Integrated Care in Parkinson's Disease: A Systematic Review and Meta-Analysis

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ABSTRACT: Background: Quality of life in Parkinson's disease (PD) is affected by motor and nonmotor symptoms, necessitating an integrated care approach. Existing care models vary considerably in numerous domains. The objectives of this study were to perform a systematic review and meta-analysis of PD integrated care models and develop recommendations for a representative model.
Methods: We conducted a systematic review of published integrated care models and a meta-analysis of randomized, controlled trials examining integrated care versus standard care. The primary outcome was health-related quality of life using a validated PD scale. We evaluated levels of care integration using the Rainbow Model of Integrated Care.
Results: Forty-eight publications were identified, including 8 randomized, controlled trials with health-related quality of life data (n = 1,149 total PD patients). Qualitative evaluation of individual care model integration guided by the Rainbow Model of Integrated Care revealed frequent clinical and professional integration, but infrequent organizational and population-based integration elements. Meta-analysis of randomized, controlled trials revealed significant heterogeneity (I^2 = 90%, P < 0.0001). Subgroup analysis including only outpatient care models (n = 5) indicated homogeneity of effects (I^2 = 0%, P = 0.52) and improved health-related quality of life favoring integrated care, with a small effect size (standardized mean difference [SMD], −0.17; 95% CI, −0.31 to −0.03; P = 0.02).
Conclusions: Outpatient integrated PD care models may improve patient-reported health-related quality of life compared with standard care; however, because of variable methodological approaches and a high risk

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of bias related to inherent difficulties in study design (eg, blinding of participants and interventionists), generalizability of these results are difficult to establish. The Rainbow Model of Integrated Care is a promising method of evaluating elements and levels of integration from individual patient care to population health in a PD context. © 2020 The Authors. *Movement Disorders* published by Wiley Periodicals, LLC on behalf of International Parkinson and Movement Disorder Society.

Key Words: integrated care; meta-analysis; multidisciplinary team; Parkinson's disease

The treatment of Parkinson's Disease (PD) remains limited to symptomatic therapies.[1] It is well recognized that both motor and a wide variety of nonmotor symptoms contribute to the overall disease burden in PD, right from the premotor to the advanced disease stages. This complexity necessitates an individually tailored, comprehensive therapeutic approach. This includes medical management (refined pharmacotherapy, deep brain stimulation) and nonpharmacological measures like physiotherapy, occupational therapy, speech therapy, or psychotherapy, as well as education and support, aiming to improve the health-related quality of life (HRQoL) of patients and caregivers. Given the heterogeneous nature of symptoms across different persons, dedicated care coordinators or PD nurses can help to achieve the individual therapeutic goals.[2]

From the perspective of patients, reported core needs include better information on self-management, sufficient interdisciplinary collaboration between different health care professionals, ample time to discuss possible future scenarios, and an individual health care professional guiding and supporting them.[3] To address these needs, multiple different integrated care models have been established worldwide, with widely varying degrees and intensities, but all aiming to offer PD patients structured and tailor-made comprehensive care programs. So far, there is limited consistency across these programs in terms of settings, team composition, or level of clinical integration. However, most programs do share certain common disciplines. In addition, results of published data have been heterogeneous with respect to study design and outcomes (including improvement in HRQoL). There is also variability in the terminology used, with care models described most commonly as "multidisciplinary," "interprofessional," "interdisciplinary," or "integrated" (see information box). Throughout the present article, "integrated care" is the terminology used for consistency, and proposals regarding terminology as a field moving forward are also discussed.

To assess these various models and to analyze the extent of care integration, the Rainbow Model of Care has been proposed.[4] It assesses the degree of care integration from a health perspective around 4 core domains (person-centeredness, service coordination, professional coordination, and organizational coordination) and 4 ancillary domains (community-centeredness, functional coordination, normative coordination, and system integration).[4] Our present meta-analysis and structured review synthesize the available data and evidence about existing integrated care models and their effects on improvement in the HRQoL of PD patients. In addition, we analyzed the level of integration of each model using the Rainbow Model framework. Finally, we offer recommendations for future integrated care projects.

Information Box: What Is the Right Terminology?[64]

Intradisciplinary: working within a single discipline.

Cross-disciplinary: viewing one discipline from the perspective of another.

Multidisciplinary: people from different disciplines working together, each drawing on their disciplinary knowledge.

Interdisciplinary: integrating knowledge and methods from different disciplines, using a real synthesis of approaches.

Transdisciplinary: creating a unity of intellectual frameworks beyond the disciplinary perspectives.

Integrated: care approach to strengthen people-centered health systems through the promotion of the comprehensive delivery of quality services across the life course; it is designed according to the multidimensional needs of the population and the individual and is delivered by a coordinated multi- or interdisciplinary team of providers working across settings and levels of care.

Methods

Review Question

This systematic review and meta-analysis assessed the following specific questions:

1. What are the existing models of integrated care in PD in terms of the settings, team composition, and levels of clinical integration?
2. In patients with PD, does provision of integrated care compared with standard care improve health-related quality of life, in a health care context that combined disciplines and/or crossed boundaries of

health care (in-patient, outpatient, primary, secondary, or tertiary settings)?

Search

We searched MEDLINE, EMBASE, the Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), and the Web of Science for relevant studies. The study protocol was submitted to PROSPERO (CRD42019115444) on December 2, 2018, and registration was confirmed on January 3, 2019. We followed the PRISMA reporting guidelines. The search strategy included terms describing or related to the condition and interventions. The search strategy for MEDLINE is included in the supplementary information. The MEDLINE search strategy was adapted for use in other electronic databases. Figure 1 presents the flow chart of the study selection process.

Studies published in the English language or with English-language translation available were included. There were no restrictions for inclusion based on geographical location or year of conducting the study. The initial search strategy for this review was conducted in November– December 2018. We repeated the search strategy in May 2019 and November 2019 to update the review before publication.

Inclusion/Exclusion Criteria

All studies meeting the following criteria were included in the review: (1) intervention included integrated care, defined as care involving a movement disorders specialist plus at least 2 other treating providers based within the center or in the community as part of the defined integrated care model (clinicians, Parkinson's nurses, allied health therapists, or others) and/or extending beyond the specialist care hospital to primary care/general neurologist/community/home; (2) participants included adults (≥18 years) with PD diagnosed as per United Kingdom Parkinson's Disease Society Brain Bank criteria and of either sex; (3) study setting was either hospital (outpatient or inpatient) or community based.[5] There was no restriction on study design for studies to be included in the systematic review. For inclusion in the meta-analysis, additional criteria were applied: (1) study design was a randomized, controlled trial or quasirandomized, controlled trial; (2) a comparator group was present that received placebo or standard care; and (3) the study reported outcomes that included a patient-reported scale for health-related quality of life validated for use in PD. Studies spanning inpatient, outpatient, community, and home settings were included without any geographical or socioeconomic status restrictions.
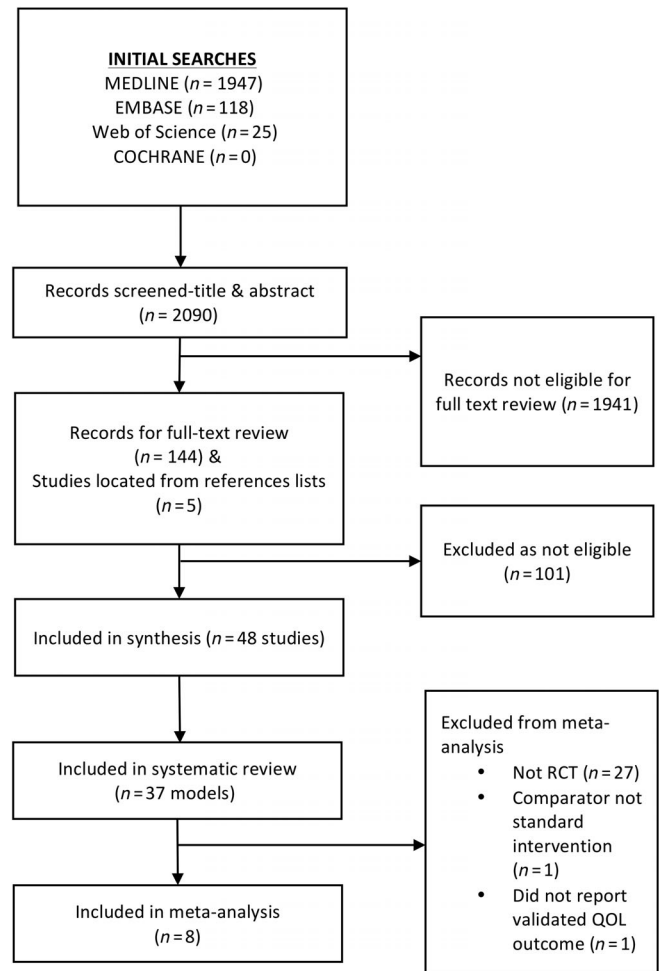

FIG. 1. Study flow diagram.

