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Reviews

Physical Therapy in Parkinson's Disease: Evolution and Future Challenges

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Abstract: Even with optimal medical management using drugs or neurosurgery, patients with Parkinson's disease (PD) are faced with progressively increasing mobility problems. For this reason, many patients require additional physical therapy. Here, we review the professional evolution and scientific validation of physical therapy in PD, and highlight several future challenges. To gain insight in ongoing, recently completed or published trials and systematic reviews, we performed a structured literature review and contacted experts in the field of physical therapy in PD. Following publication of the first controlled clinical trial in 1981, the quantity and quality of clinical trials evaluating the efficacy of physical therapy in PD has evolved rapidly. In 2004 the first guideline on physical therapy in PD was published, providing recommendations for evidence-based interventions. Current research is aiming to gather additional evidence to support specific intervention strategies such as the prevention of falls, and to evaluate the implementation of evidence into clinical practice. Although research focused on physical therapy for PD is a relatively young field, high-quality supportive evidence is emerging for specific therapeutic strategies. We provide some recommendations for future research, and discuss innovative strategies to improve the organization of allied health care in PD, making evidence-based care available to all PD patients. © 2008 Movement Disorder Society

Key words: Parkinson disease; physical therapy; review; practice guideline; community networks

BACKGROUND

Idiopathic Parkinson's diseased (PD) is a complex and progressive, incapacitating disease. PD severely threatens the quality of life[1] and causes a significant economic burden to patients and society.[2–4] PD is also a common disease and the number of patients worldwide is expected to rise considerably in the coming decades due to ageing of the population.[5,6]

Need for Allied Health Care

Even with optimal medical management using drugs or neurosurgery, patients are faced with progressively increasing impairments (e.g. in speech, mental and movement-related functions), activity limitations (e.g. self-care and mobility), and restrictions in participation (e.g. domestic life and social activities).[7–9]

For these remaining impairments, limitations, and restrictions, many PD patients resort to allied health services, such as speech therapy, occupational therapy, or physical therapy.[10] Unfortunately, current delivery of allied health care services is inadequate: many patients who require such care are not being referred, whereas other patients do receive care on questionable grounds or are treated for unnecessarily long periods of time.[10,11] Indeed, the median duration for ongoing physical therapy treatment periods is 79 weeks, with a median interval between consecutive sessions of

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8 days.[11] This unsatisfactory situation can partly be explained by: (1) the lack of strong scientific evidence for most allied health care interventions; (2) the limited knowledge and sometimes skepticism among medical doctors (e.g. neurologists, geriatricians, or general practitioners) about the added value of allied health care for PD patients; (3) the absence of PD-specific expertise among most allied health therapists[10,11]; and (4) the unavailability of certain allied health services in the community. These factors might well keep physicians from referring their patients, and also explain why treatment is suboptimal for those patients who are being referred.

Physical Therapy

The most widely used form of allied health care for PD is physical therapy.[10] The main goals of physical therapy are to improve limitations in gait, physical capacity (i.e. strength, mobility and endurance), posture, and balance.[11,12] Utilization of physical therapy within Europe is unknown. However, recent surveys suggest that the numbers vary considerably from country to country, ranging from as low as 7% in the U.K. to as much as 60% in the Netherlands.[11,12]

In this review, we describe the professional evolution and scientific validation of physical therapy in PD, and highlight several future challenges.

THEORETICAL FRAMEWORK

In 2000, Morris was the first to describe a theoretical framework supporting the use of physical therapy in PD. The model was based on the pathophysiology of movement disorders in basal ganglia disease, on scientific evidence, and on personal observations of physical therapy interventions in PD.[13] Morris described task-specific strategies to improve the performance of activities (e.g. gait, transfers such as sitting down or turning in bed, and manual activities), the prevention of falls, and the maintenance of physical capacity (e.g. muscle force and aerobic capacity). These strategies incorporate the use of external cues and cognitive movement strategies. External cues include visual, auditory, or proprioceptive stimuli that are either presented rhythmically or serially (to improve the continuation of gait) or as isolated "one-off" cues (to initiate movements such as gait or transfers). By applying external stimuli instead of the usual internal cues (which normally happens in the healthy brain), alternative circuitries in the brain can be engaged to accomplish the task, while avoiding the defective basal ganglia circuitry.[14] With cognitive movement strategies, complex movements are broken down into separate components. Subjects are trained to perform each of the components separately, and to pay conscious attention to their execution. Mental rehearsing is part of this training. Cognitive movement strategies are mainly used to improve the performance of complex movements such as transfers or manual activities. Morris also stressed the importance of involving the caregiver to optimize therapy.

In a recent update, she provided specific suggestions for physical therapy at different stages of PD, based on principles of neural adaptation and clinical research findings.[15] She also underscored the importance of early referral, for assessing patients' baseline levels of impairments, activity limitations and participation restriction, and to possibly slow down disease progression by providing locomotor training.

EVOLUTION OF THE EVIDENCE

Structured Evidence Search

The highest level of evidence for therapeutic interventions is provided by (systematic reviews of) good quality randomized controlled trials (RCTs), followed by RCTs of lower quality and other comparative studies. In the field of physical therapy in PD, the main difference between a good and a lower quality RCT turned out to be the number of patients included (powered versus underpowered). To ascertain that essential evidence was not overseen, we focused in our structured evidence search on (systematic reviews of) RCTs and controlled clinical trials (CCTs). In CCTs, patients are (1) definitely assigned prospectively to one of two or more alternative forms of health care using some quasi-random method of allocation (such as alternation, date of birth, hospital number), or (2) possibly assigned prospectively to one of two or more alternative forms of health care using a random or quasi-random method of allocation.[16] All RCTs and CCTs with sufficient data concerning the efficacy of physical therapy in PD were included.

To identify these (systematic reviews of) RCTs and CCTs, we performed a structured literature review in the electronic databases of Medline, Cinahl, Embase, PEDro, and the Cochrane Library for publications up to and including January 2008. We used the MESH-heading Parkinson Disease in combination with MESH-headings Physical Therapy Modalities, Physical Therapy (Specialty), Exercise Therapy, or Exercise Movement Techniques, or with the free text Physio-

therapy. Only publications written in Dutch, English, French, or German were included. Furthermore, we evaluated cross-references, and expert recommended references. A review was only classified as being systematic when explicit and reproducible methods had been used to present the original studies, which included at least the inclusion criteria, search dates and database(s).

In addition, to gain insight in ongoing and recently finished but not yet published RCTs and CCTs, we evaluated proceedings of conferences on physical therapy or movement disorders held in 2006, 2007, and 2008. In case of insufficient information on study designs, we contacted the principal investigator. In addition, 35 experts on physical therapy in PD were personally contacted. These experts were asked to: (1) update their list of publications; (2) provide structured information on their recently completed and ongoing trials; and (3) provide names of other recognized experts who were not yet in our list of contact persons. Finally, databases of clinical trial registers were consulted.[17–22]

Controlled Trials

Our structured literature search yielded 38 RCTs and CCTs (see Fig. 1).[23–60] Over the past decennia, both the annual number and quality of controlled trials evaluating the efficacy of physical therapy in PD have increased substantially. In 1981 the first CCT was published.[35] Since then, 37 trials have been published, 18 of which during the last 3 years (see Fig. 1). We will not discuss all these studies individually, but highlight a few important milestones.

