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The impact of caregiving on quality of life in Parkinson's disease: A systematic review

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Abstract

Objective: Parkinson's disease (PD) is a progressive neurodegenerative disease that can reduce quality of life (QOL). Previous research has explored patient specific factors that influence QOL; but understanding external factors that may also affect patient QOL, such as caregiver characteristics, can provide additional intervention targets that may improve QOL for both the person with PD and their caregiver.

Methods: We conducted a systematic review of existing literature on caregiver factors that are related to QOL for the person with PD. We developed a tailored search strategy in six databases and performed a screening procedure according to PRISMA guidelines. We synthesized findings from articles that met inclusion criteria using a narrative approach and identified themes categorizing caregiver factors associated with PD QOL.

Results: We found 32 full-text articles that fulfilled the inclusion criteria and passed the quality appraisal. Seven themes were identified, including: (1) burden, (2) strain, (3) QOL and satisfaction, (4) demographic factors, (5) psychological factors, (6) relationship factors, and (7) caregiver input.

Conclusions: Our review presents critical insights into the role of the caregiver in the QOL of a person with PD. Findings reveal several targets for intervention to improve QOL in this population.

Keywords

burden; caregiver; Parkinson's disease; quality of life; strain

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AUTHOR CONTRIBUTIONS
Kate Perepezko, Jared T. Hinkle, Elana J. Forbes, Gregory M. Pontone, Kelly A. Mills, and Joseph J. Gallo made substantial contributions to the conception/design of the work, data interpretation and drafting and critically revising the work for important intellectual content. Kate Perepezko, Jared T. Hinkle, and Elana J. Forbes contributed to data acquisition and analysis.

CONFLICTS OF INTEREST
The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

1 | INTRODUCTION

Parkinson's disease (Parkinson's disease (PD)) is a progressive neurodegenerative disease characterized by motor and non-motor symptoms that impair functioning and reduce QOL.[1-3] A previous systematic review of QOL in PD identified several patient-level factors that contribute to QOL, including depression, mobility limitations, problems in psychosocial functioning, attitude, and living environment.[4] However, models of QOL frequently reference influences outside of the individual, such as social relationships and environmental factors.[5-7] Therefore, to understand what affects QOL, we examined factors beyond patient-level factors.

One important social relationship to evaluate in PD is the relationship between the person with PD and their caregiver. With advancing disease severity, patients with PD frequently require a caregiver.[8] Caregivers provide physical and emotional care for the patient and often help with adherence to medical regimens for PD.[9-11] Caregiver support can also delay formal home care or residential nursing home placement.[12]

In other disease populations, several studies have revealed the influence of a caregiver on the QOL of the care recipient. Hoe et al. found that people with dementia who lived at home with a caregiver had higher QOL than people living in 24-h care facilities.[13] Burgener and Twigg also found that the quality of the caregiver-care recipient relationship predicted QOL and psychological wellbeing of the care recipient.[14] Another study demonstrated that caregiver burden, or the level of multidimensional burden resulting from caring for a family member and/or loved one over time that a caregiver perceives, contributed to worse QOL for the care recipient.[15,16] Caregiver strain, defined as the caregiver's experience of persistent problems and a feeling of reduced well-being that results from providing prolonged care for someone, is also associated with worse QOL for both care recipient and caregiver.[17,18]

These findings have translated to interventions targeting caregivers that improve patient outcomes. A review of dementia caregiver interventions reported on several interventions that successfully improved patient functioning and QOL.[19] Thus, improvement in QOL for PD patients may hinge on identifying and addressing modifiable caregiver characteristics that impact QOL for PD patients.

Several reviews have examined PD patient factors that affect QOL of the care recipient.[4,20,21] However, no review has examined caregiver-specific factors associated with QOL for the person with PD. The purpose of this review is to identify caregiver characteristics that influence PD patient QOL to inform the development of interventions to improve QOL in this population.

2 | METHODS

2.1 | Search strategy

A systematic review of research-based literature cataloged in PubMed, CINAHL, EMBASE, PsychINFO, Cochrane, and Web of Science was performed. The entire available time range of databases was used until January 24, 2022. The search strategy can be found in Appendix A.

2.2 | Study selection

After removing duplicates ($n = 97$), the titles and abstracts of the remaining 8, 295 articles were independently screened by two reviewers (KP and JH), consistent with PRISMA guidelines.[22] Articles were excluded during screening if they did not meet inclusion criteria or if they were not available in English. Discrepancies were resolved by a third reviewer (EF). Articles meeting the inclusion criteria and not meeting exclusion criteria were selected for full-text review (Table 1).

After the title and abstract screening was complete, 8098 articles were excluded, leaving 109 full-text articles for further screening (Figure 1). These articles were read by two reviewers (KP and JH) to determine if they met inclusion criteria. Any discrepancies were resolved again by the third reviewer (EF). After full-text review, 72 articles were excluded, leaving 32 articles for quality appraisal and data extraction. The reasons for exclusion during the full-text screening stage can be found in Figure 1.

2.3 | Quality appraisal

One reviewer (KP) used the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies to evaluate the articles that were included after full-text review.[23] Table 2 displays the questions that informed the quality appraisal. The results for the quality appraisal can be found in Appendix B.

2.4 | Data extraction and synthesis

Following quality appraisal, data were extracted from articles using a form that can be found in Appendix C. The study aim, sample size of participants with PD and their caregivers, and the study setting were recorded for all included papers. The QOL measures for the person with PD and the measures of caregiver factors were also noted. Lastly, the relationship between the caregiver factors and QOL measure and the type of analysis used were documented for each study. The data extracted from studies is presented in Table 3.

