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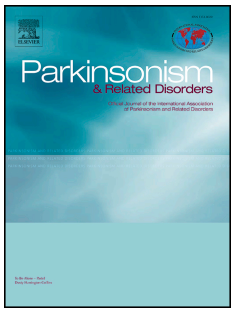

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Predictors of the psychosocial impact of being a carer of people living with Parkinson's disease: A systematic review

Kate Greenwell*[;1,2,3] William K. Gray,[3] Anna van Wersch,[4] Paul van Schaik,[4] Richard Walker[3,5]

1. National Institute for Hearing Research (NIHR) Nottingham Hearing Biomedical Research Unit, Nottingham, UK (current affiliation)

2. Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK (current affiliation)

3. Northumbria Healthcare NHS Foundation Trust, Department of Medicine, North Tyneside General Hospital, Rake Lane, North Shields, Tyne and Wear, UK.

4. School of Social Sciences and Law, Teesside University, Middlesbrough, UK

5. Institute of Health and Society, Newcastle University, Newcastle-upon-Tyne, UK

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[1] *Correspondence to: Kate Greenwell, NIHR Nottingham Hearing Biomedical Research Unit, Ropewalk House, 113 The Ropewalk, Nottingham, NG1 5DU, United Kingdom; telephone: +44 (0)115 823 2627; Email: msxkg1@nottingham.ac.uk*

Abstract

Introduction: Caring for a person with Parkinson's disease (PwP) can have a variety of negative consequences that may challenge their ability to continue their caring role. It is still unknown why some individuals adapt better than others in response to such burdens. This review is the first to synthesise and evaluate the evidence on the predictive factors of psychosocial outcomes in PwP carers.

Methods: Studies which identified predictors of psychosocial outcomes for unpaid carers were included. PsychINFO, EMBASE, AMED, BNI and CINAHL databases were searched, supplemented by scanning of references lists of included studies and relevant journals from 2008 onwards. Quality was assessed using the NICE methodology checklist for prognostic studies.

Results: Twenty-nine studies were included in the review, providing a low-level of evidence. Carer burden was investigated in 18 studies and mental health and quality of life (QoL) in seven studies each. PwP non-motor symptoms and QoL and carer depression were consistently identified as predictors for at least one psychosocial outcome. Demographics and disease factors were consistently found not to be predictors. Carer involvement and protective factors (e.g. social support, personality) demonstrated promising findings but studies were too few or factors measured inconsistently.

Conclusion: Confident conclusions could not be drawn regarding the most important predictors that should be targeted in psychosocial interventions due to methodological weaknesses and lack of theoretical testing across the current literature. Future research should build upon psychological theory to gain a better understanding of the mechanisms that explain how carers adapt to caregiving.

Introduction

Caring for a person with Parkinson's disease (PwP) can have a variety of negative physical, psychological, social and financial consequences for carers that may challenge their ability to continue their caring role. This role is often undemanding in the early disease stages but burden usually increases as the disease progresses and the PwP gradually relies more on the carer for support with everyday activities.

Carers of PwPs can be faced with increased worry and uncertainty over their future, feelings of guilt, grief and frustration, negative changes in lifestyle (including restricted work and social activities) and a worsening financial situation (mainly through loss of earnings [1-3]). This can lead to poor psychosocial outcomes including reduced quality of life (QoL), emotional and financial strain, fatigue, sleep disturbances, social isolation and an increased risk of neuropsychiatric symptoms and chronic illness [4-8].

Nevertheless, experiences vary widely [5, 9] and some carers adapt and cope well throughout the disease course [2]. There is a need to identify which factors predict poor psychosocial outcomes and to develop interventions that target these specific factors and those carers most at risk. Research has attempted to explain individual differences in psychosocial outcomes, however, no attempts have been made to systematically synthesise and evaluate this research. Lau and Au [10] carried out a meta-analysis on the correlates of carer distress in carers of PwP but focused on a limited number of factors including demographics, intensity of caregiving (e.g. years of caregiving) and disease factors (e.g. disease duration, dependency on activities of daily living). Furthermore, measures of burden, depression and stress were combined into a single variable of carer distress, therefore, they were unable to ascertain the relative contributions of predictors on specific outcomes [11].

This systematic review aims to identify potential gaps in the existing research literature by summarising and evaluating the evidence on all of the factors which predict psychosocial outcomes for carers of PwP. It is important to identify predictors, rather than just correlates, to explore the direction of associative relationships. Evidence for the effectiveness of psychosocial interventions for carers is limited and inconclusive [12]. Specifically, the current literature offers little understanding regarding the underlying causal mechanisms which explain their effectiveness. Theory application is an essential component of intervention design and evaluation [13-14], providing interventionists with an evidence-based framework that helps them identify the most appropriate targets for interventions (e.g. improving carer social support, knowledge or skills) and offering explanations for why an intervention might be effective or ineffective [14]. Therefore, the findings of this review will be used to build upon existing theoretical models of PwP carers, where possible.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15].

Inclusion criteria

Participants were unpaid carers of PwP. Outcomes were standardised or study-devised continuous measures of psychological, social, caregiving, coping or relationship outcomes. Study designs were included where the main aim was to identify predictors of carer psychosocial outcomes through statistical modelling. Studies that only considered correlations were excluded. Model building allows the

relative contribution of each variable to the outcome to be estimated by adjusting for the effects of confounding between variables. Publications were in peer-reviewed journals and written in English.

Exclusion criteria

Mixed-sample studies (including PwP carers as well as those from other disease groups) were excluded unless subsample analysis was carried out on the relevant participants. Studies that included predictors or outcomes measuring more than one construct were excluded (e.g. studies using factor analysis or combining depression and anxiety as a single predictor or outcome).

Search strategy

The electronic databases PsycINFO, EMBASE, AMED, BNI and CINAHL were searched using a combination of MeSH headings and keywords, such as 'Parkinson's disease', 'caregiver', 'burden', 'quality of life' and 'coping' (see Table 1 for example search strategy). Searches were completed up to 28th May 2013. There was no lower cut-off date for the inclusion of studies. However, initial electronic searching revealed no studies published prior to 1990 and a steady increase in the numbers of publications from 1996. For this reason, and to increase clinical relevance, searching was focussed on the period from 1996. Manual searches of publications (2008-2013) in the journals 'Parkinsonism & Related Disorders' and 'Movement Disorders' and reference lists for studies meeting the eligibility criteria were also carried out. The reference list searching had no date limit. Only one study prior to 1996 was identified and included in the review so we were confident that the electronic database searching identified all relevant articles.