During the first 15 years, most trials evaluated the efficacy of a combination of physical therapy techniques, often integrated with other allied health interventions such as occupational therapy and psychology. Furthermore, interventions aimed to improve a wide variety of problems, e.g. a combination of range of movements, balance, gait, and dexterity. In 1995, the first trial was performed that evaluated only one specific physical therapy technique that was applied to improve one particular aspect of activity limitations: the use of cognitive movement strategies to improve the performance of transfers.[39] Since then, an increasing number of trials has focused on one physical therapy technique, such as the use of cues[48,57] or treadmill training[45,52,59] to improve gait; the use of specific exercises to improve balance or falls[23,36]; or specific exercises to improve aspects of physical capacity such a range of motion,[54] endurance,[25] and strength.[24,31] The results of these trials provided a first step towards a rational basis for evidence-based physical therapy.

Other significant milestones included the evaluation of long-term efficacy, and the inclusion of a sufficient number of patients to prevent type II (false negative) errors. In 1996, the first trial was performed with long-term follow-up, until 5 months after termination of the intervention.[51] Only three subsequent trials also completed long-term evaluations over at least 3-month post treatment.[23,32,47] It was not until 2007 that long-term evaluations at 6 months, as recommended in the 2002 Cochrane reviews, were performed.[23] Finally, in 2007 the results of the first large RCT with sufficient power were published.[48]

Despite these promising developments, many important milestones have still not been achieved. Results of future well-designed trials, reported according to the CONSORT statement, remain therefore highly needed.[61,62]

Systematic Reviews

We identified 11 systematic reviews[63–73] and two best-evidence summaries of systematic reviews.[74,75] In 1994, the first systematic review on physical therapy in PD was published.[71] The first peer reviewed systematic review (in English language) was published in 2001.[64] Since then, eight subsequent reviews have followed. In addition, two of the Cochrane systematic reviews were synthesized in a systematic review of paramedical therapies for Parkinson's disease.[76] All reviews reported shortcomings of the trials reviewed. Main shortcomings were the small number of patients included, and the methodological flaws. Based on RCTs only, two Cochrane reviews reported that there was insufficient evidence to support or refute the efficacy of physical therapy in PD.[65,66] There was also insufficient evidence to support one specific form of physical therapy over another. A meta-analysis based on RCTs and CCTs reported significant summary effect sizes on ADL, stride length, and walking speed.[64] However, the authors warned that the small number of studies included, and the methodological shortcomings of the RCTs and CCTs, could have biased these results.

In addition to the systematic reviews, two groups performed a systematic review of systematic reviews.[74,75] These best-evidence summaries on the efficacy of exercise therapy included systematic reviews from 1965 up to 2002 for one review,[74] and from 2002 to 2005 in the other.[75] Only reviews that included at least one RCT were used. The quality of these reviews

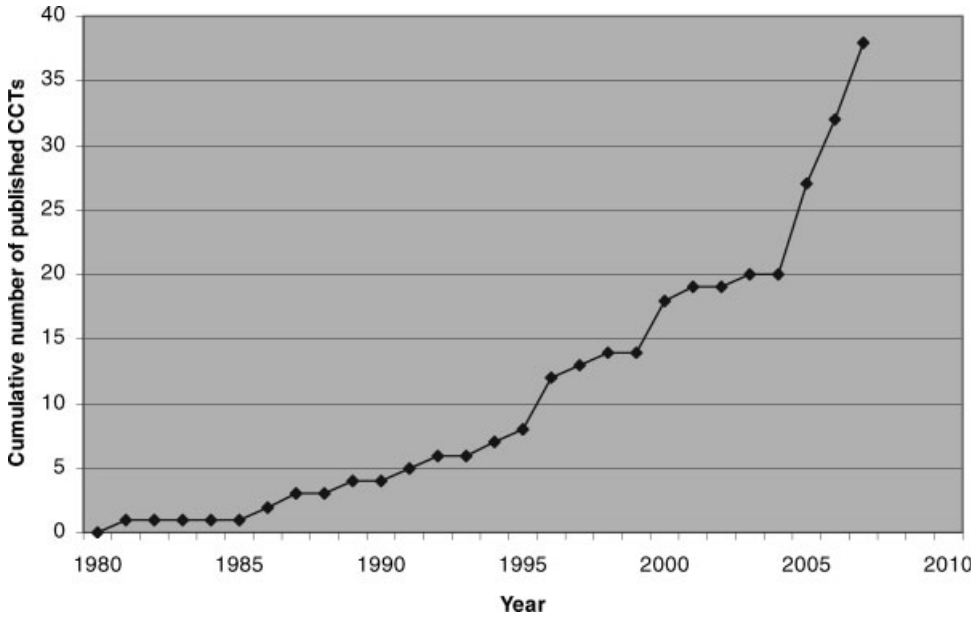

FIG. 1. Cumulative number of randomized and controlled clinical trials on the efficacy of physical therapy in PD.

was systematically assessed, and only the results of reviews with reasonable or good quality were included in the summary. For physical therapy in PD, only three of six included reviews could be used for the summary.[64–66] Based on these three reviews, both authors concluded that there are indications that physical therapy is effective in PD.

Guidelines

We identified two guidelines for physical therapy in PD.[77,78] Physical therapy in PD is often described in guidelines for medical treatment in PD,[73,79–82] but usually only briefly and not systematically. It was not until 2001 that a first evidence-based physical therapy guideline was developed. This UK guideline provided a thorough overview of scientific evidence and clinical expertise.[78] With this overview as a starting point, an evidence-based physical therapy guideline providing practice recommendations was developed in 2004.[77,83] For this guideline, all evidence related to physical therapy in PD (up to October 2003) was systematically gathered and evaluated. Evidence from research was supplemented with clinical expertise and patient values. Six specific core areas for physical therapy were identified: transfers, posture, reaching and grasping, balance, gait, and physical capacity (Fig. 2). Evidence was graded and translated into practice recommendations for both the diagnostic and therapeutic process, including outcome measures. Recommendations were arranged according to levels of evidence. The highest level of recommendation was level 2, i.e. conclusions supported by at least two independent RCTs of moderate methodological quality or with insufficient power, or other non-randomized, controlled studies. Four specific treatment recommendations reach this level 2: cueing strategies to improve gait; cognitive movement strategies to improve transfers; exercises to improve balance; and training of joint mobility and muscle power to improve physical capacity.[83] In 2006, this guideline was published online in English.

Since October 2003, the closing date for the structured literature search of the guideline, several new trials have been published. Although providing additional evidence for the efficacy of physical therapy in PD, the guideline recommendations remain valid and only need to be updated on details (Table 1).

Ongoing Trials

The response to our query for research information was 74% (responders are listed in the Acknowledgments, as well as responders to our query for research information following our visit to databases of clinical trial registers). Two authors reported that they were no longer involved in research of physical therapy in PD. We did not identify other experts in the field of physical therapy in PD that had not yet been contacted. Nineteen ongoing or completed but still unpublished RCTs and CCTs were identified (Table 2).