We employed a narrative approach to describe and synthesize the results of the included articles.[24] The results section was divided into themes characterized by caregiver factors that were associated with the QOL of people with PD. These themes included: burden, strain, QOL and satisfaction, psychological factors, demographics, and relationship factors. Next, we followed a process that has been described in previous reviews to create a “summary of association” score for each theme.[24-26] We determined if the association between the caregiver factor within each theme and PD QOL was significant and whether the factors were positively or negatively related to QOL. A summary score was used to describe the proportion of evidence within each theme that supported an association (i.e. a significant relationship). We then classified the evidence based on this “summary of association” score according to categories defined in previous reviews: unrelated (0%–33% of studies supporting association), unclear (34%–59% of studies supporting association) or related (60%–100% of studies supporting association).[24-26]

3 | RESULTS

3.1 | Participant and study characteristics

We identified 32 papers to include in our review. These articles were published between 2002 and 2021. All included papers used a quantitative analysis method. Most papers ($n = 17$) used correlation analysis, 12 papers used regression analysis, two papers used a chi-square test, two papers used t-tests, one paper used structural equation modeling, and one paper used an ANOVA. Most study designs were cross-sectional ($n = 30$) and two studies were longitudinal. The median sample size for caregivers was 87 (range: 15–6154). The median sample size for people with PD was 91 (range: 15–7209).

Several different instruments were used to measure QOL in people with PD. The most frequently used instrument was the Parkinson's Disease Questionnaire-39 (PDQ-39) ($n = 20$).[27] Other measures of QOL included the Parkinson's Disease Questionnaire-8 (PDQ-8)[28] ($n = 6$), the 36-Item Short Form Survey (SF-36)[29] ($n = 3$), Visual Analogue Scale (VAS)[30] ($n = 2$), QOL in Alzheimer's disease (Quality of Life in Alzheimer's Disease)[31] ($n = 2$), 12-Item Short Form Survey (SF-12)[32] ($n = 1$), Schedule for the Evaluation of Individual QOL Questionnaire[33] ($n = 1$), Questions on Life Satisfaction scale[34] ($n = 1$), McGill QOL Questionnaire[35] ($n = 1$), Patient-Reported Outcomes Measurement Information System[36] ($n = 1$), and the Euroqol (EQ-5D) ($n = 1$).[37]

3.2 | Narrative synthesis

After identifying similar caregiver factors across included studies, we developed seven themes that represented the findings reported in the included studies. These themes included: (1) burden, (2) strain, (3) QOL and satisfaction, (4) demographics, (5) psychological factors, (6) relationship factors, and (7) caregiver input. The following sections describe the key findings for each theme and the summary of association score.

3.3 | Caregiver burden

The most frequently reported caregiver factor was caregiver burden ($n = 10$). Nine studies reported a significant relationship between caregiver burden and PD QOL, resulting in a summary of association of 90% which indicates caregiver burden is related to PD QOL.[38-47] In most studies ($n = 8$), worse caregiver burden was associated with worse QOL for the PD patient. One article did not report the direction of the association between caregiver burden and PD QOL, only reporting a significant p-value.[38]

Importantly, all the articles that did report a significant association between these variables relied on univariable analyses (e.g., correlations, t-test, ANOVA) and therefore did not account for potential confounders of the relationship between caregiver burden and PD QOL. The article that did not find a significant relationship between these variables did employ regression, controlling for scores on the Parkinson Fatigue Scale, Nonmotor Symptom Scale, and caregiver QOL.[47] However, this study focused on advanced PD patients using levodopa-carbidopa intestinal gel and therefore the findings may not be transferable to the general PD population.

3.4 | Caregiver strain

Another caregiver measure that was evaluated was caregiver strain (*n* = 6). All six studies identified a significant relationship between caregiver strain and PD QOL (summary of association = 100%).[38,48-58] In these studies, higher caregiver strain was associated with worse QOL for the PD patient. Most articles examined this relationship with univariable analyses; however, one article did report the results of a regression analysis that accounted for patient sex, age, comorbidities, Hoehn and Yahr stage, mobility, verbal fluency, recall scores, and the use of treatments for depression, psychosis, and cognition.[48] This study still found a significant relationship between caregiver strain and QOL among a large, national sample of people with PD.

3.5 | Quality of life and satisfaction

Another theme that was identified during this narrative approach was caregiver QOL and satisfaction. Findings motivating this theme reported on overall caregiver QOL as measured by a QOL scale and caregiver satisfaction with life and support. Six articles reported on the relationship between this caregiver factor and PD QOL, with most articles (*n* = 4) revealing a positive relationship.[50,59-64] Two articles did not find significant associations between these variables.[47,54] Most articles (*n* = 4) relied on univariable analyses, however, one article that did not report a significant relationship between caregiver QOL and PD QOL, employed a regression analysis, controlling for scores on the Parkinson Fatigue Scale, Nonmotor Symptom Scale, and caregiver burden among a sample with advanced PD who used levodopa-carbidopa intestinal gel. The summary of association score for findings contributing to this theme was 60%, indicating these factors are related.

3.6 | Demographics

There were two papers that reported on three caregiver demographic factors and their relationship to PD QOL. One study examined the relationship between caregiver age and gender on PD QOL and found no significant relationship.[55] This study used a regression analysis, controlling for patient mutuality score, UPDRS Part 3 score, Nonmotor Symptom Scale score, and Montreal Cognitive Assessment score. Another study evaluated the relationship between caregiver education and PD QOL. These authors did find that lower caregiver education was related to worse scores on PD patient SF-36 subdomains (emotional role, social functioning, and pain).[65] The summary of association score for caregiver demographics is 33% indicating these factors are unrelated.

