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ORIGINAL COMMUNICATION

Patient-centered integrated healthcare improves quality of life in Parkinson's disease patients: a randomized controlled trial

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Abstract

Introduction Improving quality of life (QoL) is a key issue when dealing with Parkinson's disease (PD). Integrative care shows potential to achieve improvements in QoL. Here, we analyzed whether a community-based, open-label, integrated approach improves QoL in PD patients.

Methods PD patients were screened for eligibility and evaluated by a university-based PD specialist, a PD nurse, and a general neurologist at a local practice. Patients were randomly assigned to a control group (CG), receiving standard German neurological treatment including a baseline assessment and follow-up visit at 6 months, or an interventional group (IG) who received an individually tailored therapy plan and additional home visits. Patients and investigators were not blinded for either intervention. Primary outcome analysis compared the differential change of PDQ-39 from baseline to 6-month follow-up between CG and IG. Between-group changes in mood, motor/non-motor functioning, and cognition were secondary outcomes.

Results 300 patients were included and randomized equally to IG and CG. 132 IG and 125 CG patients had a valid PDQ-39 at follow-up and qualified for the modified ITT analysis. PDQ-39 improved more in IG compared to CG [2.2 points (95% CI − 4.4 to 0.1); $p = 0.044$]. Likewise, change scores between IG and CG favored IG for UPDRS III ($p < 0.001$, mean change 3.3, 95% CI − 4.9 to − 1.7) and PD-NMS ($p < 0.001$, mean change 11.3, 95% CI − 17.1 to − 5.5).

Conclusions Data show that an integrated approach, compared to regular PD care, improves QoL as well as motor and nonmotor PD symptoms over 6 months. Future studies need to address the cost–benefit ratio and whether positive effects can be maintained beyond intervention.

Keywords Parkinson · Integrated care · Multidisciplinary · Allied health · Quality of life

Introduction

Parkinson's disease (PD) is a complex disorder that causes motor and non-motor symptoms. It affects both the patient and the caregivers [9], leading to a severe reduction in QoL.

Reduced QoL is monitored with clinical rating measures, and the PDQ-39 is among the recommended scales established by the International Parkinson and Movement Disorder Society [8, 11]. An annual increase of about 2–2.5 points per year in the PDQ-39 [7, 23] is reflected by an increase of approximately 2 points in the UPDRS [14] and results in increasing annual costs for health care [20].

In recent years, the concept of PD as a disease with a dominant motor symptom complex has evolved towards a multifaceted syndrome with different pathologies [2]. The individual course of the disease varies accordingly among

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patients, and therapy has to be tailored individually, considering the individual's needs and priorities [2].

The German healthcare system offers PD patients access to community-based outpatient neurological care, as well as health care support including physiotherapy, speech therapy and occupational therapy. However, uniform interdisciplinary team care approaches have not been developed. Furthermore, the "interface" between inpatient and outpatient management to date remains unsatisfactory, there is no established communication network to ensure that patient treatments are coordinated.

Here, we conducted a randomized controlled clinical study to test the hypothesis that an integrated patient-centered healthcare approach, combining the expertise of a community-based general neurologist, a hospital-based movement disorder specialist and a specially trained PD nurse, will—compared to the standard neurological practice model—result in an improved QoL for PD patients.

Materials and methods

Study design

This study was designed as a randomized controlled clinical study with two treatment arms and a follow-up period of 6 months in the greater area of Cologne, Germany.

The Cologne Parkinson Network (CPN) formed the CPN study group, consisting of a movement disorders specialist, who also worked as a consultant neurologist at the University Hospital of Cologne (UHC), Department of Neurology, 25 community-based neurologists working at their local practice, and a PD nurse.

The trial was conducted between 01/02/2012 (first patient first visit) and 07/27/2015 (last patient last visit) and was approved by the local ethics committee of the medical faculty of the University of Cologne (No. 11-233).

Participants

1400 PD patients were screened for their eligibility by community neurologists and presented in quarterly joint CPN consultations to the movement disorder specialist and the PD nurse. Patients were included when meeting the following criteria: clinical diagnosis of PD according to the UK Brain Bank criteria, ability to complete the study questionnaires in German, and age between 25 and 85 years. In addition, the following exclusion criteria were applied: unstable medical condition as a co-morbidity, living at a distance of more than 60 km away from the UHC, major depression (BDI-2 > 30 points), and cognitive decline (PANDA < 14 points). All patients gave written informed consent.

