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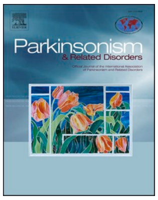

Review article

Effect of deep brain stimulation on caregivers of patients with Parkinson's disease: A systematic review

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ABSTRACT

Background: Caregivers of patients with Parkinson's Disease (PD) often provide important support in the pre- and postoperative phase of Deep Brain Stimulation (DBS). DBS-associated changes of patient-functioning may affect caregiver wellbeing and impact the support system. Factors influencing caregiver-wellbeing under these circumstances are incompletely known.

Objective: to systematically review studies of sufficient methodological quality on the impact of DBS on caregivers of PD patients.

Methods: using PRISMA guidelines, major databases were searched up to May 2020. Five subcategories were identified: Caregiver burden, Caregiver cognitive and psychiatric functioning, Caregiver Quality of Life (QoL), Marital Satisfaction/Conflicts, and Caregiver Satisfaction. Quality was assessed using an in-house checklist.

Results: 293 studies were identified; 12 were ultimately included. Caregiver burden, psychiatric and cognitive functioning and QoL remained relatively unchanged. Results on marital satisfaction/conflicts were contrasting: an increase in marital conflicts despite improved relationship quality scores DBS. Caregiver satisfaction with surgery was low with 50–58% of caregivers being disappointed with DBS outcomes. Concerning caregiver related factors: a higher preoperative caregiver QoL, younger age, lower scores on psychiatric rating scales, and more favourable preoperative relationship quality scores, were associated with better caregiver wellbeing. A favourable patient-profile includes younger age and age-at-onset, shorter disease duration, lower medication requirements, and lower scores on psychiatric rating scales.

Conclusion: Although most patient- and caregiver-related subdomains remained unchanged after DBS, dissatisfaction among caregivers and marital problems may constitute a large risk for a well-functioning patient-caregiver dyad. Early recognition of potential problem situations may improve post-DBS care for both patients and caregivers.

1. Introduction

Parkinson's Disease (PD) is a progressive neurodegenerative disorder with rapidly increasing incidence rates worldwide, and is characterized by several debilitating motor- and non-motor symptoms [1]. Patients suffering from medication-induced motor complications may be eligible for Deep Brain Stimulation (DBS), a surgical option which may relieve motor complications and improve patients' Quality of Life (QoL) [2]. DBS is a complex intervention, which may abruptly change patients' situation and functional status [3]. Not only may this affect the way PD patients interact towards their caregivers, it also requires an adaptation of behaviour of the caregiver towards the patient [4,5].

A good caregiver support system is crucial in PD management [6,7]. Caregiver burden has been studied previously in PD, both in the general PD population [6–9], and with specific regard to DBS patients [10–15]. Caregiver burden was reported similar in both the general PD population, and in caregivers of DBS patients [10]. Severity of PD symptoms, psychological distress and disabilities negatively impacts both QoL and

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burden in caregivers of PD patients [16,17]. In turn, distress among caregivers negatively influences the wellbeing of PD patients [9], leading to an undermining interaction within the patient-caregiver dyad (e.g. patient-spouse, patient-child, etc.). Aside from the impact on burden [12,14], QoL [5,14], and marital satisfaction [5], effective support provided by caregivers represents substantial health-economic benefits, such as through reduced demand of nursing home facilities [7,9].

The interaction between caregivers and PD patients is particularly important in DBS candidates, as patients may be heavily dependent on a good social support system especially shortly after surgery [18,19]. However, studies have shown that 50–58% of caregivers express negative valuations after DBS [5,20], which may account for increases in marital dissatisfaction and conflicts [4,5]. Early recognition of potential problem situations and modifiable factors influencing caregiver burden and/or satisfaction after DBS may provide targets for supporting a functional patient-caregiver dyad. There is currently insufficient information on the effect of DBS on caregivers of PD patients, as well as on factors influencing the caregivers valuations. The aim of this study was therefore to systematically review the impact of DBS on caregivers of PD patients, and to identify potential targets to improve caregiver valuations after DBS.

2. Method

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines is used in this systematic review [21]. Potentially relevant articles were searched on PubMed, Embase, Web of Science, COCHRANE and Emcare using suitable keywords (see appendix A).