Study selection

The titles and abstracts of the articles were screened for relevance by one author (KG). The full text articles retained were assessed independently for inclusion by two authors (KG, WKG) using a study selection form[1] and disagreements were resolved via discussion (see Figure 1).

Data extraction

Details on the participants, recruitment methods, study design, predictive factors, outcomes and key findings were captured independently by two authors (KG, WKG) using a structured data extraction form[1] which was piloted before use. The methodological quality of each study was assessed independently by the same authors against a modified version of the NICE methodology checklist for evaluating the risk of bias in prognosis studies [16]. The six criteria under which quality was judged were: 1) representativeness of the sample; 2) potential bias due to loss to follow-up; 3) predictors appropriately assessed; 4) outcomes appropriately assessed; 5) potential confounders accounted for; and 6) statistical analysis appropriate (see Table 3).

In addition, three authors (KG, WKG, AvW) independently assessed each study on their use of theory in statistical model building and whether their findings were used to refine existing theory. The choice of the variables investigated is crucial to the integrity of the statistical model and the validity of the conclusions drawn. Using a theoretical framework during study design and data analysis can help ensure that all potentially important variables are investigated and allow further testing of the accuracy and applicability of this theory across different contexts [14]. Any disagreements were resolved via discussion or consultation with a fourth author (PvS).

Data synthesis

Data synthesis was performed using narrative methods. Due to the diversity of outcomes and predictors included in the studies a meta-analysis was not possible.

Results

Design, setting, recruitment strategies and participants

Eighty-one full text articles were reviewed and 29 studies included in the review (see Figure 1; and Table 2 for key characteristics of each study). Table 3 provides an overall summary of the characteristics of the studies included. Three studies used a longitudinal design and twenty-six a cross-sectional design. Of the longitudinal studies, one [17] followed carers across two short time points (baseline and year 1). The other two studies [18-19] assessed three time-points in the same cohort across a ten-year period (baseline, year 2, year 10). Loss to follow-up at ten years was around 50%. Among those approaching participants by post who reported a response rate (n=5), the mean response rate was acceptable (54.6%; range 35.2-88%).

There was no consistent definition of carer across the reviewed studies and few gave clear inclusion or exclusion criteria. Among the studies reporting PwP-carer relationships (n=25), spouses dominated the samples (range 53.5-100%), with 14 studies recruiting spouses only. Other relationships included offspring, siblings, daughter/son in-laws, niece/nephews, friends and neighbours. All but one [20] of the carer samples were predominantly female. Details of the carer role, level of involvement or caring duties were rarely given. Only four studies [21-24] reported

duration of caregiving (range 3.8-8.1 years) and only one [22] reported daily caregiving hours (mean 3.3 hours).

Methodological quality assessment

As can be seen in Table 4, none of the studies provided sufficient information on the source population to judge whether studies were at risk of sampling bias and few compared respondents and non-respondents. None of the three longitudinal studies were able to demonstrate that their loss to follow-up was unrelated to key study characteristics and, therefore, the likelihood of attrition bias is high.

Most studies adequately measured potential predictors (n=21) and outcomes (n=26), sufficient to limit any potential measurement bias. However, only three studies [18, 25-26] made significant attempts to account for potential important confounders, including PwP and carer demographics, PwP disease factors and carer involvement.

Twenty-four studies met the methodological criteria for statistical analysis. Although some studies referenced psychological theory, notably O'Connor and McCabe [17], most variables included in the statistical models appeared to be chosen relatively arbitrarily and were not based on a pre-determined theory or framework. None of the studies attempted to test or refine psychological theory.

Key findings

The individual study results are summarised in Tables 5-8 and key findings in relation to the most common outcomes studied are summarised below.

Carer burden

Eighteen studies measured subjective carer burden, defined as "the extent to which caregivers perceived their emotional or physical health, social life, and financial status as suffering as a result of caring" [27, p 261]. The most commonly used

scales were Zarit's Caregiver Burden Inventory (ZCBI) [20, 23, 28-32], the Carergiver Strain Index (CSI) [26, 33] and Role Strain subscales of the Family Caregiving Inventory [18, 34-35].

Seven of the ten studies exploring PwP depression identified it as a predictor of carer burden [6, 20, 29, 33, 35-37]. Tanji et al. [33] found that depression was a predictor in their USA, but not their Japanese, sample. Leroi et al. [20] reported that depression only predicted greater carer burden in PwP with impulse control disorders. Two of the three studies exploring mental status identified it as a predictor of greater carer burden [30-31].

Across the three studies exploring neuropsychiatric symptoms, one study found a positive relationship [38], one identified a relationship but did not specify the direction of the relationship [29], and the last revealed that neuropsychiatric symptoms were not a predictor [6]. Greater carer depression (especially among spouse caregivers [30]) was a predictor in four studies [30-31, 33, 39] with only two studies failing to find a relationship [29, 38]. Poorer carer social support was found to be a predictor in two studies [23, 30], but not in another two [36, 39]. One study found a relationship in offspring, but not spouse, carers [30]. There was a lack of consistency regarding how social support was measured, which included social support from community and state or family [30], the family subscale of the perceived social support scale [23], social network contacts [39] and size of social network [36].

Studies consistently failed to find relationships between PwP or carer demographics and carer burden. Nine studies (see Table 5) explored PwP demographics, including age, gender, education and social class, but only one found a relationship with younger PwP age and male gender [40]. Findings in relation to PwP disease factors

and motor complications were inconsistent, although all four studies that investigated disease duration found it not to be a predictor.

Mental health

Mental health outcomes included measures of global mental health, depression, anxiety, stress and affect. Depression was measured using the Centre for Epidemiologic Studies-Depression scale [19, 24, 35], Beck Depression Inventory [6, 36], Geriatric Depression Scale [36], Hamilton Depression Scale [29, 41] and Montgomery-Åsberg Depression Rating Scale [29]. Medical Outcomes Study Mental Health Index [32] measured global mental health. Anxiety was assessed using Spielberger's State-Trait Anxiety Inventory [24] and stress with the Perceived Stress Scale [24]. The multiple affect adjective checklist (MAACL-R) measured depression, anxiety, positive affect, hostility and sensation-seeking in one study [42].