Outcomes

For the systematic review, outcomes included identification of the settings, team composition, components of care, and levels of clinical integration achieved by existing models of integrated care. Frequencies of levels of integration are reported for included studies regarding the 4 overarching elements of the Rainbow Model of Integrated Care: clinical levels of integration (microlevel person-centered care elements), professional and organizational levels of integration (mesolevel population-based care), and system integration (macrolevel population-based care).[6] The presentation of frequencies is qualitative in nature, and there was no quantitative data analysis comparing the Rainbow Model levels of integration. For the meta-analysis, the main outcome parameter was patient-reported health-related quality of life. The 39-item PDQ-39 questionnaire and a shortened version, the PDQ-8, are both validated and widely used measures to assess the quality of life in PD patients.[7-9]

Data Extraction

Titles and/or abstracts of studies retrieved using the search strategy were screened independently by 2 review team members (R.R., L.B.). The full text of studies that meet the inclusion criteria were retrieved and independently assessed for eligibility. Disagreements were resolved through discussion with a third reviewer (C.E.). After removal of duplicates, data were extracted from the included studies using a standardized, prespecified data extraction form. The data extraction form captured details of the study (author, year of publication, study design, geographic location), population (inclusion/exclusion criteria, number of participants, baseline characteristics), intervention (setting, team composition, and duration and frequency of intervention), comparator (if any), levels of integration, outcomes assessed, and information for assessment of the risk of bias. The 2 review team members extracted the data independently, and discrepancies were resolved through discussion mutually and with a third team member when required.

Risk of Bias Assessment

Studies included in the meta-analysis were assessed for internal validity using the Cochrane risk-of-bias assessment tool. Two review team members independently applied the tool for included studies (R.R., L.B.). Discrepancies were resolved by mutual discussion.

Data Synthesis and Publication Bias Assessment

We summarized the data regarding existing models of interdisciplinary/integrated care in terms of the team composition, settings, level of integration achieved, and outcomes monitored/reported. We pooled the results from randomized, controlled trials that have reported the same outcome measure (HRQoL) using a random-effects meta-analysis with standardized mean differences. We calculated the 95% CI and 2-sided P values for the outcome measure. Heterogeneity between studies in effect measures was assessed using the I^2 statistic. An I^2 value of more than 50% was considered significant heterogeneity. RevMan version 5.3 was used to perform the meta-analysis and generate a funnel plot for visual inspection of potential publication bias. In addition to visual/graphic examination of the funnel plot, mathematical methods for examining publication bias included those recommended by Begg and Mazumdar, as well as Egger, Smith, Schneider, and Minder, and were analyzed using Comprehensive Meta-Analysis version 3.[10,11]

Rainbow Model of Integrated Care

The Rainbow Model of Integrated Care provides a validated framework to evaluate the level of integration of diverse health care models.[4] In practice, it defines 4 major domains of integration: clinical, professional, organizational, and systems integration. The Rainbow Model specifically identifies practices consistent with care integration for each domain. For this analysis, models that explicitly documented at least 1 practice recommended for care integration in a particular domain were considered to have achieved care integration in that domain. Two authors independently graded the studies for care integration, and discrepancies were resolved through mutual consensus and an adjudicator when required.

Results

The combined searches retrieved 2090 records (Fig. 1). After removal of duplicates and screening of titles/abstracts, 149 records were chosen for full-text review. We included 48 records in the qualitative review, from which 37 studies met the inclusion and exclusion criteria. The study characteristics of 8 randomized, controlled trials (RCTs) included in the quantitative meta-analysis[12-19] and 19 other experimental studies included in the systematic review are presented in Table 1.[20-47] The remaining 10 articles included in our systematic review were nonexperimental (ie, review articles or descriptions of care models) and are detailed separately in Supplementary Table 1.[48-57]

Systematic Review of Care Models

We identified 37 individual reported models from 48 articles that met our definition of integrated care. Integrated care practices were reported from varying locations worldwide (see supplementary materials, Supplementary Fig. 2 for geographical map), although large parts of the world remained underrepresented. Table 1 presents the characteristics and results of all studies, including the RCTs included in the meta-analysis, as well as other studies included in the systematic review (nonrandomized, controlled trials, pretest/posttest designs, observational cohort studies, and retrospective chart reviews).[12-47] In the online supplementary materials, Supplementary Table 1 presents articles with detailed descriptions of proposed care models and other related reviews of care models specific to integrated care in PD.[48-57] Core team members included in the models are shown in Figure 2.

The majority of care models incorporated elements from 2 broad themes with overlapping features. Many studies (n = 26) focused on the process of care coordination including medical and surgical management, consultations, and allied health care.[12,15,16,27,30,32,33,35,37-43,46,47,49-57] The other major theme was delivery of multidisciplinary rehabilitation in various settings (n = 11).[13,14,17-19,28,29,34,44,45,48] Among the care coordination models, 24 were primarily based

TABLE 1. Study characteristics

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
Eggers et al, 2018[10,18]	Outpatient neurology clinic and home visits, Germany	Movement disorders specialist General neurologist PD specialist nurse	PDQ-39	H&Y UPDRS-III NMSS BDI-II PANDA LEDD	Baseline, 3 months, 6 months	132:125	Usual care	Individualized treatment plan based on recommendations of all core team members Home visits and telephone hot line managed by PD nurse PD nurse coordinated pharmacological intervention changes with speech and physical therapists Pharmacologic modifications based on assessment of PD nurse and feedback from patients and therapists
Ferrazzoli et al, 2018[11,19-23]	Inpatient specialist center, Italy	Movement disorders specialist Physical therapist Occupational therapist Speech therapist Clinical psychologist Neuropsychologist	PDQ-39	UPDRS-III PDDS TUG BBS MMSE MoCA FAB WCST TMT A&B BDI STAI-Y	Baseline, 1 month, 2 months, 3 months, 4 months	186:48	Usual care	MIRT (multidisciplinary rehabilitation treatment) 4-week program involving 4 daily rehabilitation sessions for 5 days (each session is 1 hour) First and second sessions: physical therapy/aerobic exercise Third session: occupational therapy Fourth session: speech therapy Day 6 of each week, 1 hour of additional physical exercise on equipment only (no therapist present) Possible additions based on weekly team meetings and individual patient needs: Hydrotherapy Robotic-assisted walking training Virtual reality training Psychoeducational groups
Monticone et al, 2015[12]	Inpatient, Italy	Specialist physician (physiatrist) Specialist PD nurse Occupational therapist Speech therapist Psychologist	MDS-UPDRS-III	PDQ-39 BBS FIM	Baseline, 8 weeks, 12 months posttreatment	35:35	General physical therapy	8-week inpatient program involving motor training, cognitive training, and ergonomic education Daily physical therapy (90 minutes), twice weekly cognitive training sessions (30 minutes each), 1 ergonomic session weekly (30 minutes)
Gage et al, 2014[13,24]	Community, UK	General neurologist Specialist PD nurse Gerontologist Physical therapist Occupational therapist Speech therapist Nonnurse coordinator Community mental	Self-Assessment PD Disability Scale	PDQ-8 UPDRS I-IV NMSS Barthel ADL Frenchay Activities Index EQ-5D SF-36	Baseline, 6 weeks, 24 weeks, 36 weeks	144:83	Usual care	Members of the multidisciplinary treatment team also met prior to the trial to discuss and agree on the details of the intervention, including the roles and protocol to be followed by individual therapists. The goals of the agreed-on care plan were

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
		health team Parkinson's UK support worker		HADS VAS CSI TUG GHQ-12 Falls (self-reported) Speech Self Report Questionnaire Abridged Emerson and Enderby Screening Assessment Rating Scale Yale Depression Screen Self-Efficacy Scale				reviewed and ratified at team meetings throughout the duration of the program in both intervention groups. Group A: home visits to develop and implement tailored individual plans over 6 weeks, written educational PD fact sheets distributed. Most patients received 1 visit from one of the professionals each week. Individual plans included referrals to other professionals when indicated, including to a neurologist, a community mental health team, and a Parkinson's UK support worker. Also referrals to community support resources. Face-to-face treatment team meetings twice in each 6-week cycle to discuss patient plans and progress and further individualize patient treatment plans. Group B: same intervention as group A plus ongoing support for 4 months from a care assistant trained in Parkinson's starting at the end of the 6-week intervention, characterized by 1 hour per week per patient (via a mix of home visits and telephone contacts). Ongoing communication with team and further input provided from specialists when warranted. Intervention group data were combined for meta-analysis.
van der Marck et al, 2013[14]	Outpatient specialist center and general neurology clinic, Canada	Movement disorder specialist PD nurse General neurologist Social worker (program coordinator)	PDQ-39	UPDRS-III UPDRS I–IV MADRS SCOPA-PS LEDD CSI	Baseline, 4 months 8 months	61:61	Usual care with general neurology	Individually tailored care from the movement disorders specialist neurologist, supported by PD nurse and social worker. Patients also offered to see a social worker for psychological or home-care issues and a PD nurse for changes in symptoms, medication issues, and all other PD-related questions.
Tickle-Degnen et al, 2010[15]	Outpatient specialist center and home visits, USA	Movement disorder specialist	PDQ-39	None	Posttreatment, 2 months, 4 months	76:41	Usual care	Group 1: 3 hours of self-management rehabilitation per week and two 1.5-hour

