available for carers, including social welfare payments and the provision of social care assistance, evidence suggests only 55% of UK carers say they receive the support they need [61]. Barriers to accessing support include carers not being appropriately identified by services, a lack of knowledge about available support, a lack of appropriate signposting, and complex application processes [61,62]. This highlights the fact that legislation change alone is not enough to provide a supportive environment to carers; it is also essential that such support is publicised and easily accessible in order to promote carer wellbeing.

Conclusion

A key contribution of the systematic literature review was highlighting several limitations in the evidence base regarding HD carer wellbeing, particularly regarding the need for theoretically driven research examining more holistic conceptualisations of carer wellbeing using large samples, which I was able to address in the research paper. The research findings extend the existing evidence base by identifying that satisfaction with family relationships and friendships are significant predictors of both positive and negative indicators of wellbeing. However, overall the papers highlight that there is still much to learn

about both the factors that influence wellbeing in carers of HD and the underlying psychological processes which support adaptation to this challenging role.

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Section Four: Ethics Section

Ethics Application

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Research Ethics Application Form v1.8.1

Research Ethics Application Form v1.8.1 RECR

Psychosocial factors and quality of life in carers of people with HD - Approved

Information Regarding this Research Project

Are you conducting a research project?

(for more information on research projects please see our ethics pages)

(•) Yes ( ) No

Does your research only involve animals?

( ) Yes (•) No

Are you undertaking this research as/are you filling this form out as:

- ( ) Academic/Research Staff
- ( ) Non Academic Staff
- ( ) Staff Undertaking a Programme of Study
- (•) PhD or DClinPsy student
- ( ) Undergraduate, Masters, Master by Research, MPhil or other taught postgraduate programme

Which Faculty are you in?

Faculty of Health and Medicine

Which department are you in?

Health Research

Will your project require NHS REC approval? (If you are not sure please read the guidance in the information button)

○ Yes ◉ No

Do you need Health Research Authority (HRA) approval? (Please read the guidance in the information button)

○ Yes ◉ No

Have you already obtained, or will you be applying for ethical approval, from another institution outside of Lancaster University? (For example, an external institution such as: another University's Research Ethics Committee, the NHS or an institution abroad (eg an IRB in the USA)? Please select one of the following:

◉ No, I do not need ethical approval from an external institution.
○ Yes, I have already received ethical approval from an external institution.
○ Yes, I will be applying for ethical approval from an external institution after I have received confirmation of ethical approval from my Faculty Research Ethics Committee (FREC) at Lancaster University, if the FREC grants approval.

Is this an amendment to a project previously approved by Lancaster University?

○ Yes ◉ No

Will your research involve any of the following? (Multiple selections are possible, please see i icon for details)

☐ Human Participants
☑ Data relating to humans (Secondary/Pre-existing data only)
☐ Data collection from online sources such as social media platforms, discussion forums, online chat-rooms
☐ Human Tissue
☐ None of the above

Project Information

Please confirm/amend the title of this project.

Psychosocial factors and quality of life in carers of people with HD

Estimated Project Start Date 03/01/2023

Estimated End Date 31/08/2024

Is this a funded Project?

○ Yes ◉ No

Research Site(s) Information

Will you be recruiting participants from research sites outside of Lancaster University? *(E.g. Schools, workplaces, etc; please read the guidance in the information button for more information)*

○ Yes ◉ No

Applicant Details

Are you the named Principal Investigator at Lancaster University?

◉ Yes ○ No

Please check your contact details are correct. You can update these fields via the personal details section located in the top right of the screen. Click on your name and email address in the top right to access "Personal details". For more details on how to do this, please read the guidance in the information button.

First Name

Hannah

Surname

Ross

Department

Health research

Faculty

Health and Medicine

Email

h.ross@lancaster.ac.uk

Principal Investigator

You have stated that you are the Principal Investigator for this project.

First Name

Hannah

Surname

Ross

Department

Health research

Email

h.ross@lancaster.ac.uk

Supervisor Details

Search for your supervisor's name. *If you cannot find your supervisor in the system please contact rso-systems@lancaster.ac.uk to have them added.*

First Name

Fiona

Surname

Eccles

Department

Health Research

Faculty

Faculty of Health and Medicine

Email

f.eccles@lancaster.ac.uk

Do you need to add a second supervisor to sign off on this project?

○ Yes ◉ No

Additional Team Members

Other then those already added, please select which type of team members will be working on this project:

- ☐ I am not working with any other team members.
- ☑ Staff
- ☐ Student
- ☑ External

Please list all external contacts here:

First Name

Maria

Surname

Dale

Organisation

Leicester Partnership NHS Trust

Search for the names of all other internal staff here:

First Name

Jane

Surname

Simpson

Department

Health Research

Faculty

Faculty of Health and Medicine

Email

j.simpson2@lancaster.ac.uk

Data Origin

Is the data you will be using in the public domain or from data repositories?

(•) Yes ( ) No

Do you intend to use data about humans from online sources such as social media platforms, discussion forums, or online chat rooms?