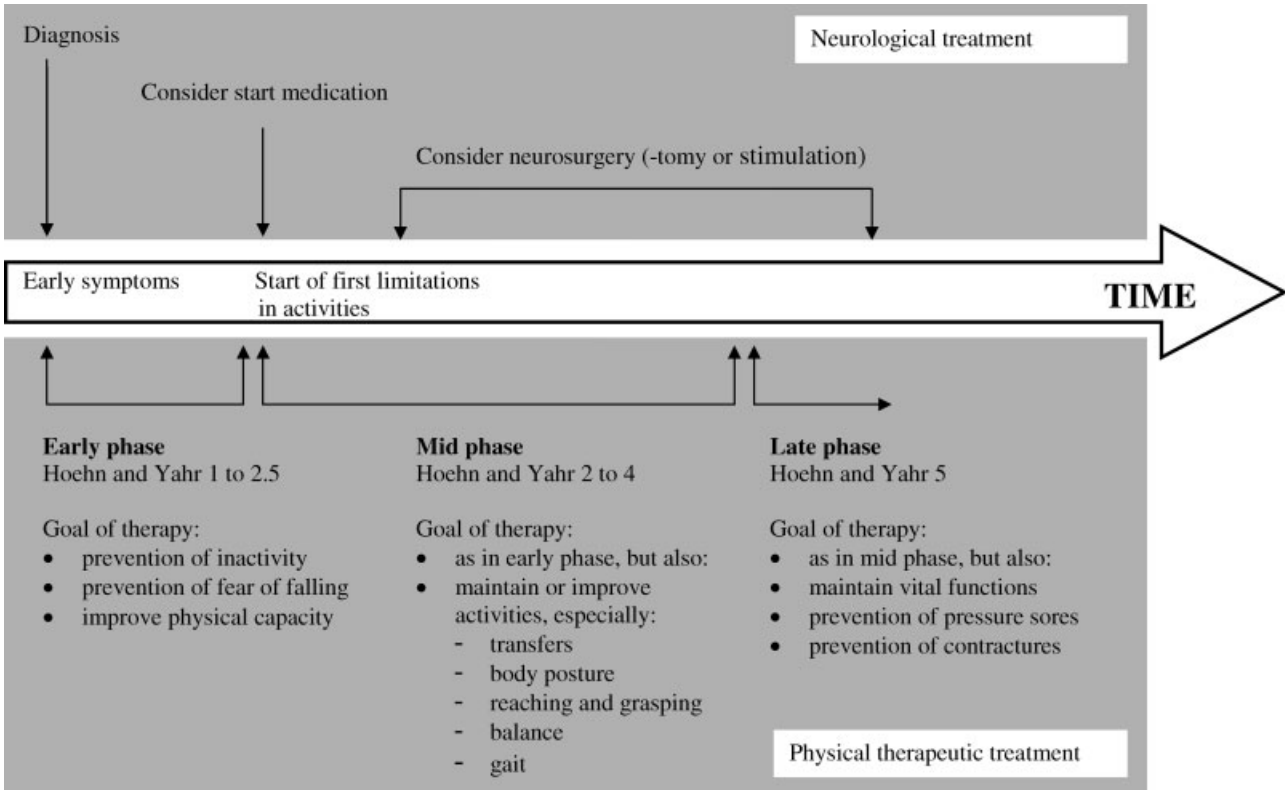

FIG. 2. Specific treatment goals of physical therapy in PD.

These studies give insight into current conceptions about trial design, selected interventions and outcome measures. Furthermore, they provide valuable information for researchers who intend to undertake new research in this field. We will highlight a few details.

Overall, these new studies show good improvements in design and intervention compared to older studies in the field. The median (targeted) number of included patients is 42. Nine of the trials are large (60 patients) to very large (over 700 patients). The majority of studies follow their patients for a prolonged time after terminating the intervention, with a median follow-up time of 3 months. In all studies, goals for the interventions cover at least one of the core areas of physical therapy in PD.[83] A limitation of these studies is that 8 of the 19 studies were not registered in a clinical trials register. Furthermore, the efficacy of physical therapy to improve limitations in reaching and grasping has not been studied.

TABLE 1. *Update guideline recommendations (October 2003 to December 2007)*

Study	New recommendation	Level
Nieuwboer[48]	Cueing strategies improve posture and gait, and the confidence to carry out functional activities without falling.	3
Nieuwboer[48]	Cueing strategies have no long-term effects at 6-weeks follow-up (duplicating evidence found by Thaut et al.[84]).[a]	2
Rochester[85,86]	Auditory cues, more than visual cues, improve gait during performance of a secondary motor task.	3
Dibble[31]	A high-force, eccentric resistance training of the lower extremities improves stair descent, the 6-minute walk, and muscle volume.	3
Mak[43]	Audiovisual cues enhance the performance of sit-to-stand.	3

[a]These results were found when cues were absent during the assessments. In daily life, PD patients will use the cues in the circumstances they need them, for example to increase their gait velocity when crossing a street. Therefore, the results might be an underestimation of the real effect when using the cues. Future study might consider assessing the patients while using the cues.

TABLE 2. *Unpublished ongoing randomized controlled trials of physical therapy in Parkinson's disease*

Principal investigators	PD population	*N*	Experimental intervention(s)	Control intervention(s)	Core area[a]	Follow-up after termination intervention	Primary outcome measure(s)	End date	Clinical trials register
Bilney B, Dodd K, O'Brien M	HY 1–4, 18–80 year	25 reached	10 weeks, 30 sessions progressive resistance strength training: twice a week group training, once a week at home	Usual care	Phys cap	4 weeks	Muscle strength maximum force (isometric, isokinetic)	Finished	Yes
Canning CG	HY 1–2.5, 30–80 year, sedentary, 1 yr no falls	20 reached	6 weeks home-based treadmill training	None	Gait	7 weeks	6 minute walk test	2007	Yes
Canning CG	HY 1–4, 30–80 yrs, falls or risk of falling	25 reached	6 months, 3 times per week (40 to 60 min) home exercise of leg strengthening and balance; a monthly exercise class by a physical therapist; cueing strategies to manage freezing; advice on falls prevention and a falls diary	Advice on falls prevention and a falls diary	Balance	No	PD falls risk score	2008	Yes
Canning CG	HY 1–4, 30–80 yrs, Falls or risk of falling	230 target	6 months, three times per week (40 to 60 min) home exercise of leg strengthening and balance; a monthly exercise class by a physical therapist; cueing strategies to manage freezing; advice on falls prevention and a falls diary	Advice on falls prevention and a falls diary	Balance	No	Number of falls	2010	Will be[b]
Capato T, Pimentel Piemonte ME	HY 2–3	42 target	5 weeks, 10 sessions (45 min) motor training with visual and auditory cues	(1) 5 weeks, 10 sessions (45 min) motor training without cues (2) no treatment	Balance	No	Berg balance, postural stress	Finished	No
Dawes D, Sackley C	HY 1–2	20 target	3 months, regular exercise (community leisure centre, fitness instructor) and $\leq$2 hrs physical therapy advice	Usual care, no exercise provision	PhysCap	6 months	PASE	2009	Yes[c]