Eligibility was initially assessed by screening titles and abstracts by two independent reviewers (MMvH and VJG) on May 6st 2020, based on the following inclusion criteria: 1. Cohorts with idiopathic Parkinson's disease, essential tremor, or dystonia, 2. Intervention: DBS, 3. Observational data on caregivers/spouses/partners available, 4. Original research article, 5. Adult patients and caregivers, 6. $N \geq 3$ and 7. article in English. The quality threshold for inclusion was based on an in-house checklist for quality assessment (range 0–22, higher scores reflect lower quality, see appendix B); low-quality studies (score < 11) were excluded [22,23]. Data extraction was performed using piloted forms (see appendix C). Inclusion for full-text screening was based on mutual agreement (MMvH and VJG), or decided after discussion of discrepancies and re-reading of the pertinent sections until mutual agreement was reached. Cohen's kappa for interrater agreement (two reviewers) was calculated. The articles were a posteriori categorized in the following five domains: 1. Caregiver burden, 2. Caregiver cognitive and psychiatric functioning, 3. Caregiver QoL, 4. Marital Satisfaction/Conflicts, and 5. Caregiver Satisfaction.

3. Results

The search strategy performed on May 6st 2020 yielded 293 articles (Fig. 1), which lead to 30 articles selected for full-text evaluation (Kappa = 0.832). After reading of the full-texts, 12 articles were included (Table 1).

3.1. Caregiver burden

Six studies reported data on caregiver burden (Table 2) [10–15]. Caregiver burden after STN DBS was relieved in one study [14], unchanged in four studies [10–14], and not reported in one study [15]. One study found no significant linear difference between Zarit Burden Inventory (ZBI) scores at baseline and one year follow-up (i.e. 2 points improvement on an 88-point scale) [14], however improvement was reported in the same cohort upon evaluating ZBI changes differently by using predefined cut-off scores [24] (no p-value reported) [14]. Another study searched for overload in caregivers (applying a cut-off value of 47 on the ZBI scale): 54,5% of caregivers experienced overload, similar for both a DBS and non-DBS group [10].

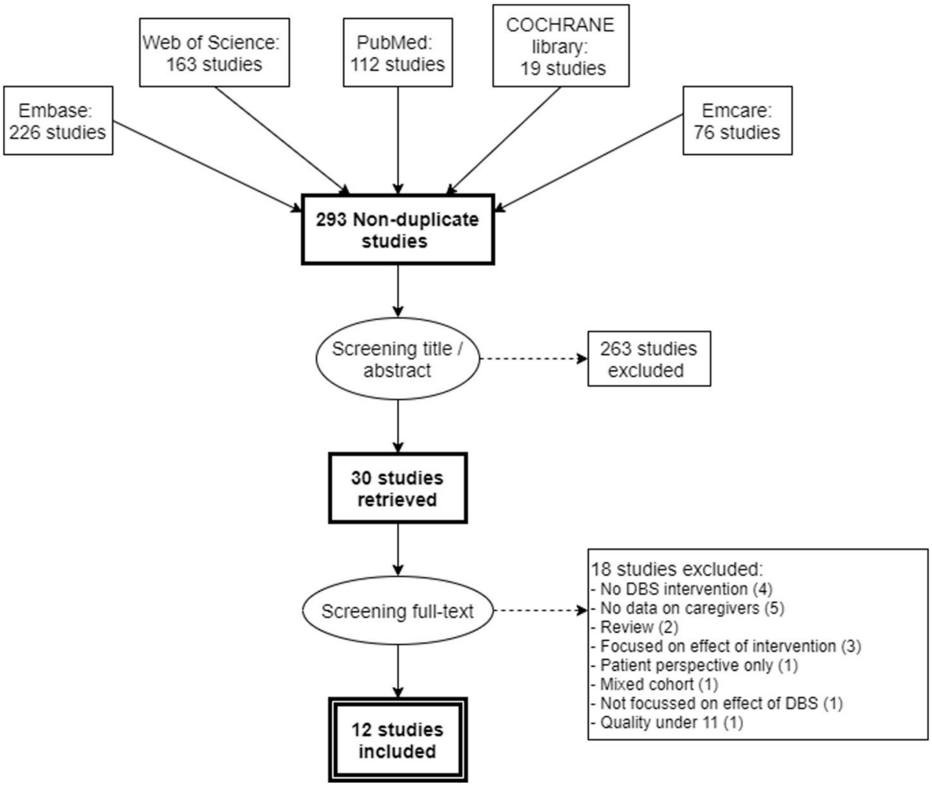

Fig. 1. PRISMA flow diagram.

Table 1
Included studies.