( ) Yes (•) No

Has consent for the use/reuse of the data for research purposes been obtained?

(•) Yes ( ) No ( ) I don't know

Will you protect confidentiality and anonymity in your (re)analysis of the data?

(•) Yes ( ) No ( ) I don't know

Data Analysis

Do you intend to conduct a secondary analysis of existing research data?

(•) Yes ( ) No

Was the data ethically obtained and was approval granted from a research ethics committee for its use?

(•) Yes ( ) No ( ) I don't know

Does the consent obtained from participants cover the proposed re-use of the research data for your current project?

(•) Yes ( ) No ( ) I don't know

Will you obtain the data in anonymised format?

(•) Yes ( ) No ( ) I don't know

General Queries

Does the funder or any organisations involved in the research have a vested interest in specific research outcomes that would affect the independence of the research?

( ) Yes (•) No ( ) I don't know

Does any member of the research team, or their families and friends, have any links to the funder or organisations involved in the research?

(•) Yes ( ) No ( ) I don't know

Can the research results be freely disseminated?

(•) Yes ( ) No ( ) I don't know

Will you use data from potentially illicit, illegal, or unethical sources (e.g. pornography, related to terrorism, dark web, leaked information)?

( ) Yes (•) No ( ) I don't know

Will you be gathering/working with any special category personal data?

(•) Yes ( ) No ( ) I don't know

Are there any other ethical considerations which haven't been covered?

( ) Yes (•) No ( ) I don't know

REC Review Details

Based on the answers you have given so far you will need to answer some additional questions to allow reviewers to assess your application.

It is recommended that you do not proceed until you have completed **all of the previous questions**.

Please confirm that you have finished answering the previous questions and are happy to proceed.

☑ I confirm that I have answered all of the previous questions, and am happy to proceed with the application.

You have stated that you are research only involves data.

☑ Please confirm that your research will have no direct involvement with human participants.

Questions for REC Review

Summarise your research protocol in lay terms (indicative maximum length 150 words).

Note: The summary of the protocol should concisely but clearly tell the Ethics Committee (in simple terms and in a way which would be understandable to a general audience) what you are broadly planning to do in your study. Your study will be reviewed by colleagues from different disciplines who will not be familiar with your specific field of research and it may also be reviewed by the lay members of the Research Ethics Committee; therefore avoid jargon and use simple terms. A helpful format may include a sentence or two about the background/ "problem" the research is addressing, why it is important, followed by a description of the basic design and target population. Think of it as a snapshot of your study.

Huntington's disease (HD) is a rare and fatal degenerative brain disease which causes motor impairment, cognitive decline, behavioural changes, and psychological difficulties. People with HD have complex care needs and are often cared for by family and friends. Providing care is challenging and studies have found that carers of people with HD report lower quality of life and mental wellbeing than carers of people with other conditions. However, relatively little research has been conducted with this group to find out what factors influence their wellbeing, which could improve the support they are offered. This study will analyse quantitative data which has previously been collected via a large international study to examine whether the care needs of the person with HD are risk factors for lower quality of life and lower mental wellbeing in carers. It will also examine whether social support can help protect carer wellbeing.

State the Aims and Objectives of the project in Lay persons' language.

• To explore which clinical (in the person with HD) and demographic (in both person with HD and carer) factors predict carer wellbeing and quality of life.
• To explore which social factors (for carer) predict carer wellbeing and quality of life.
• To investigate whether social support factors can act as a protective buffer against the negative impacts on their wellbeing.

Information about the Research

Will you be sharing your data with any other organisation?

(•) Yes ( ) No

Confirm you will ensure a data sharing agreement is in place which is GDPR compliant.

☑ I confirm that I will ensure a data sharing agreement is in place which is GDPR compliant

What are your dissemination plans? E.g publishing in PhD thesis, publishing in academic journal, presenting in a conference (talk or poster).

Doctoral Thesis
Presentation to DClinPsy trainees and staff in Y3
Plan to publish systematic review and empirical paper produced as part of the thesis
Will seek out opportunities to attend a conference with the research (poster/presentation)
Press release or lay summary of research and findings to be shared with participants and public via Enroll-HD website/newsletter
I will also provide updates and feedback to people who participated in my consultation phase via email and meetings as preferred by them.

General Queries

You have stated that at least one member of the research team has links to the funder or organisations involved in this project. Please explain the relationship and how you will mitigate or manage this conflict of interest.

Maria Dale works as a clinical psychologist in an NHS service for people with Huntington's disease. This service is one of the sites which participates in the Enroll HD study. As such there is unlikely to be a conflict of interest which requires mitigation.

You have indicated that you will be gathering/working with special category data. Please confirm here how you will comply with data protection law (GDPR) for use of special category personal data.

It will be necessary to work with data related to participant's genetic and health status in order to complete the project.

Participants have provided explicit consent for their data to be processed be researchers conducting scientific research such as this project (meeting conditions a and j). The outcomes of research will have relevance for health and social care (condition h) as they may inform the provision of health and social care for families affected by HD. This project is in the public interest given the significant impact of HD on individuals, families, and health and social care systems and the relative lack of research currently available about factors contributing to the wellbeing and quality of life of carers of people with HD.