Of five studies that explored PwP depression as a predictor of carer depression, two found a positive relationship [6, 36], one reported a relationship but failed to report its direction [29] and two did not find a relationship [35, 41].

Findings regarding PwP neuropsychiatric symptoms, carer gender and carer social support as predictors of mental health were inconsistent (see Table 6). Again, there was a lack of clarity regarding how social support was measured. Konstam et al. [42] found a relationship between emotional social support and the depression subscale of the MAACL-R using statistical modelling. However, they failed to report the direction of the relationship or the measure of social support used.

In five studies that considered PwP and carer demographics (see Table 6), only the longitudinal study of Lyons et al. [19] noted a predictive relationship. Female carers demonstrated greater baseline and faster increase of depression. Likewise, PwP

disease factors and motor symptoms were only found to be predictive in two of six studies, with little or no consistency.

Quality of life and other outcomes

Studies investigating carer QoL or other outcomes are summarised in Table 7 and 8, respectively. A variety of generic and disease-specific QoL measures were used, including the SF-12v2 [26], SF-8 [43], GHQ-12 [6], GHQ-30 [36], PDQ-Carer [21], Scale of QoL of Caregivers (SQLC) [25] and the World Health Organisation QoL questionnaire [17].

Four studies explored the relationship between PwP and carer QoL using generic (e.g. SF-36) and disease-specific measures (e.g. PDQ-39) and a relationship was revealed for three studies [21, 26, 43]. Martinez-Martin et al. [25] did not find any relationships; however, PwP QoL was assessed by the carer using proxy measures. PwP dependency in activities of daily living (ADL) [6, 25], cognitive impairment [6, 25], carer age [21, 25] and years of caregiving [21, 26] were also identified as predictors but this relationship was found only once across each of the two studies. No studies identified a predictive relationship between carer QoL and age, gender, education, disease duration or disease stage.

Discussion

The included studies focused on three main outcomes: carer burden, mental health and QoL. The results presented can perhaps be best understood if viewed from the theoretical framework proposed by Goldsworthy and Knowles' stress-appraisal model [44]. Their work extends previous stress-appraisal models [11, 45-48] for use with PwP carers. They describe three main elements. First, the model proposes that

carer well-being is influenced by disease factors, which act as 'primary stressors', placing a steadily increasing and prolonged physical and mental strain on the carer. Second, the model acknowledges that individuals respond to disease differently, undergoing two levels of stress appraisal: (a) 'primary appraisal' of the PwP's need for care (as opposed to actual disability), whereby individuals evaluating the disease as highly threatening will provide a greater amount of care to the PwP (as measured by informal hours to caregiving); and (b) 'secondary appraisal' of the caregiving situation, as measured by carer burden. In the model, carer burden is hypothesised to mediate relationships of predictors with other outcomes (i.e. QoL), as well as being an outcome itself. Finally, the model proposes several mediators (e.g. perceived social support, quality of PwP-carer relationship, frequency of breaks) which ameliorate the effects of the primary stressor on secondary appraisal and other outcomes. The stress-appraisal model explained between 64% and 69% of the variance in carer QoL and burden, respectively [44]. However, it was tested on a relatively small sample size, 22% of which were paid caregivers. Despite these limitations, the model provides a useful starting point for theory testing and refinement (see Figure 2).

Primary stressors

In the studies identified, PwP depression, mental status and neuropsychiatric symptoms were consistent predictors of carer burden. PwP neuropsychiatric symptoms also predicted carer depression and QoL, though relatively few studies explored these outcomes. However, there was less support for the impact of PwP motor symptoms and more generic disability factors. Disease duration, disease stage, ADL and motor symptomology were among the most commonly explored variables but were rarely found to be predictors. Although this review cannot assess

the relative contributions of each predictor, psychological and non-motor symptoms appear to be more important than physical symptoms and levels of disability. This seems to contradict the findings of Lau and Au's meta-analysis [10], which found that PwP motor symptoms and dependency in activities of daily living were more strongly correlated with carer burden than PwP depression, disease stage, longer disease duration and cognitive impairment. Perhaps PwP disease factors are significant on bivariate analysis but no longer reach significance once more influential predictors are added on multivariate analysis. This hypothesis is supported by a hierarchical regression study of carer burden, included in this review [35], in which ADL was no longer significant once non-motor symptom measures (i.e. PwP depression, cognitive impairment) were added.

Relationships were found between PwP and carer factors within similar domains, that is, between PwP and carer depression and between PwP and carer QoL. Perhaps PwP QoL and depression act as primary stressors or, alternatively, these findings may be explained by interdependent dyadic relationship processes, whereby the cognitions, emotions and behaviour of one partner or relative is dependent on the same factors in the other [49].

Stress appraisal

Despite its likely importance as a confounding variable [50], only five studies explored carer involvement. Intensity of caregiving (informal hours and years of caregiving) was shown to be correlated with carer burden in Lau and Au's meta-analysis [10]. With regards to primary appraisal, informal hours of caregiving was found to be a predictor of carer burden in one out of two studies in this review but was not found to predict depression or QoL. Goldsworthy and Knowles reported that the effect of informal hours of caregiving on burden and QoL was mediated by

perceived social support and frequency of breaks, thereby perhaps explaining the inconsistent findings.

Furthermore, subjective measures of caregiving hours are open to participants' own interpretations of what constitutes 'caregiving' and offer little detail on the type of care given. Other measures of caregiving (e.g. caregiving experience, type of caregiving) did not predict outcomes, but these were generally poorly reported and measured. Further research should utilise validated measures which provide a more detailed understanding of the type and extent of carer involvement (e.g. 'amount of direct care' scale [7]). It would also be interesting to assess the PwP's perceptions of the care provided, as some carers believe they are giving greater support than the care recipient feels they are receiving [51].