Author + year	Centre	Design	N patients	N caregivers	Age caregivers	Domain of interest	QI	Comments
Baumann-Vogel 2020 [28]	University Hospital Zurich, Switzerland	Cross-sectional	56	56	?	Marital satisfaction	*	
Crespo- Burillo 2018 [10]	Hospital Universitario Miguel Servet, Spain	Cross-sectional	22	22	63.4 ± 10.8	Caregiver burden, Psychiatric functioning	***	Compared DBS with other treatment options
Lewis 2014 [25]	University of Cologne, Germany	Longitudinal follow-up	28	28	56.11 ± 14.66	Psychiatric functioning	***	
Lewis 2015 [20]	University of Cologne, Germany	Longitudinal follow-up	25	25	60.00 ± 10.92	Psychiatric functioning, QoL, caregiver satisfaction	**	
Lewis 2014 [26]	University of Cologne, Germany	Longitudinal follow-up	27	27	56.26 ± 14.91	Psychiatric functioning	**	Not all caregivers were partners
Lezcano 2004 [27]	Hospital of Cruces, Baracaldo, Spain	Longitudinal follow-up	14	?	?	QoL	*	
Mosley 2018 [11]	Asia-Pacific Centre for Neuromodulation, Australia	Longitudinal follow-up	64	64	58 ± 8,4	Caregiver burden, Marital satisfaction	***	1 caregiver was the adult child of the patient
Mosley 2019 [15]	Asia-Pacific Centre for Neuromodulation, Australia	Longitudinal follow-up	10	10	57.0 (35–70)	Caregiver burden, Marital satisfaction, Caregiver satisfaction	*	
Oyama 2014 [12]	NPF QII Clinical study, USA	Cross-sectional	275	275	?	Caregiver burden, Psychiatric functioning	**	Matched case-control
Schüpbach 2006 [5]	Centre d'Investigation Clinique, Paris, France	Longitudinal follow-up	29	24	?	Psychiatric functioning, Marital satisfaction, Caregiver satisfaction	*	
Soileau 2014 [13]	University of Michigan Medical School, USA	Longitudinal follow-up	12	?	?	Caregiver burden	*	
Soulas 2012 [14]	Henri Mondor Hospital, Créteil, France	Longitudinal follow-up	26	26	62,7 ± 8,8	Caregiver burden, Psychiatric functioning, QoL	**	

QI: Quality Index (max. 22 points, higher scores indicate lower risk of bias), * 11–13 points (medium quality), ** 14–16 points (high quality), *** ≥17 points (very high quality).

Table 2
Caregiver burden.

Author + year	Instrument	Follow-up duration	Change in symptoms?	Factors of influence[a]		Comments[b]
Crespo-Burillo 2018 [10]	ZBI	n.a.	No difference			ZBI cut-off scores [24]: moderate to severe burden.
Mosley 2018 [11]	ZBI	0.5 years	No difference	Caregiver-reported empathy (empathy quotient)	+	ZBI cut-off scores [24]: little to no burden
				Patient depressive symptoms (BDI II)	–	
				Patient impulsiveness (Barrat Impulsiveness scale)	–	
				Patient set shifting and prepotent inhibition (Hayling Category A Errors)	–	
				Patient hypersexuality (QUIP-RS)	–	
				LEDD	–	
				Stimulation-related psychiatric symptoms	–	
Mosley 2019 [15]	Semi- structured interviews	1 year	Not reported	Patient stimulation-related psychiatric symptoms	–	
				Patient neuropsychiatric symptoms	–	
Oyama 2014 [12]	MCSI	n.a.	No difference	Time since surgery	+	
				Patient age	–	
Soileau 2014 [13]	CBI	0.5 years	No difference	Cognition (MoCA)	0	
				Motor function (UPDRS III)	0	
Soulas 2012 [14]	ZBI	1 year	Improved using cut-off scores. No sig. linear difference.	Patient age	–	ZBI cut-off scores(24): mild to moderate burden.
				Motor function (UPDRS III)	0	
				Caregiver age	0	
				Age-at-onset	0	
				Patient QoL (PDQ-39)	0	

BDI: Becks Depression Inventory; CBI: Caregiver Burden Inventory; LEDD: Levodopa equivalent daily dose; MCSI: Multidimensional Caregiver Strain Index; MoCA: Montreal Cognitive Assessment; PDQ-39: Parkinson's Disease Questionnaire 39; QUIP-RS: Questionnaire for Impulsive-Compulsive disorders in PD Rating Scale; UPDRS: Unified Parkinson's Disease Rating Scale; ZBI: Zarit Burden Inventory.

[a] - significant negative influence, + significant positive influence, 0 no significant influence.