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
		Specialist PD nurse General neurologist Physical therapist Occupational therapist Speech therapist						group clinic sessions (18 hours total). Group 2: 4.5 hours of self-management rehabilitation per week, two 1.5-hour group clinic sessions, and one 1.5-hour individual home or community session for transference of self-management skills to their locations of daily living (27 hours total). Group training sessions included physical exercise, speech exercises, functional training, and discussions.
Guo et al, 2009[16]	Outpatient specialist center, China	Movement disorder specialist Specialist PD nurse General neurologist Physical therapist Occupational therapist Speech therapist Psychologist Dietician	PDQ-39	UPDRS-II UPDRS-III SEADL Zung SDS Global PMS CMS	Baseline, 4 weeks, 8 weeks	23:21	Same lectures, 1 rehabilitation session, then usual care	Intervention group data were combined for meta-analysis. Three group education lectures encouraging participation and interactive dialogue followed by integration with a personalized rehabilitation program. First lecture: nutrition in PD (by nutritionist) Second lecture: mood issues in PD (by psychologist) Third lecture: movement symptoms (by physical and occupational therapists), followed by 24 half-hour sessions of individualized rehabilitation for 8 weeks.
Wade et al, 2003[17]	Outpatient specialist center and general neurology clinic, UK	Specialist PD nurse Physical therapist Occupational therapist Social worker (program coordinator)	PDQ-39	UPDRS NHPT EQ-5D SF-36 HADS VAS	Baseline, 24 weeks	53:41	Usual care	Multidisciplinary group education program and individualized rehabilitation, 1 full day once weekly for 6 weeks. 2 hours of individual treatment in the morning, followed by group activities in the afternoon.

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation Setting(s)	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
Study	Design and sample size	Core team members included in intervention implementation		Outcomes	Times		Intervention	Control group received intervention after 24 weeks.

Randomized, quasi-randomized, and nonrandomized trials included in systematic review

| van der Marck et al, 2013[25] | Nonrandomized, controlled trial
Intervention
n = 150
Control
n = 151 | Outpatient PD specialist center, general neurology center, community
Combination of PD expert referral center and ParkinsonNet (IMPACT), Netherlands | Core team members included in intervention implementation

Available to intervention group only: movement disorders neurologist, ParkinsonNet trained allied health professionals (physiotherapy, speech therapy, occupational therapy)

Available to both intervention and control group: general neurologist, PD nurse, and allied health professionals *without* ParkinsonNet training (physiotherapy, occupational therapy, speech therapy, psychologist, psychiatrist, social worker, dietician, rehabilitation specialist, sexologist, sleep specialist, geriatrician, nursing home specialist) | ALDS
PDQL
UPDRS-III
BELA-A-k
Costs (during study period) | BL
2 months
4 months
6 months
8 months | | —Intervention group received individualized comprehensive assessment with a movement disorders specialist and allied health care providers with specialized training in PD (ParkinsonNet), including physiotherapy, speech therapy, and occupational therapy
—Control group receives care from general neurologists and allied health professionals *without* ParkinsonNet training
—Both groups had access to a regional network of other allied health professionals
Results:
—At 4, 6, and 8 months, mean ALDS and PDQL showed small but statistically significant higher scores in intervention group than in control group
• However, when controlling for baseline disease severity (Hoehn & Yahr), groups did not significantly differ
Secondary outcome results:
—No group differences in UPDRS-III, BELA-A-k, or costs | |

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
Lindskov et al, 2007[26]	Nonrandomized, controlled trial; Intervention n = 48; Control (delayed intervention) n = 48	Outpatient PD specialist center; Multidisciplinary educational program, Sweden	Movement disorders neurologist, PD nurse, occupational therapist, physiotherapist, speech therapist, psychologist, social worker, dietician, dental hygienist	SF-12, PCS, MCS, LEDD	BL, 1 month post			Multidisciplinary educational program lasting 6 weeks, consisting of weekly 2-hour sessions. • First hour: interactive dialogues led by 1–2 core team members on topics related to their subspecialty. • Second hour: team members demonstrated relaxation, speech, and exercises to PD patients, and PD family members took part in a nurse-led support group. Results: —No group differences over time regarding change scores on SF-12, PCS, or MCS —Significantly higher increase in LEDD in control group
Trend et al, 2002[27]	Pretest/posttest; PD patient and caregiver pairs; n = 137	Outpatient PD specialist center; Intensive multidisciplinary rehabilitation program, UK	Intervention: physiotherapist, occupational therapist, speech therapist, PD nurse, consultant neurologist, care manager. Education: presentations made by benefits agent, chiropodist, continence adviser, dietician, pharmacist, Parkinson's Disease Society welfare visitor, PD nurse, consultant neurologist	HADS-D, HADS-A, EQ-5D utility index, EQ-5D thermometer, Timed walk, Gait (number of paces), Emerson voice and articulation assessment	1 week, 6 weeks			Cognitively intact PD patients and caregiver pairs attended weekly sessions (5.5 hours each) in a day unit including multidisciplinary individualized rehabilitation and group education for 6 weeks over a 3-year period (maximum of 6 PD patient/caregiver pairs per session). Results: Significant improvement in primary outcomes including depression (HADS-D) and quality of life (EQ-5D utility index and thermometer), but no significant improvement in anxiety (HADS-A). —Significant improvements in all secondary outcomes
Carne et al, 2005[28,29]	Retrospective chart reviews; Study 1[28] n = 43; Study 2[29] n = 49	Outpatient PD specialist center; Parkinson's Disease Research, Education, and Clinical Center (PADRECC), USA	Studies 1 and 2: movement disorders neurologist seen by 100% of patients and makes referrals to PD nurses, physiatrists, neuropsychologists, rehabilitation specialists (physical, occupational, and speech therapy under this umbrella), support groups, home exercise programs, disease and wellness educational programs	Studies 1 and 2: UPDRS-III; Rate of PD medication increases; Rate of PD medication decreases	Study 1: 1 year; Study 2: 1 year 2 years 3 years			Both studies examined the efficacy of a multidisciplinary treatment model employed at the PADRECC, where UPDRS-III change scores evaluated to compare "responders" (change score less than or equal to 0) versus "nonresponders" (greater than 0) at follow-up. Study 1: greater proportion of PD patients classified as responders (n = 32) versus nonresponders (n = 11) at follow-up; no significant group differences in medication changes. Study 2: entire sample showed mean improvement in UPDRS-III scores, and greater proportion of PD patients classified as responders (n = 37) versus nonresponders (n = 12) across all follow-up periods

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
Cohen et al, 2007[30]	Observational cohort study n = 73	Inpatient, movement disorders specialist center Fast-track DBS rehabilitation, USA	Preoperative evaluation: movement disorders neurologist, neuropsychologist Perioperative/postoperative: neurosurgeon, movement disorders neurologist, neuropsychologist physiatrist, physical therapist, speech therapist, occupational therapist, psychiatrist, clinical psychologist, dietician, case managers	FIM (total, cognitive, and motor scores) UPDRS-III LEDD	BL (preoperative) Discharge 3 months 1 year		Multidisciplinary postoperative management to maximize DBS programming and patient functional outcomes and rapidly reduce dopaminergic medications in an inpatient setting (2–3 weeks; average stay, 17.3 days) Results: —Significant improvement in total FIM, motor FIM, and cognitive FIM at discharge —Significant improvement in UPDRS-III at 3-month follow-up compared with preoperative score —Significant LEDD reduction at 3-month follow-up —Maintenance of treatment benefit demonstrated regarding preoperative and 1-year UPDRS-III in proportion of sample with follow-up data (n = 27)	
Ellis et al, 2008[32]	Pre-test post-test n = 68	Inpatient rehabilitation, movement disorders specialist center Inpatient multidisciplinary rehabilitation program, USA	Core team members delivering daily rehabilitation interventions: physical therapist, speech therapist, occupational therapist Additional core team members: movement disorders neurologist, neurorehabilitation specialty neurologist, movement disorders fellow, PD nurses, and case managers	FIM (total, cognitive, and motor scores) Timed Up and Go test 2-Minute Walk Test Finger-Tapping Test	BL Discharge		Individualized inpatient rehabilitation in which PD patients worked with all core team members for a total of 3 hours daily, 5–7 days per week (average length of stay, 20.8 days) Pharmacological adjustments were made based on data collected each day of treatment Results: —Significant improvements in all outcome measures at discharge for entire sample —Subset of patients whose medications were never adjusted for (ie, received rehabilitation only; n = 10), showed significant improvements in total FIM, motor FIM, and cognitive FIM at discharge	

