



RESEARCH ARTICLE

Innovative technology-based interventions in Parkinson's disease: A systematic review and meta-analysis

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Abstract

Objective: Novel technology-based interventions have the potential to improve motor symptoms and gait in Parkinson's disease (PD). Promising treatments include virtual-reality (VR) training, robotic assistance, and biofeedback. Their effectiveness remains unclear, and thus, we conducted a Bayesian network meta-analysis. **Methods:** We searched the Medline, Embase, Cochrane CENTRAL, and [Clinicaltrials.gov](https://www.clinicaltrials.gov) databases until 2 April 2024 and only included randomized controlled trials. Outcomes included changes in UPDRS-III/MDS-UPDRS-III score, stride length, 10-meter walk test (10MWT), timed up-and-go (TUG) test, balance scale scores and quality-of-life (QoL) scores. Results were reported as mean differences (MD) or standardized mean differences (SMD), with 95% credible intervals (95% CrI). **Results:** Fifty-one randomized controlled trials with 2095 patients were included. For UPDRS (motor outcome), all interventions had similar efficacies. VR intervention was the most effective in improving TUG compared with control (MD: -4.36 , 95% CrI: -8.57 , -0.35), outperforming robotic, exercise, and proprioceptive interventions. Proprioceptive intervention significantly improved stride length compared to control intervention (MD: 0.11 m, 95% CrI: 0.03 , 0.19), outperforming VR, robotic and exercise interventions. Virtual reality improved balance scale scores significantly compared to exercise intervention (SMD: 0.75 , 95% CrI: 0.12 , 1.39) and control intervention (SMD: 1.42 , 95% CrI: 0.06 , 2.77). Virtual reality intervention significantly improved QoL scores compared to control intervention (SMD: -0.95 , 95% CrI: -1.43 , -0.52), outperforming Internet-based interventions. **Interpretation:** VR-based and proprioceptive interventions were the most promising interventions, consistently ranking as the top treatment choices for most outcomes. Their use in clinical practice could be helpful in managing motor symptoms and QoL in PD.

Introduction

With the fast aging of the world's population, the prevalence of Parkinson's disease (PD),^{1,2} a neurodegenerative condition, will increase significantly. In 2016, it was estimated that the 6.1 million people live with PD globally.³ From 1990 to 2016, the age-standardized rate of prevalence had increased by 22%, and age-standardized change in disability-adjusted life years has also increased.⁴ PD patients present with bradykinesia, defined as slowness of

movement and reduction in amplitude or speed as movements, are continued, in combination with either rest tremor, rigidity, or both.^{5–8} Postural instability often present later in the course of the disease. Such symptoms vastly affect patients' motor ability and their quality of life (QoL).^{9,10}

There is increasing interest in motor-cognitive rehabilitation therapies for PD patients but their effectiveness remains to be clarified.¹¹ Pharmacologic therapies including dopaminergic drugs such as levodopa and dopamine

agonists² are frequently associated with long-term complications such as dyskinesias and motor fluctuations^{2,6} and can also aggravate nonmotor parkinsonian symptoms such as hallucinations, cognitive impairment, and orthostatic hypotension. Several motor features, including gait and balance, do not typically respond to levodopa.¹² Another common treatment is deep brain stimulation, which involves sending electrical signals to specific brain nuclei. While it has been proven effective in improving quality of life and “appendicular” motor symptoms such as limb tremor, it remains insufficient in reducing axial motor symptoms such as gait impairment and postural abnormalities¹³ and has been shown to worsen speech intelligibility.¹⁴