[b] ZBI cut-off scores according to Stagg B, Larner A. Zarit Burden Interview: Pragmatic study in a dedicated cognitive function clinic. Progress in Neurology and Psychiatry. 2015; 19.

Factors with a significant positive influence on caregiver burden included the caregiver-reported empathy of the patient [11], and time since surgery [12]. Patient-reported symptoms of depression [11] and higher patient-age [12,14] influenced caregiver burden negatively. Other factors with a negative influence on caregiver burden included patients' attentional impulsiveness, impaired set-shifting and prepotent inhibition, symptoms of hypersexuality, higher Levodopa equivalent daily dose (LEDD) [11], higher age of the caregiver and a younger age-at-onset [14], and stimulation-related psychiatric symptoms (rated by psychiatrists and neurologists) [11,15]. Change in motor function did not correlate with change in caregiver burden [13,14]. One study using semi-structured interviews reported that neuropsychiatric symptoms were of greater influence on caregiver burden than motor symptoms [15].

3.2. Caregiver cognitive and psychiatric functioning

Six studies described caregiver cognitive and psychiatric functioning (Table 3) [5,10,14,20,25,26], the latter being either symptoms of anxiety [10,20], depression [5,10,14,20,25,26], or apathy [20]. In general, caregiver cognitive and psychiatric functioning was relatively unchanged after DBS.

Depressive symptoms were relieved in one study [14], demonstrated by a decrease in the number of depressed caregivers one year after surgery (23% of caregivers improved (n = 6) vs. 15% of caregivers who worsened (n = 4)). However, in the ‘improved’ group, four out of six caregivers had a depression at baseline (BDI-II > 18), suggesting presence of a regression-to-the-mean phenomenon [14]. In contrast, one study reported deterioration of caregivers depressive symptoms, with confirmed depression in eight out of twenty-four caregivers two years after a successful DBS surgery (preoperative characteristics were not provided) [5]. Four studies did not find a difference between either a DBS and a non-DBS group in a cross-sectional setting [10], or between baseline BDI-II scores and scores at 1 year follow-up [20,25,26]. One study showed an initial decrease in depressive symptoms of two points on the BDI-II scale, from preoperative conditions to 3 months follow-up. However, scores rose again to pre-DBS levels when assessed one year after surgery [20].

Caregivers symptoms of anxiety were reduced three months after DBS, but returned to baseline levels at one year follow-up in one study [20]. Symptoms of anxiety were not significantly different in a group of caregivers of patients who received STN-DBS, compared to caregivers of patients who received other treatments in a cross-sectional setting [10]. Caregiver cognition, and apathy scores [25,26] did not significantly change between baseline and follow-up [20].

The strongest and only significant predictor for depression at 1-year follow-up was the baseline BDI score [14]. No factors influencing other psychiatric domains or cognition were reported.

3.3. Caregiver QoL

Three studies reported results on caregiver QoL (Table 4) [14,20,27], with inconsistent results. Caregiver QoL was reported to improve significantly by 68% two years after STN DBS [27], whereas patients perceived a 62% improvement of QoL [27]. In contrast, a different study described a non-significant deterioration in caregiver QoL. Moreover, based on relative change indices, more caregivers deteriorated after DBS than improved (SF36 Physical Health: 15% of caregiver improved vs. 35% deteriorated; SF36 Mental Health (MH): 23% of caregivers improved vs. 42% deteriorated) [14]. A third study divided caregivers into two groups based on postoperative semi-structured interviews at 3 months follow-up and at one year follow-up: a ‘positive statements’ group and a ‘negative statements group’ based on responses given by the caregivers. The ‘positive statements’ group showed a significant improvement in the SF-36MH component scores, whereas the ‘negative statements’ group did not [20].

Factors with a positive influence on caregiver QoL were the caregivers preoperative QoL (SF-36MH) [14], as well as giving ‘positive statements’ during a postoperative semi-structured interview [20]. Factors with a negative influence on caregiver QoL included caregivers’ age [20], and duration of PD [14]. Patients’ mood (BDI and AES) had a negative influence on to caregiver QoL [20].

3.4. Marital satisfaction/conflicts

Four articles reported data on marital satisfaction and conflicts

Table 3

Caregiver cognitive and psychiatric functioning.