Data Storage

How long will you retain the research data?

It is standard practice for research data to be retained by the department for a period of 10 years.

How long and where will you store any personal and/or sensitive data?

During project: stored as encrypted files on password protected OneDrive hosted by Lancaster University, shared with student, supervisor, and field supervisor.
After completion: encrypted data files will be shared via OneDrive with DClinPsy administrative staff for long term storage. Data will be transferred electronically using a secure method that is supported by the University. The data will be saved on a password protected file space on the university server for a period of 10 years.

Please explain when and how you will anonymise data and delete any identifiable record?

The files provided by Enroll HD will already be anonymised and will be transferred via secure transfer and encrypted files.

Project Documentation*

Important Notice about uploaded documents:

When your application has been reviewed if you are asked to make any changes to your uploaded documents please highlight the changes on the updated document(s) using the highlighter so that they are easy to see.

In addition to completing this form you must submit all supporting materials.

Please indicate which of the following documents are appropriate for your project:

- [x] Research Proposal (DClinPsy)
- [ ] Advertising materials (posters, emails)
- [ ] Letters/emails of invitation to participate
- [ ] Consent forms
- [ ] Participant information sheet(s)
- [ ] Interview question guides
- [ ] Focus group scripts
- [ ] Questionnaires, surveys, demographic sheets
- [ ] Workshop guide(s)
- [ ] Debrief sheet(s)
- [ ] Transcription (confidentiality) agreement
- [ ] Other
- [ ] None of the above.

As you are in a DClinPsy course please upload your Research Proposal for this project.

Documents

Type	Document Name	File Name	Version Date	Version	Size
Research Proposal	Research protocol V2	Research protocol V2.docx	28/11/2022	1	225.9 KB

Declaration

Please Note

Research Services monitors projects entered into the online system, and may select projects for quality control.

All research at Lancaster university must comply with the LU data storage and governance guidance as well as the General Data Protection Regulation (GDPR) and the UK Data Protection Act 2018. (Data Protection Guidance webpage)

- [x] I confirm that I have read and will comply with the LU Data Storage and Governance guidance and that my data use and storage plans comply with the General data Protection Regulation (GDPR) and the UK Data Protection Act 2018.

Have you that you have undertaken a health and safety risk assessment for your project through your departmental process? (Health and Safety Guidance)

- [x] I have undertaken a health and safety assesment for your project through my departmental process, and where required will follow the appropriate guidance for the control and management of any foreseeable risks.

When you are satisfied that this application has been completed please click "Request" below to send this application to your supervisor for approval.

Signed: This form was signed by Dr Fiona Eccles (f.eccles@lancaster.ac.uk) on 28/11/2022 14:00

Please read the terms and conditions below:

- You have read and will abide by Lancaster University's Code of Practice and will ensure that all staff and students involved in the project will also abide by it.
- If appropriate a confidentiality agreement will be used.
- You will complete a data management plan with the Library if appropriate. Guidance from Library.
- You will provide your contact details, as well as those of either your supervisor (for students) or an appropriate person for complaints (such as HoD) to any participants with whom you interact, so they know whom to contact in case of questions or complaints?
- That University policy will be followed for secure storage of identifiable data on all portable devices and if necessary you will seek guidance from ISS.
- That you have completed the ISS Information Security training and passed the assessment.
- That you will abide by Lancaster University's lone working policy for field work if appropriate.
- On behalf of the institution you accept responsibility for the project in relation to promoting good research practice and the prevention of misconduct (including plagiarism and fabrication or misrepresentation of results).
- To the best of your knowledge the information you have provided is correct at the time of submission.
- If anything changes in your research project you will submit an amendment.

Applicant Only: To complete and submit this application please click "Sign" below:

Signed: This form was signed by Hannah Ross (h.ross@lancaster.ac.uk) on 28/11/2022 13:06

Research Protocol

Psychosocial factors and quality of life in carers of people with HD

Lead Researcher

Hannah Ross, Trainee Clinical Psychologist, Division of Health Research

Health Innovation One, Sir John Fisher Drive, Lancaster University, Lancaster. LA1 4AT

Research Supervisors

Name	Job role	Organisation/Address	Supervisory role
Fiona Eccles	Research tutor, lecturer	Lancaster University	Theoretical, methodological
Maria Dale	Clinical Psychologist	Leicester Partnership NHS Trust, Mill Lodge, The Rise, Narborough, Leicestershire, LE19 4SL	Theoretical, methodological, clinical expertise
Jane Simpson	Professor	Lancaster University	Theoretical, methodological

Lay Summary

Huntington's disease (HD) is a rare and fatal degenerative brain disease which causes motor impairment, cognitive decline, behavioural changes, and psychological difficulties. People with HD have complex care needs and are often cared for by family and friends. Providing care is challenging and studies have found that carers of people with HD report lower quality of life and mental wellbeing than carers of people with other conditions. However, relatively little research has been conducted with this group to find out what factors influence their wellbeing, which could improve the support they are offered. This study will analyse quantitative data which has previously been collected via a large international study to examine whether the care needs of the person with HD are risk factors for lower quality of life and lower mental wellbeing in carers. It will also examine whether social support can help protect carer wellbeing.