3.7 | Psychological factors

There were five different psychological factors (e.g. cognitive status, depression, personality, perception of patient anxiety and depression) that were investigated in the articles included in this review. Most of these factors were found to have a relationship with PD QOL, resulting in a summary of association score of 66% (related). Lubomski et al. found that care recipients who had caregivers with mild cognitive impairment also had worse QOL.[57] Bartolomei et al. revealed that caregiver depression was correlated with worse PD QOL.[49] Another study investigated the relationship between specific caregiver personality traits and care recipient QOL. Ma et al. found that caregiver neuroticism was not significantly associated with PD QOL, while higher caregiver conscientiousness scores associated with better PD QOL.[66] The authors also controlled for patient age, gender, disease duration, UPDRS score, and patient neuroticism and conscientiousness in this analysis. Lastly, Kudlicka et al. reported on the relationship between caregivers' rating of their care recipient's anxiety and depression. The caregiver rating of anxiety was found to be significantly related to PD QOL, while the rating of depression was not.[67]

3.8 | Relationship factors

In addition to identifying individual caregiver factors that contributed to QOL for the care recipient, some papers looked at factors related to the relationship between the caregiver and care recipient and how they affect PD QOL. Three papers investigated the quality of interactions between the caregiver and care recipient, labeled as mutuality score or couple satisfaction.[68-73] From the analyses conducted in these included articles, the quality of interactions and PD QOL was found to be unrelated (summary of association = 33%). The only paper that had a significant association between the relationship quality and PD QOL, conducted this analysis with PD QOL subscales.[73] The authors only reported a significant association between relationship satisfaction and the social support subscale on the PDQ-39.

3.9 | Caregiver input

Four papers examined the relationship between having a caregiver and PD QOL. Three papers found a negative relationship between having a caregiver or having higher carer input and PD QOL (summary of association score = 75%, related).[54,74,75] While these authors did report a significant negative relationship between these variables, it is important to consider the cross-sectional nature of these relationships. All studies reporting on this factor were cross-sectional and therefore, it is impossible to determine the directionality of this association and, therefore, causality. It is likely that people with PD are more likely to need a caregiver when their QOL deteriorates. In fact, a couple of studies included in this section support this idea. Hand et al. found that QOL score was worse for people with PD who had high care input compared to moderate or low care input.[74] These researchers also observed significant differences on both the mobility and activities of daily living subscales of the PDQ-39, with people with PD who had high caregiver input also having worse scores on those subscales. This finding suggests that lower QOL scores contribute to the need for a caregiver due to increased disability. Additionally, Navarta-Sanchez et al. found no significant relationship between presence of a caregiver and PD QOL after controlling for age, gender, brief coping, benefit finding, disease severity, psychosocial adjustment, and resources.[75] Similarly, Dahodwala et al. found that worse QOL was related to higher odds of having a caregiver present during a clinical visit, however, caregiver presence was also more likely with higher disease severity (Hoehn & Yahr stage 4-5 compared to stage 1).[48] These analyses suggest that having a caregiver is more strongly associated with worse disability and longer disease duration which can affect QOL, rather than worse QOL resulting from having a caregiver.

4 | DISCUSSION

We aimed to identify and describe the literature exploring the role of the caregiver in QOL for people with PD. We synthesized research examining caregiver factors associated with care recipient QOL, including caregiver burden, strain, QOL and satisfaction, psychological factors, demographic factors, relationship factors, and caregiver input. Our analysis revealed that one of the most influential and commonly studied caregiver factors was caregiver strain. All articles that investigated the relationship between caregiver strain and PD QOL found a significant relationship between these two variables. Additionally, caregiver burden, psychological factors, and caregiver input were also found to be associated with PD QOL, whereas demographic factors and relationship quality were not. These studies provide some insight into the influential role of a caregiver, however, many relied on univariable analyses and cross-sectional study designs. More research is needed on this topic to better understand the relationship between caregiver factors and QOL for people with PD.

Our systematic review is the first to summarize studies examining the role of the caregiver in the QOL of people with PD. We followed Cochrane's robust methodological procedures during the review process and had more than one reviewer at each stage to reduce bias. We also performed a search in six databases for relevant papers but acknowledge the potential to miss other sources in the gray literature. However, given the observational nature of these studies, we focused on manuscripts whose methods would withstand the scrutiny of peer review.

One major implication of the findings of this review is that several potential targets for interventions that can improve QOL for people with PD were identified. Existing treatments and interventions to improve QOL in this population typically target the person with Parkinson's disease[62,63]; however, caregivers are common and highly affected by the disease as well.[8] This review identified several caregiver characteristics and qualities that could be addressed with an existing intervention known to improve patient QOL in other disease states or could justify and inform the development of a new caregiver intervention.

In addition to informing the design of interventions to improve QOL for people with PD, this review also highlights the importance of evaluating caregiver health and needs during regular clinical visits. Routine caregiver evaluations during care recipient clinic visits have been proposed.[52,64] A study by Riffin, Wolff, and Pillemer surveyed US primary care physicians to assess the current practices and barriers to evaluating caregivers during primary care visits. This study revealed how rare caregiver evaluations are in this setting and found that a lack of time was the most common barrier to conducting such an assessment.[76] Participants in the study also identified facilitators of routine caregiver evaluation, such as better referral options and an easier referral mechanism.[76] PD demands a multi-disciplinary approach to care, with many patients having a movement disorders specialist, psychiatrist/psychologist, physical therapist, occupational therapist, speech-language therapist, and social worker on their medical care team.[77-79] However, referrals for caregivers are less common.[80] Future research should evaluate the feasibility of incorporating caregiver assessments into movement disorder specialist visits. Several low-burden, self-administered questionnaires are available to assess caregiver burden or strain.[17,81,82] Incorporating these measures into routine clinical visits could have implications for caregiver and care recipient health outcomes. Caregivers who fall within a risk category could be referred to additional services to prevent worsening of their own health and the health of their care recipients.