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
Fleisher et al, 2018[33,34]	Retrospective chart review n = 85 Mixed sample: PD, n = 67; DLB, n = 4; PSP, n = 4; MSA n = 2; CBS, n = 1; HD, n = 1; Atypical parkinsonism not otherwise specified, n = 6	Home visits Edmond J. Safra Interdisciplinary Home Visit Program (HVP) for Advanced Parkinson's Disease, USA	Movement disorders neurologist, PD nurse, social worker (also serves as program coordinator)	Feasibility indices CSI-SF after 4 visits completed Rate of hospital-ization and emergency department visits	End of fourth visit (CSI-SF) 2 years			Quarterly home visits with all team members to homebound patients at risk for loss to follow-up. After each visit, comprehensive interdisciplinary note sent to all patient care providers and referrals to other specialists coordinated within 1–5 days, and interim phone call check-ins within 2–4 weeks. Feasibility: —Total of 272 visits across the sample (median of 4 visits; range, 1–7 visits), median visit duration, 70 minutes; median travel time, 30 minutes —83.5% of visits completed all defined activities, home safety assessments performed at 98.2% of visits, advanced directives addressed with 89.4% of patients Satisfaction (CSI-SF; range, 0–100): —48.8% of patients completed (median score, 98.1) —31.4% of caregivers completed (median score, 96.3) Utilization over 2 years of HVP implementation: —Subset with longitudinal data who completed at least 2 home visits (n = 61), significant decrease in hospitalization and emergency department visits during HVP implementation compared with rate 12 months prior to HVP implementation
Frundt et al, 2018[35]	Pre-test post-test n = 184 Mixed sample: PD, n = 169 Atypical PD, n = 5 (3 PSP, 1 FTD, 1 CBS) Uncertain diagnosis, n = 10	Outpatient PD specialist center Hamburg Parkinson's Day-Clinic (HPDC), Germany	Movement disorders neurologist, PD nurse, occupational therapist, physiotherapist, speech therapist, psychotherapist, music therapist, consultant of social services, nutritional advisers	MDS-UPDRS III AIMS PDNMS BDI-II MoCA PDSS-2 King's Pain Scale QUIP PDQ-39	Day of admission Day of discharge			Patients attended 5 days for 7–8 hours each day over the course of 3 weeks and individualized treatment plans are implemented. Movement neurologist and PD nurse assess motor and nonmotor symptoms at each visit and further individualize plan and refer to other core team members based on patient needs. Results: —Significant improvements observed across all outcome measures on day of discharge compared with day of admission —Largest proportions of patient improvement observed for PDQ-39 (77.6%), MDS-UPDRS III (77.0%), and King's Pain Scale (70.1%)
Hack et al, 2015[36]	Pilot study, pre-test post-test n = 7	Home visits Operation House Call (OHO), USA	Movement disorders fellows, movement disorders neurologists, neurosurgeon, neuropsychologist, psychiatrist, physical therapist, occupational therapist, speech therapist, social worker	UPDRS-III H&Y	BL 1 year			Aiming to provide a person-centered model and health care access to PD patients in a rural setting without health insurance and unable to afford transportation Movement disorders fellows perform all home visits and present during video rounds with all other members of the interdisciplinary team to make recommendations for referrals and coordinate care Results: significant improvement in UPDRS-III at 1-year follow-up and trend toward significant improvement in "on" H&Y

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
Higuchi et al, 2016[37]	Observational cohort study n = 164	Outpatient PD specialist center University of Florida Health Center for Movement Disorders and Neurorestoration Interdisciplinary Team, USA	Movement disorders neurologist, neurosurgeon, neuropsychologist, psychiatrist, physical therapist, occupational therapist, speech therapist	Rate of unintended hospitalizations PDQ-39 UPDRS-III	Preoperative/postoperative 6 months 12 months			Examined the impact of interdisciplinary DBS screening on unintended hospitalizations and quality of life postoperatively. Risks and benefits for each DBS candidate discussed at interdisciplinary team meeting requiring input from all 7 core team members and consensus achieved prior to intervention. Team members described major and minor concerns for patients regarding their risk of unintended postoperative hospitalizations. Results: —Of 164 PD patients screened, 133 were deemed appropriate for DBS —Postoperatively, unintended hospitalizations (UH) occurred in 21% of patients (n = 28) —Major concerns for those with UH during screening came primarily from neurology, neuropsychology, and psychiatry (most common major concerns: cognition, anxiety, depression) —PDQ-39 at 12 months: patients with a score of 200 or higher were significantly more likely to have an UH —No group differences in UPDRS-III
Holloway et al, 2006[31]	Pilot study/program evaluation n = 22	Outpatient PD specialist center Care Pathway framework for PD, UK	Movement disorders neurologist, PD nurse	Semistructured interviews	12 months			Examine use of Care Pathway framework for PD to simplify referral processes and improve communication across health and social network referral sources to facilitate individualized, interdisciplinary treatment plans Care Pathway elements include an information pack listing local resources, a problems/needs form, clinic summary documentation, and service record sheet; the latter 2 documents were questionably effective, and the service record form was rarely completed based on structured interviews at 12 months Authors stated that although patients expressed satisfaction and providers expressed enthusiasm with various aspects of the framework, their "situations showed very little change overall."
Jones et al, 2016[38]	Program evaluation	Outpatient PD specialist center Canberra Hospital and Health Service PD and Movement Disorder (PMD) Service, Australia	PD nurse specialist (lead care provider and coordinator), movement disorders neurologist, general neurologist	Discussions with stakeholders and patients	Evaluation of first 2 years of program			PMD Service provides nurse-led education, clinical support, and care coordination in the Australian Capital Territory Primary objectives: —Improve patient care, self-management, quality of life, well-being, and caregiver burden —Improve knowledge and skills of health care professionals —Avoid unnecessary hospital and nursing home placements Results of program evaluation: —Questionnaires completed by patients and health care professionals reported improved understanding of the disease and management plan — No discernable change in hospital admissions rates after program initiation compared with prior rates
Miyasaki et al, 2012[39]	Pretest/posttest n = 65	Outpatient PD specialist center Palliative care program for PD and related disorders, Canada	Movement disorders neurologist, nonnurse coordinator, palliative care physician, wound care counselor, spiritual adviser	ESAS-PD	3 months			Patients are evaluated by care coordinator in each clinic visit and discussed with movement disorders neurologist and palliative care physician to reach consensus regarding interventions and referrals to other health care providers based on individualized assessments and patient needs —Patients, with assistance from caregivers, completed the ESAS-PD at the first visit and second visit Results: ESAS-PD total score significantly lower at second visit, and symptoms that responded most to interventions included dysphagia, constipation, anxiety, pain, and drowsiness

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
Vaughan et al, 2017[40]	Retrospective chart review n = 29	Outpatient PD specialist center Interdisciplinary PD Comprehensive Care Clinic (CCC), USA	Movement disorders neurologist, PD nurse practitioners, sleep medicine specialist, geriatrician, neuropsychologist, psychiatrist, physical therapist, occupational therapist, speech therapist, social worker	AAN quality indicators UPDRS-III	BL 12 months			Patient and caregivers attending the CCC met with team members from each key specialty area for a 2-day evaluation of motor and nonmotor symptoms to develop individualized treatment plans. Record review of patients participating in CCC compared with a matched sample of patients receiving standard specialist care at the center to evaluate how many AAN quality indicator measures were completed at the 12-month follow-up Results: —PD patients who participated in the CCC received significantly more assessments recommended by AAN (average 10/10 quality indicators) than a matched sample of PD patients receiving standard of care at the center (average 5/10 quality indicators) —No significant group differences in UPDRS scores
Rompen at al, 2019[41]	Retrospective electronic medical record review n = 14,000 (approximately)	Professional network-based multidisciplinary allied health care Kaiser Permanente	Physical therapist, speech therapist, occupational therapist, general neurologist, movement disorders specialists	Percentage of patients receiving specialized allied health care	2 years			Nine interventions delivered through creation of a network of health care providers modeled on the Dutch ParkinsonNet: (1) professional training of providers, (2) facilitate creation of networks, (3) codesigning care plans, (4) organize information technology, (5) train the trainers, (6) inform involved providers, (7) streamline referrals and concentration of care, (8) educate patients, (9) build a network for movement disorders specialists Results: —Proportion of patients receiving specialized allied health care improved from 30% at baseline to 55% in year 1 and 67% in year 2. Demonstrated feasibility of transferring care models from one health care system to another.
Ritter et al, 2019[42]	Pretest/posttest n = 83	Inpatient multidisciplinary rehabilitation program (3 weeks) Baerum, Norway	Occupational therapist, physical therapist, doctors, neurologists, nurses, sports educators, cognitive behavioral therapists, nutritionists	PDQ-39, GSE	3 weeks			Patients were admitted for 3 weeks and a primary contact coordinated among 10 health care disciplines to achieve goals set by the patient. Both individual and group sessions were provided at a frequency of physical therapy of at least 30 minutes 3 times a week, group speech therapy twice a week, and additional components (CBT, disease-specific educational groups, etc.) in an individualized manner. Results: —Higher functional status ($P < 0.001$), general self-efficacy ($P < 0.01$), and quality of life ($P < 0.001$) at 3 weeks compared with baseline
Marumoto et al, 2019[43]	Quasi-randomized, controlled trial n = 80	Inpatient Enhanced Multidisciplinary Care (EMC) versus multidisciplinary rehabilitation (MR) Hyogo, Japan	EMC neurologists, physiatrists, physical therapists, occupational therapists, speech therapists, psychologists/ medical social worker, nurse, music therapists, physical education instructors, pharmacists, nutritionists	UPDRS, PDQ-39, MMSE, LEDD	8 weeks, 17 hours/week for both groups			Compared enhanced multidisciplinary care with multidisciplinary rehabilitation, both in inpatient settings Results: —Quality-of-life scores significantly improved with EMC compared with MR