Years of caregiving was found to predict QoL in one of two studies but did not predict carer burden or affect. However, as spouse carers dominated samples, years of caregiving is more likely to reflect disease duration (i.e. a primary stressor), rather than primary appraisal, which was only identified as a predictor once in this review. Pinquart and Sörenson [50] found that caregiving duration in carers of older adults was weakly associated with carer burden and depression. They explained this finding by arguing that psychosocial outcomes represents a U-shaped curve with greatest distress being at the midpoint of care as individuals adapt to their caregiving role over time.

Other models of stress and illness have suggested that coping strategies (i.e. one's cognitive, emotional or behavioural responses to stress or illness) are an important form of appraisal [47, 52-54]. Two studies examined coping strategies and found relationships with mental health but did not meet this review's inclusion criteria regarding participants studied [55] and analysis used [56]. It is unclear from the

evidence to date where this form of appraisal would be situated within the stress-appraisal model. One hypothesis would be that coping strategies are situated between primary and secondary appraisal (see Figure 2). Furthermore, these relationships may be bidirectional in that a perceived greater PwP need for care may determine the type of coping strategies chosen (e.g. help-seeking) and that greater carer involvement may also be the consequence of an individual's appraisal of their preferred coping style (e.g. problem-focused coping).

Few studies assessed variables that could be conceptualised as secondary appraisal. Carer burden was used as an outcome measure in 18 studies and only in one as a predictor, demonstrating a relationship with mutuality [57]. Perceived uplifts of caregiving, such as appreciating the closeness with the PwP, feeling useful, experiencing pride in handling crises, have also been shown to be important predictors of burden and depression [46, 50] but were not assessed by any of the studies.

Protective factors

Carer social support was identified as a predictor in half of the studies exploring carer burden. Promising findings were also found for mental health; however, only two studies explored this factor. Social support was identified as an important protective factor by Goldsworthy and Knowles in line with other stress and illness models [47, 52]. Social support may provide a *direct (main) effect*, whereby support promotes well-being, irrespective of whether stress is experienced, or an *indirect (buffer) effect* by which social support protects individuals from the negative effects of high stress [58]. In contrast, carer social support did not predict carer QoL across two studies. Perhaps the relationship between carer QoL and social support was mediated by carer burden (via secondary appraisal), a hypothesis supported by Goldsworthy and

Knowles [44]. However, there was little agreement across studies regarding how social support was measured and conceptualised and so results should be interpreted with caution. Interestingly, the two studies that conceptualised social support in terms of social contact or size of network failed to find any relationships with psychosocial outcomes. Perhaps *perceptions* of support, rather than the *actual* social support given, is influential.

Two longitudinal studies found that carer personality factors, including optimism and pessimism, predicted baseline depression [19] and carer burden at year 10 [18]. Furthermore, carers' perceptions of meaning in one's life (but not meaning specific to caregiving), sense of coherence and self-efficacy were all found to be predictors of at least one psychosocial outcome. It has also been argued that self-efficacy may serve as a form of primary appraisal in which individuals evaluate their ability to face, as well as deal, with the stressor [53, 59-60]. These factors were not included in Goldsworthy and Knowles' model but various conceptualisations have been included in general stress and illness models [52], as well as other carer models [47]. Introducing such constructs could help explain a greater proportion of the variance in psychosocial outcomes, thus improving the accuracy and applicability of this model (see Figure 2).

Additional variables

Although not included in Goldsworthy and Knowles' model [44], carer depression was a relatively consistent predictor of carer burden. Perhaps these are inter-related concepts or, alternatively, carer depression may act as a secondary stressor, adding to the burden experienced. It may be useful to introduce carer depression into future models (see Figure 2).

Carer demographics were rarely identified as a predictor and only one study found a significant relationship for PwP demographics, consistent with previous meta-analyses [10] and systematic reviews [61]. It is likely that such variables, alongside other characteristics such as relationship to PwP, provide moderating effects, rather than having a direct influence on psychosocial outcomes [50].

Methodological quality

The studies provided relatively low-level evidence for the predictors of carer psychosocial outcomes and demonstrated similar limitations to those identified in systematic reviews of carers for people with other conditions [61]. Furthermore, the use of theoretical models, to inform the design of studies and the interpretation of data, would have added substantially to the quality of most of the studies [13-14]. Such a theory-driven approach is lacking across the current literature but is needed to better understand which intervention components are needed to bring about changes in psychosocial outcomes and the factors which moderate intervention success [12].

The presence of sampling bias could not be established due to poor reporting of, and comparisons with, the source population. Samples were dominated by older, female spouses, which may reflect the older age of disease onset and prevalence bias towards males in the PwP population and the fact that spouses are the most common form of support. Samples were recruited mainly from medical settings or patient or carer support groups and were biased towards those experiencing mild to moderate disability. It will be of value to recruit younger and non-spousal carers and carers of institutionalised PwP, all of whom who may not be the primary carer but may nonetheless still face significant but different caregiver challenges [2, 62-63].

Longitudinal studies

Only three studies adopted a longitudinal design, so drawing conclusions regarding causation is not possible. Moreover, none of the three longitudinal studies met the methodological criteria relating to attrition bias. Further longitudinal studies are needed to identify potential causal factors. However, it is important to note that such studies can be costly and loss to follow-up can be a major limitation.

Limitations

Due to the diversity between studies and lack of theoretical modelling, a meta-analysis was not possible. Furthermore, electronic database searching was limited to studies published after 1996. However, the reference list searching was carried out without date limitations to ensure any key studies published prior to this date were captured. Finally, although the quality assessment tool has not been validated for use in cross-sectional studies of predictors, it was chosen based on widely-accepted quality criteria [64] and offered the most useful tool for assessing risk of bias as part of a narrative review.

Conclusion

Research into PwP carers has grown over the last 20 years and starts to acknowledge the essential role that carers play. This review is the first to systematically synthesise and evaluate the evidence on the factors that predict psychosocial outcomes in PwP carers. Its broad scope provides some support for existing theory and suggested areas for future research development. Methodological weaknesses in the studies identified and a lack of theoretical testing limits the extent to which conclusions can be drawn. However, there were some promising findings for PwP non-motor symptoms, QoL and carer depression, which may represent potential targets for future interventions.