The findings of review also point to a dearth of research examining the relationship between caregiver factors and PD QOL using rigorous methods. Most articles included in this review only evaluated the relationship between the caregiver factor and PD QOL, without accounting for other influential factors. Future research is needed to more systematically study this relationship using multivariate approach to control for potential confounders of the caregiver factor-PD QOL relationship. There are several variables that have previously been shown to influence both PD QOL and the caregiver. For example, most people with PD experience a worsening of symptoms and that require greater caregiver involvement and a reduction in QOL around disease durations of 10 years[65,66,83] Additionally, other variables such as level of disability and cognitive status have also been shown to influence both PD QOL and the caregiver.[71-73]

Furthermore, all studies included in this review were cross-sectional, which only allows us to determine associations between variables and prevents any investigation of causality. Within the caregiver input theme, the reliance on cross-sectional analyses demands a cautious interpretation of the findings. The results reported in this section differ from what has been observed in other caregiving literature, namely, several articles contained findings that having a caregiver was associated with worse QOL. In contrast, in the general caregiving literature the presence of a caregiver has been associated with better outcomes for the care recipient. This discrepancy highlights the need for further, longitudinal investigation of this relationship to determine directionality.

5 | LIMITATIONS

We broadly defined our search strategy to capture all measures of QOL in PD and all study designs. While this approach likely increased the number of articles we included in the review and provided a more comprehensive overview of this topic, it also prevented us from conducting a meta-analysis[84] making direct comparison across studies more challenging. One general requirement for a meta-analysis is that the studies are “sufficiently homogenous in terms of subjects involved, interventions, and outcomes to provide a meaningful summary.”[85] Unfortunately, even though we had similar outcomes across studies (QOL), the study designs and participant characteristics varied greatly, meaning the results of a meta-analysis would be less meaningful (see Table 3). However, as this is the first review looking at the role of the caregiver in PD QOL, we believe that a narrative summary provides the best method to synthesize information across the studies that were included. We also employed the Popay framework,[24] which has been used in other systemic reviews to synthesize information and compare the level of evidence, to address this limitation.

6 | CONCLUSION

Caregivers play a critical role in the management of Parkinson's disease. Our review reveals that caregiver strain is one of the most influential caregiver-level factors that contributed to

QOL for people with PD. Caregiver burden, psychological factors, caregiver presence were also found to be associated with PD QOL, whereas demographic factors and relationship quality were not. The findings from this review can inform novel interventions targeting these modifiable caregiver factors. Our research emphasizes the importance of considering the caregiver and their health during clinical visits for people with Parkinson's disease. Our review also indicates the need of additional research investigating the relationship between caregiver factors and PD QOL.

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

APPENDIX A

Search Strategy

(“Parkinson Disease”[Mesh] OR parkinson[tiab] OR parkinson's [tiab] OR parkinsons[tiab])

#2 (“Caregivers”[Mesh] OR “Spouses”[Mesh] OR caregiver*[tiab] OR “caring intervention”[tiab] OR “care giver*”[tiab] OR “caregiving”[tiab] OR “care giving”[tiab] OR spouse*[tiab] OR “significant other*”[tiab] OR “family caring”[tiab] OR “family caregiver*”[tiab] OR “family partner*”[tiab] OR husband*[tiab] OR wives[tiab] OR wife[tiab] OR partner[tiab] OR “adult children” [tiab] OR relatives[tiab] OR sibling*[tiab] OR spouse*[tiab] OR carer*[tiab] OR “informal care*”[tiab])

#3 (animals[mh] NOT humans [mh])

#4 (#1 AND #2) NOT #3

APPENDIX B

Quality Appraisal Results

	Research question	**Study population**	**Response rate**	**Inclusion criteria**	**Sample size**	**Exposure measure**	**Timeframe**	**Different exposure levels**	**Exposure measurement**	**Repe expo**
Bartolomei 2018	1	1	1	1	1	N/A	N/A	1	1	N/A
Caap-Ahlgren 2002	1	1	1	1	1	N/A	N/A	1	1	N/A
Chu 2019	1	1	1	1	1	N/A	N/A	1	1	N/A

	Research question	**Study population**	**Response rate**	**Inclusion criteria**	**Sample size**	**Exposure measure**	**Timeframe**	**Different exposure levels**	**Exposure measurement**	**Repe expo**
Dahodwala 2018	1	1	1	1	1	N/A	N/A	1	1	N/A
daSilva 2008	1	1	1	1	1	N/A	N/A	1	1	N/A
Demeulemeester 2015	1	1	1	1	1	N/A	N/A	1	1	N/A
Hand 2018	1	1	1	1	1	N/A	N/A	1	1	N/A
Henry 2020	1	1	1	1	1	N/A	N/A	1	1	N/A
Karlstedt 2017	1	1	1	1	1	N/A	N/A	1	1	N/A
Karlstedt 2018	1	1	1	1	1	N/A	N/A	1	1	N/A
Kelly 2012	1	1	1	1	1	N/A	N/A	1	1	N/A
Kudlicka 2014	1	1	1	1	1	N/A	N/A	1	1	N/A
Lubomski 2021	1	1	1	1	1	N/A	N/A	1	1	N/A
Ma 2018	1	1	1	1	1	N/A	N/A	1	1	N/A
Martinez-Martin 2005	1	1	1	1	1	N/A	N/A	1	1	N/A
Miyashita 2011	1	1	1	1	1	N/A	N/A	1	1	N/A
Muller 2010	1	1	1	1	1	N/A	N/A	1	1	N/A
Navarta-Sanchez 2016	1	1	1	1	1	N/A	N/A	1	1	N/A
Oguh 2013	1	1	1	1	1	N/A	N/A	1	1	N/A
Peters 2011	1	1	1	1	1	N/A	N/A	1	1	N/A
Prizer 2020	1	1	1	1	1	N/A	N/A	1	1	N/A
Rajiah 2017	1	1	1	1	1	N/A	N/A	1	1	N/A
Ricciardi 2015	1	1	1	1	1	N/A	N/A	1	1	N/A
Rodriguez-Violante 2015	1	1	1	1	1	N/A	N/A	1	1	N/A
Rosqvist 2019	1	1	1	1	1	N/A	N/A	1	1	N/A
Tan 2019	1	1	1	1	1	N/A	N/A	1	1	N/A
Tanji 2008	1	1	1	1	1	N/A	N/A	1	1	N/A
Torny 2018	1	1	1	1	1	N/A	N/A	1	1	N/A
Trang 2020	1	1	1	1	1	N/A	N/A	1	1	N/A
Valldeoriola 2021	1	1	1	1	1	N/A	N/A	1	1	N/A
Viwattanakulvanid 2014	1	1	1	1	1	N/A	N/A	1	1	N/A
Yuksel 2018	1	1	1	1	1	N/A	N/A	1	1	N/A