Randomization and masking

Qualifying patients were randomly assigned in a 1:1 ratio to either the intervention group (IG) or control group (CG). Research staff without clinical or research involvement in the study performed randomization using randomization lists with a randomized allocation sequence. Because the IG had access to the PD nurse through home visits and medication changes during the study, neither patients nor study team was blinded to treatment allocation.

Procedures

In the CG, patients were included in the study only during the quarterly joint CPN consultations, which took place at the community neurologists' office, and continued standard German neurological treatment. This included visits to the local neurologists practice about every 3 months (baseline, 3, 6 months). Once included, the PD nurse obtained questionnaires (PDQ-39, PD-NMS, BDI-2) and surveyed clinical parameters (e.g. UPDRS III) at baseline and every 3 months in the regular ON-state. Patients had access to regular physiotherapy, occupational or speech therapy. As there is a lack of structured and/or available PD-specific psychotherapeutic or cognitive training programs in the greater area of Cologne, we did not recommend this on a regular basis. Access to therapies and medication was the same for both treatment arms. For a detailed overview of all procedures, see Table 1.

The IG treatment additionally included the development of an individual treatment plan, regular home visits of a PD nurse (every 3 months or, whenever necessary, on short notice) and a telephone hotline. This resulted in dynamic and highly individualized therapies. Individual treatment plans were reviewed every 4 weeks and adapted according to individual patients' needs. In both groups, alterations of drug therapy were implemented according to the guidelines of the German Society of Neurology [4]. Furthermore, the PD nurse coordinated the therapeutic pharmacological intervention with the program of speech therapists or physiotherapists. This allowed rapid therapeutic modifications to be made, as needed.

Outcomes

The comparative change of the PDQ-39 as a measure for QoL [11], from baseline to 6-month follow-up between CG and IG, was set as the primary outcome parameter. The PDQ-39 includes eight subdomains with items for mobility, activities of daily living, emotional well-being, stigma, social support, cognitions, communication and bodily

Table 1 Overview of procedures

Procedure	Part of CG	Part of IG	Acting team member
Regular Parkinson's consultation hours (every 3 months)	Yes	Yes	Community neurologist, movement disorder expert, PD nurse
Individual treatment plan (based on recommendations of community neurologist, movement disorder expert, PD nurse)	No	Yes	Community neurologist, movement disorder expert, PD nurse
Home visits	No	Yes	PD nurse
Telephone hotline	No	Yes	PD nurse
Therapeutic modifications due to assessment of PD nurse, feedback of patients, feedback of therapists	No	Yes	Community neurologist, movement disorder expert, PD nurse

Table 2 Overview of time points and according assessments

Test	Baseline	Follow-up I (after 3 months)	Follow-up II (after 6 months)
PDQ-39	X	X	X
H&Y	X	X	X
UPDRS III	X	X	X
NMSS	X		X
BDI-2	X		X
PANDA	X		X
Medication	X	X	X

discomfort. Higher levels of impairment are reflected by a higher scoring. An individually clinically relevant difference over 6-month time corresponds to a change of the PDQ-39 of 1.6 points [10]. Changes in mood (Beck Depression Inventory, BDI-2), motor (United Parkinson's Disease Rating scale, Part III, UPDRS-III) and non-motor functioning (Non-motor Symptom Score, NMS-Score) and cognition (Parkinson Neuropsychometric Dementia Assessment, PANDA) between baseline and 6-month follow-up between groups were evaluated as secondary outcome parameters (see also Table 2). Daily medication was converted to the levodopa equivalence dose according to published conversion rates [16]. As safinamide has no published conversion rates, the equivalence calculation for amantadine was used. Outcome parameters were obtained at baseline, 3 and 6 months.

Details of hospital admissions (reason for admission, length of stay) were assessed by detailed interviews with the patients either during consultation hours in the joint consultation or home visits. In cases of uncertainty about the medical circumstances of the admission, or lack of details (e.g. regarding the length of the hospital stay), either the admitting hospital or family doctors were contacted and a discharge summary was reviewed.

Patients of the IG were asked after 6 months about their overall satisfaction with their individualized treatment. The score ranged from 1 = very disappointed to 10 = completely satisfied. Patients of the CG were not asked about their satisfaction as these patients did not receive the dynamic therapeutic regimen.

Statistical analysis

The sample size calculation was based on published data on the PDQ-39 in patient populations with a mean disease duration of about 8 years [1, 21]. These data showed a mean PDQ-39 of 25 (SD 8) points. To detect a relevant effect size of 0.4, i.e. 40% of the standard deviation, with 80% power at two-sided significance level 0.05, the *t* test for independent samples requires 200 evaluable patients (100 patients per treatment arm). Moreover, to ensure subgroup analyses and to account for a drop-out rate of up to 15%, we planned to include 300 patients.