Author + year	Domain (instrument)	Follow-up duration	Change in symptoms	Factors of influence[a]		Comments
Crespo- Burillo 2018 [10]	Anxiety (HADS-A)	n.a.	No difference			
	Depression (HADS-D)		No difference			
Lewis 2014 [25]	Cognition (MMSE)	1 year	No difference			
	Depression (BDI-II)		No difference			
Lewis 2014 [26]	Cognition (MMSE)	1 year	No difference			
	Depression (BDI-II)		No difference			
Lewis 2015 [20]	Anxiety (STAI-S)	1 year	Improved at 3 months; returned to baseline at 1 year			
	Apathy (AES)		No difference			
	Cognition (MMSE)		No difference			
	Depression (BDI-II)		Improved at 3 months; returned to baseline at 1 year			
Schüpbach 2006 [5]	Depression (diagnosed by psychiatrist)	2 years	Deterioration			
Soulas 2012 [14]	Depression (BDI-II)	1 year	Improved	Caregiver baseline BDI	+	Applying a cut-off (BDI-II > 18) to classify depression
				Caregiver age	0	
				Caregiver sex	0	
				Patient age	0	
				Age-at-onset	0	
				Motor function (UPDRS III)	0	
				Patient QoL (PDQ-39)	0	
				Disease duration	0	
				LEDD	0	

AES: Apathy Evaluation Scale; BDI: Becks Depression Inventory; HADS-A/D: Hospital Anxiety and Depression Scale; LEDD: Levodopa equivalent daily dose; MMSE: Minimal Mental State Examination; PDQ-39: Parkinson’s Disease Questionnaire 39; STAI: State Trait Anxiety Inventory; UPDRS: Unified Parkinson’s Disease Rating Scale.

[a] - significant negative influence. +Significant positive influence, 0 no significant influence.

Table 4
Caregiver QoL.

Author + year	Instrument	Follow-up duration	Change in symptoms	Factors of influence[a]		Comments
Lewis 2015 [20]	SF-36	1 year	Positive group: partially improved (MH) Negative group: no difference	Caregiver age Mood patient (BDI and AES)	– –	Divided the population into two groups based on valuations during semi-structured interviews
Lezcano 2004 [27]	SQLC	2 years	Improved			
Soulas 2012 [14]	SF-36	1 year	Non-significant deterioration. Based on relative change indices, more caregivers deteriorated than improved.	Caregiver preoperative SF-36 MH Disease duration	+ –	

AES: Apathy Evaluation Scale; BDI: Becks Depression Inventory; SQLC: Scale of Quality of Life for Caregivers; SF-36: Short-Form health survey 36 (MH: Mental Health component).
[a] - significant negative influence, + significant positive influence, 0 no significant influence.

Table 5
Marital Satisfaction/conflicts.

Author [b] year	Instrument	Follow-up duration	Change in symptoms	Factors of influence[a]		Comments
Baumann- Vogel 2020 [28]	PFB-K, DCI	n.a.	Marital satisfaction: Improvement Marital conflicts: Increase of conflict behaviour			
Mosley 2018 [11]	RQI	0.5 years	Deterioration	Caregiver burden	–	Poorer relationship quality results in higher burden
Mosley 2019 [15]	Semi-structured interviews	1 year	Caregivers felt “helpless and overwhelmed” after DBS			
Schüpbach 2006 [5]	Unstructured interviews	2 years	Deterioration			50% of couples reported marital conflicts prior to surgery

DCI: Dyadic Coping Interview; PFB-K: short version of the partnership Questionnaire; RQI: Relationship Quality Index.
[a] - significant negative influence.
[b] Significant positive influence, 0 no significant influence.

(Table 5) [5,11,15,28], with seemingly contrasting results on an increase in relationship quality paralleled with a reduction in marital satisfaction. One study reported an increase in relationship satisfaction in 40% of the couples after 17 months follow-up, compared to a decrease in quality in 14% of the couples. Of the 40% improved couples, 29% were deemed to have ‘mild improvement’ and 11% ‘strong improvement’. All couples with deterioration were deemed ‘mild deterioration’ [28]. Couple dyadic coping increased for the subdomains communication of stress, supportive dyadic coping, delegated dyadic coping, and shared dyadic coping. In contrast, 39% of couples showed an increase of conflict behaviour, whereas 15% of the couples showed a decrease [28].

A reduction of marital satisfaction after DBS was found in two other studies [5,11]. One study reported a negative correlation of the Relationship Quality Index and caregiver burden (i.e. poorer relationship quality resulted in higher caregiver burden) [11]. Semi-structured interviews revealed changes in the relational dynamic, enduring even after the recovery period, resulting in feelings of helplessness and overwhelmed by DBS-induced changes in patients [15]. A different study reported worsening in marital life in 50% of couples (25% reported improvement, another 25% reported no change in marital life) after a follow-up of 18–24 months. In six out of twenty-four cases, patients rejected their partners whereas in eleven out of twenty-four cases the partner rejected the patient [5].