APPENDIX C

Data Extraction Form

Title
Lead author
Country in which the study conducted

Title
Aim of study
Study design
Inclusion criteria
Exclusion criteria
Total number of caregiver participants
Total number of participants with PD
Analysis used
Primary findings
Additional notes (optional)

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Key points

- Several caregiver-specific characteristics are associated with quality of life (QOL) for the care recipient with Parkinson's disease, including caregiver QOL, burden, strain, conscientiousness, and education level.
- Findings reveal several targets for interventions to improve QOL in this population.
- The findings of this review uncover a dearth of research examining the relationship between caregiver factors and QOL for the care recipient using rigorous, longitudinal methods. Future research is needed to study this relationship more systematically.

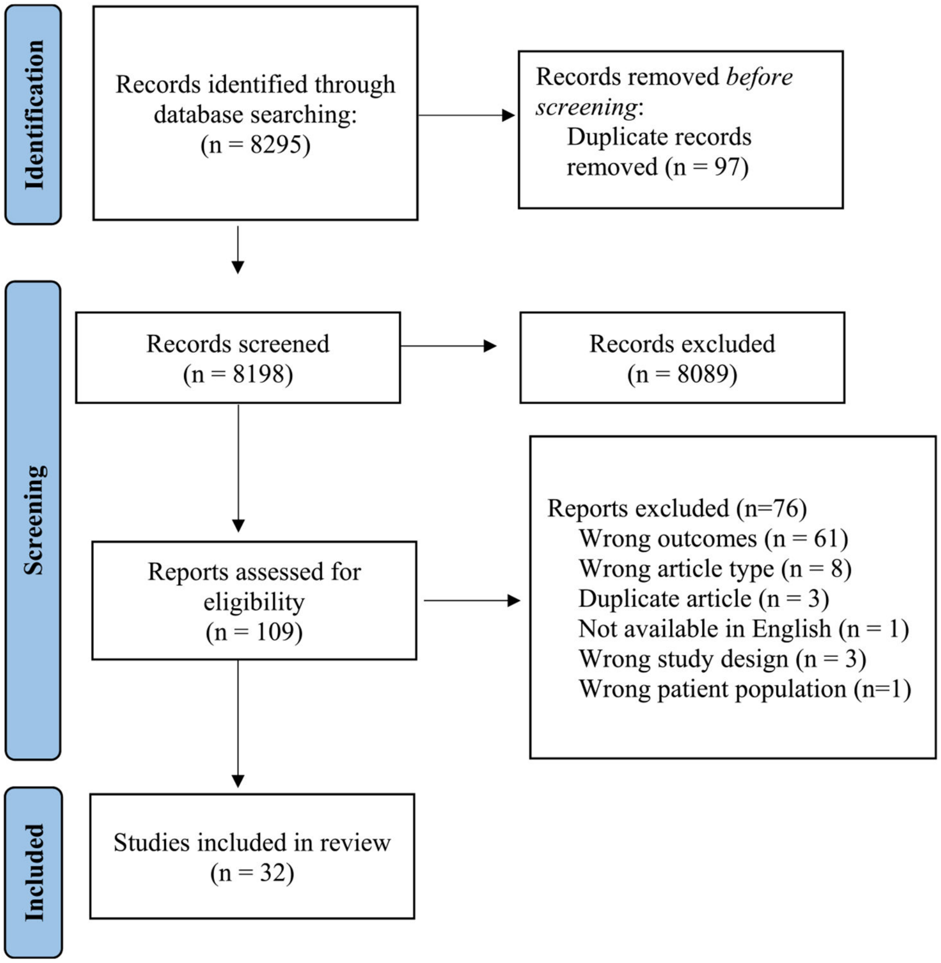

FIGURE 1.

Study selection process (CONSORT diagram)

TABLE 1

Exclusion and inclusion criteria for a systematic review of quality of life (QOL) in Parkinson's disease and the caregiver

Inclusion criteria	Exclusion criteria
Article topic relates to Parkinson's disease and quality of life	Article topic was not related to Parkinson's disease and quality of life.
Study sample included both caregivers and people with Parkinson's disease	Article did not include both caregivers and PWP in their sample.
Peer-reviewed articles available in English.	Articles is not peer-review, not in English. The record type is a review, book, abstracts only/conference proceedings.
Measured and reported on quality of life for the person with Parkinson's disease.	Study design uses an animal model.
Evaluated the relationship between a caregiver factor and PWP QOL.	

TABLE 2

Quality Appraisal criteria

Criteria
1. Was the research question or objective in this paper clearly stated?
2. Was the study population clearly specified and defined?
3. Was the participation rate of eligible persons at least 50%?
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?
5. Was a sample size justification, power description, or variance and effect estimates provided?
6. For the analyses in this paper, were the exposure(s) of interest measured before the outcome(s) were measured?
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?
8. For exposures that can vary in amount or level, did the study examine different levels of exposure as related to the outcome (e.g., categories of exposure or exposure measured as a continuous variable)?
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
10. Was the exposure(s) assessed more than once over time?
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
12. Were the outcome assessors blinded to the exposure status of participants?
13. Was loss to follow-up after baseline 20% or less?
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure (s) and outcome(s)?