Continuous variables were summarized by mean ± standard deviation and qualitative variables by count (percentage). Continuous outcomes were evaluated over time using mixed models for repeated measures (MMRM) with fixed terms for baseline value, group, time and an interaction group × time (unstructured variance-covariance matrix). Differences between groups and time points were derived from estimated marginal means and tested by pairwise contrasts. Conditional on these variables any missing values were assumed to have occurred at random (MAR condition).

Calculations were done with the software SPSS Statistics (Version 24; IBM Corp., Armonk, NY, USA).

Monitoring

To ensure data quality, the Cologne Centre for Clinical Studies (ZKS Cologne), an independent clinical research organization, monitored 30% of the data. The data quality was rated as extremely high by the ZKS Cologne with less than 1% findings (two queries with a discrepancy of less than 5%).

The study was registered in the German Register for Clinical studies (DRKS00003452).

Results

A total of 1400 patients were screened for eligibility and 300 patients were included and agreed to participate in the study between January 2, 2012, and July 27, 2015 (see Fig. 1). The 1100 screened patients who did not participate did not fulfill the inclusion criteria ($n = 823$; age, distance to UHC, co-morbidities, demented, depressed) or were not interested in or did not see a need for an ongoing multidisciplinary care program ($n = 277$). The 300 interested and qualifying patients were randomly assigned to the IG and CG (150 per group). In total, 257 patients (132 patients in the IG and 125 patients in the CG) completed the study with a follow-up at 6 months (14% drop-out rate).

From a clinical perspective, patients in both groups were comparable in terms of motor symptoms (UPDRS III), disease duration, or LEDD. Likewise, demographic details such as sex or age did not vary significantly across groups (see Table 3).

Primary outcome

PDQ-39 significantly improved in the IG compared to the CG over the 6-month period ($p = 0.044$). The mean group difference as a change from baseline over 6 months was 2.20 points (95% CI − 4.4 to − 0.1). The interaction between mean group change and the effects of time/group revealed a significant influence of both effects ($p = 0.006$, $F = 7.739$), suggesting that the finding was influenced by both treatment and time. The PDQ-39 remained stable over the first 3 months in both groups ($p = 0.642$, mean group difference as a change from baseline over 3 months = 0.5 points, 95% CI − 1.6 to 2.5; see also Table 4 and Fig. 2). At all, 53% of patients in the IG improved at least 2.2 points over the 6-month period.

Regarding the subscores, the further analysis revealed relevant improvements of the IG between baseline and 6-month follow-up in the domains emotional well-being (mean group difference 2.6 points, $p = 0.03$), stigma (mean group difference 2.3 points, $p = 0.038$), communication (mean group difference 1.8 points, $p = 0.131$) and physical discomfort (mean group difference 4.3 points, $p = 0.044$).

Secondary outcomes

For motor symptoms, there was a significant reduction in UPDRS part III over the first 3 months in the IG ($p < 0.001$), and a significant between-group difference ($p = 0.003$). Over the 6-month period, UPDRS-III significantly improved in the IG compared to the CG ($p \leq 0.001$). The mean group difference as a change from baseline over 6 months was 3.30