3.5. Caregiver satisfaction

Three studies reported data on caregiver satisfaction (Table 6) [5,15,20], defined as either satisfaction with results of DBS surgery [5], and satisfaction with the postoperative situation [15,20]. Overall, studies report negative valuations for caregiver satisfaction.

One study showed that above 50% of caregivers considered STN-DBS to negatively impact themselves (at 3 months follow-up: 10 out of 24 caregivers described the outcome of DBS to be negative, 8 were positive and 6 were indeterminate; at 1 year follow-up 11 out of 20 caregivers were negative, and 9 were positive). Four out of six caregivers who were ambiguous at three months follow-up transferred to the ‘negative’ group at 1 year [20]. A different study showed that 58% of caregivers were disappointed by the outcome of the DBS operation at eighteen months to

Table 6
Caregiver satisfaction with surgery.

Author + year	Instrument	Follow-up duration	Change in symptoms	Factors of influence[a]		Comments
Lewis 2015 [20]	Semi-structured interviews	1 year	Negative	Caregiver age Caregiver QoL (SF-36)	– –	
Mosley 2019 [15]	Semi-structured interviews	1 year	Positive			Caregivers stated that despite complications of DBS, they would make the same choice for surgery again
Schüpbach 2006 [5]	Unstructured interviews	2 years	Negative			

DBS: Deep Brain Stimulation; SF-36 Short Form Health Questionnaire 36; QoL: Quality of Life.
[a] - significant negative influence, + significant positive influence, 0 no significant influence.

twenty-four months follow-up [5].

In contrast, one study stated that despite neuropsychologic complications of DBS, both caregivers and patients would make the same decision to undergo the surgery again, because of the significant motor improvement and lower required dose of medication [15]. Older age of the caregiver and worse caregiver SF-36MH scores had a significant negative influence on their satisfaction scores at one year follow-up [20].

4. Discussion

Caring for patients with PD may be challenging and accompanies several lifestyle and relational changes [9]. DBS is known for its substantial improvement in the wellbeing of patients [2], however, its impact on PD caregivers is unclear. The aim of this study was therefore to systematically review the effects of DBS on caregivers of PD patients, and to identify potential targets to improve caregiver valuations after DBS.

Caregiver burden did not significantly change in the majority of studies, regardless of design, follow-up, or baseline caregiver burden [10–14]. These results suggest that despite substantial motor improvement, burden in caregivers of PD patients is not relieved after DBS which in turn may explain unfavourable satisfaction scores expressed by caregivers after DBS [5,20]. One study stated that this could be explained by the fact that patients were happy with their “new” life, although the caregiver had trouble adjusting to this altered lifestyle [26]. Nevertheless, both patient and caregivers reported that they would opt for DBS again [15], likely due to the symptomatic improvements in patients induced by DBS. The significance of the results on caregiver burden appear dependent on the type of analysis [14]. As caregiver burden did not worsen either, it may be argued that DBS maintains preoperative caregiver burden whereas caregiver burden might have deteriorated without DBS, although this constitutes a counterfactual contrast.

The results on caregiver QoL are varying in both directions [13,20,27]. The results appear influenced by the choice of QoL instrument (the specific scale SQLC demonstrated an improvement, whereas the more generic SF-36 scale did not), and type of analysis [14]. Moreover, all three studies were limited by small sample sizes (data on 14–26 caregivers, respectively).

Psychiatric functioning among caregivers, including symptoms of depression, anxiety, and apathy, appears relatively unchanged after STN DBS, although some inconsistency was observed on caregiver depression [5,14]. However, the study that reported relief of depression used a BDI cut-off of 18 (out of 63 points), indicative of minimal-mild depression vs. moderate-severe depression [29], whereas the study that reported deterioration among caregivers assessed the presence of depression through evaluation by a psychiatrist.