TABLE 2. *(Continued)*

Principal investigators	PD population	*N*	Experimental intervention(s)	Control intervention(s)	Core area[a]	Follow-up after termination intervention	Primary outcome measure(s)	End date	Clinical trials register
Fisher BE	≥18 year, HY 1–4	30 reached	8 weeks, 24 sessions of high-intensity exercises	(1) 8 weeks, 24 sessions of low-intensity exercises (2) 6 education classes	Gait, transfers, other: neuroplasticity	6 months	UPDRS, gait (kinematic, kinetic), Sit-to-stand (kinematic, kinetic), neuroplasticity (TMS)	Finished	No
Goodwin V	HY 1–4, >2 falls past year	248 target	10 weeks, once a week (60 min), group based strength and balance exercises led by a physiotherapist; twice a week unsupervised home exercises	Usual care	Balance	20 weeks	Number of falls	2009 April	Yes
Kamsma YPT, Dijkstra B, Zijlstra W	HY 2–4, 55–85 year	35 reached	12 weeks, 12 sessions (60 min) home-based physical therapy: cognitive movement strategies for transfers and gait	(1) 12 weeks, 12 sessions (1hr) usual care physical therapy, (2) no physical therapy	Transfers, gait	3 months (n = 16)	Parkinson activity Scale (scores of video observation recorded at home)	2007	No
Morris ME, Iansek R	21–85 year	180 target	8 weeks, 8 sessions (120 min): (1) individualized movement strategy training, (2) progressive functional strength training	8 weeks, 8 sessions of 2 hrs training of social life skills	Balance, gait, transfers	3 months 12 months	Number of falls	2009	Yes
Morris ME, Iansek R	HY 1–4, 21–85 year	28 reached	maximum 16 sessions (45 min) in 2 weeks, inpatient movement strategy training	2 weeks, maximum 16 sessions (45 min): inpatient musculoskeletal exercises	Gait, transfers	3 months	Walking speed, UPDRS	Finished	Yes
Munneke M, Bloem BR	20–80 year	708 reached	Optimized organization of care (ParkinsonNet) in order to implement evidence-based guidelines	Usual organization of physical therapy care	All, other: organization of care	Not applicable (but patients followed for 15 months)	Quality of care, costs, satisfaction, health: PSI-PD, PDQ-39 (mob)	Finished	Yes
Pimentel Piemonte ME	HY 2–3	60 target	4 weeks, 8 sessions, motor training and cognitive movement strategies	4 weeks, 8 sessions, motor training	Gait	3 months	20 meter walk, UPDRS (ADL)	Finished	No

TABLE 2. *(Continued)*

Principal investigators	PD population	*N*	Experimental intervention(s)	Control intervention(s)	Core area[a]	Follow-up after termination intervention	Primary outcome measure(s)	End date	Clinical trials register
Pimentel Piemonte ME	HY 2-4	60 target	12 months 5 days a week, individualized home-based exercises, every 15 days physical therapy consult	12 months, once every three months, general guidance on PD	Phys cap, balance, gait	No	PDQL, UPDRS	Finished	No
Sandrini G, Pacchetti C	HY 2–4, 67 (5.8)	40 reached	4 weeks, 20 sessions (60 to 90 min), neurorehabilitation based on rhythmic auditory cues	4 weeks, 20 sessions (60–90 min), neurorehabilitation based on visual cues (parallel transverse lines)	Gait	3 months	Gait (double limb support, speed, cadence, step width and stride length), EMG	Finished	No
Protas EJ	HY 2–3	70 target	2 months, treadmill based gait and step perturbation program	2 months, standard physical therapy exercise endurance program	Balance	5 months	Falls, gait (temporal, spatial), Balance	2011	No
Schenkman ML	>50 year, HY 2–3	170 target	(1) 16 months flexibility and function exercises: 8 weeks, 3 times a week individualized treatment, followed by 8 weeks three times a week group treatment, then 2 weeks twice a week and 2 weeks once a week, and then for 11 months once a month (2) 16 months endurance training: 16 weeks 3 times a week, then 2 weeks twice a week, then 2 weeks once a week, and then 11 months once a month	16 months, once a month a group session usual care (National Parkinson Foundation home-based exercise program)	Balance, phys cap	16 months	Functional reach, economy of movement (oxygen consumption), Functional capacity (CS-PFP)	2009	Yes
Sheppard S	40–80 year, HY 1–3	23 reached	12 weeks, 24 sessions (75 min), group exercise: e.g. flexibility, balance, physical capacity)	(1) 12 weeks, 12 sessions (75 min) education: active learning, action plan development (2) combination of experimental and control intervention	Balance, phys cap, (QOL)	3 months	Timed up and go, activities balance confidence, self-efficacy (SSEMCD)	Finished	Yes
Thaut M	HY2–3, >50 year	60 target	3 weeks, 15 sessions (30 min), home-based RAS-gait training	(1) 3 weeks, 15 sessions (30 min), home-based gait exercise, no cues, (2) no-training	Gait	9 weeks	Gait (velocity, stride length, cadence, symmetry), measures of rhythmic motor synchronization	2008	No

HY, Hoehn and Yahr; PhysCap, physical capacity (i.e. strength, mobility and endurance); UPDRS, Unified Parkinson's Disease Rating Scale; SSEMCD, Stanford Self-Efficacy for Managing Chronic Disease; PSI-PD, Patient Specific Index for Parkinson's Disease; Modified PAS, Modified Parkinson Activity Scale; PASE, Physical Activity Scale for the Elderly; TMS, transcranial magnetic stimulation (cortical silent period duration).

[a]According to the evidence-based physical therapy guideline[83]; balance also includes falls.

[b]Trial commences mid 2008.

[c]Part of the Long Term Fitness Enablement (LIFE) Study.

The results of these large, well designed studies are expected to fill the current knowledge gaps of evidence-based physical therapy in PD. For example, the ongoing trial of Morris et al. promises to increase our insights into falls prevention strategies, whereas the ongoing trial by Schenkman et al. is likely to provide new evidence on interventions targeting physical capacity (Table 2).

FUTURE CHALLENGES

Optimizing Trial Design

Quality assessments that were done as part of the systematic reviews show that many published trials had serious methodological limitations. These limitations may have produced unjustified conclusions about the efficacy. Bias in study design and the common practice of using multiple outcome measures might have provided false positive results. On the other hand, false negative results may have resulted from use of inappropriate outcome measures (i.e. without particular relevance to patients, carers, or physical therapists; and without proven responsiveness), lack of power, and insufficient contrast between the experimental and control groups.

In addition, a wide variety of different outcome measures is currently being used to evaluate the same goal. In their recent review, Kwakkel et al. reported the use of 31 different outcome measures to evaluate ADL after physical therapy in PD.[69] This inconsistency in outcome measures precludes good comparison of study results and prohibits pooling of data.

Future studies are needed to further underpin any recommendations for everyday clinical practice, and to increase the levels of their evidence. Limitations of trials completed so far provide lessons for optimizing the design of future trials. Several significant milestones in the quality of studies have been reached, but many more goals remain to be reached. Four important issues should be taken into account: (1) design and recruitment; (2) delivery of physical therapy; (3) outcome measures; and (4) publication. We will briefly discuss these below.

Design and Recruitment

The most important limitations in study design that need to be tackled in future studies are proper randomization of treatment arms with a concealed allocation, and blinding of patients. Blinding of therapists is also often neglected, but this can only be avoided when two interventions are compared, keeping the therapists unaware of the preferred intervention.