Key areas for future research

- Better use of theoretical models in study design and data analysis can ensure all relevant predictors are identified and further our understanding of the psychological processes of change necessary for success in psychosocial interventions.
- Further longitudinal studies are needed to identify potential causal factors.
- It will be of value to recruit younger and non-spousal carers and carers of institutionalised PwP to better understand the experience of all who provide unpaid care or support to PwP.
- Use of validated measures assessing the type and extent of carer involvement.

Note [1]The study selection and data extraction form is available on request from the corresponding author.

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Contributions

Design/conception – Kate Greenwell, Anna van Wersch, Richard Walker. Literature and database search – Kate Greenwell. Data extraction – Kate Greenwell, William K. Gray. Methodological quality assessment – Kate Greenwell, William K. Gray, Anna van Wersch, Paul van Schaik. Writing of initial draft of the manuscript – Kate

Greenwell, William K. Gray. All authors critically revised and approved the final manuscript

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Figure captions

Figure 1.Identification of included studies

Figure 2. New conceptual model highlighting potential directions for future research

Table 1: Example search strategy for EMBASE

1	exp PARKINSON DISEASE/ OR Parkinson*.ti,ab
2	exp CAREGIVER/ OR Carer*.ti,ab OR Caregiv*.ti,ab OR “Care giv*”.ti,ab OR EXP FAMILY/ OR family.ti,ab OR families.ti,ab OR exp RELATIVE/ OR relatives.ti,ab OR exp SPOUSE/ OR spous*.ti,ab OR husband*.ti,ab OR wife.ti,ab OR wives.ti,ab OR partner*.ti,ab
3	Burden.ti,ab OR exp CAREGIVER BURDEN/ OR Strain.ti,ab OR exp QUALITY OF LIFE/ OR “Quality of life”.ti,ab OR “QOL”.ti,ab OR Distress.ti,ab OR psychosocial.ti,ab OR “social support”.ti,ab OR mutuality.ti,ab OR exp SOCIAL SUPPORT/ OR “well-being”.ti,ab OR “negative affect” OR “positive affect” OR meaning.ti,ab OR reward.ti,ab OR Coping.ti,ab OR Cope.ti,ab OR exp COPING BEHAVIOR/ OR impact.ti,ab OR consequence*.ti,ab OR adjust*.ti,ab
4	1 AND 2 AND 3
5	4 [Limit to: English Language and Publication Year 1996-Current]

Table 2: Characteristics of included studies

	Study characteristics						Carer characteristics		
Study	Country	Design	Sample size	Recruitment	Approached	PwP variables investigated	Mean age (years)	Female (%)	Spouse of the PwP (%)
Tanji et al. (2013) [33]	Japan & USA	CS	178	Medical setting	Medical/clinic	Yes	69.5 (Japan) 65.7 (USA)	NR	100
Morley et al. (2012) [21]	UK	CS	238	Community*	By post	Yes	68.2	74.4	92
Carter et al. (2012) [65]	USA	CS	74	Community*	Unclear	No	62	NR	80
Shin et al. (2012) [30]	South Korea	CS	91	Medical setting	Medical/clinic	Yes	66.4 (spouse) 45.8 (offspring)	50.0 (spouse) 53.7 (offspring)	54.9
Leroi et al. (2012) [20]	UK	CS	71	NR	Unclear	Yes	62.7	39.4	53.5
Shin et al. (2012) [31]	South Korea	CS	42	Medical setting	Medical/clinic	Yes	60.0	61.9	NR
Peters et al. (2011) [26]	UK	CS	704	Community*	By post	Yes	67.1	71.9	88.9
O'Connor & McCabe (2011) [17]	Australia	L	60	Community*	By post	No	68.8	NR	NR
Miyashita et al. (2011) [43]	Japan	CS	273	National register	By post	Yes	NR	NR	NR

Carter et al. (2010) [34]	USA	CS	65	Clinical trial database	Unclear	No	61.7	70.8	100
Sarandol et al. (2009) [29]	Turkey	CS	57	Medical setting	Medical/clinic	Yes	NR	59.6	61.4
McRae et al. (2009) [22]	USA	CS	70	Community*	By post	No	65.5	74.3	95.7
Lyons et al. (2009)[18]	USA	L	255	Clinical trial database	Unclear	No	63.7	69	100
D'Amelio et al. (2009) [38]	Italy	CS	40	Medical setting	Medical/clinic	Yes	63.6	NR	100
Tanji et al. (2008) [57]	USA	CS	96	Medical setting	Medical/clinic	Yes	63.7	66.7	100
Carter et al. (2008) [35]	USA	CS	219	Clinical trial database	Secondary data	Yes	64	71	100
Martinez-Martin et al. (2005) [25]	Spain	CS	57	Medical setting	Medical/clinic	Yes	58.8	66.7	73
Lyons et al. (2004) [19]	USA	L	311	Clinical trial database	Unclear	No	63	72	100
Marsh et al. (2004) [28]	USA	CS	50	Medical setting; community*	Secondary data	Yes	NR	NR	NR
Konstam et al. (2003) [42]	USA	CS	58	Medical setting	Medical/clinic	No	66.6	63.8	89
Caap-Ahlgren & Dehlin (2002) [39]	Sweden	CS	65	Medical setting	Medical/clinic	Yes	67	36.9**	89.2
Edwards & Scheetz (2002) [23]	USA	CS	41	Medical setting; community*	By post	Yes	66.8	68.3	100

Thommessen et al. (2002) [37]	Norway	CS	58	Longitudinal epidemiology study database	Secondary data	Yes	70.8	NR	100
Fernandez et al. (2001) [41]	USA	CS	45	Medical setting	Medical/clinic	Yes	NR	NR	100
Hooker et al. (2000) [24]	USA	CS	87	Medical setting; community*	Various methods	No	66.9	63.2	100
Aarsland et al. (1999) [6]	Norway	CS	58	Longitudinal epidemiology study database	Unclear	Yes	70.8	66	100
Wallhagen & Brod (1997) [32]	USA	CS	45	Medical setting; community*	Secondary data	Yes	69	68.9	100
Miller et al. (1996) [36]	UK	CS	54	Medical setting; community*	Unclear	Yes	65.6	NR	100
Calder et al. (1991) [40]	UK	CS	65	Community*	Unclear	Yes	NR	NR	95.4

Key: NR = not reported; CS = cross-sectional; L = longitudinal

*Examples of community recruitment include prevalence studies, patient or carer support groups, internet, newsletters, word of mouth.