Only one study quantified the number of marital conflicts after DBS [5], although an association with pre-existing marital problems is suggested. Two theories underlying marital conflicts were suggested: 1. the patient rejects the partner after feeling ‘cured’, which lead to a feeling of overprotection by the caregiver who has become accustomed to this state of dependency, or 2. the caregiver rejects the patient because the patient improved ‘insufficiently’ to the caregivers liking [4,5]. Alterations in the in the patient-caregiver dynamic after DBS are likely to be sudden and potentially disruptive of a previously stable situation. Another reason could be that patients changed (e.g. behaviourally) after surgery, which could influence marital satisfaction as well. Furthermore, it was suggested that the moral obligation of the caregiver to remain with their partner after the patients physical dependence was reduced after DBS [5]. Nevertheless, relationship quality and caregiver burden were negatively correlated in a longitudinal study [11], suggesting in turn that a reduction of caregiver burden following DBS may have beneficial effects in marital satisfaction as well. The discrepancy in results on marital satisfaction can be explained by differences in measurement instrument, i.e. questionnaires aimed at marital satisfaction [28] vs. semi-structured interviews [5] focussing on marital conflicts, the latter allowing more room for exploration of (negative) valuations. Moreover, Baumann-Vogel et al. applied a cross-sectional post-DBS design with questionnaires on valuations before surgery, which carries the risk of recall bias [28].

Several factor influencing caregiver wellbeing have been identified (Fig. 2). Although most factors were evaluated only once and results require further validation, a favourable caregiver-profile with regard to caregiver wellbeing appears to include higher preoperative caregiver QoL [14,20], younger age [14,20], lower scores on psychiatric rating scales [14], and more favourable valuations of the relationship quality [11]. A favourable patient-profile with regard to caregiver wellbeing appears to include younger age [11,14], younger age-at-onset [14], shorter disease duration [14,20], lower LEDD [11], and lower scores on psychiatric rating scales [11,14,20]. Awareness of these favourable patient- and caregiver-profiles may benefit outcomes in both groups. For example, more extensive preoperative education including the caregiver may lead to improved informed decision making on DBS, including awareness of potential outcomes of caregivers and the effect of DBS on patient-caregiver dyads, rather than the impact on the patient only. Furthermore, through early identification of patients and caregivers “at risk”, counselling and possibly interventions can be offered to counteract any negative effects [11]. We speculate that knowledge of these influencing factors may also help manage patients’ and caregivers’ expectations prior to surgery [30].

Several interventions have been described that may benefit caregivers of DBS patients. In the study by Baumann-Vogel et al., 27% of the couples reported a need for professional help following DBS, indicating a need for specilized support during the post-DBS period [28]. A study by Flores et al. (which did not met our inclusion criteria) described a psychoeducational programme for patients and caregivers to counteract maladjustment after DBS, with an emphasis on familial- and couple relationships. A decrease in anxiety symptoms after the programme was seen in caregivers, after two years follow-up. However, burden did not differ between the psychoeducation group and the control group. Simultaneously, patient characteristics that significantly changed after the psychoeducational program were a decrease in depression at both one and two years after surgery, and a lower anxiety score at one year after surgery [31]. A different study by Haahr et al. developed a series of intervention-meetings with a specialized DBS nurse after surgery, resulting in significant improvements in adjusting to life after DBS for both patients and caregivers, as well as adjusting to coping with PD in general [32]. Similarly, a randomized controlled trial conducted in a general PD population showed that a patient-education programme administered to patients and caregivers alike yielded improvements in the domains ‘psychosocial problems’ and ‘need for help’ for the caregivers [33].

Limitations of the available studies include the small sample sizes of most longitudinal studies. Most results were not replicated or verified, which is particularly impeding in a setting with these small sample sizes. Furthermore, follow-up time of one year was used in most studies, and in only two studies [5,27] was two years follow-up used. Given that PD is a chronic progressive disease, long-term results of DBS on caregivers beyond two years follow-up is required from future studies, although disease progression may play an important role during long-term follow-up. Moreover, severe dysfunction such as potential development of dementia or admission to nursing-home facilities after DBS, are not discussed in any of the reviewed studies. Furthermore, although the search strategy included studies on caregivers of patients with tremor and dystonia, no studies reported results for these patient groups and results cannot be extrapolated to other DBS-indications. Differences in DBS target, i.e. subthalamic, thalamic, or pallidal DBS, was not studied although this may effect behavioural differences post-DBS with consequences for the patient-caregiver dyad as well. Several other factors that may have differed between studies, but still have a potential influence,