Furthermore, most prior studies were underpowered. Although large (n = 142), even the study by Ashburn et al. was underpowered for their goals (i.e. falls prevention).[23] Future studies should therefore include sufficient numbers of patients, based on power analyses tailored to the primary research question and a single primary outcome measure. A specific challenge here is the difficulty in recruiting sufficient patients in an RCT of physical therapy in PD.[40,87] For example, in a study with randomization between "medical treatment with additional physical therapy" versus "medical treatment without additional physical therapy," less than 15% of eligible patients was willing to participate.[40] The main reason for not willing to participate was that patients were already receiving physical therapy (often as maintenance therapy), and were unwilling to be randomly allocated with a 50% chance to the "no physical therapy" arm. This recruitment problem might lead to a selection bias and precludes automatic generalization of the findings to the overall PD population.

Future RCTs can benefit from this knowledge and avoid the recruitment problem, e.g. using a randomly assigned cross-over design or a design of randomly assigned clusters in which not patients are randomly assigned, but for example therapists. In addition, to reduce the within-subject variability (mainly introduced by time-dependent fluctuations in dopamine levels in patients with PD), RCTs with a repeated measurement design are advocated for future trials. In 2006 the first RCT with a sufficient number of included patients was published: a cross-over study carried out through international collaboration between three university medical centers.[48] A first example of a cluster RCT is currently being carried out: the ParkinsonNet trial (Table 2). Besides overcoming problems in recruitment, this design also offers the possibility to blind patients for the intervention arm received.

When choosing a cross-over design, a sufficient time span between the two research periods is crucial, in order to avoid a carry over of long-term treatment effects into the next treatment period. When choosing a cluster RCT, a sufficient contrast between control and experimental clusters needs to be warranted. Especially when controls clusters are providing "usual care" this is a major concern.

Finally, a limitation in prior research designs was the period of follow up, which was often absent or only brief (typically less than 4 weeks). Although most ongoing studies are using a much longer follow-up,

many studies still fail to reach the recommended minimal follow-up period of 6 months.[66]

Delivery of Physical Therapy

Experience in the field of stroke indicates that training effects highly depend on the intensity of physical therapy, both in terms of frequency and duration of treatment.[88] However, prior studies in PD hardly provide insights into the optimal treatment frequency and duration of therapy. A challenge is posed by the progressive nature of PD which leads to increasing limitations, so improvements following intervention will likely deteriorate again with time. Therefore, we need to gain much better insights into the optimal delivery of interventions over time.

Outcome Measures

Most studies lack appropriate primary outcome measures that can measure clinically relevant changes afforded by physical therapy. There are several problems. First, many studies selected multiple "primary" outcome measures, thereby increasing the probability of finding positive results by accident. This strategy is, to some extent, understandable because the wide range of problems typically experienced by each individual patient makes it difficult to choose just one outcome measure, knowing that this will likely not capture all aims of a multifaceted physical therapy intervention. But in reality there can of course—by definition—be only one primary outcome measure, and this needs to be defined prior to onset of the trial. Second, the selected outcome measures were not always tailored to the goal (i.e. the efficacy of physical therapy in PD) and were therefore insufficiently responsive to change. Most of the applied outcome measures have been developed for other goals than evaluating the efficacy of physical therapy in PD. For example, most items of the widely used UPDRS concern impairments (e.g. rigidity and leg agility in the Motor Section) or activities which will not improve with physical therapy (e.g. speech and swallowing in the ADL Section) and are therefore not likely to detect change.

In future trials, primary outcome measures should be selected which are responsive and in line with the aim of the intervention studied. Consensus needs to be reached about which outcome measures can be applied in future trials. The Outcome Measure in Rheumatology (OMERACT) initiative could be used as an example.[89] Outcome measures should be selected for each core area of physical therapy in PD: gait, posture and balance, transfers, dexterity and physical capacity. The outcome measure to be chosen in a study then depends on the specific aim of the intervention being studied.

Seeing the nature of physical therapy, which mainly aims to improve activity limitations, priority needs to be given to outcome measures at the level of activities. However, improvements in clinical measures may not necessarily correspond to improvements in how the patient functions or feels. Therefore, a patient-reported measure should be used in addition to a physiologic outcome measure such as gait velocity.[90,91]

Considering the diverse nature of activity limitations seen across different individual PD patients, even within one physical therapy core area, it will be difficult if not impossible to choose a 'one-size-fits-all' outcome measure. A patient-reported, patient-specific outcome measure can bypass this problem by evaluating the specific activity limitations that are most bothersome to each individual patient. Examples of patient-specific instruments are the MACTAR,[92] the Patient Specific Functional Scale,[93] the Patient Specific Index,[40,94] the COPM,[95] and the PSI-PD (Nijkrake et al., submitted).

Finally, we will briefly discuss the widely heard concern that concurrent changes in antiparkinson medication during a trial may obscure the "pure" effects of physical therapy. It is obviously true that medication regimes should ideally be kept constant if one aims to determine the intrinsic efficacy of physical therapy. In everyday clinical practice, this is often not feasible, certainly when patients have to be followed for prolonged periods of time, as is recommended.[66]

In this case, a good alternative is to carefully document any changes in drug therapy throughout the study period, and to treat these medication adjustments either as a confounder or, better even, as a secondary outcome measure. A conceivable outcome is that physical therapy may obviate the need to drastically increase the dose of antiparkinson medication.

Publication

New trials should be registered in a database for clinical trials before the start of patient recruitment. The results of these trials should be published according to the CONSORT statement.[61,62]

Implementation of Evidence Into Clinical Practice

There are three important problems in everyday clinical practice that threaten the quality of physical therapy in PD: (1) most physical therapists lack PD-specific expertise; (2) the small volume of PD patients treated annually by each individual physical therapist;

(3) and the generally poor communication between health care providers involved in PD care (e.g. between physical therapists and referring neurologists). The lack of PD-specific expertise is partly inherent to the low volume of PD patients treated by each therapist. Even in the Netherlands where physical therapy is commonly prescribed, each therapist typically treats at most 3 patients each year.[10,11] Additional reasons for the lack of expertise include the absence of practical guidelines and the lack of high quality, competence oriented education.[10,11] One guideline has become available in 2004,[83] but simple publication does not necessarily guarantee widespread use in clinical practice (i.e. dissemination alone does not automatically guarantee implementation).[96] Considerable attention should therefore be focused on guideline implementation. However, it is unclear which guideline implementation strategies are likely to be most efficient.[97]

One option to tackle all three of the aforementioned problems is the development of community-based networks of dedicated health professionals specialized in PD. Such regional networks have recently been introduced in the Netherlands under the name ParkinsonNet.[98] The central idea is that—within a given region—PD patients should preferentially be treated by a small group of selected professionals with a high degree of expertise in PD (this includes both allied health professionals and physicians). This expertise is gained initially during an intensive training course, and is maintained at a high level because patients are being referred specifically to these ParkinsonNet therapists. Consequently, their treatment volume increases considerably, allowing therapists to continuously apply and extend their expertise in clinical practice. Furthermore, the participating allied health professionals receive continuous education, supported by a web-based training and communication facility. Finally, a PD-specific electronic patient record (EPR) is used which supports clinical decision making based on published evidence, offers support for communication and provides routine feedback from patients to the health care provider through internet-based surveys. Treatment duration can be reduced by providing therapists with clear criteria to stop treatment when the goals have been reached. The ParkinsonNet concept assumes an active role for patients and their families (patient empowerment), for example using a simple screening tool for self-assessment and self-referral, and by clarifying to patients where the ParkinsonNet therapists can be found in their region. Patients also have access to their own EPR.