(Continues)

TABLE 1. Continued

Randomized, controlled trials included in meta-analysis

Study	Settings	Core team members included in intervention implementation	Primary outcome[a]	Secondary outcomes	Times	Sample size (IG:CG)	Control	Intervention description
		MR neurologists, physiatrists, physical therapists, occupational therapist, speech therapist, medical social worker						
Harris et al, 2019[44]	Clinical process redesign in the emergency department Sydney, Australia	Emergency department physician, neurologist, nurses, pharmacists, speech pathologists	Medication documentation, medication errors		3 months		Care Pathway for PD patients presenting to the ED was redesigned to include (1) a clinical pathway and educational program, (2) electronic medical record alert, (3) pharmacy electronic referral alert, (4) PD information brochure access, (5) green paper medication chart sticker, (6) relocation of PD medications. Results: —50% reduction in medication errors, 21% improvement in timely PD medication administration, reduced length of ED stay	
Connor et al, 2019[45]	Care Coordination for Health Promotion and Activities in Parkinson's Disease (CHAPS) VA Medical Centers, USA Randomized control study n = 328	Nurse case manager, PD specialists/ neurologists, primary care physicians, psychiatrist, physiatrist, physical therapist, occupational therapist, speech therapist, social worker	AAN PD quality indicators, HUI3, UPDRS, MOS, GSE, CAHPS, PACIC, WHO-5, PHQ-2, PHQ-9		24 months		Compared with the effects of a nurse-led guided care management program to standard care Results: —Increased adherence to PD quality-of-care indicators as documented in the EMR —Screening instrument for depression showed improvement in the intervention group compared with usual care	

Retrospective audit of medical records, pretest/posttest interviews n = 71

AAN, American Academy of Neurology; ADLs, activities of daily living; AIMS, Abnormal Involuntary Movement Scale; ALDS, Academic Medical Centre linear disability score; BBS, Berg Balance Scale; BDI, Beck Depression Inventory; BELA-A-k, belastungsfragebogen Parkinson angehörigen-kurzversion; BL, baseline; CAHPS, Consumer Assessment of Healthcare Providers and Systems; CBS, corticobasal syndrome; CBT, cognitive behavioral therapy; CSI-SF, Caregiver Satisfaction Survey – Short Form; CSI, Caregiver Strain Index; CMS, caregiver's mood status; DBS, deep brain stimulation; DLB = dementia with Lewy bodies; ED, emergency department; ESAS-PD, Edmonton Symptom Assessment System Scale for PD; EQ-5D-3L, EuroQol-5D; FAB, Frontal Assessment Battery; FIM, Functional Independence Measure; GHQ-12, General Health Questionnaire-12; GSE, General Self-Efficacy Scale; FTD, frontotemporal dementia; HADS-A, Hospital Anxiety and Depression Scale (Anxiety subscale); HADS-D, Hospital Anxiety and Depression Scale (Depression subscale); HUI3, Health Utilities Index 3; H&Y, Hoehn & Yahr; LEDD, levodopa-equivalent daily dose; MADRS, Montgomery Asberg Depression Scale; MBT, MiniBestTest; MCS, mental health composite score of the SF-12; MDS-UPDRS-III, Movement Disorder Society Unified Parkinson's Disease Rating Scale, Part III Motor Examination; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; MOS, Medical Outcomes Study Social Support Scale; MSA, multiple systems atrophy; NHPT, nine-hole peg test; NMSS, Non-Motor Symptom Scale; PACIC, Patient Assessment of Chronic Illness Care; PANDA, Parkinson Neuropsychometric Dementia Assessment; PCS, physical health composite score of the SF-12; PDQ-8, Parkinson's Disease Questionnaire–8; PDQ-39, Parkinson's Disease Questionnaire–39; PDDS, Parkinson's Disease Disability Scale; PMS, patient's mood status; PHQ-2, -9 = Patient Healthcare Questionnaire; PSP, progressive supranuclear palsy; QUIP, Questionnaire for Impulsive-Compulsive Disorders; TUG, Timed Up and Go test; TMT A&B, Trail Making Test A&B; SCOPA-PS, Scales for Outcomes in Parkinson's Disease – Psychosocial; SEADL, Schwab and England Activities of Daily Living; SF-36, 36-Item Short Form Health Survey; SF-12, 12-Item Short Form Health Survey; STAI-Y, State Trait Anxiety Inventory; SDS, Zung Self-Rating Depression Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAS, Visual Analog Scale; WCST, Wisconsin Card-Sorting Test; WHO-5, WHO Well-Being Index 5.
[a]Primary outcome listed in RCTs included in meta-analysis is that which the study authors identified as their primary outcome.
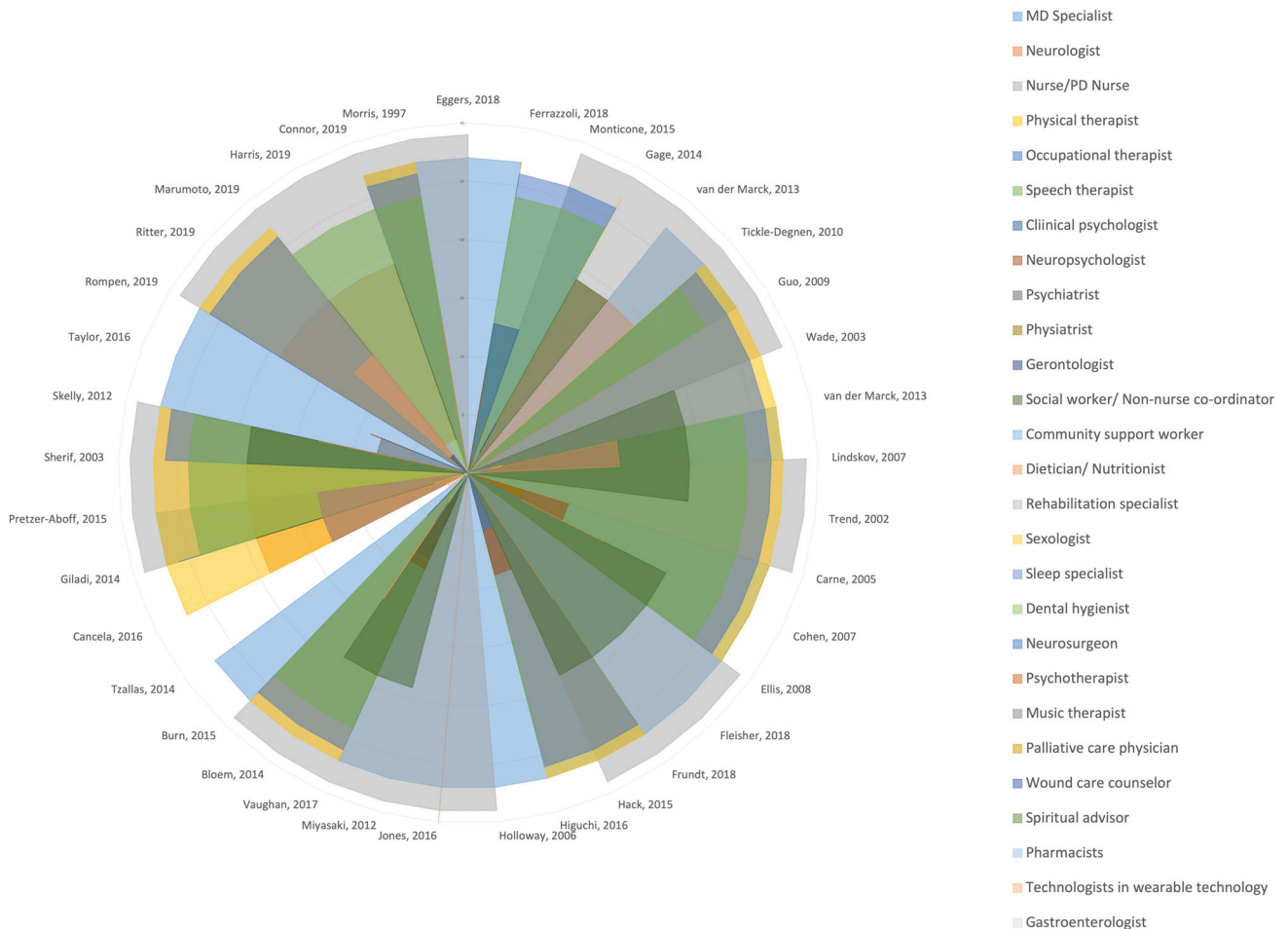
FIG. 2. Composition of teams in models included in the systematic review. The radial bars radiating towards each study represent the team members in that study. The length of the radial bar represents the frequency at which each profession/ specialty is represented when data is combined across all studies. For example, PD nurse/ nursing professional (grey bar) was the most common team member across studies, which is represented by the length of the grey bar. This is followed by movement disorder (MD) specialist (light blue bar), physical therapist (yellow bar) and others. For a more detailed representation of team composition of an individual model, please see online supplementary material Figure S3. [Color figure can be viewed at wileyonlinelibrary.com]