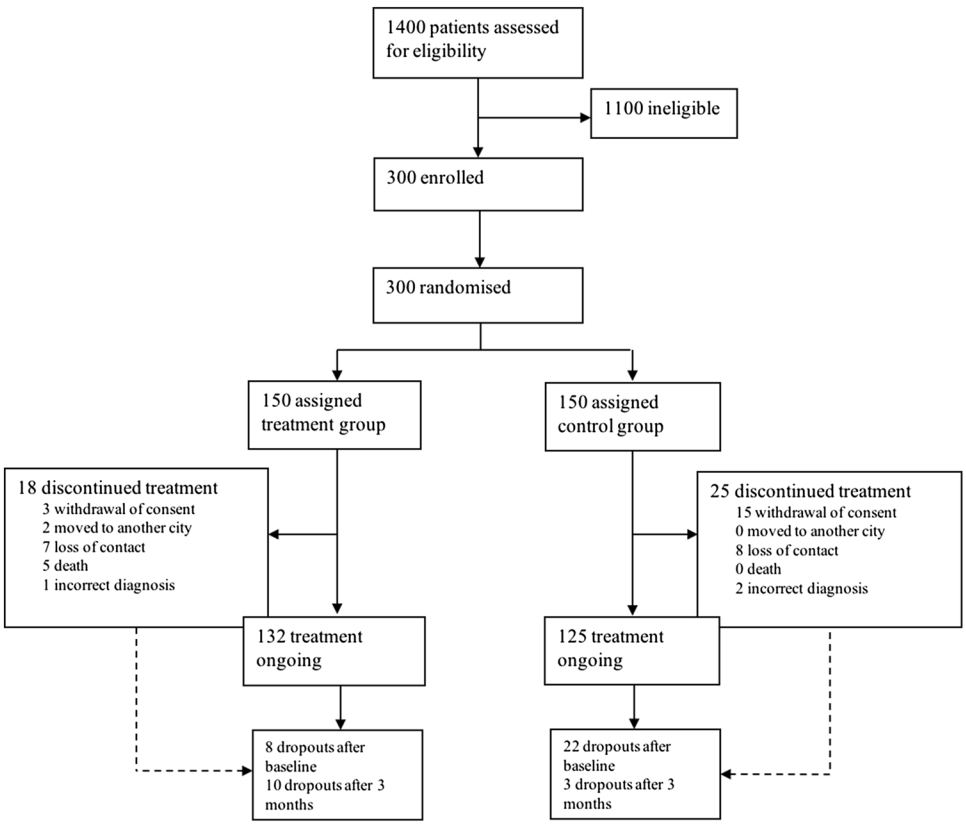

Fig. 1 Trial profile according to CONSORT

Table 3 Baseline characteristics IG and CG

Outcome parameter	Intervention group (mean and SD)	IG (*n*)	Control group (mean and SD)	CG (*n*)	*p* value
Age (years)	69.8 ± 8.4	131	69.9 ± 7.8	132	0.924
Women/men		47/85		52/80	0.518
Disease duration/time since diagnosis (years)	6.2 ± 6.2	126	5.5 ± 5.2	124	0.716
Hoehn and Yahr stage	2.5 ± 0.8	132	2.6 ± 0.8	125	0.687
Primary outcome: PDQ-39 total score	26.0 ± 14.8	132	27.7 ± 15.6	125	0.407
Subscale mobility	32.1 ± 26.6	132	31.9 ± 24.3	125	0.882
Subscale activities of daily living	27.9 ± 23.6	132	28.9 ± 23.2	125	0.661
Subscale emotional well-being	27.3 ± 20.9	132	31.9 ± 19.6	125	0.072
Subscale stigma	17.4 ± 16.1	132	19.6 ± 20.2	125	0.815
Subscale social support	14.2 ± 19.6	132	14.5 ± 18.7	125	0.561
Subscale cognition	30.9 ± 19.6	132	33.3 ± 21.1	125	0.436
Subscale communication	22.0 ± 18.8	132	2.9 ± 21.1	125	0.927
Subscale bodily discomfort	36.0 ± 23.0	132	39.2 ± 23.4	125	0.266
Secondary outcomes					
UPDRS III	28.3 ± 9.1	132	28.0 ± 8.7	125	0.938
PANDA	24.7 ± 3.8	131	24.7 ± 3.5	125	0.795
BDI-2	12.0 ± 8.2	132	12.6 ± 7.3	125	0.266
NMS	53.9 ± 29.6	132	62.3 ± 34.6	125	0.057
Daily LEDD	612.9 ± 431.3	132	612.4 ± 390.6	125	0.659
Other					
Medication use in %					
Levodopa	34%	132	34%	125	0.921
Dopamine agonist	30%	132	31%	125	0.885
COMT inhibitor	9%	132	9%	125	0.927
MAO B blocker	16%	132	15%	125	0.862
Amantadine	11%	132	11%	125	0.911
Anticholinergic	0%	132	0.71%	125	0.101
Deep brain stimulation	4%	132	2.8%	125	0.422

The *p* values are from Pearson's chi-square test (nominal data) or Kruskal–Wallis test (at least ordinal data), respectively

points (95% CI − 4.9 to − 1.7). 56% of the patients in the IG improved after 6 months at least within the range of the mean improvement of 3.3 points.

The scores of the PD-NMS improved after 6 months in favor of the IG ($p < 0.001$, mean change 11.3, 95% CI − 17.1 to − 5.5). The effect of group was highly significant ($p < 0.001$). 68% of the patients in the IG improved after 6 months at least within the range of the mean improvement of 11.3 points.

Regarding the subscores, the further analysis revealed significant improvements of the IG between baseline and 6-month follow-up in the domains gastrointestinal tract (mean group difference 2.4 points, $p \leq 0.001$), urinary tract (mean group difference 2.6 points, $p \leq 0.001$), and miscellaneous (e.g. pain or sweating; mean group difference 1.6 points, $p = 0.001$).