TABLE 3

Methodological characteristics of included articles

Study	Study Aim	Sample	Study design	Sample size (PWP)	Sample Size (CG)	Caregiver Measures	Quality of Life Measures	Analysis Method	Relationship between CG factor and PWP QOL
Bartolomei 2018	To examine the relationship of sleep quality and depression in patients with PD with burden, mood, and quality of life of their caregivers.	Outpatient clinic	Cross sectional study	57	57	CBI, BDI	PDQ-39	Pearson correlation and Spearman correlation	Caregivers' burden and depression were interrelated (Pearson's correlation $p <$ 0.001) and both correlated with PD quality of life.
Caap-Ahlgren 2002	To identify various factors in PD patients and their caregivers that are of supposed importance with respect to caregiver burden.	Outpatient clinic	Longitudinal study	65	65	CBI	PDQ-39	Spearman correlation	The correlation between PDQ-39 and caregiver burden: 0.48 ($p < 0.005$)
Chu 2019	To determine the relationships between QOL and life satisfaction among PD patients and their caregiver.	Active members of the Malaysia Parkinson's Disease Association (MPDA)	Cross sectional study	20	20	Life satisfaction Scale	PDQ-39	Pearson Correlation	Correlation between PDQ-39 and life satisfaction scale was 0.46 (significant 2-tailed)
Dahodwala 2018	To compare access to caregiving between men and women with Parkinson's disease (PD).	Participants enrolled in the National Parkinson Foundation Parkinson's Outcomes Project	Cross-sectional	6154	7209	Caregiver attending visit MCSI	PDQ-39	Linear regression (Cross-sectional)	Higher PDQ-39 score was related to higher odds of having a caregiver accompany to baseline visit (1.02; 95% CI: 1.01–1.02) and MCSI score (0.34; 95% CI: 0.30–0.37).
daSilva 2008	To evaluate the quality of life of patients with PD; measure the caregivers stress level; and to confront the caregivers stress levels with the patient's quality of life, relating them to the disease gradation.	Outpatient clinic	Cross-sectional	43	43	CSS	PDQ-39	Chi-Square test Spearman Correlation	PDQ-39 versus CSS ($p =$ 0.0017, $r = 0.4646$).
Demeulemeester 2015	To investigate the perception of patients and partners of their own as well as of each other present and former quality of life and to explore a possible correlation of these estimates with measures of disease burden.	Outpatient clinic	Cross sectional study	50	50	VAS	VAS	Pearson correlation	Quality of life of the PD patient was correlated with caregiver QOL (0.395, $p = 0.005$)
Hand 2018	To examine the baseline care needs of the cohort living at	Participants in the Northumbria	Cross-sectional	132	115	Presence of caregiver	PDQ-39	Chi-squared Test	There was a significant difference in PDQ-39 score

Study	Study Aim	Sample	Study design	Sample size (PWP)	Sample Size (CG)	Caregiver Measures	Quality of Life Measures	Analysis Method	Relationship between CG factor and PWP QOL
	home and detail the levels of formal and informal care required to meet these needs.	Care Needs Project.				Duration of caregiving Tasks performed Current health problems they had which they felt negatively affected their ability to fulfill their caring role.			for those with informal caregiver (32.97; 22.71–42.86 compared to those without an informal caregiver (18.7; 14.455–30.295), $p < 0.001$.
Henry 2020	To assess the relationship among a range of PD symptoms and four measures of caregiver QOL.	Outpatient clinic	Cross sectional study	181	181	PDQ-Carer Demographic information (age, sex, relationship to care recipient, how often they see the care recipient, and how many hours per week they spend with the care recipient)	PDQ-39	Correlation	All subscales of the PDQ-39 were correlated with PDQ-Carer subscales ($p < 0.01$ or lower).
Karlstedt 2017	To identify factors associated with mutuality, HRQOL, and caregiver burden.	Baseline data from a longitudinal study.	Cross sectional study	51	51	CBI MS Caregiver gender and age	PDQ-8	Multiple linear regression	The significant predictors of PDQ-8 Total score were MS score (beta = 433, = 0.001) and NMSQuest score (beta = 0.498, $p < 0.001$) contributed significantly to the explained variance of PDQ8SI scores. Caregiver gender (−4.329; 95% CI −11.565–2.907) and caregiver age (−0.190; 95% CI: −0.551–0.171) were not significant predictors of PDQ-8 total score.
Karlstedt 2018	To disentangle different pathways that could explain the effect of PD specific symptoms on patients' HRQOL.	Outpatient clinic	Cross sectional study	51	51	CBI MS Caregiver gender and age	PDQ-8	Structural equation modeling	With increasing severity of motor and nonmotor symptoms, patients' mutuality decreased which leads to worse PDQ-8.
Kelly 2012	To consider the relationship between HRQOL in people with PD and their caregivers.	Participants were drawn from general medical practitioners, neurologists, Parkinson's	Cross sectional study	97	97	MCSI	EQ-5D PDQ-39 VAS	Spearman rank correlations coefficient	A small but significant negative relationship was found using the EQ-5D and VAS, but not the unweighted VAS, suggesting that poorer HRQOL in people with PD is associated