Further important elements of ParkinsonNet include improved communication among all health professionals involved in PD care, and structuring of the referral process (by promoting dedicated referrals to ParkinsonNet therapists). The merits of this ParkinsonNet concept are currently being evaluated in a large cluster-randomized study (Table 2). Specifically, the ParkinsonNet trial should provide insights into the barriers for implementing such regional networks, and how a successfully implemented ParkinsonNet may affect e.g. the quality of referrals, the quality of patient care and the costs for society. The first results of the ParkinsonNet trial suggest that the implementation of ParkinsonNet increases the treatment volume per therapist from around 4 patients per year to 12, increases the quality of care, while it decreases the treatment duration and the costs for society.[99]

The question arises whether this ParkinsonNet concept can also be extrapolated to other countries, where the organization of health care may be different and where other funding models are in place. Generally speaking, implementation of network care will be hampered by a health care system that offers separate funding for the different components of the network. We suspect that single-payer systems where the government guarantees that every citizen will have a health insurance (with an option for private insurance), as is present in countries such as the United Kingdom, Germany or Canada, will facilitate implementation. In contrast, a pluralistic health care system such as found in the U.S.A. might provide barriers for implementation. The levels of funding of allied health care (which can differ markedly across different countries) may also hamper implementation, for example when patients have to pay for at least part of the costs themselves. Nevertheless, we expect that barriers provided by the organization of health care systems may be overcome by the incentives, as indicated above, that are offered to e.g. governments, health insurance companies or other funding bodies, for example by improving the efficiency of care, by actively engaging patients in their own health program, by avoiding unnecessarily prolonged treatments, and by decreasing overuse or inappropriate use of care.

Note that the ParkinsonNet concept is probably most viable within densely populated areas. Other initiatives, targeted to less densely populated areas, use e.g. competence-based education ("train the trainer"). According to this concept, existing health care resources within communities (e.g. sports instructors) or caregivers are trained to carry out parts of the evidence based practice, such as the promotion of an ongoing physical activity program. This can be supported by computer

based learning environments, including the application of an (interactive) CD-ROM.

CONCLUSION

Following publication of the first randomized controlled trial in 1981, the quantity and quality of clinical trials evaluating the efficacy of physical therapy in PD has evolved rapidly. In 2004 the first guideline on physical therapy in PD was published, providing recommendations for evidence-based interventions. Large and well-designed ongoing trials are promising to increase the current levels of evidence that support the use of physical therapy strategies, e.g. to prevent falls or to improve physical capacity. Furthermore, initiatives are underway to implement newly acquired evidence into clinical practice, and to gain future insight into barriers and effect modifiers for implementation of guidelines. Seeing the complex nature of PD, improvement of the organization of care needs to be high up the agenda.

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REFERENCES

1. Schrag A, Jahanshahi M, Quinn N. How does Parkinson's disease affect quality of life? A comparison with quality of life in the general population. Mov Disord 2000;15:1112–1118.
2. Noyes K, Liu HS, Li Y, Holloway R, Dick AW. Economic burden associated with Parkinson's disease on elderly Medicare beneficiaries. Mov Disord 2006;21:362–372.
3. Cubo E, Alvarez E, Morant C, et al. Burden of disease related to Parkinson's disease in Spain in the year 2000. Mov Disord 2005;11:1481–1487.
4. Dodel RC, Berger K, Oertel WH. Health-related quality of life and healthcare utilisation in patients with Parkinson's disease: impact of motor fluctuations and dyskinesias. Pharmacoeconomics 2001;19:1013–1038.
5. Dorsey ER, Constantinescu R, Thompson JP, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology 2006;68:384–386.
6. Rijk MCd, Tzourio C, Breteler MM, et al. Prevalence of parkinsonism and Parkinson's disease in Europe: the EUROPARKINSON Collaborative Study. European Community concerted action on the epidemiology of Parkinson's disease. J Neurol Neurosurg Psychiatry 1997;62:10–15.
7. Giladi N, Balash Y. The clinical approach to gait disturbances in Parkinson's disease: maintaining independent mobility. J Neural Transm Suppl 2006;70:327–332.
8. Poewe W. The natural history of Parkinson's disease. J Neurol 2006;253:2–6.
9. Rascol O, Goetz C, Koller W, Poewe W, Sampaio C. Treatment interventions for Parkinson's disease: an evidence based assessment. Lancet 2002;359:1589–1598.
10. Nijkrake MJ, Bloem BR, Keus SH, Mulleners W. Quality of allied health care in Parkinson's disease. Mov Disord 2006;21:S131.
11. Keus SHJ, Bloem BR, Verbaan D, et al. Physiotherapy in Parkinson's disease: utilization and patient satisfaction. J Neurol 2004;251:680–687.
12. Mutch WJ, Strudwick A, Roy SK, Downie AW. Parkinsons-disease—disability, review, and management. Br Med J 1986; 293:675–677.
13. Morris ME. Movement disorders in people with Parkinson disease: a model for physical therapy. Phys Ther 2000;80:578–597.
14. Debaere F, Wenderoth N, Sunaert S, van HP, Swinnen SP. Internal vs external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback. Neuroimage 2003;19:764–776.
15. Morris ME. Locomotor training in people with Parkinson disease. Phys Ther 2006;86:1426–1435.
16. Cochrane Eyes and Vision Group Quick guide for handsearchers. Available at: www.cochraneeyes.org [cited 2008 Jan. 7].
17. U.S. National Institutes of Health Registry. Available at: http://clinicaltrials.gov [cited 2008 Feb. 21].
18. *meta*Register of Controlled Trials (*m*RCT). Available at: www.controlled-trials.com/mrct [cited 2008 Feb. 21].
19. Australian New Zealand Clinical Trials Registry. Available at: www.anzctr.org.au [cited 2008 Feb. 21].
20. University Hospital Medical Information Network. Available at: www.umin.ac.jp [cited 2008 Feb. 21].
21. Nederlands Trial Register. Available at: www.trialregister.nl [cited 2008 Feb. 21].
22. United Kingdom's National Health Service (NHS). The National Research Register (NRR). Available at: www.nrr.nhs.uk, Issue 3, July, 2007 [cited 2008 Feb. 21].
23. Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan LD, Fitton C. A randomized controlled trial of a home-based exercise programme to reduce the risk of falling among people with Parkinson's disease. J Neurol Neurosurg Psychiatry 2007; 78:678–684.
24. Bridgewater KJ, Sharpe M. Trunk muscle training and early parkinson's disease. Physiother Theory Pract 1997;13:139–153.
25. Burini D, Farabollini B, Iacucci S, et al. A randomised controlled cross-over trial of aerobic training versus Qigong in advanced Parkinson's disease. Eura Medicophys 2006;42:231–238.
26. Caglar AT, Gurses HN, Mutluay FK, Kiziltan G. Effects of home exercises on motor performance in patients with Parkinson's disease. Clin Rehabil 2005;19:870–877.
27. Cakit BD, Saracoglu M, Genc H, Erdem HR, Inan L. The effects of incremental speed-dependent treadmill training on postural instability and fear of falling in Parkinson's disease. Clin Rehabil 2007;21:698–705.
28. Comella CL, Stebbins GT, Brown-Toms N, Goetz CG. Physical therapy and Parkinson's disease: a controlled clinical trial. Neurology 1994;44(Part 1):376–378.
29. Craig LH, Svircev A, Haber M, Juncos JL. Controlled pilot study of the effects of neuromuscular therapy in patients with Parkinson's disease. Mov Disord 2006;21:2127–2133.
30. Dam M, Tonin P, Casson S, et al. Effects of conventional and sensory-enhanced physiotherapy on disability of Parkinson's disease patients. Adv Neurol 1996;69:551–555.