Balance and gait are motor outcomes that are frequently affected in PD. These alterations are often associated with diminished functional ability, poor prognosis, and frequent falls.¹⁵ To supplement pharmacological and surgical treatment, there has been an increasing focus on using technology-based interventions to improve motor outcomes and quality of life.^{16–19} Virtual-reality (VR) training has been effective in improving motor function in chronic stroke patients.²⁰ VR technology can provide PD patients with a safe and effective environment to undergo training and rehabilitation.¹⁶ Rehabilitation assisted by robotic machines also serve to help patients achieve better motor outcomes by acting as a force multiplier for conventional physiotherapy and training.¹⁷ Rehabilitation approaches such as peripheral stimulation are noninvasive, and they show potential in improving motor outcomes.¹⁸ Internet-based interventions are also of note as they improve access to care for patients,¹⁹ hence allowing for better follow-up with patients that can contribute to positive outcomes. As motor functions may be influenced by one's cognitive ability,²¹ interventions that integrate motor and cognitive aspects have the potential to lead to better motor outcomes in rehabilitation.^{22–24} Technology-based interventions, such as the addition of a VR component to treadmill training, show promise in delivering outcomes in both motor and cognitive domains through an integrated motor-cognitive approach.²⁵ Therefore, these technology-based interventions may be used to complement ongoing pharmacological or surgical treatment and improve rehabilitation outcomes for patients.

However, for technology-based interventions, there are few large-scale randomized controlled trials evaluating the effectiveness of available interventions, and very few studies have directly compared the interventions against each other. Randomized controlled trials comparing several treatments are usually not feasible²⁶ due to sample size limitations, and conclusions concerning the effectiveness of these interventions are varied. To our knowledge, there

is no existing study that directly compares the effects of these interventions. To address this gap in knowledge, we conducted a network meta-analysis, which allows for direct and indirect comparison²⁶ among Internet-based, proprioceptive, robotic, and VR interventions against active and inactive controls, and their effects on QoL, gait, and balance parameters. For this study, Internet-based interventions were defined as any form of telemedicine, or any intervention which involved the input of healthcare professionals remotely via online means. Proprioceptive interventions were defined as any intervention that increased the proprioceptive input to the patient (e.g., through mechanical pressure stimulations or vibrations). Robotic interventions, inclusive of gait and balance training assistance, utilized robotic means to facilitate sensorimotor rehabilitation to the patients.²⁷ Virtual reality interventions generate an environment in which the patient can interact in a manner that is similar to a physical place.²⁸

With improved understanding of the impact of these interventions, the potential of these interventions can be better maximized to improve overall rehabilitation outcomes.

Methods

Search strategy

This network meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (PROSPERO CRD42022301160).²⁹ The PRISMA checklist can be found in Supplementary Material S1. The Medline, Embase, Cochrane CENTRAL, and Clinicaltrials.gov databases were searched from inception until 2 April 2024. The search strategy involved keywords and MeSH terms synonymous to “Parkinson Disease”, “robotics”, “internet-based”, “virtual reality”, “biofeedback”, “physical stimulation”, “exergaming”, and “rehabilitation”. References of related reviews were screened to ensure a comprehensive search. A copy of the search strategies can be found in Supplementary Material – Table S1.

Study selection and data extraction

Four independent authors (CEY, ECKH, NYO, and CJKL) carried out the eligibility assessment in an independent and blinded manner. The authors screened the titles and abstracts before retrieving and reviewing the full texts. A third independent author (ASM) was involved in the resolution of disputes. Only randomized controlled trials with more than 10 participants in each arm were included. Observational studies, case-control studies,

reviews, meta-analyses, editorials, commentaries, conference abstracts, and non-English language articles were excluded. Studies were included if they (i) were randomized controlled trials that (ii) evaluated outcomes related to balance and gait (iii) in patients with PD.

The primary study outcomes were changes in measures for UPDRS (motor outcome), stride length, 10-meter walk test (10MWT), timed up-and-go (TUG) test, balance scale scores, and QoL indices.

All controls for the studies, excluding the proprioceptive studies, were either usual care or active controls, where participants engaged in exercise or conventional physical therapy. For three-armed studies with two active controls, the more common active control was chosen. For three-armed studies with an active control and usual care, all three arms were included. For the proprioceptive studies, controls were placebos. For the reporting of the results, active controls are labeled "Exercise," while usual care/placebo are labeled "Control."

Data were extracted by four authors (YCE, ECKH, NYO, and CJKL) in an independent and blinded manner. The following variables were extracted: (i) baseline demographics: age, gender, disease duration, MDS-UPDRS/UPDRS Section III scores and (ii) changes in MDS-UPDRS/UPDRS Section III score, stride length, 10MWT, TUG test, balance scale scores (e.g., Mini Balance Evaluation Systems Test scores and Parkinson Disease Questionnaire Scores), and Quality of Life scores (e.g., SF-36 and PDQ-39).