Aims and objectives

- To explore which clinical (in the person with HD) and demographic (in both person with HD and carer) factors predict carer wellbeing and quality of life.
- To explore which social factors (for carer) predict carer wellbeing and quality of life.
- To investigate whether social support factors can act as a protective buffer against the negative impacts on their wellbeing.

Rationale

Huntington's disease (HD) is a rare and fatal neurogenerative condition that affects approximately 12.3 persons per 100,000 in the UK (Evans et al., 2013) and 2.71 per 100,000 worldwide (Pringsheim et al., 2012). HD is caused by a genetic mutation which expands the cytosine-adenine-guanine (CAG) trinucleotide repeat in the huntingtin allele and carriers of the mutated gene have a 50% chance of passing it on to their children (Novak & Tabrizi, 2010; Wider & Lüthi-Carter, 2006). HD is characterised by progressive motor impairment and cognitive decline, behavioural changes, and psychological difficulties (Walker, 2007; Wider & Lüthi-Carter, 2006). Formal diagnosis is made based on motor impairment, with onset generally between 40-50 years and a mean life expectancy of 20 years post-diagnosis (S. E. Folstein, 1987). Symptoms are initially subtle but deteriorate to dementia and immobility, resulting in complex difficulties that require daily care support. Often this day-to-day care is provided by family or friends (informal carers) until the very late stages.

Caring for someone with HD is undoubtedly a challenging role. The progressive nature of HD means that informal carers must continually adapt to the changing needs of the person with HD. Particular features of the disease, such as unpredictable and aggressive behaviour, irritability, and perseveration, can be challenging to manage (Oliveri & Pravettoni, 2017; Sobel

& Brookes Cowan, 2000; Williams et al., 2009, 2012). In addition to managing challenging care needs, carers of people with HD report difficulties including having to balance caring with childcare and working; experiencing difficult emotions such as guilt, loss, and shame; concerns about the genetic implications of HD; financial difficulties; social stigma; and lack of appropriate formal support (Aubeeluck et al., 2012; Roscoe et al., 2009; Sherman et al., 2020; Williams et al., 2007; Williams, Skirton, et al., 2009). Given the broad range of potential stressors, it is perhaps unsurprising that carers of people with neurological conditions like HD are more likely to report distress, higher levels of carer burden and depression, and lower overall quality of life (QoL) than carers of people with other conditions (Joling et al., 2010; Mitchell et al., 2015).

Several models have been developed to explain the mechanisms through which providing informal care impacts on wellbeing outcomes (Gérain & Zech, 2019b; McLeod, 2012; Pearlin et al., 1981; Pearlin & Bierman, 2013; Sörensen et al., 2006). These models suggest that characteristics of the caregiving role, such as symptom severity and functional impairment for the person with the condition, and the amount of time spent providing care, act as stressors which can directly influence carer wellbeing. However, they also argue that the influence of these stressors on wellbeing can be moderated by the availability of psychosocial resources which can help to buffer against or intensify the stressfulness of the role, such as coping skills, personal appraisals, and social support.

Most studies examining the impact of patient and carer-based stressors on carer wellbeing in HD have used carer burden as a measure of wellbeing. For example, one study (n=26) found that the severity of motor symptoms, cognitive functioning difficulties, and depressive symptoms had significant positive correlations with carer burden (Cubo et al., 2010). However, Yu at al. (2019) (n=20) examined a range of HD symptomatology (e.g. motor, functional, cognitive, and behavioural) and carer-related variables (e.g. demographic

characteristics, time spent caring) and found that only being the main carer and lower functional ability in the person with HD were associated with increased carer burden. Whilst cognitive function has consistently been found to predict carer burden (Banaszkiewicz et al., 2012; Hergert & Cimino, 2021; Wibawa et al., 2020), other patient-based stressors such as motor symptoms and psychological/behavioural symptoms were predictors in some studies (Banaszkiewicz et al., 2012; Hergert & Cimino, 2021) but not others (Wibawa et al., 2020) .

Relatively few studies have examined quality of life and depression in carers of people with HD. One study found that poorer quality of life in carers was correlated with cognitive function, functional capacity, and depression in the person with HD (Ready et al., 2008) and that depression in the person with HD correlated with depression in carers (Pickett et al., 2007). However, in a small study involving people with late-stage HD and their carers, no associations were found between HD symptomatology and the level of involvement in caring and measures of carer life satisfaction, self-rated general health, and depressive symptoms (Roscoe et al., 2009). Similarly, Yu et al (2019) found no associations between patient or carer characteristics and carer quality of life. Just one study examined predictors of quality of life in carers of people with HD, finding that that motor symptoms and depression in participants with HD were independent predictors of carer quality of life (Banaszkiewicz et al., 2012) .