Table 3. Summary of the key characteristics of the 29 studies included

World region	North America: 14 Europe: 11 (5 from the UK) Asia: 4 (2 from Japan, 2 from South Korea) Australia: 1 * One study included subjects from Japan and the USA
Recruitment strategy	Medical: 10 By post: 6 Secondary data analysis: 4 Mixed methods: 1 Not reported: 8
Ethnicity of carers (n = 7)	Range: 87.8-98.9% white
Co-habitation between carer and PwP (n = 15)	Range: 80.9-100%
Mean age of PwP (n = 21)	Range: 63.0-72.4 years
Mean disease duration for PwP (n = 15)	Range: 5.6- 12.2 years
Mean Hoehn and Yahr stage for PwP [66] (n = 10)	Range: 2.2-3.4

Table 4: Methodological quality assessment

		Meets criteria for methodological quality	Does not meet criteria for methodological quality	Unclear whether meets criteria for methodological quality
1.	The study sample represents the population of interest with regard to key characteristics, sufficient to limit potential bias to the results	None	None	All studies (none of the studies described their sample in relation to the wider population of PwP)
2.	In longitudinal studies, loss to follow-up is unrelated to key characteristics (that is, the study data adequately represent the sample), sufficient to limit potential bias	None	3 studies [17-19] (Only three studies were longitudinal)	None
3.	The potential predictor of interest is adequately measured in study participants, sufficient to limit potential bias	21 studies [6, 17-21, 24-26, 29-30, 32-33, 35-37, 39-41, 43, 65]	5 studies [22-23, 28, 34, 57]	3 studies [31, 38, 42]
4.	The outcome of interest is adequately measured in study participants, sufficient to limit potential bias	26 studies [6, 17-26, 28-36, 39-43, 65]	2 studies [37, 57]	1 study [38]
5.	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the predictor of interest	3 studies [18, 25-26]	25 studies [6, 17, 19-24, 28-41, 43, 57, 65]	1 study [42]
6.	The statistical analysis is appropriate for the design of the study, limiting potential for the presentation of invalid results	24 studies [6, 17-26, 28, 30-35, 37, 39, 42-43, 57, 65]	None	5 studies [29, 36, 38, 40-41]

Table 5: Key findings for studies of carer burden

	Significant predictors of greater caregiver burden	Predictors investigated, but not found to be significant
PwP demographics	• Younger age [40] • Male gender [40]	• Age [6, 30-31, 33, 37, 39] • Gender [6, 26, 29-31, 33, 37, 39] • Education [6, 29-31] • Social class [40]
PwP disease factors & motor symptoms	• Greater functional impairment [36]* • Greater difficulties with ADL [6, 23, 28] • Reduced ability to self-care [40] • Greater disease stage [38-39] and perceived disease severity [32] – Greater disease stage predicted carer burden at year 10 but not faster increases in burden over this period [18] • Greater dopaminergic load in PwP with impulse control disorders [20] • Greater falls in the Japanese (not USA) sample [33] • Greater motor symptomology in offspring but not spouses [30] • Poorer QoL (mobility and social support subscales only) [26]	• Disease duration [33]**[6, 26, 36, 39] • Disease stage [33]** [6, 30-31, 40] • ADL [29-31, 33, 35, 37] • Motor symptoms [6, 28-29, 31, 38] and complications [30-31] • QoL [39] • Gait, speech, freezing, fluctuation and postural instability [33] • Comorbidity [29, 33] • Medication use [33]**
PwP non-motor symptoms	• Greater behavioural disturbance [40] • Greater cognitive impairment [6, 35, 37] (Specifically in PwP with apathy [20]) • Greater depression [6, 35-37] (Specifically in USA, but not Japanese sample [33] and PwP with impulse control disorders [20] – Relationship direction not reported [29] • Greater neuropsychiatric symptoms [38] – Relationship direction not reported [29] • Presence of psychosis [28] • Poorer mental status [31] (Specifically in spouses [30])	• Behavioural abnormalities [29] • Depression [28, 38-39] • Cognitive impairment [28-31, 33, 38, 40] • Presence of dementia [40] • Anxiety [36] • Neuropsychiatric symptoms [6] • Mental status [29]
Other PwP factors	• Less perceived control over symptoms [32]	• Perceived control over disease progression [32] • Sense of coherence [39]

		• Whether receiving public home care [6]
Carer demographics	• Gender (relationship direction not reported) [26] • Younger spouse age group (40-55 years) predicted greater carer burden, compared to older spouses (70+ years) [34] • Wives demonstrate greater carer burden at year 10 and faster increases in carer burden over this period, compared to husbands [18]	• Age [18, 31, 33, 39] • Gender [31, 34, 39] • Education [29, 31, 33] • Years of marriage [33] • Occupational status [29, 33] • Cohabitation with PwP [31]
Carer involvement	• Greater hours spent caring per week [26]	• Daily caregiving duration, whether carer has had previous experience and additional caregiving [29] • Years of caregiving [26]
Carer psychological factors	• Greater depression [30-31, 33, 39] (Specifically in spouses [30])	• Depression [29, 38] • Anxiety [29] • Psychological well-being [23]
Protective factors	• Poorer social support [23] (specifically from community and state in offspring caregivers [30]) • Less help from others (USA sample only) [33] • Poorer baseline mutuality predicts burden at year 10 (Specifically, in wives but not husbands) [18] • Less sense of coherence [39] • Less baseline optimism and greater baseline pessimism predicts greater carer burden at year 10 [18]	• Marital satisfaction [23] • Social support [36, 39] • Receiving assistance during caregiving [29]
Other carer factors	• Poorer spouse physical health [34]	• QoL [30-31] • Physical health [29] • Comorbidity [33]

Key: *Measured using more than one scale, only one significant; **These were significant on bivariate analysis but were excluded on the multivariate analysis due to multicollinearity. Note: The study by D'Amelio et al [38] was particularly poorly presented and it was often unclear which variable was used as the outcome, with the terms 'distress', burden' and 'stress' being used inter-changeably.