in the outpatient setting with or without care coverage extending to home or community.[12,15,16,27,30,33,35,37-43,47,49-57] Two models were specifically tailored for perioperative evaluation of patients for deep brain stimulation, and another targeted neuropsychiatric symptoms in a comprehensive manner.[32,39,57] All the other care models were generic in terms of the health care needs of persons with PD. One study reported an inpatient care coordination model specific to PD patients presenting to the emergency department.[46] Strategies for care coordination varied — a majority of the models involved a point of contact for the patient or caregiver who functioned as a manager to coordinate communication and consultations among the patient and other providers. The primary coordinator role was taken up by specialist nurses, movement disorders neurologists, or others such as the social worker.[12,14,16,30,33,40-42,46,47,51] This eliminated the

need for the entire care team to be present at a single site at the same time. Additional telephonic support and home visits were used across many models to facilitate this strategy. Team meetings among the health care providers at frequencies ranging from daily to monthly were reported as a means of sharing information among the provider team members. Two studies reported the use of information technology–based platforms for the monitoring of patients' day-to-day needs, coordination and feedback from the care provider, one utilized a telehealth solution.[53,55,56] Other care coordination models used a 'one-stop-clinic' approach, where care providers from multiple domains met the patient at the same location over a day or two.[35,37-39,49,54] Two models furthered this approach by taking health care provider teams to the patient's home.[35,38] Yet another model of care coordination involved initial management at expert centers followed by routine care delivery at the

community level through an integrated network of allied health care professionals.[27,50] Multidisciplinary rehabilitation models were either inpatient- (n = 6) or outpatient (n = 6)–based. Compared with the care coordination models, the focus of these studies was on multidisciplinary interventions with physical therapist, occupational therapist, and speech language pathologist playing prominent roles.

Levels of Integration

Figure 3 illustrates frequencies of individual elements of each Rainbow Model level of care integration. With regard to clinical integration (microlevel person-centered care), all included studies described explicit consent for proposed care, and the majority of studies emphasized fostering self-management for PD patients and providing educational and support opportunities, whereas the least frequently included element was specified clinical decision support tools at the point of care. Standardized processes of service coordination within institutions was the most common level of professional integration (population-based care at the mesolevel) described, whereas multidisciplinary professional education opportunities were least frequent. Other elements extending to population-based care, including mesolevel organizational integration and macrolevel systems integration were less frequently achieved, highlighting challenges for translating individualized care to broader population-based care leading to improved public health.

Meta-Analysis

Description of Studies

The 8 included RCTs were conducted between 2003 and 2018: 2 in Italy, 2 in the UK, and 1 each in Germany, the United States, Canada, and China.[12-19] There were 1149 participants overall, who were all community-dwelling adults with PD. Sample sizes of the individual studies ranged from 44 to 257 persons living with PD. Mean age of the study participants was 69.4 ± 8.8 years. Mean duration of illness was 7.4 ± 5.8 years as reported in 7 studies.[12-14,16-19] Modified Hoehn & Yahr stage ranged from 1.0 to 4.0.[12-15,17]

The settings for the intervention were fully inpatient in 2 studies.[13,14] Among the outpatient interventions, 4 were delivered at a specialist center setting with extension of care to general neurology or home-based care delivery in 2.[16-19] Care delivery was through home visits alone in 1 study and involved specialist care delivered in a general neurology setting with extension to home in one.[12,15] All studies delivered the intervention face to face on an individual basis, with additional group therapy in 4.[12,17-19]

Core team members involved in the included studies are shown in Figure 2. All studies involved a multidisciplinary team for intervention delivery. The patient/caregiver were included for active care delivery in terms of self-management or monitoring in 4 studies.[12,14,16,18] The duration of the intervention program varied from 6 to 32 weeks for the outpatient studies.

Comparison groups involved standard care in all studies. For 2 studies in which more than 1 multidisciplinary intervention was tested, we pooled the data for the multidisciplinary interventions into a single intervention group.[15,17]

All included studies reported measures to assess HRQoL that are validated or recommended for PD as a primary or secondary outcome.[7] Additional outcomes reported include Unified Parkinson's Disease Rating Scale (UPDRS) items II and III, activities of daily living (Schwab and England scale, Functional Independence Measure, Parkinson's Disease Disability Scale), gait (Berg Balance Scale, Timed Up and Go test, falls, stand-walk-sit time), nonmotor symptom assessment scales (Non Motor Symptoms Scale, Becks Depression Inventory-2, Parkinson Neuropsychometric Dementia Assessment, Self-Rating Depression Scale, Montgomery Asberg Depression Rating Scale, Scales for Outcomes in Parkinson's Disease-Psychosocial, Hospital Anxiety Depression Scale), medication dosages (levodopa-equivalent daily dose), hospital admissions, patient satisfaction, and caregiver strain (Caregiver Strain Index). One study reported costs analysis.[15] None of the included studies reported adherence to care quality measures. Adverse events were documented in 2 studies — one reported no adverse events and the other minor adverse events (transient pain, mood disturbances, autonomic, and sensory problems), which were similar in frequency in both the intervention and control groups.[14,17] No major adverse events were reported.

Risk of Bias in Included Studies

The risk of bias assessment for included studies is presented in the supplementary materials (Supplementary Fig. 1a,b). The trials covered a wide range of methodological quality and no study achieved low risk in all the seven criteria assessed. Specifically, high risk of performance bias was common to all the studies because of practical issues associated with blinding of participants and personnel. Analysis for the presence of possible publication bias was mixed. The Begg and Mazumdar rank correlation test was not significant ($P = 0.13$, 1-tailed); however, visual inspection of the funnel plot was asymmetric (Supplementary Fig. 1c), and Egger's regression intercept test was significant ($P = 0.01$, 1-tailed), suggesting the presence of publication bias in this literature.