No significant changes were detected in the additional secondary outcome parameters cognition (PANDA) and depressive symptoms (BDI-2).

Changes in the overall dosage of dopaminergic medication were similar across groups: LEDD increased slightly over 6 months with a mean of 29 mg (IG)/35.1 mg (CG, $p = 0.723$). The total number of dosage adjustments over 6 months was comparable between groups (IG: $n = 257$ adjustments, CG: $n = 270$).

In total, the number of hospitalizations was not significantly higher in one group [45 (IG) vs. 51 (CG) hospitalizations, $p > 0.05$; see Table 5]. A more detailed analysis revealed no relevant differences in the total number of hospitalizations to subspecialties.

IG patients rated their overall satisfaction with the treatment with a mean score of 8.6 out of 10.

Table 4 Changes of outcome parameters between baseline and 6 months for each group and differences between groups

Outcome	Group	Raw data		Change from baseline (mixed model for repeated measures)							
		Baseline		3-month FU		6-month FU		3-month FU		6-month FU	
		Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)	*n*	EMM (95% CI)	*p* (*F*; *df*1, *df*2)	EMM (95% CI)	*p* (*F*; *df*1, *df*2)
PDQ-39	IG	26.0 (14.8)	132	25.9 (15.1)	126	24.6 (15.1)	132	0.4 (− 1.0 to 1.8)	0.578 (0.3; 1, 253.1)	− 1.5 (− 3.0 to 0.0)	0.057 (3.7; 1, 254.2)
	CG	27.7 (15.6)	125	27.5 (15.6)	125	28.3 (15.7)	125	− 0.1 (− 1.5 to 1.4)	0.917 (0.0; 1, 248.2)	0.8 (− 0.8 to 2.3)	0.335 (0.9; 1, 254.3)
	IG-CG							0.5 (− 1.6 to 2.5)	0.642 (0.2; 1, 250.6)	− 2.2 (− 4.4 to − 0.1)	**0.044 (4.1; 1, 254.4)**
LEDD	IG	612.9 (431.3)	132	614.7 (429.0)	128	641.8 (424.0)	130	11.1 (− 13.8 to 36.0)	0.380 (0.8; 1, 250.1)	25.2 (− 5.9 to 56.2)	0.112 (2.5; 1, 249.8)
	CG	612.4 (390.6)	125	616.1 (384.9)	125	647.5 (373.2)	124	3.7 (− 21.5 to 29.0)	0.772 (0.1; 1, 247.7)	33.2 (1.4 to 65.0)	**0.041 (4.2; 1, 249.2)**
	IG-CG							7.4 (− 28.1 to 42.8)	0.682 (0.2; 1, 248.9)	− 8.0 (− 52.5 to 36.4)	0.723 (0.1; 1, 249.5)
UPDRS-III	IG	28.3 (9.1)	132	26.4 (9.1)	129	26.5 (8.8)	128	−1.8 (−2.8 to −0.8)	**< 0.001 (12.0; 1, 252.4)**	− 1.8 (− 2.9 to − 0.6)	**0.002 (9.6; 1, 250.8)**
	CG	28.0 (8.7)	125	28.4 (9.1)	124	29.6 (9.0)	124	0.5 (− 0.6 to 1.5)	0.399 (0.7; 1, 251.2)	1.5 (0.4 to 2.7)	**0.009 (6.9; 1, 248.8)**
	IG-CG							− 2.3 (− 3.7 to − 0.8)	**0.003 (9.2; 1, 251.8)**	− 3.3 (− 4.9 to − 1.7)	**< 0.001 (16.4; 1, 249.8)**
PDNMS	IG	53.9 (29.6)	132	–	–	45.8 (28.8)	128	–	–	− 10.0 (− 14.0 to − 5.9)	**< 0.001 (23.5; 1, 249)**
	CG	62.3 (34.6)	125	–	–	62.1 (30.5)	124	–	–	1.3 (− 2.8 to 5.4)	0.529 (0.4; 1, 249)
	IG-CG							–	–	− 11.3 (− 17.1 to − 5.5)	**< 0.001 (14.7; 1, 249.0)**
PANDA	IG	24.7 (3.8)	131	–	–	25.0 (4.4)	126	–	–	0.2 (− 0.4 to 0.8)	0.478 (0.5; 1, 246)
	CG	24.7 (3.5)	125	–	–	25.2 (4.1)	123	–	–	0.5 (− 0.1 to 1.1)	0.134 (2.3; 1, 246)
	IG-CG							–	–	− 0.3 (− 1.1 to 0.6)	0.569 (0.3; 1, 246.0)
BDI-2	IG	12.0 (8.2)	132	–	–	11.1 (8.0)	132	–	–	− 0.9 (− 1.8 to − 0.0)	**0.045 (4.1; 1, 253)**
	CG	12.6 (7.3)	125	–	–	12.6 (8.3)	124	–	–	0.3 (− 0.7 to 1.2)	0.566 (0.3; 1, 253)
	IG-CG							–	–	− 1.2 (− 2.5 to 0.1)	0.071 (3.3; 1, 253)