Table 6: Key findings for studies of carer mental health

	Significant predictors of poorer carer mental health*	**Predictors investigated, but not found to be significant**
PwP demographics		• Age [6] • Gender [6, 29] • Education [6, 29]
PwP disease factors & motor symptoms	• Longer disease duration [41] • ADL (relationship direction not reported) [29]**	• ADL [6, 35] • Age of disease onset [41] • Disease duration [6, 36] and stage [6, 36, 41] • Perceived severity does not predict mental health [32] • Motor symptoms [6, 29, 41] • Comorbidity [29] • Functional impairment [36]***
PwP non-motor symptoms	• Greater cognitive impairment predicts carer depression [35] • Greater neuropsychiatric symptoms (Specifically aberrant motor behaviour) [6] • Greater depression [6, 36] – Relationship direction not reported [29]	• Cognitive Impairment [6, 29, 41] • Presence of hallucinations, delusions, urinary and bowel incontinence and sleep disturbances [41] • Neuropsychiatric symptoms, mental status and behavioural abnormalities [29] • Depression [35, 41] • Anxiety [36]
Other PwP factors	• Less perceived control over symptoms predicts poorer mental health [32]	• Perceived control over disease progression does not predict mental health [32] • Whether receiving public home care [6]
Carer demographics	• Being female predicts greater baseline depression [19] • Females have faster increases in depression levels over a ten-year period [19]	• Gender did not predict depression, stress or anxiety [24]**** • Age, education and income does not predict affect [42]

		• Education and occupational status [29]
Carer involvement		• Daily caregiving duration, whether carer has had previous experience caregiving and additional caregiving [29] • Type of caregiving, years of caregiving and caregiving limitations do not predict affect [42]
Carer psychological factors		• Anxiety [29]
Protective factors	• Lower levels of optimism and higher levels of pessimism [19] • Greater existential vacuum (i.e. lack of meaning) [42] • Less existential transcendence and greater perceptions of personal choice/responsibility predicts greater anxiety [42] • Greater existential vacuum (i.e. lack of meaning) predicts greater hostility and dysphoria [42] • Greater purpose predicts greater positive affect and sensation-seeking [42] • Emotional social support (relationship direction not reported) [42]	• Social support [36] • Receiving assistance during caregiving [29] • Finding meaning through caregiving does not predict affect [42]
Other		• Physical health [29] • Health comparison does not predict affect [42]

Key: * The outcome measure is depression, unless specified; **Measured using more than one scale, only one significant; ***Measured using more than one scale; ****Age and carer involvement were also included in the model as potential confounders but the findings were not reported for these variable

Table 7: Key findings for studies of carer quality of life

	Significant predictors of poorer carer quality of life	Predictors investigated, but not found to be significant
PwP demographics		• Age [6, 25] • Gender [6, 25-26] • Education [6]

PwP disease factors & motor symptoms	• Greater difficulty with ADL [25]
	• Poorer QoL [43]
	  • Mobility and cognitive impairment subscales of PDQ-39 [21]
	  • Mobility and social support subscales of PDQ-39 (direction not reported) [26]
		• Disease duration [6, 25-26, 36] and stage [6, 25, 36]
		• Age of disease onset [25]
		• Functional impairment [36]*
		• ADL [6]
		• QoL (including carer proxy ratings) [25]
		• Motor symptoms [6, 25] and complications [25]

PwP non-motor symptoms	• Greater neuropsychiatric symptoms (Specifically delusions and agitation) [6] • Greater cognitive impairment [6] • Greater depression [36]	• Anxiety [36] [25] • Depression [6, 25] • Mental state [25] • Cognitive impairment [25]
Other PwP factors		• Whether receiving public home care [6]
Carer demographics	• Less income at baseline predicted poorer QoL at year 1 [17] • Older carer age [21]	• Age, habitat and education [25] • Gender [25-26] • Economic pressure at baseline did not predict QoL at year 1 [17]
Carer involvement	• Greater years of caregiving [21]	• Hours spent caring per week [26] • Years of caregiving [26] • Continuity of care [25]
Psychological factors	• Poorer mood at baseline predicted poorer QoL at year 1 [17]	
Protective factors		• Marital relationship satisfaction and social support satisfaction at baseline did not predict QoL at year

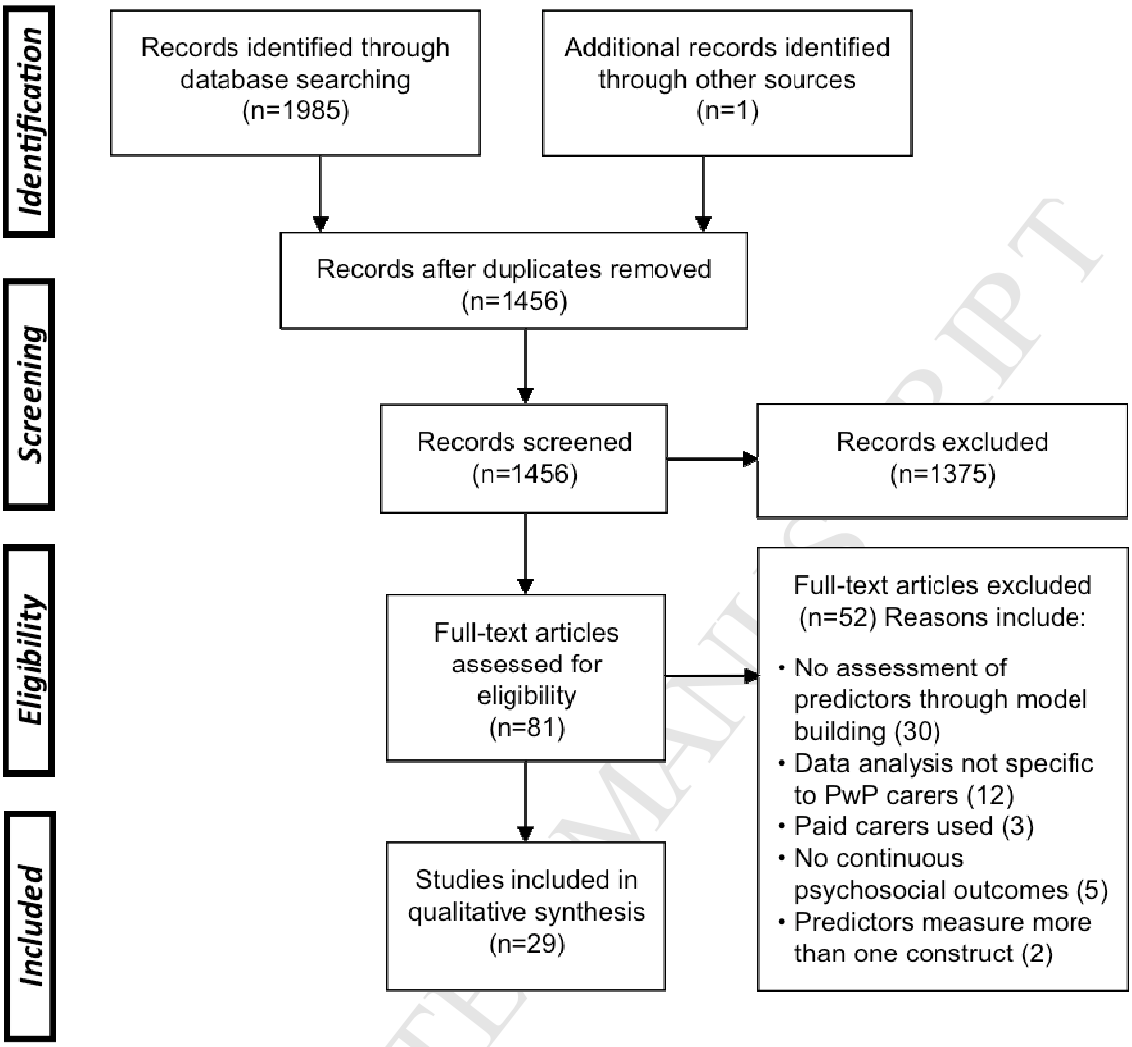
	1 [17] • Social Support [36]