Study	Study Aim	Sample	Study design	Sample size (PWP)	Sample Size (CG)	Caregiver Measures	Quality of Life Measures	Analysis Method	Relationship between CG factor and PWP QOL
		Victoria network and advertisements in local papers.							with higher caregiver strain experienced by their caregivers. The correlation of PDQ-39 with MCSI scores (rs = 0.3 at $p < 0.001$) confirmed that poorer self-rated health in people with PD was associated with increased strain in their caregivers.
Kudlicka 2014	To evaluate how EF contributes to QOL and health status for the PwPD and caregiver burden.	Outpatient clinic	Cross sectional study	50	65	CBI caregiver rating of BRIEF-A	LSS PDQ-39	Multiple regression analyses	The BRIEF-A caregiver rating was the strongest and the only individually significant predictor of QOL-health, whereas the depression rating only approached significance. The model explained 32% of the variance in QOL-health. The BRIEF-A caregiver rating was the strongest and the only individually significant predictor of QOL movement disorders. The model explained 26% of the variance in QOL-movement disorders. The BRIEF-A self-rating was the strongest and the only individually significant predictor of PDQ-39. The model explained 34% of the variance in health status.
Lubomski 2021	To examine MCI in PD patients and their caregivers to determine if caregiver cognition affected their PD relative.	Outpatient clinic	Cross-sectional study	103	81	MoCA	SF-36	*T*-tests	PD patients without MCI were noted to experience an even lower QOL when their caregiver had MCI, compared to a caregiver with no MCI. This difference was observed on the physical component of the SF-36 [PCS 50.9 (SD 22.3) versus 55.8 (SD 16.1), $t = -2.5$, $p = 0.015$ and the mental components 60.5 (SD 18.4) versus 64.8 (SD 19.3), $t = -2.3$, $p = 0.028$].
Ma 2018	To explore neuroticism and conscientiousness personality factors of the patient and family caregiver associated with quality of life (QOL) of PD patients	Outpatient clinic	Cross sectional study	134	134	NEO-FFI	PDQ-39	Multivariate stepwise linear regression analysis with a forward selection.	The neuroticism of the caregiver was not significantly related to the three domains of QOL, while conscientiousness of the caregiver was added to the predictor of PDQ-39 (beta = −0.22).

Study	Study Aim	Sample	Study design	Sample size (PWP)	Sample Size (CG)	Caregiver Measures	Quality of Life Measures	Analysis Method	Relationship between CG factor and PWP QOL
Martinez-Martin 2005	To assess the impact of PD on informal caregivers of patients and identify the main factors related to caregiver strain.	Outpatient Clinic	Cross sectional study	64	64		PDQ-39	Spearman Correlation	Caregiver quality of life was correlated with patient quality of life ($r = -0.600$, $p < 0.001$).
Miyashita 2011	To clarify the QOL of patients with intractable neurological diseases and their caregivers.	Survey sent to homes	Cross sectional study	418	418	SF-8	SF-36	correlation and regression	The patients' mental health and caregivers' mental component summary were moderately correlated (standardized beta [SB] = 0.34, $p < 0.001$).
Muller 2010	To report the analysis of the survey outcomes on QOL, insurance, disability and caregiver burden in patients with PD and their carers.	Not described.	Cross sectional study	2603	2603	BSFC	PDQ-8	Spearman Correlation	Correlation between PDQ-8 & BSFC = 0.25 ($p < 0.0001$)
Navarta-Sanchez 2016	To explore potential clinical, social and attitudinal determinants of psychosocial adjustment and QOL in PD patients and informal caregivers	Three settings in a community context: The Navarre association of Parkinson's patients, a Neurology outpatient clinic and a primary care practice in Pamplona (Spain)	Cross sectional study	83	91	SQLC	PDQ-39	Multiple linear regression	The presence of a caregiver was not a significant predictor of PDQ-39 (−1.61 (−9.14,5.90) $p = 0.67$)) after controlling for age, gender, brief coping, benefit finding, disease severity, psychosocial adjustment, and resources.
Oguh 2013	To determine what measures of PD disability, demographics, and patient quality of life are associated with caregiver strain among caregivers of patients with PD.	Data was obtained from the National Parkinson Foundation's quality Improvement Registry (NPF-QII)	Cross sectional study	826	826	MCSI	PDQ-39	Spearman Correlation	The total PDQ-39 score was correlated with MCSI score ($r = 0.567$, $p < 0.00$).
Peters 2011	To explore to what extent patient self-reported health, as measured on the disease-specific Parkinson's Disease Questionnaire (PDQ-39), is associated with carer strain and self-reported quality of life.	A postal survey was carried out of both patients and caregivers through local branches of Parkinson's UK.	Cross sectional study	704	901	CSI	PDQ-39	Correlation	The PD Index was found to be highly associated with caregiver burden as measured on the CSI ($r = 0.56$, $p < 0.001$, $n = 422$).
Prizer 2020	To assess whether caregiver presence was associated with variations in patient presentation and outcomes	Baseline data from a 3-site randomized controlled trial	Cross-sectional	210	175	Presence of a caregiver	PDQ-39, PROMIS-29, McGill QOL, QOL-AD	Regression	Quality of life as measured by the QOL-AD questionnaire was better for individuals with caregivers compared to those

Study	Study Aim	Sample	Study design	Sample size (PWP)	Sample Size (CG)	Caregiver Measures	Quality of Life Measures	Analysis Method	Relationship between CG factor and PWP QOL
	in a palliative PD and atypical PD population.								without caregivers ($p < 0.0001$). Differences in QOL between people with caregivers and those without caregivers as measured by other scales did not reach significance.
Rajiah 2017	To examine the impact of clinical features on PD patients' QOL, and the impact of PD patients' QOL on their caregivers' burden.	Malaysian Parkinson's Disease Association	Cross-sectional	122	122	ZBI	PDQ-39	Correlation	ZBI score was correlated with PDQ-39 score ($r = 0.76$, $p < 0.005$).
Ricciardi 2015	To evaluate the relationship quality and satisfaction in couples, in which one partner had PD, obtaining the perspective of both patients and partner and examine the impact of alexithymia, empathy, depression, and anxiety on ratings of relationship quality and satisfaction.	PD patients and their spousal caregivers were recruited at “Centro Studi Lorenzon” in Treviso, Italy, in the context of a free workshop series	Cross sectional study	15	15	DAS,CoSI	PDQ-39	Backward Step-wise regression	CoSI was a significant predictor of PDQ-39 social support subscale (beta = −0.606, $p = 0.004$).
Rodriguez-Violante 2015	To analyze the relationship between caregiver burden and PD patients' quality of life.	Outpatient clinic	Cross sectional study	201	250	ZBI	PDQ-8	*t*-test correlation	PDQ-8 score was higher for patients who had caregivers with burden (44.3+/−31) compared to those without burden (28.3 +/−20.6), $p = 0.004$. A moderate correlation was observed between PDQ-8 and ZBI ($r = 0.35$, $p < 0.001$)
Rosqvist 2019	To describe and assess satisfaction with care in a sample of patients with late stage PD in Sweden and to identify factors associated with patient satisfaction with care as well as to describe and assess their informal caregivers' satisfaction with support and to identify factors associated with caregivers' satisfaction with support.	Outpatient clinic	Cross sectional study	76	107	Caregiver satisfaction with support	SEIQOL	logistic regression	PWP quality of life was not significantly associated with caregiver satisfaction with support ($p = 0.623$).
Tan 2019	To investigate the characteristics of PD patients related to different levels of caregiver burden.	Outpatient clinic	Cross sectional study	104	104	ZBI	PDQ-39	ANOVA	The median PDQ-39 scores was significantly higher in the high caregiver burden group compared to no-or little group (30.7 vs. 16.2, p-value 0.002). The high caregiver burden