Despite some promising findings, the conflicting evidence regarding the associations between caregiving stressors on wellbeing of carers of people with HD remains unclear, as evidenced by the range of conflicting findings. In addition, many studies have used small sample sizes <40 (e.g., Cubo et al., 2010; Ready et al., 2008; Roscoe et al., 2009; Wibawa et al., 2020; M. Yu et al., 2019) , potentially leaving them underpowered and making it difficult to generalise the results. It should also be noted that wellbeing is a multifaceted concept, which is not accounted for solely by the absence of burden or distress (Simons & Baldwin,

2021) . Therefore, the focus on carer burden and the lack of studies looking at other factors likely to contribute to wellbeing, like quality of life or psychological health, is also a weakness in the current evidence-base.

Qualitative research suggests that carers of people with HD value being able to draw on social support resources, including family relationships, friendship, and respite support, to manage the impact of the role (Williams, Ayres, et al., 2009; Williams, Skirton, et al., 2009). Similarly, one small-scale study found that higher satisfaction with social support was correlated with increased life satisfaction (Roscoe et al., 2009) . Interestingly, this study found that the actual level of social support available to participants (as measured by how often support was offered by others, rated from never to often) was not correlated to life satisfaction, suggesting that carers' perception of the adequacy of their social support is more important than the amount of social support available. Although access to social support resources appears important, carers of people with HD commonly report strain in personal relationships and feelings of isolation (Sherman et al., 2020; Williams, Ayres, et al., 2009; Williams, Skirton, et al., 2009). Furthermore, they are at greater risk of losing social connections compared to carers of people with other neurological conditions (McCabe et al., 2009) . Carers also report experiencing shame and stigma from others due to misunderstandings about HD symptoms and a distressing lack of knowledge about HD among healthcare professionals, reflecting a lack of reliable support within wider society (Roscoe et al., 2009; Sherman et al., 2020; Skirton et al., 2010). These findings suggest that social support could be a particularly salient contributing factor to the wellbeing of carers of people with HD. However, it remains unclear whether social support predicts carer wellbeing or whether it moderates relations between caregiving stressors and wellbeing in carers of people with HD.

Therefore, this study will examine links between caregiving stressors and wellbeing outcomes. In addition, I will test whether social support is a protective factor which moderates the impact of caregiving stressors on carer wellbeing. This research topic has been influenced by a review of the literature and through consultation with carers of people with HD which I conducted in October 2022. By using a large longitudinal dataset, the proposed study could generate findings which are more generalisable and support the development of interventions which support carer psychological wellbeing. This project is relevant to clinical psychology as it aims to increase understandings of the underlying processes through which stressors can lead to psychological distress in carers of people with HD. It is important to understand these links to develop appropriate and holistic interventions that maintain carer wellbeing. It would also help to ensure that health and social care providers have a good understanding of the challenges carers of people with HD face. Not only could this reduce suffering among carers, evidence also suggests that higher carer quality of life could improve health outcomes for people with neurodegenerative disorders (Lwi et al., 2017) .

The research questions are:

1. What is the relation between carer stressors, social support, and carer quality of life, and depressive symptoms?
2. Does social support moderate the relation between carer stressors and carer quality of life and depressive symptoms?

It is expected that:

1. Carer stressors including higher cognitive and behavioural symptoms in people with HD and demographic and carer factors (e.g., years spent caring) will predict higher depression and lower QoL in carers.
2. Measures of social support will predict lower depression and higher QoL in carers.

3. Social support will moderate (reduce the strength of) the relation between stressor and carer wellbeing outcomes.

Method

Participants and data source

This study will use data already collected from matched caregivers and people with manifest HD (aged 18+) participating in the Enroll-HD study https://www.enroll-hd.org/. Participants with manifest HD (i.e. those who are showing unequivocal motor symptoms) will be selected for this study as care needs are likely to be higher in this group than those who are not yet showing symptoms but do know they have the HD genetic mutation. Established in 2011, Enroll-HD is a worldwide prospective observational study of people with HD and their families, which aims to increase knowledge about HD and contribute to improving health and wellbeing. There are currently 21,116 participants drawn from sites in North America, Latin America, Europe, Asia, Australia, and New Zealand. The study is sponsored by the CHDI Foundation who fund drug-discovery research projects for HD. The available sample size of those meeting the inclusion criteria is hard to determine in advance without access to the dataset, but it is not anticipated that obtaining a sufficient sample will be a problem give the large size of the dataset.

Recruitment for Enroll-HD is ongoing as the study aims to recruit all eligible participants, which includes carriers of the mutated gene, family members who are not related by blood to the carrier, blood relatives of the gene carrier without the HD gene mutation, and community controls with no relations affected by HD. Participants are recruited through specialist HD clinics and word of mouth (e.g. invited by a relative, through fliers, websites etc.). To obtain informed consent, participant information about Enroll-HD is provided in oral and written form (actual documentation varies due to the international nature of the study) following which participants are asked to sign a consent form, which includes giving consent

for the data to be used for secondary analyses. Consent is obtained from a legal representative for individuals who are judged not to have mental capacity according to local regulations and best practice. Participants can withdraw from the study at any time without reason.