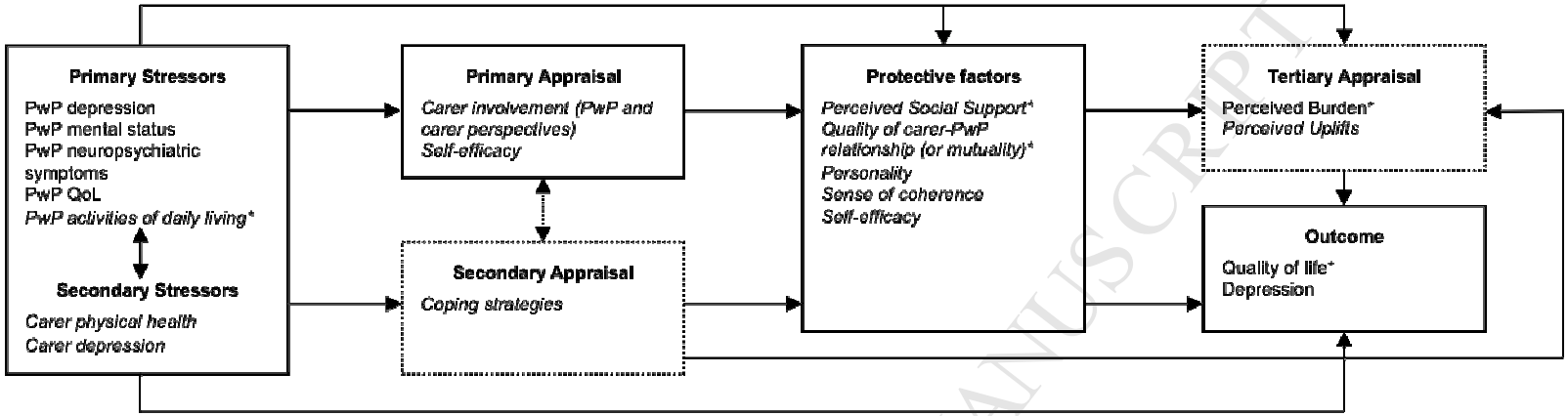
Key: *Measured using more than one scale

Table 8: Key findings for studies with other carer outcomes

Outcome measure	Significant predictors of outcome	Predictors investigated, but not found to be significant
Revised UCLA Loneliness Scale [22]	• Less years of carer education, poorer carer physical health and poorer self-efficacy predicts greater carer loneliness	• PwP age, disease stage, disease duration, subjective memory complaint • Carer age and perception of interactions with PwP
Mutuality Scale	• In final model, only greater carer burden predicted poorer mutuality [57]	• PwP age, disease duration*, disease stage, ADL*/**, motor symptoms* and complications*, mental status, speech and gait impairment, postural instability*, dyskinesia, tremor, rigidity, bradykinesia, motor fluctuations*, facial expression, urinary incontinence*, cognitive impairment, mental health, comorbidity and QoL [57] • Carer gender [34, 57] • Carer age, years of marriage, comorbidity, mental health and physical and mental* QoL [57] • Carer age group and physical health [34]
Preparedness [34]		• Carer gender, age group and physical health
Rewards of meaning [34]	• Younger spouse age group (40-55 years) predicted lower levels of rewards of meaning, compared to older spouses (70+ years)	• Carer gender and physical health
Marwit and Meuser Caregiver Grief Inventory - Short Form [65]	• Greater cognitive impairment predicted greater pre-death grief	• Hallucinations, depression and anxiety • Presence of motor fluctuations

Key: *These were significant on bivariate analysis but were excluded on the multivariate analysis due to multicollinearity; **Measured using more than one scale





Notes: Variables marked in italics and dotted lines require further investigation. Variables marked with an asterisk were also included in Goldsworthy and Knowles' stress-appraisal model [46] and boxes with dotted lines represent modifications to its conceptual framework.

Highlights

- Patient non-motor symptoms and quality of life widely predicted psychosocial outcome
- Greater carer depression consistently predicted poorer psychosocial outcomes
- Demographics and disease factors were consistently found not to be predictors.
- Confident conclusions could not be drawn regarding the most important predictors
- Future research should build upon psychological theory to improve understanding

Appendix I. PRISMA Statement Checklist [15]

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5 & 22 (Table 1)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Fig 1; pg 21
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 2; pg7-9, 23-25
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 4; pg 9-10, 25
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 5-8; pg 8-11, 28-33
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19