Bold values indicate statistically significant changes ($p < 0.05$)

EMM estimated marginal mean, *FU* follow-up, *SD* standard deviation, *IG* intervention group, *CG* control group

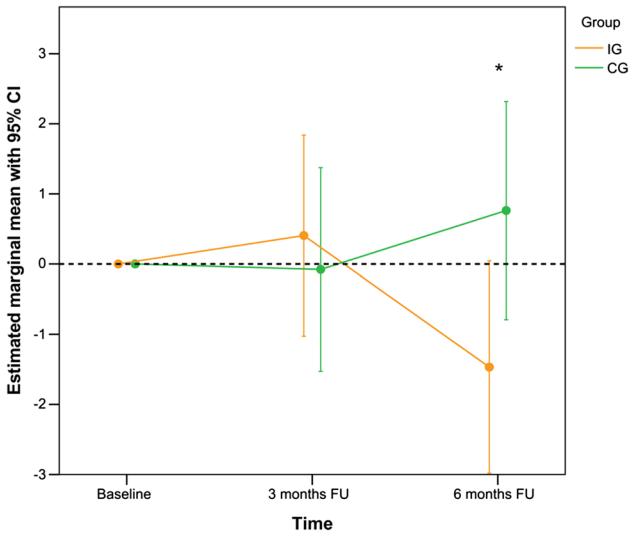

Fig. 2 Changes of the primary outcome parameter PDQ-39 over 6-month time in the intervention group and control group. The asterisk indicates the significant change between IG and CG between baseline and 6-month FU

Discussion

Treating PD patients is complex due to highly specialized treatment options, well-informed and often demanding patients, as well as increasingly long life spans with associated sociodemographic and economic impact. This may call for integrated care approaches dealing with the individual needs of PD patients.

In this randomized controlled trial, we assessed the efficacy of an integrated care approach, where patients were treated by a "PD team", which was comprised of a general neurologist, a movement disorder specialist and a PD nurse, within their familiar environment, i.e. either at the local practice of their primary neurologist or at home. Compared with standard care, the primary outcome parameter QoL improved in the intervention group in a clinically and statistically relevant manner. Recently, large clinical trials in PD have selected QoL as primary outcome, since this parameter has been recognized as one of the key factors in successful patient-centered care [5, 22]. As Peto and colleagues suggested, a clinically relevant difference over 6-month time corresponds to a change in PDQ-39 of 1.6 points [10]. Accordingly, the 2.2-point change in PDQ-39 total score observed in our study represents a relevant modification of daily restrictions. As an example from drug trials, levodopa vs. levodopa-sparing therapy and MAOBI vs. dopamine agonists improved PDQ-39 mobility scores about 1.4–1.8 points over a period of 3 years [5]. Additionally, the finding of improvements in the domains emotional well-being, stigma, communication and physical discomfort speak for an improved patient empowerment in terms of

Table 5 Number of total hospitalizations, hospitalizations due to emergency admissions and due to falls in the intervention/control group

	Orthopedics	Neurology	Cardiology	General medicine	Oncology	Urology	Psychiatry	Temporary nursing home	Total	*p*
Intervention group	7	17	4	13	1	3	0	0	45	> 0.05***
Hospitalizations due to emergency admissions	3	4	0	2[a]	0	0	0	0	9	
Hospitalizations due to falls	3	1	0	0	0	0	0	0	45	
Control group	7	18	8	8	5	3	1	1	51	
Hospitalizations due to emergency admissions	3	3	0	2[b]	0	0	1	0	9	
Hospitalizations due to falls	2	0	0	0	0	0	0	0	2	

***Significant difference between number of total hospitalization days between IG and CG

[a]Emergency due to pancreatitis (one hospitalization) and bronchitis (one hospitalization)

[b]Emergency due to acute obstipation (one hospitalization) and diarrhea (three hospitalization)

disease acceptance or coping. Thus, depending on the chosen methods and included patients, the non-invasive features of our trial support the use of an integrated care approach as a valid strategy to improve QoL for PD patients.