Study	Study Aim	Sample	Study design	Sample size (PWP)	Sample Size (CG)	Caregiver Measures	Quality of Life Measures	Analysis Method	Relationship between CG factor and PWP QOL
									group had significantly higher median scores for domain 2 (ADL, p-value 0.005), domain 4 (stigma, p-value 0.005), and domain 6 (cognition, p-value 0.002) compared to no-or little group.
Tanji 2008	To assess the association between mutuality of the marital relationship in Parkinson's disease with disease severity, disability, mental health, quality of life, and caregiver burden.	Outpatient clinic	Cross sectional study	96	96	MS	SF-12v2	Correlation	Spouse reported mutuality was not significantly correlated with physical health QOL ($p = 0.20$) or mental health QOL ($p = 0.10$).
Torny 2018	To determine correlations between the intensity of disease burden and characteristics of patients and their spouses.	Outpatient clinic	Cross sectional study	38	38	ZBI	PDQ-8	Correlation	PDQ-8 was correlated with ZBI score ($r = 0.27$, $p = 0.007$).
Trang 2020	To determine predictors of general QOL in a population of PDRD patients with high needs and advanced disease and to compare patient ratings of general QOL to health-related QOL and general patient QOL as reported by caregivers.	Baseline data obtained from a multisite randomized controlled trial of outpatient palliative care	Cross-sectional	210	175	HADS, FACIT, QOL-AD, ZBI	QOL-AD, PDQ-39	Regression (Elastic Nets Model)	Caregiver burden (ZBI) was associated with PDQ-39 ($r = 0.1105$, $p = 0.0394$).
Valldeoriola 2021	To assess, the effect of 6-month treatment with LCIG on the QOL of patients with APD using the self-reported PDQ-39.	Outpatient clinics	Longitudinal	62	62	SQLC, ZBI, CSI, GAS, GDS	PDQ-39	Regression	Improvements in patients' QOL (PDQ-39) did not correspond with improvements in caregivers' QOL (SQLC) or caregiver burden (ZBI).
Viwattanakulvanid 2014	To determine and analyze the main determinants of caregiver burden and examine the impact of nocturnal dis-abilities of PD patients on their caregivers.	Multicenter, national outpatient centers	Cross sectional study	89	89	ZBI	PDQ-8	Correlation	PDQ-8 was correlated with ZBI score ($r = 0.38$, $p < 0.001$).
Yuksel 2018	To assess the impact of early-stage PD on caregiver burden with disease severity, duration, disability and psychiatric symptoms.	Outpatient clinic	Cross sectional study	30	30	ZBI	SF-36	Student t test, Mann Whitney U test	Lower caregiver education was related to SF-36 subdomains of the patients (emotional role, social functioning, and pain), $p < 0.05$).

Abbreviations: BDI, Beck Depression Inventory; BRIEF-A, Behavior Rating Inventory of EF-Adult Version; BSFC, Burden Scale for Family Caregivers; CBI, Caregiver Burden Inventory; CoSI, Couple Satisfaction Index; CSI, Caregiver Strain Index; CSS, Caregiver Stress Scale; DAS, Dyadic Adjustment Scale; EQ-5D, EuroQOL; FACIT, Functional Assessment of Chronic Illness Therapy; GAS, Goldberg Anxiety Scale; GDS, Goldberg Depression Scale; HADS, Hospital Anxiety and Depression Scale; HRQOL, Health Related Quality of Life; LCIG, Levodopa-Carbidopa Intestinal Gel; LSS, Life

Satisfaction Scale; MCI, Mild Cognitive Impairment; MCSI, Multidimensional Caregiver Strain Index; McGill QOL, McGill Quality of Life Questionnaire; MoCA, Montreal Cognitive Assessment; MS, Mutuality Scale; NEO-FFI, Neuroticism Extraversion Openness Five-Factor Inventory; Outpatient clinics, Clinic that provides care for patients without requiring a hospital stay; PDQ-Carer, Parkinson's disease Questionnaire for Caregivers; PDQ-39, Parkinson's disease Questionnaire-39; PDQ-8, Parkinson's disease Questionnaire-8; PDRD, Parkinson's Disease and Related Disorders; PROMIS-29, Patient-Reported Outcomes Measurement Information System; QOL-AD, Quality of Life in Alzheimer's Disease; SEIQOL, Schedule for the Evaluation of Individual QOL Questionnaire; SF-36, Short Form-36 Health Survey; SF-8, Short Form-8 Health Survey; SF-12v2, Short Form-12 Health Survey; SQLC, Scale of Quality of Life of Caregivers; VAS, Visual Analog Scale; WPAI, Work Productivity and Activity Impairment.