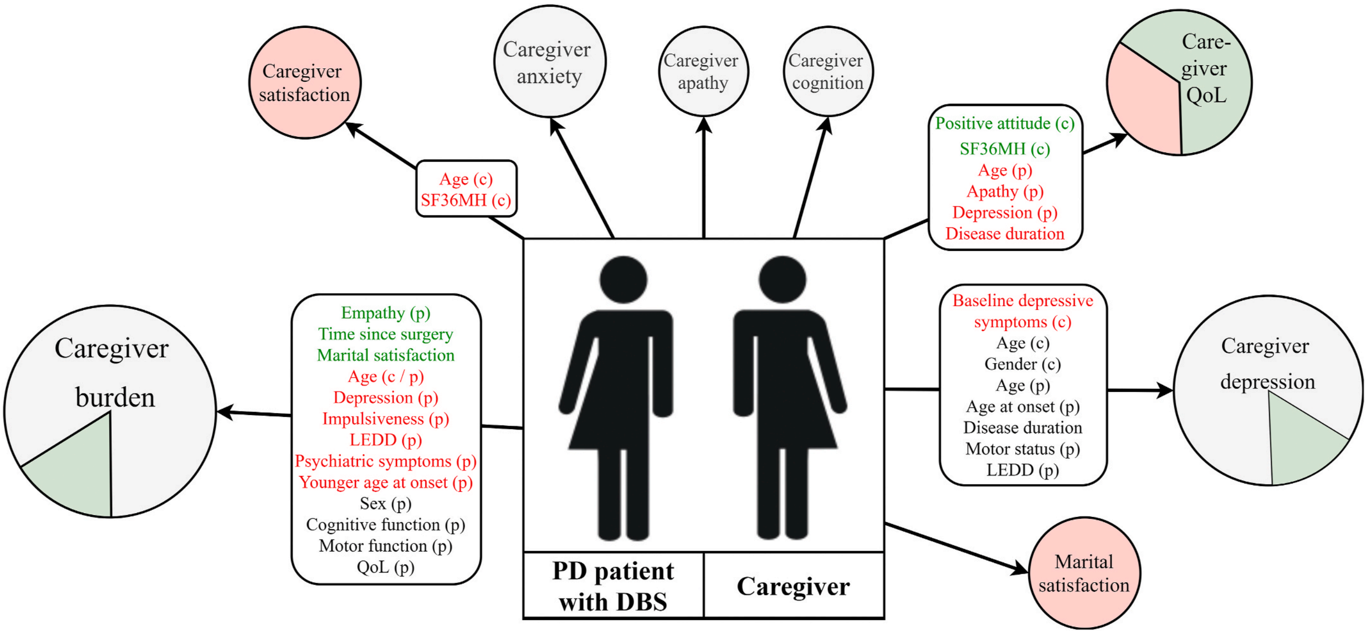

Fig. 2. Patient- and caregiver profiles with regard to caregiver wellbeing.

were not studied, such as living environment (at home or institutionalized, social-, and cultural differences). A previous systematic review reported that social functioning inconsistently improved after DBS [34], a factor with probable influence on the patient-caregiver-dynamic as well which was not studied in this context. Moreover, in the selected studies the caregivers were mostly partners, although this is not necessarily always the case and differences in the relationship between caregiver and patient may be of influence as well.

Strengths of this review include the systematic approach and the use of the PRISMA guidelines. The quality assessment allows the reader to weigh the contribution of each study individually. Limitations of this review include the lack of a quantitative synthesis of the results, due to the large heterogeneity in study-design, reporting and scale used to assess caregiver well-being. Furthermore, adjudication in case of disagreement on study-inclusion was based on discussion and mutual agreement between the original reviewers, rather than by a third reviewer. Reasons for exclusion during the title- and abstract screening were not systematically recorded.

Given the small sample size and lack of verification of findings, future research should focus on modelling caregiver wellbeing after DBS in larger, longitudinal settings in order to provide further insight into potentially modifiable factors to ultimately improve both caregiver- and patient wellbeing, as well as studying previously described interventions for caregivers in this context. Furthermore, PD is currently the only studied disorder in relation to both DBS and impact on caregivers and future studies should investigate other diseases for which DBS is an approved intervention as well.

In conclusion, we have provided a systematic overview of studies on the impact of DBS on caregivers of PD patients. Although caregiver burden, caregiver psychiatric functioning and caregiver QoL appear relatively unaffected by DBS at group-level, caregivers can display a dissatisfaction with the outcome of DBS, as well as reporting of marital conflicts. Awareness of factors influencing caregiver wellbeing after DBS is crucial for maintaining a good social support system and is beneficial to both patients, caregivers, and the patient-caregiver dyad.

Outer circles indicate the studied caregiver domains (red: negative impact of DBS on caregiver domain; green: positive impact; grey: no change; multicolored circles indicate discrepancy between studies; size of the circles reflect the number of studies with results for the pertaining domains). Factors of influence are denoted in the middle boxes, either patient-related factors (p) or caregiver-related factors (c). Red font indicates a significant unfavourable impact; green font indicates a significant favourable impact; grey font indicates no significant impact.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2020.09.038.

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