Participants are invited to take part in the study on an annual basis during routine clinical care appointments. Demographic data are collected for both participants with HD and carers. Participants with HD complete a range of clinical assessments including general physical health, motor function, cognitive function, mental health and behavioural symptoms, and quality of life for participants with HD. Participants who are carers complete measures related to quality of life and mental wellbeing. Data are collected by trained clinical personnel who undergo regular re-certification.

Measures

It is anticipated that data on the following measures will be extracted from the database for use in this study.

Measures for HD participants

Problem Behaviours Assessment-Short Form (PBA-s; Callaghan et al., 2015)

An 11-item semi-structured interview which assesses behavioural symptoms of HD, including mood disturbance and executive functioning. The interview is conducted with the participant with HD and another informant with good knowledge of them. Each item is scored for severity and frequency on a 5-point scale. There are depression, psychosis, apathy, irritability/aggression, and executive functioning subscales. Scores for items in each sub-scale are multiplied to provide an overall score, with higher scores indicating more severe symptoms. It has been shown to have good inter-rater reliability (Callaghan et al., 2015)(Callaghan et al., 2015).

Unified Huntington's Disease Rating Scale (UHDRS; Kieburtz, 1996).

A rating scale to measure functioning in the core clinical domains affected by HD assessed by experienced clinicians. Two subscales, motor function and functional capacity, are collected in Enroll-HD. Items can be summed to give a performance rating for each subscale. Each sub-scale has high internal consistency (.83-.95) (Kieburtz, 1996)(Kieburtz, 1996) and it is used widely in HD studies.

Cognitive Function

Cognitive function is a broad concept which encompasses a range of mental processes including memory, attention, visual-spatial ability, executive functioning, and verbal ability. Therefore, I plan to use a range of measures which assess different aspects of cognitive function in participants with HD.

Verbal Fluency Test.

Assessments of verbal fluency are commonly used in cognitive assessments, drawing on various elements of cognition including memory retrieval and executive control (Shao et al., 2014)(Shao et al., 2014). Participants are asked to name as many words beginning with the same letter (phonological fluency) and as many words as possible in a particular semantic category (semantic fluency). Performance on these tasks has been found to be impaired in HD (e.g., Ho et al., 2002)(e.g., Ho et al., 2002)

Stroop Interference Test *(SIT; Stroop, 1935)*

A test of cognitive flexibility, processing speed, and ability to inhibit responses. Colour names are presented in an ink colour incongruent to the word (e.g. the word “yellow” is written in orange letters) and participants are required to say the colour of the ink. Responses made within 45 seconds are recorded and summed to make total correct and total incorrect answers. Performance on this task has been found to be impaired in HD (e.g., Paulsen, 2011)(e.g., Paulsen, 2011).

Symbol Digit Modalities Test *(SDMT; Smith, 1973).*

A measure of visual attention and processing speed. Participants must correctly match as many symbols and numbers according to a provided key as possible within a 90 second period. Correct matches are summed to provide a total score. Performance on this task has been found to be impaired in HD (e.g., Paulsen, 2011).

Trail Making Test *(TMT; Reitan, 1958).*

A two-part test which has been found to measure various facets of cognitive function including processing speed, visual processing, attention, working memory, and executive functions in people with HD (O'Rourke et al., 2011) . Part A requires participants to connect numbers in ascending order. In Part B participants have to connect alternating letters and numbers in ascending order (e.g. A-1, B-2, etc.). Each section is timed, and completion time and number of errors is recorded. Performance on these tasks has been found to be impaired in people with HD (O'Rourke et al., 2011) .

Mini-mental state examination *(MMSE; Folstein et al., 1975)..*

A measure of overall cognitive function which 11-items that assess five areas of cognitive function: orientation, registration, attention and calculation, recall, and language. Scores on each item are summed to provide a total score (0-30), with higher total scores indicating better overall cognitive function. A score of ≥24 indicates normal cognitive function. The MMSE is commonly used to clinical practice and research to screen for cognitive impairment. Meta-analytic reviews have found that the MMSE can distinguish participants with dementia from those without dementia effectively (e.g., Tsoi et al., 2015) .

Carer measures

Huntington Disease Quality of Life for Carers (HDQoL-C Aubeeluck & Buchanan, 2007) **.**

A multi-dimensional self-report measure of quality of life designed for carers of people with HD. The scale has 47 items and is split into three sections. Items in section one capture demographic characteristics, including items such as whether the carer lives with the person with HD or is their main carer. Items in section two relate to satisfaction with various facets of life and are scored from 0-dissatisfied to 10-satisfied. Items in section three assess the frequency with which respondent's experience various practical and emotional aspects of caregiving, rated from 0-never to 10-always. A recent validation using Enroll-HD data found the HDQoL-C had good internal consistency and reliability (Aubeeluck et al., 2019b) . We plan to use single items relating to carer demographics and characteristics of the caregiving role, overall QoL rating, and indicators of social support in the analyses.