Statistical analysis

All analyses were conducted in RStudio (Version 4.0.3). The Bayesian network meta-analysis was performed with the *BUGSnet* package. Mean differences (MD), standardized mean differences (SMD), and 95% credible intervals (95% CrI) were used. MD was calculated for stride length, 10MWT, and TUG test as these were continuous outcomes. A variety of scales were used for the outcomes of UPDRS (motor outcome), balance, and QoL scores. Hence for these outcomes, we calculated SMD, which is often employed to compare and meta-analyse heterogeneous measures of an outcome.^{30,31} Treatment groups were namely (i) Internet-based, (ii) proprioceptive, (iii) robot, and (iv) VR. For the purposes of analysis and reporting, we used the operational definitions as laid out in the introduction. Additionally, bio-feedback and physical stimulation treatment groups were combined under the proprioceptive group as they exert their treatment effects with the same principle of increasing the level of proprioceptive input to the patient.^{32–36} Exergaming studies were subsumed under the VR treatment group if they had elements of immersive or nonimmersive VR (e.g., Xbox Kinect). We conducted Markov Chain Monte Carlo simulations using vague priors³⁷ and a generalized linear model

with Gaussian family distribution and an identity link function.³⁸ The setting of 10,000 burn-ins, 100,000 iterations, and 1,000 adaptations was used when conducting the analysis. Trace and density plots were used to assess for model convergence and consistency. Deviance information criterion and individual datapoint posterior mean deviance contribution were used to compare goodness of fit between the consistency and inconsistency models.³⁸ The deviance information criterion was also used to select between a fixed-effects or random-effects model.³⁸ The random-effects model was ultimately chosen for all outcomes as it minimized the deviance information criterion. The output of the network analysis was presented as a heat plot, in which a blue cell indicates a positive value and a yellow cell indicates a negative value. For TUG, UPDRS (motor outcome), and QoL, a negative value indicates an improvement in the outcome (favoring the treatment arm). For balance score, 10MWT, and stride length, a positive value indicates an improvement in the outcome measure (favoring the treatment arm). Surface under the cumulative ranking (SUCRA) scores are presented for each outcome, ranking the interventions in terms of effectiveness, with higher SUCRA scores reflecting a higher likelihood that the treatment is most beneficial.

Risk-of-bias assessment

The revised Cochrane Risk-of-Bias tool for randomized trials (ROB2) was used to evaluate for risk of bias in the included studies. The ROB2 tool evaluates bias across 5 features: (i) the randomization process, (ii) deviations from intended interventions, (iii) missing outcome data, (iv) measurement of the outcome, and (v) selection of the reported result. Two independent and blinded authors (ECKH and NYO) assessed all included studies for risk-of-bias (Supplementary Material – Table S4), and disagreements were resolved through discussion with a third independent author.

Publication bias

Publication bias was assessed via visually inspecting for funnel plot asymmetry, using the R packages *netmeta* and *dmetar*. Funnel plots are presented in Supplementary Material – Figures S1–S6. Funnel plots were largely symmetrical throughout the different outcomes.

Results

Summary of included studies

A total of 5146 studies were identified after the search in the four databases. After de-duplication, 1289 studies

were screened. Full-text reviews were done for 157 studies, and eventually, 51 randomized controlled trials were included in this network meta-analysis, involving 2095 patients were included in the final analysis. Six Internet-based,^{39–44} 14 proprioceptive,^{18,35,36,45–55} 12 robotic,^{17,27,56–65} and 19 VR^{22,66–83} studies were included (Fig. 1). For most of the studies, the treatment effects were measured without the technology (i.e., motor and QoL outcomes were measured when the patients were not receiving the intervention at the point of evaluation).

All controls for the studies, excluding the proprioceptive studies, were either usual care or active controls. For the proprioceptive studies, controls were placebos.