Non-motor symptoms [12] were significantly ameliorated in the intervention group as shown by an overall reduction of more than 11 points in the PD-NMS score. The predominance of changes in the categories gastrointestinal tract and urinary system points towards the significant influence of non-motor symptoms on QoL improvements. In our study, patients' UPDRS changed by 3.3 points in the intervention group, which is just within the range of a clinically important change (= 3 points) as reported by Hauser et al. [6]. Importantly, the daily levodopa equivalent dose did not change in both groups. Improved QoL, as well as changes in secondary outcomes, therefore, cannot be ascribed to an increasing dosage of dopaminergic medication over time. Our data suggest that the observed improvements in the IG are related to individualized therapy rather than simple adaptation of medication, e.g. to improved timing of the medication, installation of complementary therapies (physiotherapy, speech therapy, occupational therapy) or intensive counseling of patients and caregivers through the PD nurse.

One can argue that due to the stable hospital admissions the clinical relevance of this model of care might be limited. However, we would like to point out that significant changes in patient-related outcomes, e.g. the PDQ-39, pinpoint towards a relevant meaning for PD patients in their everyday life.

The following characteristics of our integrated care model may underlie the observed positive effects: (1) selection of neurologists with a high commitment to PD patients, PD therapy and evidence-based guidelines, (2) collaboration in a multidisciplinary team with team-based decisions on changes of the therapeutic regimen, (3) instant modification of therapy plans once symptom deteriorations were observed, and (4) at-home and community-based care instead of hospital-based assistance.

We consider the multidisciplinary expertise, and most importantly the PD nurse, to be one of the most innovative aspects of our integrated care program.

Contrary to, e.g. common practice in the UK, the involvement of a PD nurse is exceptional in Germany. The PD nurse ensured a faster response to patients' queries, improved communication structures, and better access to patients. Furthermore, the PD nurse was closely involved in patient counseling, including aspects of coping with PD and social concerns. The easy availability of the PD nurse (via telephone) for all minor and major problems provided patients with security and immediate feedback in case of questions or uncertainties. Therapy plans were supervised by the PD nurse, who acted as a case manager. The role of a PD nurse as an important player in PD care is multifaceted [15] and related to enabling patients' self-management of the neurological condition, QoL and caregiver support. Thus, the "therapeutic effects" of the PD nurse have to be discussed. IG patients received more attention, social support and personal, individualized care through the PD nurse. These services were not available to the CG. As the treatment was not an invasive procedure, which is prone to show substantial placebo-associated improvements [3], the chance for observed results being due to a placebo effect is relatively low.

Until recently, there was no evidence-based guidance on how to design integrated care models. This gap has narrowed with the experience gained through the Dutch ParkinsonNet [19]. This structured, multidisciplinary approach offers demonstrable health benefits. Additionally, the Canadian-Ontario scenario revealed in a single-center approach an improvement of QoL as measured using the PDQ-39 [18]. To date, further randomized control trials (RCT) are lacking.

From the few published studies, the Dutch ParkinsonNet [19] and the Canadian-Ontario study [18] are comparable in terms of a structured integrated care approach. Both trials lasted for 8 months. Van der Marck et al. reported in 2012 that they achieved an improvement of QoL through ongoing individually tailored care from a multidisciplinary team [18]. Compared to our study, patients were not visited at home and no general neurologist was included in the team. Additionally, in the Canadian study, a selection bias of patients has to be considered due to the recruitment of patients referred to a movement disorder center. The Dutch ParkinsonNet study group chose another approach: patients received an individually tailored comprehensive assessment in an expert tertiary referral center and were subsequently referred to existing regional networks of allied health professionals [19]. The results in terms of QoL improvements were moderate and disappeared after baseline correction. An advantage of the Dutch concept was the evidence-based training of the large multiprofessional team to achieve the best therapy results for the patients. A recent mixed-method analysis yielded that the ParkinsonNet approach enhances multidisciplinary collaboration between healthcare professionals [17]. Again, the local neurologist or home visits of a PD nurse were not included in the study design—the integrated care was initiated in an expert center and either stayed there (Canada) or was handed over to local allied health professionals (The Netherlands). In contrast, our concept focused on delivering primary care in the patients' familiar environment.

Some shortcomings of our approach must be considered. Due to the study design, the intervention was not blinded, neither for the patients nor the team members. As the interventions were rather heterogeneous, the specific impact of the different components on the individual outcomes is difficult to assess. Allied health professionals were not included as regular team members in the

consultations, as they varied among individual patients. An integration of patients' therapists would have been desirable but was beyond the available organizational means. Thus, the interindividual different therapeutic regimen of, e.g. physiotherapy might be one confounding factor of a favorable outcome of the IG.