Hospital Depression and Anxiety scales (HADS; Zigmond & Snaith, 1983)..
This self-report 14-item measure generates sub-scale scores for anxiety, irritability, and depression. Each item is rated from 0-3 depending on how much it has reflected the participant's experience in the last week, with higher total scores indicating higher levels of symptoms. A systematic review of 747 studies using this scale found it to be reliable and valid in a variety of populations (Bjelland et al., 2002) . We understand that this measure is collected for gene-negative control participants who are also carers of participants with HD and hope to be able to link this with HDQoL data to provide a more robust measure of depression in carers.

Demographic data

Demographic data will be extracted about carers and participants with HD. It is anticipated this is likely to include gender, age, ethnicity, geographic location, and relationship of carer to the person with HD to patient.

Proposed analysis

Without access to the data it is difficult to determine the exact data analysis plan. We propose to take the steps outlined below if possible, though this may be subject to change upon accessing the data. Data will be analysed using RStudio or SPSS including Hayes PROCESS macro (https://www.processmacro.org/index.html). After data cleaning, descriptive statistics, preliminary analyses, and parametric assumption checks will be conducted. We plan to use baseline data (i.e. data collected when participants complete the survey for the first time) as this will allow us to obtain the maximum number of participants.

Descriptive statistics

Descriptive statistics will be produced, including:

- Breakdown of participants (carers and people with HD) by gender, age, relationship to patient, ethnicity, and geographic location.
- Means, standard deviations, and range for each subscale score in the PBA-s, HADS, and UHDRS scores, and individual items from HDQoL used in analysis.

Analysis 1

Bivariate correlations will be conducted of the variables of interest to establish whether there are significant relationships between them. This may inform which variables will be included in the multiple regression. The variables are anticipated to be:

1. Caregiving stressors – patient characteristics: cognitive ability, functional and motor ability (UHDRS), and behavioural symptoms (PBA-s) and; caregiver characteristics: age, sex, length of time spent caregiving, main carer, and living in the same household as the person with HD (HDQoL)
2. Social support variables (drawn from HDQoL)
3. Carer wellbeing (HADS if possible, or HDQoL).

Analysis 2

A multiple regression will be conducted to determine whether caregiving stressors, carer characteristics and social support stressors predict carer wellbeing outcomes of depression and satisfaction with quality of life.

Analysis 3

A moderation analysis will be taken to identify whether social support factors moderate the impact of stressor on these outcomes. The independent variables will be statistically significant stressors identified in the regression. The dependent variables will be carer satisfaction with quality of life and depression taken from the HDQol-C. The moderator variables will be the social support variables.

Practical issues

There are no costs associated with this project. In order to access the data it is necessary to submit a project proposal for scientific review by the CHDI Foundation which may cause a delay in access to data. The CHDI Foundation also require applicants to submit detailed information about the digital information security precautions they have in place. We liaised with the Head of IT Security at Lancaster University and relevant IT staff in Lancashire and South Cumbria Foundation NHS Trust (because I will use my NHS trust laptop to handle the data) and Leicester Partnership Foundation NHS Trust (for Maria Dale) to help prepare the relevant paperwork for review by Enroll-HD. We can submit the data security paperwork to the ethics committee once complete if required. These practicalities have been accounted for in my proposed timescale.

Ethical concerns

- Participant privacy – The dataset is anonymised so sensitive personal data will not be able to be linked to an individual. I will sign and abide by the conditions set out in the Enroll-HD Data Use Agreement (DUA) to ensure participant confidentiality.
- Data storage and transfer – Data files will be encrypted for transfer and processed following General Data Protection Regulation and Data Protection Act (2018) principles. It will be kept on password protected university data store, accessible only to the researcher and supervisors. Once the project has been examined, the data will be transferred securely to the research coordinator of the DClinPsy for storage for 10 years, with oversight from Fiona Eccles, research supervisor. After 10 years it will be destroyed.

Timescales

August-November 2022 - Ethics application

October 2022 – HD/Carer Stakeholder meetings

October-January 2022– Apply for access to Enroll-HD data

February-March 2023 – Receive Enroll-HD data, data cleaning

April-June 2023 – Empirical data analysis

July- December 2023– Write up empirical work

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Appendices

Appendix 4-A Ethical Approval

Name: Hannah Ross

Supervisor: Fiona Eccles

Department: Health research

FHM **REC Reference:** FHM-2022-0933-RECR-2

Title: Psychosocial factors and quality of life in carers of people with HD

Dear Hannah Ross,

Thank you for submitting your ethics application in REAMS, Lancaster University's online ethics review system for research. The application was recommended for approval by the FHM Research Ethics Committee, and on behalf of the Committee, I can confirm that approval has been granted for this application.