The six most reported outcomes were changes in UPDRS (motor outcome) score (as measured by UPDRS-III or MDS-UPDRS-III), stride length, 10MWT, TUG test, balance scale scores (e.g., Mini Balance Evaluation Systems Test scores and Parkinson Disease Questionnaire Scores), and Quality of Life scores (e.g., SF-36 and PDQ-39). A summary of the included trials is included in Tables S2 and S3. The mean age of included patients ranged from 53.5 to 76.1 years for the intervention arms and 53.5 to 77.7 years for the control arms. Total duration of intervention and the duration of follow-up/ last time of clinical assessment are reported in Table S3. Majority of the interventions lasted between 4 and 12 weeks, with follow-up duration lasting between 4 and 12 weeks. Majority of included participants in the control and intervention arms had their functional ability rated between Hoehn and Yahr Scale Stages II and III.

Network analysis of interventions

For all interventions, differences in effect sizes are presented. SUCRA scores are presented in Table 1.

UPDRS (motor component)

All interventions performed similarly for UPDRS (motor component) (Fig. 2). Comparing SUCRA scores, VR (SUCRA: 79.63) performed the best, followed by robotic (SUCRA: 72.95), Internet-based (SUCRA: 42.53), exercise (SUCRA: 36.87), proprioceptive intervention (SUCRA: 36.26), and control (SUCRA: 31.75).

TUG

Virtual reality intervention significantly outperformed control interventions (MD: -4.36 , 95% CrI: -8.57 , -0.35) (Fig. 3). Comparing SUCRA scores, VR (SUCRA: 79.51) performed the best, followed by robotic (SUCRA: 75.93), exercise (SUCRA: 46.03), proprioceptive intervention (SUCRA: 43.66), and control (SUCRA: 4.87).

Stride length

Proprioceptive intervention significantly improved stride length (Fig. 4) compared to control intervention (MD: 0.11 m, 95% CrI: 0.03, 0.19). Comparing SUCRA scores, proprioceptive intervention (SUCRA: 75.17) performed the best, followed by VR (SUCRA: 68.79), exercise (SUCRA: 51.17), robotic (SUCRA: 45.87), and control (SUCRA: 8.99).

10-meter walk test

Proprioceptive intervention significantly improved 10MWT speed (Fig. 5) compared to control interventions (MD: 0.14 m/s, 95% CrI: 0.05, 0.22). Comparing SUCRA scores, robotic intervention (SUCRA: 77.78) performed the best, followed by proprioceptive intervention (SUCRA: 66.01), Internet-based intervention (SUCRA: 51.44), VR (SUCRA: 47.51), exercise (SUCRA: 43.05), and control (SUCRA: 14.23).

Balance scale scores

Virtual reality improved balance scale scores significantly (Fig. 3) compared to exercise intervention (SMD: 0.75, 95% CrI: 0.12, 1.39) and control intervention (SMD: 1.42, 95% CrI: 0.06, 2.77). Comparing SUCRA scores, VR (SUCRA: 87.00) performed the best, followed by robotic intervention (SUCRA: 68.66), then Internet-based intervention (SUCRA: 45.03), exercise (SUCRA: 43.26), and control (SUCRA: 15.37). Two studies by Picelli et al.^{57,58} reporting on balance scale scores had potentially overlapping patient cohorts. A sensitivity analysis was hence performed by preserving the study with a greater sample size.⁵⁷ The effect sizes and SUCRA score ranking remained consistent, with VR outperforming other modalities.

QoL scores

Virtual reality intervention improved QoL scores (Fig. 6) significantly compared to Internet-based interventions (SMD: -0.70 , 95% CrI: -1.38 , -0.04) and control interventions (SMD: -0.95 , 95% CrI: -1.43 , -0.52). Exercise intervention also improved QoL scores significantly compared to control intervention (SMD: -0.82 , 95% CrI: -1.28 , -0.40). Comparing SUCRA scores, VR intervention (SUCRA: 90.24) performed the best, followed by exercise (SUCRA: 76.79), then robotic intervention (SUCRA: 62.69), proprioceptive intervention (SUCRA: 36.73), Internet-based intervention (SUCRA: 27.9), and control (SUCRA: 5.64).