31. Dibble LE, Hale TF, Marcus RL, Droge J, Gerber JP, LaStayo PC. High-intensity resistance training amplifies muscle hypertrophy and functional gains in persons with Parkinson's disease. Mov Disord 2006;21:1444–1452.
32. Ellis T, de Goede CJ, Feldman RG, Wolters EC, Kwakkel G, Wagenaar RC. Efficacy of a physical therapy program in patients with Parkinson's disease: a randomized controlled trial. Arch Phys Med Rehabil 2005;86:626–632.
33. Formisano R, Pratesi L, Modarelli FT, Bonifati V, Meco G. Rehabilitation and Parkinson's disease. Scand J Rehabil Med 1992;24:157–160.
34. Gauthier L, Dalziel S, Gauthier S. The benefits of group occupational therapy for patients with Parkinson's disease. Am J Occup Ther 1987;41:360–365.
35. Gibberd FB, Page NG, Spencer KM, Kinnear E, Hawksworth JB. Controlled trial of physiotherapy and occupational therapy for Parkinson's disease. Br Med J (Clin Res Ed) 1981;282:1196.
36. Hirsch MA, Toole T, Maitland CG, Rider RA. The effects of balance training and high-intensity resistance training on persons with idiopathic Parkinson's disease. Arch Phys Med Rehabil 2003;84:1109–1117.
37. Hurwitz A. The benefit of a home exercise regimen for ambulatory Parkinson's disease patients. J Neurosci Nurs 1989;21:180–184.
38. Inzelberg R, Peleg N, Nisipeanu P, Magadle R, Carasso RL, Weiner P. Inspiratory muscle training and the perception of dyspnea in Parkinson's disease. Can J Neurol Sci 2005;32:213–217.
39. Kamsma YPT, Brouwer WH, Lakke JPWF. Training of compensatory strategies for impaired gross motor skills in patients with Parkinson's disease. Physiother Th Pract 1995;11:209–229.
40. Keus SHJ, Bloem BR, van Hilten JJ, Ashburn A, Munneke M. Effectiveness of physiotherapy in Parkinson's disease: the feasibility of a randomised controlled trial. Parkinsonism Relat Disord 2007;13:115–121.
41. Lehman DA, Toole T, Lofald D, Hirsch MA. Training with verbal instructional cues results in near-term improvement of gait in people with Parkinson disease. J Neurol Phys Ther 2005;29: 2–8.
42. Lun V, Pullan N, Labelle N, Adams C, Suchowersky O. Comparison of the effects of a self-supervised home exercise program with a physiotherapist-supervised exercise program on the motor symptoms of Parkinson's disease. Mov Disord 2005;20:971–975.
43. Mak MK, Hui-Chan CW. Cued task-specific training is better than exercise in improving sit-to-stand in patients with Parkinson's disease: a randomized controlled trial. Mov Disord 2007;23:501–509.
44. Marchese R, Diverio M, Zucchi F, Lentino C, Abbruzzese G. The role of sensory cues in the rehabilitation of parkinsonian patients: a comparison of two physical therapy protocols. Mov Disord 2000;15:879–883.
45. Miyai I, Fujimoto Y, Ueda Y, et al. Treadmill training with body weight support: its effect on Parkinson's disease. Arch Phys Med Rehabil 2000;81:849–852.
46. Mohr B, Muller V, Mattes R, et al. Behavioral treatment of Parkinson's disease leads to improvement of motor skills and tremor reduction. Behav Ther 1996;27:235–255.
47. Nieuwboer A, De Weerdt W, Dom R, Truyen M, Janssens L, Kamsma Y. The effect of a home physiotherapy program for persons with Parkinson's disease. J Rehabil Med 2001;33:266–272.
48. Nieuwboer A, Kwakkel G, Rochester L, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. J Neurol Neurosurg Psychiatry 2007;78:134–140.
49. Pacchetti C, Mancini F, Aglieri R, Fundaro C, Martignoni E, Nappi G. Active music therapy in Parkinson's disease: an integrative method for motor and emotional rehabilitation. Psychosom Med 2000;62:386–393.
50. Palmer SS, Mortimer JA, Webster DD, Bistevins R, Dickinson GL. Exercise therapy for Parkinson's disease. Arch Phys Med Rehabil 1986;67:741–745.
51. Patti F, Reggio A, Nicoletti F, Sellaroli T, Deinite G, Nicoletti F. Effects of rehabilitation therapy on Parkinsons' disability and functional independence. J Neurol Rehabil 1996;14:223–231.
52. Protas EJ, Mitchell K, Williams A, Qureshy H, Caroline K, Lai EC. Gait and step training to reduce falls in Parkinson's disease. Neurorehabilitation 2005;20:183–190.
53. Qutubuddin AA, Cifu DX, rmistead-Jehle P, Carne W, McGuirk TE, Baron MS. A comparison of computerized dynamic posturography therapy to standard balance physical therapy in individuals with Parkinson's disease: a pilot study. Neurorehabilitation 2007;22:261–265.
54. Schenkman M, Cutson TM, Kuchibhatla M, et al. Exercise to improve spinal flexibility and function for people with Parkinson's disease: a randomized, controlled trial. J Am Geriatr Soc 1998;46:1207–1216.
55. Sidaway B, Anderson J, Danielson G, Martin L, Smith G. Effects of long-term gait training using visual cues in an individual with Parkinson disease. Phys Ther 2006;86:186–194.
56. Tamir R, Dickstein R, Huberman M. Integration of motor imagery and physical practice in group treatment applied to subjects with Parkinson's disease. Neurorehabil Neural Repair 2007;21:68–75.
57. Thaut MH, McIntosh GC, Rice RR, Miller RA, Rathbun J, Brault JM. Rhythmic auditory stimulation in gait training for Parkinson's disease patients. Mov Disord 1996;11:193–200.
58. Toole T, Hirsch MA, Forkink A, Lehman DA, Maitland CG. The effects of a balance and strength training program on equilibrium in Parkinsonism: a preliminary study. Neurorehabilitation 2000;14: 165–174.
59. Toole T, Maitland CG, Warren E, Hubmann MF, Panton L. The effects of loading and unloading treadmill walking on balance, gait, fall risk, and daily function in Parkinsonism. Neurorehabilitation 2005;20:307–322.
60. Yekutiel MP, Pinhasof A, Shahar G, Sroka H. A clinical trial of the re-education of movement in patients with Parkinson's disease. Clin Rehabil 1991;5:207–214.
61. CONSORT Group. Consolidated Standards of Reporting Trials (CONSORT) Statement. Available at: http://www consort-statement.org [cited 2008 Mar. 10].
62. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. Lancet 2001;357:1191–1194.
63. Crizzle AM, Newhouse IJ. Is physical exercise beneficial for persons with Parkinson's disease? Clin J Sport Med 2006;16:422–425.
64. de Goede CJT, Keus SHJ, Kwakkel G, Wagenaar RC. The effects of physical therapy in Parkinson's disease: a research synthesis. Arch Phys Med Rehabil 2001;82:509–515.
65. Deane KH, Jones D, Ellis-Hill C, Clarke CE, Playford ED, Ben Shlomo Y. A comparison of physiotherapy techniques for patients with Parkinson's disease. The Cochrane Library 2002 (Issue 3):[CD002815] Available at: URL:PM:11279765.
66. Deane KH, Jones D, Playford ED, Ben Shlomo Y, Clarke CE. Physiotherapy versus placebo or no intervention in Parkinson's disease. The Cochrane Library 2002 (Issue 3) Available from: URL:PM:11687029.
67. Gage H, Storey L. Rehabilitation for Parkinson's disease: a systematic review of available evidence. Clin Rehabil 2004;18:463–482.
68. Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL. The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis. Mov Disord 2008;23:621–640.
69. Kwakkel G, de Goede CJT, van Wegen EEH. Impact of physical therapy for Parkinson's disease: a critical review of the literature. Parkinsonism Relat Disord 2007;13(Suppl 3):S478–S487.
70. Lim I, Van Wegen E, de Goede C, et al. Effects of external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review. Clin Rehabil 2005;19:695–713.
71. Nieuwboer A, De Weerdt W, Nuyens G, Hantson L, Feys H. Een literatuurstudie naar de effecten van fysiotherapie bij de ziekte van Parkinson. Ned Tijdschr Fysiother 1994;5:122–128.