Clinical Integration

Professional Integration

Organizational Integration

Systems Integration
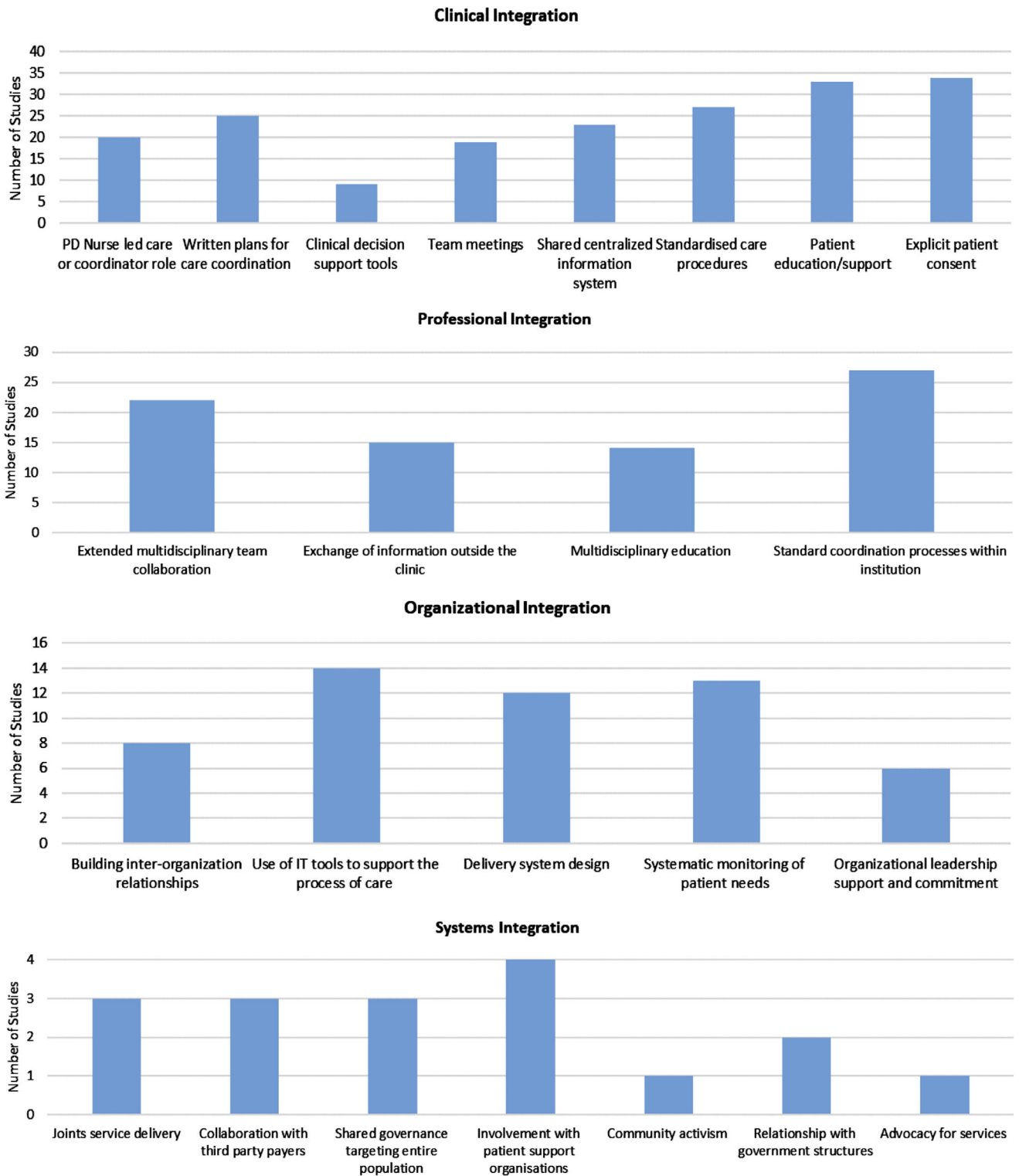
FIG. 3. Rainbow model levels of integration. [Color figure can be viewed at wileyonlinelibrary.com]

Effects of Interventions — Quality of Life

HRQoL scores were available for 1149 participants. HRQoL measures used were PDQ-39 (n = 7) and PDQ-8 (n = 1). We used a stepwise approach for the meta-analysis. Pooling data from all the available RCTs (n = 8) resulted in significant heterogeneity ($I^2 = 90\%$). Various factors including the intervention that was delivered, setting, duration of follow-up and quality of the studies were considered to be contributing to the heterogeneity. One single study that reported a short-

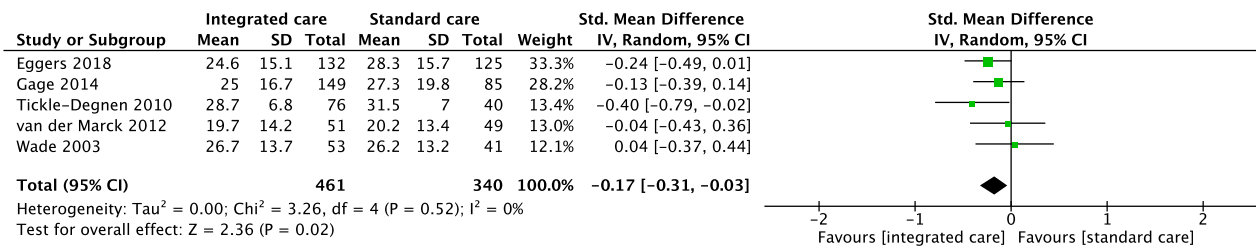| Study or Subgroup	Integrated care			Standard care			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Eggers 2018	24.6	15.1	132	28.3	15.7	125	33.3%	−0.24 [−0.49, 0.01]	
Gage 2014	25	16.7	149	27.3	19.8	85	28.2%	−0.13 [−0.39, 0.14]	
Tickle–Degnen 2010	28.7	6.8	76	31.5	7	40	13.4%	−0.40 [−0.79, −0.02]	
van der Marck 2012	19.7	14.2	51	20.2	13.4	49	13.0%	−0.04 [−0.43, 0.36]	
Wade 2003	26.7	13.7	53	26.2	13.2	41	12.1%	0.04 [−0.37, 0.44]	
Total (95% CI)			461			340	100.0%	−0.17 [−0.31, −0.03]	

Heterogeneity: Tau^2 = 0.00; Chi^2 = 3.26, df = 4 (P = 0.52); I^2 = 0%
Test for overall effect: Z = 2.36 (P = 0.02)

Favours [integrated care] Favours [standard care]

FIG. 4. Forest plot of meta-analysis exploratory subgroup analysis. Forest plot of data from studies assessing the effect of integrated care delivered in the out-patient setting on Health Related Quality of Life at six months or beyond, compared to standard care showing significant effect in favor of integrated care (SMD −0.17 [−0.31 - −0.03], I^2 = 0%). [Color figure can be viewed at wileyonlinelibrary.com]

term outcome (assessment at the end of 8 weeks of intervention) showed a significant effect in favor of integrated care (SMD, −4.10; 95% CI, −5.17 to −3.02; P < 0.001).[18] Although this study contributed only 7.6% to the overall results in terms of weight, we performed a sensitivity analysis excluding it. In this model, we pooled data from the remaining 7 studies that reported long-term outcomes (at least 6 months), that did not alter the results and still revealed significant heterogeneity (I^2 = 74%). This model included studies of integrated care delivered both in the outpatient and the inpatient settings. The patient population in the inpatient studies was significantly older than in the outpatient studies, and the intensity and frequency of intervention was different among these groups. Considering the heterogeneity in the population and intervention, we performed a post hoc exploratory subgroup analysis pooling data from studies assessing outpatient integrated care models separately (Fig. 4). Heterogeneity using the I^2 statistic was 0% for this subgroup. Pooled data from the outpatient programs reporting long-term outcome suggested a significant effect of integrated care on quality of life in PD compared with standard care (SMD, −0.17; 95% CI, −0.31 to −0.03; P = 0.02). A single study that reported short-term outcome (8 weeks) in the outpatient setting showed a significant effect in favor of integrated care (SMD, −4.10; 95% CI, −5.17 to −3.02; P < 0.001).[18] Significant heterogeneity (I^2 = 92%) limited the interpretation of pooled results from the 2 studies done in an inpatient setting.[13,14]

Discussion

This systematic review identified several unique models of health care offering multidisciplinary and integrated care to patients with PD. We identified models operating across inpatient hospital care, outpatient hospital care, and community-based settings. Most models achieved clinical integration as assessed by the Rainbow Model of Integrated Care; however, the highest level of care integration, systems integration, was achieved by only a few models.[18,27,35,37,50,54]

Although integrated care models were reported from a number of geographic locations, there were limited data available from large parts of the world, particularly Asia and Africa. We performed a meta-analysis to identify the effects of integrated care on health-related quality of life, which is an important patient-reported outcome that reflects the holistic effects of an intervention on physical, mental, and social domains. When considering the interventions overall, significant heterogeneity limited pooling of data across studies. In addition to the variability of interventions delivered, differences in the population, geographic setting, and timing of outcome assessment could contribute to the observed heterogeneity. Hence, we performed an exploratory subgroup analysis combining interventions delivered in the outpatient and inpatient settings and reporting short-term and longer-term outcomes separately. The meta-analysis of pooled data from randomized, controlled trials identified a modest yet significant favorable effect of outpatient-based integrated care on quality of life compared with usual care, without significant heterogeneity.

Many Models Available — But Are They Comparable?

This work demonstrates substantial variety in integrated care approaches with varying levels of care integration in PD. Although our subgroup analysis revealed no statistical heterogeneity for the HRQoL outcome, it is questionable whether these individual models are really comparable and whether the outcome data are truly combinable. We asked whether integrated care as an entity affected HRQoL and prespecified a definition of integrated care. Although the individual components and settings may vary across different models, they all meet the core definition of integrated care. Further data from head-to-head comparisons may be required to understand the strengths and weaknesses of the various individual models. However, previous studies in other fields such as chronic pulmonary disease, cancer care, and chronic kidney disease have successfully assessed the effect of multidisciplinary and integrated care using similar techniques, despite individual variations in

models.[58-61] As the primary outcome parameter for HRQoL reported in all RCTs was homogenous, we could combine the outcomes. Although the effect size was modest, the strongest improvements in HRQoL were seen in outpatient settings, which reflect the nature of integrated care as a model for chronic diseases that takes place mainly in outpatient settings. These results emphasize the role of integrated care in care coordination and care management rather than solely the effects of distinct therapeutic approaches (eg, physiotherapy or speech therapy only). It is also important to note that individual components of each care model included in the present review are interventions that are commonly used in isolation rather than specifically developed for integrated care programs. Although types of individual interventions included in respective models are variable and no 2 care models were identical, we defined each as "integrated care" according to specific criteria in an effort to conduct a quantitative analysis, as well as evaluate care models using the Rainbow Model.