We assessed QoL in PD patients but unfortunately did not include the assessment of the caregiver burden. This missing aspect would be of interest as caregiver burden is closely associated with patients' QoL [13], and it should be addressed in future studies.

Before presenting a patient in the joint CPN consultation, the local neurologist decided which patients out of his practice should be considered for further consultation. This yielded a total of 1400 patients presented in the joint consultations during this study. Thus, a selection bias, e.g. in favor of complex patients with treatment difficulties or higher disease severity, cannot be ruled out.

The fairly high number of drop-outs (14%) should be carefully taken into account. One of the major causes for dropping out of the trial was withdrawal of consent ($n = 23$, 8%); despite thorough informed consent, patients realized after randomization to the control group that there would not be any benefit, which leads to the withdrawal of consent.

Although the conclusions of benefit from the integrative care model need to be treated with caution, as the German healthcare system differs in many aspects from those in other countries, major components of the integrated care concept investigated here can easily be implemented elsewhere.

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The CPN study group

The CPN study group included the following community neurologists:

Susanne Adams, MD; Karl Assmann, MD; Angela Böhme, MD; Eckhard Bonmann, MD; Gisela Buchberger, MD; Birgit Cremer, MD; Christian Dortmann, MD; Johannes Faulhaber, MD; Marius Fischer, MD; Mehran Ghaemi, MD; Martin Hettmann, MD; Christine Hofmann, MD; Sabine Kersting, MD; Gereon Nelles, MD; Wei-Chi Liu, MD; Rainer Maelger, MD; Kyra Merzbach, MD; Oliver Scharwat, MD; Joachim Schläfer, MD; Christian Schmiegelt, MD; Dirk Schulze Zumloh, MD; Annette Semmroth, MD; David Svoboda, MD; Hans-Hermann Winter, MD; Sonja Wirtz, MD; Gilbert Wunderlich, MD.

Author contributions CE: literature search, figures, study design, data collection, data analysis, data interpretation, and writing. RD: data collection and data analysis. JS: figures, data collection, data analysis, data interpretation, and review of the manuscript. GRF: data interpretation and review of the manuscript. MH: data analysis and data interpretation. LT: study design, data analysis, data interpretation, writing, and review of the manuscript.

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Compliance with ethical standards

Conflicts of interest C. Eggers has received honoraria for speaking engagements and consultancy from Abbvie Pharma, Bial Pharma, Medtronic, Zambon Pharma, TEVA Pharma, GE Healthcare, and UCB Pharma. The institution of C. Eggers, not C. Eggers himself, received funding by the German Research Foundation (DFG) via the Clinical Research Group 219, the medical faculty of the University of Cologne via the "Köln Fortune program", Medtronic Inc. and the German Parkinson Foundation (Deutsche Parkinson Vereinigung). R. Dano has no conflicts of interest. J. Schill has no conflicts of interest. G.R. Fink receives royalties from the publication of the book *Funktionelle MRT in Psychiatrie und Neurologie* and *Neurologische Differentialdiagnose*; received honoraria for speaking engagements from Bayer, TEVA, GlaxoSmithKline, and Boehringer Ingelheim; and receives research support from the Bundesministerium für Bildung und Forschung, the Deutsche Forschungsgemeinschaft and the Marga- and Walter-Boll Foundation. M. Hellmich has no conflicts of interest. L. Timmermann is consultant for Medtronic Inc, Boston Scientific, Bayer Healthcare, UCB Schwarz Pharma, received honoraria in symposia sponsored by TEVA Pharma, Lundbeck Pharma, Bracco, Gianni PR, Medas Pharma, UCB Schwarz Pharma, Desitin Pharma, Boehringer Ingelheim, GlaxoSmithKline, Eumecom, Orion Pharma, Medtronic, Boston Scientific, Cephalon, Abbott, and GE Medical. The institution of Prof. Timmermann, not Prof. Timmermann himself, received funding by the German Research Foundation (DFG) via the Clinical Research Group 219, the German Ministry of Education and Research (BMBF), Manfred und Ursula Müller Stiftung, Klüh Stiftung, Hoffnungsbaum e. V., NBIA DISORDERS SOCIETY USA, the medical faculty of the University of Cologne via the "Köln Fortune program", Medtronic Inc. and the German Parkinson Foundation (Deutsche Parkinson Vereinigung).

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