As Principal Investigator/Co-Investigator your responsibilities include:

- ensuring that (where applicable) all the necessary legal and regulatory requirements in order to conduct the research are met, and the necessary licences and approvals have been obtained.
- reporting any ethics-related issues that occur during the course of the research or arising from the research to the Research Ethics Officer at the email address below (e.g. unforeseen ethical issues, complaints about the conduct of the research, adverse reactions such as extreme distress).

- submitting any changes to your application, including in your participant-facing materials (see attached amendment guidance).

Please keep a copy of this email for your records. Please contact me if you have any queries or require further information.

Yours sincerely,

Dr Laura Machin

Chair of the Faculty of Health and Medicine Research Ethics Committee

fhmresearchsupport@lancaster.ac.uk

Appendix 4-B Huntington's Disease Quality of Life for Carers Questionnaire (Short Version)

Section 1

This section asks for information about yourself.

What is your year of birth?	……
What is your gender?	☐ Male ☐ Female
How many years of formal education do you have?	…… Years
Do you have a job?	☐ YES, FULL TIME ☐ YES, PART-TIME ☐ NO
What is your marital status?	☐ Single ☐ Married ☐ Partnership ☐ Separated ☐ Divorced ☐ Widowed
How long have you known about Huntington's Disease in the family of the affected person(s)?	…… Years
How long have you been caring for an HD affected family member?	…… Years
Are you the main carer for the person with HD?	☐ YES ☐ NO
The affected person is my:	☐ Sibling ☐ Spouse/Partner ☐ Parent ☐ Child ☐ Other
Have you previously cared for any other HD affected person?	☐ YES ☐ NO

- *if so,* what is /was their relationship to you? The affected person is my (e.g. spouse, sister, parent etc): ……..

Do you have children at risk / symptomatic? ☐ YES ☐ NO

How many family members live in your household? …….……..….

Do you live in the same household as the HD person(s)? ☐ YES ☐ NO

Section 2

The next set of questions asks how *satisfied* you are with different areas of your life.

Please circle the number that best describes how *satisfied* you are with each area of your life.

1. How *satisfied are you* with your PHYSICAL HEALTH?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

2. How *satisfied are you* with your PSYCHOLOGICAL HEALTH?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

3. How *satisfied are you* with what you HAVE ACHIEVED IN LIFE?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

4. How *satisfied are you* with your FAMILY RELATIONSHIPS?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

5. How *satisfied are you* with your RELATIONSHIPS WITH YOUR FRIENDS?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

6. How *satisfied are you* with FEELING A PART OF YOUR SOCIAL ENVIRONMENT?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

7. *How satisfied are you* with THE MEDICAL TREATMENT THAT YOUR HD AFFECTED RELATIVE RECEIVES?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

8. *How satisfied are you* with THE PROFESSIONAL SUPPORT YOU RECEIVE?

dissatisfied satisfied

0 1 2 3 4 5 6 7 8 9 10

Section 3

This next set of questions asks how you *feel* about different aspects of your life.

Please circle the number that best describes how you *feel* about each area of your life.

Negative feelings sub-scale

7. I *feel* SAD

never always

0 1 2 3 4 5 6 7 8 9 10

7. I *feel* DEPRESSED

never always

0 1 2 3 4 5 6 7 8 9 10

8. I *feel* STRESSED

never always

0 1 2 3 4 5 6 7 8 9 10

5. I *feel* EXHAUSTED

never always

0 1 2 3 4 5 6 7 8 9 10

5. I *feel* A SENSE OF GRIEVING
never always

0 1 2 3 4 5 6 7 8 9 10

5. I *feel* A SENSE OF LOSS
never always

0 1 2 3 4 5 6 7 8 9 10

5. I *feel* A SENSE OF ANGUISH
never always

0 1 2 3 4 5 6 7 8 9 10

5. I *feel* FULL OF FEAR
never always

0 1 2 3 4 5 6 7 8 9 10

Positive feelings sub-scale

4. I *feel* THERE IS HOPE FOR THE FUTURE
never always

0 1 2 3 4 5 6 7 8 9 10

6. I *feel* SUPPORTED
never always

0 1 2 3 4 5 6 7 8 9 10

13. I *feel* COMFORTED BY MY BELIEFS
never always

0 1 2 3 4 5 6 7 8 9 10

14. I *feel* THAT I CAN COPE
never always

0 1 2 3 4 5 6 7 8 9 10

14. I *feel* THAT I AM SAFE
never always

0 1 2 3 4 5 6 7 8 9 10

14. I *feel* THAT MY ROLE AS A CARER IS REWARDING

never always

0 1 2 3 4 5 6 7 8 9 10

14. I *feel* SATISFIED WITH MY OVERALL QUALITY OF LIFE

never always

0 1 2 3 4 5 6 7 8 9 10

Reference: Aubeeluck, A., Stupple, E. J. N., Schofield, M. B., Hughes, A. C., van der Meer, L., Landwehrmeyer, B., & Ho, A. K. (2019). An International Validation of a Clinical Tool to Assess Carers' Quality of Life in Huntington's Disease. *Frontiers in Psychology*, *10*. https://doi.org/10.3389/fpsyg.2019.01658