Comparing these models in a clinical trial environment reveals the difficulties in conducting this type of study: many variables cannot be thoroughly controlled. This hampers the assessment of multifaceted interventions. Blinding the participants and intervention providers is another major challenge in practice and may contribute to significant bias, especially when using patient-reported outcomes. Subject attrition and cointerventions may also be higher with nonblinded study designs.[62] Most of the included studies did not report how they dealt with this potential bias. However, so far, no solution has been developed to control for the various varying and influencing factors in a complex model of care.

We decided to use the most often chosen primary outcome (namely, HRQoL) for further assessment and comparison of the various models. We acknowledge that this outcome alone might not reflect the best efficacy of a multifaceted intervention. There could be other informative outcomes such as measures recommended by the World Health Organization (WHO) to assess functionality, health, and disability, for example, the WHO Disability Assessment Schedule, a generic assessment instrument for health and disability across all diseases, including neurological disorders or a Likert scale self-reported global rating of well-being.[63] Currently, only a very few studies in PD use these tools as outcomes. Probably, selection of outcomes based on the conceptual framework of the International Classification of Functionality in future studies may enlarge the evidence in integrated care models. However, these outcomes were inconsistently reported in the published studies, precluding their use for a meta-analysis.

One solution to assess the extent of integrated care could be the Rainbow Model of Integrated Care

Measurement Tool (RMIC-MT), which allows for measurement of the degree of integrated care from a health professional and managers' perspective.[64] Patient-perceived care coordination is assessed through a consumer version of the RMIC-MT.[65] The RMIC-MT could be used as a future tool for outcome assessment of integrated care models.

Another point to consider here is the global variability: most models are developed and adopted according to local/regional conditions and requirements. There is not a "one-size-fits-all" approach that has been developed up to this point, which makes results heterogeneous and comparability complex. Learning from this variability can be driven through scenarios for, for example, Delphi panels, to identify the crucial team members to deliver integrated care. It is not only the heterogeneity of models but also the different interpretations or inconsistencies in terminology that adds to the difficulties in developing a unified approach.[66]

These definitions focus on team aspects, whereas the term *integrated care* sets the patient at the center. After thorough reflection within the task force and a search for definitions, we decided to use the term *integrated care* throughout this article, as we considered this the most appropriate wording to describe a care approach to strengthen people-centered health systems through the promotion of the comprehensive delivery of quality services across the life span. Integrated care is designed according to the multidimensional needs of the population and the individual and is delivered by a coordinated multi- or interdisciplinary team of providers working across settings and levels of care. This definition follows the World Health Organization and describes the ultimate aim of the best possible integration of a model into an existing health care system.[67] We are aware that this definition does not fully reflect many of the applied models; however, we propose that the term *integrated care* should be used in the future to describe models of coordinated and interdisciplinary care for PD patients (and caregivers).

What Has to Be Considered to Deliver Future Integrated Care in PD?

Despite many open questions, there are already some key findings that could be considered for the implementation of current or future integrated care models in PD. A recent practice-based evidence approach has suggested some major recommendations for the organization of integrated clinical care teams in PD (Radder et al, submitted). Furthermore, there are some team members who have not been identified as "classic" candidates of an integrated care model for PD, for example, the specialist in vascular medicine, gastroenterologist, pulmonologist, neuro-ophthalmologist, urologist, geriatrician/elderly care physician, palliative care specialist,

and the dentist. The inclusion of these specialties might increase awareness about the complexity of PD-associated nonmotor symptoms and lead to initiation of more efficient referrals to the appropriate health care professionals.[68] Indeed, a recent RCT showed extended multidisciplinary care to be better than standard multidisciplinary rehabilitation in PD.[45]

With further evolution of digital infrastructures, integrated care models have the large potential to harmonize health care pathways, personalize health care utilization according to individual needs, and facilitate communication between health care providers.[69] However, systematic data on these emerging techniques and applications are currently limited.

As researchers continue to work toward discovery of disease-modifying strategies to slow down, halt, or even reverse the neurodegenerative process associated with PD, it is important to highlight that the primary goals of integrated care models may shift in the future. At such time, when significant strides have been realized in this realm and some form of disease modification has actually become available, the composition of team members and overall structure of integrated care programs might have to be revisited.

Strength and Weaknesses of the Methodology

Using the term *parkinsonism* is open to the question of whether Parkinson;s disease or atypical parkinsonian syndromes (APS) are included in a trial, and if PD or APS patients are adequately included.[70] Two non-RCTs included in the systematic review included PD and APS patients, although the large majority in both studies (79% or more) of the total sample comprised PD patients.[35,37] Broadly, if integrated care models intend to emphasize individual person-centered assessment and care, including all parkinsonian syndromes, is logical, as the assessments and treatments will be tailored to their needs. However, from an analytic perspective, in future trials, it is recommended that subgroup analysis of PD patients be performed, as well as atypical syndrome subgroup analysis if sample size allows.

There is a growing body of evidence over the past decades that sex-specific issues have a larger impact on women with PD. Female sex is independently associated with more nonmotor symptoms and a poorer HRQoL in PD.[71] Women assess severity and burden of the disease differently.[72,73] Furthermore, the therapeutic access for women is different, for example, women are less likely to undergo deep brain stimulation.[74] Just recently it has been brought to the discussion that women with PD are underrepresented in clinical trials, with a skew of more than 7% male PD patients.[75] These findings could not be confirmed because of a lack of specific data in the RCTs. Future trials should incorporate data on sex diversity to address sex-specific issues accordingly.

In evaluating the 8 RCTs included in the overall meta-analysis, although the methodological strength of using a randomized, controlled design across the individual studies is favorable for a higher degree of certainty, no study achieved low risk in all the criteria of risk of bias assessment. In addition, all were judged to be at high risk of performance bias related to practical difficulties associated with blinding of participants and intervention personnel. On an individual study level as well as in our meta-analytic results, we thus grade the level of certainty according to the GRADE framework to be very low.

As previously noted, there are no solutions to control for the inherent variability and influencing factors in a complex integrated care model. In addition, integrated care models aim to tailor interventions depending on the assessment of specific patient needs and team member communication in an effort to individualize treatment plans. Because of the inherent variability in aspects of care models, considerable resources required to develop and implement integrated care models, and the vital inclusion of shared decision-making processes among patients and team members providing interventions to personalize care, recommendations for integrated care models — including our own — will qualify as "weak" according to GRADE criteria. Thus, although our conclusions suggest a possible positive effect of integrated care on quality of life in PD, this should be further studied in trials if methods are proposed and developed in the future to control for the myriad influencing factors in an integrated and complex model of care. Overcoming these methodological challenges may improve the certainty of evidence and strength of recommendations.

Considerations for Future Integrated Care Trials

Despite the large variety of existing studies and the various approaches of integrated care projects, several recommendations for future integrated care trials can be derived. First, a controlled study design including blinding of patients and health care professionals is a major precondition for any future RCT. However, because of the multicomponent intervention designs, including several nonpharmacological interventions in which the blinding of health care providers is not possible, guarantee of a true double-blinding of conditions is challenging. One partial solution can be a cluster randomization design, which has been used successfully before to evaluate complex care interventions in PD.[76] Second, a true placebo-design is hardly achievable. Thus, a head-to-head design, comparing the standard of care with a new intervention design is the most

favorable approach. Third, the inclusion of detailed description of the interventions, level and strategy of integration among the disciplines and health services is fundamental to facilitating the study's reproducibility and comparison of results. Fourth, researchers and clinicians should be encouraged to install new integrated care models incorporating elements of a clinical trial design as much as feasible when installing new integrated care outfits to enlarge knowledge about the effectiveness of integrated care models and the factors that promote optimal outcomes.

After analysis of the existing data, we recommend for future trials to incorporate details about: (1) the integration level among the professionals (shared evaluations/purposes/interventions), (2) the level of patient empowerment (education, shared decision making), (3) the level of expertise of professionals, (4) frequency and duration of each intervention, (5) the model for integration of the crossed boundaries of health care, and (6) the level of patients' education. Additional recommendations for future studies include evaluation of cost-effectiveness and feasibility within the respective health care system and country, identification of individual components of care models yielding the largest improvements in outcomes, and how to implement best practice in the broadest sense achievable (eg, in regions or settings where resources may be limited). Few studies report comprehensive costs of delivering integrated care, including implementation and maintenance costs, as well as additional costly outcomes such as hospital admissions, emergency service utilization, and others. Future studies should assess these for diverse settings and different models to understand the impact of integrated care on actual costs. Apart from the economic impact, challenges in delivering integrated care vary in different health care settings. Integrating such care models into existing health care frameworks may require reforms at organizational levels. Communication between team members is a vital component of integrated care and may require targeted solutions. Above all, maintaining the patient-centeredness of any care model requires an ongoing feedback and modification mechanism in which the patient and caregiver play equally vital roles.■

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Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

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