72. Rubinstein TC, Giladi N, Hausdorff JM. The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. Mov Disord 2002;17:1148–1160.
73. Suchowersky O, Gronseth G, Perlmutter J, Reich S, Zesiewicz T, Weiner WJ. Practice parameter: neuroprotective strategies and alternative therapies for Parkinson disease (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2006;66:976–982.
74. Smidt N, de Vet HC, Bouter LM, Dekker J. Effectiveness of exercise therapy: a best-evidence summary of systematic reviews. Aust J Physiother 2005;51:71–85.
75. Taylor NF, Dodd KJ, Shields N, Bruder A. Therapeutic exercise in physiotherapy practice is beneficial: a summary of systematic reviews 2002-2005. Aust J Physiother 2007;53:7–16.
76. Deane KH, Ellis-Hill C, Jones D, et al. Systematic review of paramedical therapies for Parkinson's disease. Mov Disord 2002; 17:984–991.
77. Keus SHJ, Hendriks HJM, Bloem BR, et al. KNGF Guidelines for physical therapy in Parkinson's disease. Ned Tijdschr Fysiother 2004;114(Suppl 3): Available at: www.kngf.nl or www.cebp.nl [cited 2008 Mar. 10].
78. Plant R, Walton G, Ashburn A, Lovgreen B, Handford F, Kinnear E. Guidelines for physiotherapy practice in Parkinson's disease. Newcastle, U.K.: University of Northumbria, Institute of Rehabilitation; 2001.
79. Italian Neurological Society and Italian Society of Clinical Neurophysiology. Guidelines for the Treatment of Parkinson's Disease 2002. Treatment of Parkinson's disease. Neurol Sci 2003;24 (Suppl 3):S165–S213.
80. Horstink M, Tolosa E, Bonuccelli U, et al. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society—European section. I. Early (uncomplicated) Parkinson's disease. Eur J Neurol 2006;13:1170–1185.
81. Horstink M, Tolosa E, Bonuccelli U, et al. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES). II. Late (complicated) Parkinson's disease. Eur J Neurol 2006;13:1186–1202.
82. Olanow CW, Watts RL, Koller WC. An algorithm (decision tree) for the management of Parkinson's disease (2001): treatment guidelines. Neurology 2001;56(Suppl 5):S1–S88.
83. Keus SH, Bloem BR, Hendriks EJ, Bredero-Cohen AB, Munneke M. Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research. Mov Disord 2007;22:451–460.
84. Thaut MH, McIntosh KW, McIntosh GC, Hoemberg V. Auditory rhythmicity enhances movement and speech motor control in patients with Parkinson's disease. Funct Neurol 2001;16:163–172.
85. Rochester L, Hetherington V, Jones D, et al. The effect of external rhythmic cues (auditory and visual) on walking during a functional task in homes of people with Parkinson's disease. Arch Phys Med Rehabil 2005;86:999–1006.
86. Rochester L, Nieuwboer A, Baker K, et al. The attentional cost of external rhythmical cues and their impact on gait in Parkinson's disease: effect of cue modality and task complexity. J Neural Transm 2007;114:1243–1248.
87. Ashburn A, Ruth MP, Louise F, Claire B, Lindsay MD, Carolyn F. Recruitment to a clinical trial from the databases of specialists in Parkinson's disease. Parkinsonism Relat Disord 2007;13:35–39.
88. Kwakkel G. Impact of intensity of practice after stroke: issues for consideration. Disabil Rehabil 2006:28:823–830.
89. Fried BJ, Boers M, Baker PRA. A method for achieving consensus on rheumatoid-arthritis outcome measures—the Omeract Conference process. J Rheumatol 1993;20:548–551.
90. FDA. Draft guidance for industry on patient-reported outcome measures: use in medicinal product development to support labelling claims. Available at: www.fda.gov/cber/gdlns/prolbl.pdf [cited 2008 Mar. 10].
91. Hobart JC, Cano SJ, Zajicek JP, Thompson AJ. Rating scales as outcome measures for clinical trials in neurology: problems, solutions, and recommendations. Lancet Neurol 2007;6:1094–1105.
92. Tugwell P, Bombardier C, Buchanan WW, Goldsmith CH, Grace E, Hanna B. The MACTAR Patient Preference Disability Questionnaire—an individualized functional priority approach for assessing improvement in physical disability in clinical trials in rheumatoid arthritis. J Rheumatol 1987;14:446–451.
93. Stratford P, Gill C, Westaway M, Binkley J. Assessing disability and change on individual patients: a report of a patient specific measure. Physiother Can 1995;47:258–263.
94. Beurskens AJ, de Vet HC, Koke AJ, et al. A patient-specific approach for measuring functional status in low back pain. J Manipulative Physiol Ther 1999;22:144–148.
95. Law M, Polatajko H, Pollock N, McColl MA, Carswell A, Baptiste S. Pilot testing of the Canadian Occupational Performance Measure: clinical and measurement issues. Can J Occup Ther 1994;61:191–197.
96. Engers AJ, Wensing M, van Tulder MW, et al. Implementation of the Dutch low back pain guideline for general practitioners—a cluster randomized controlled trial. Spine 2005;30: 595–600.
97. Grimshaw J, Eccles M, Thomas R, et al. Toward evidence-based quality improvement—evidence (and its limitations) of the effectiveness of guideline dissemination and implementation strategies 1966–1998. J Gen Intern Med 2006;21:S14–S20.
98. Munneke M, Keus SHJ, Nijkrake M, et al. ParkNet: a multifaceted strategy to implement practice guidelines for physiotherapy in Parkinson's disease. Parkinsonism Rel Disord 2008;14(Suppl 1):S64.
99. Keus SHJ, Nijkrake M, Bloem BR, et al. ParkNet implementation: evaluation of health benefits. Parkinsonism Relat Disord 2008;14(Suppl 1):S9.