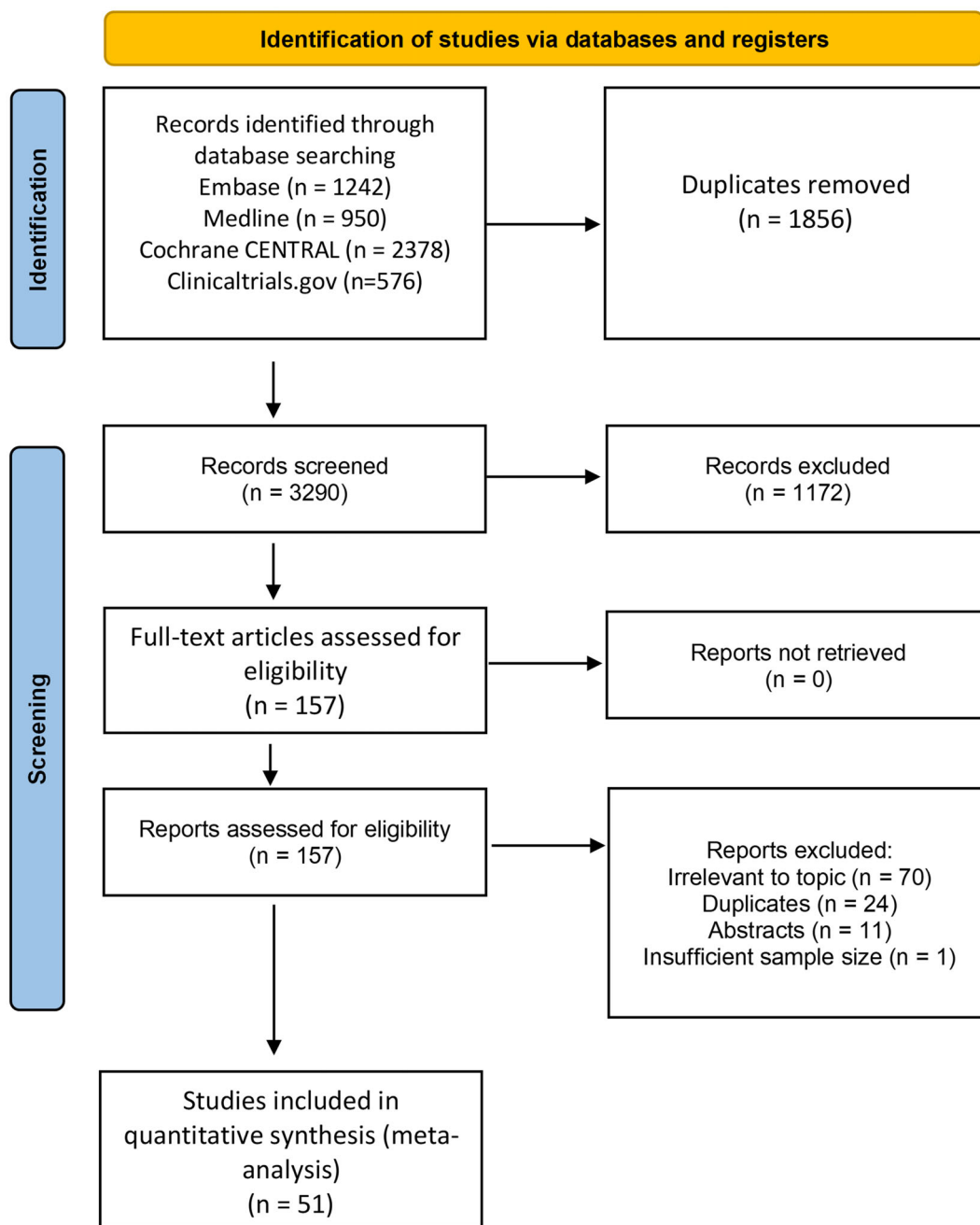


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Quality assessment

Risk-of-bias assessment using the ROB2 tool is provided in Table S4. Most of the studies are at low to moderate risk of bias. For the studies with moderate risk of bias, this was largely due to the impossibility of blinding the patients to the intervention that they receive in most studies (e.g., robotic intervention), hence causing the

second domain of the ROB2 tool to be flagged as “Some concerns.”

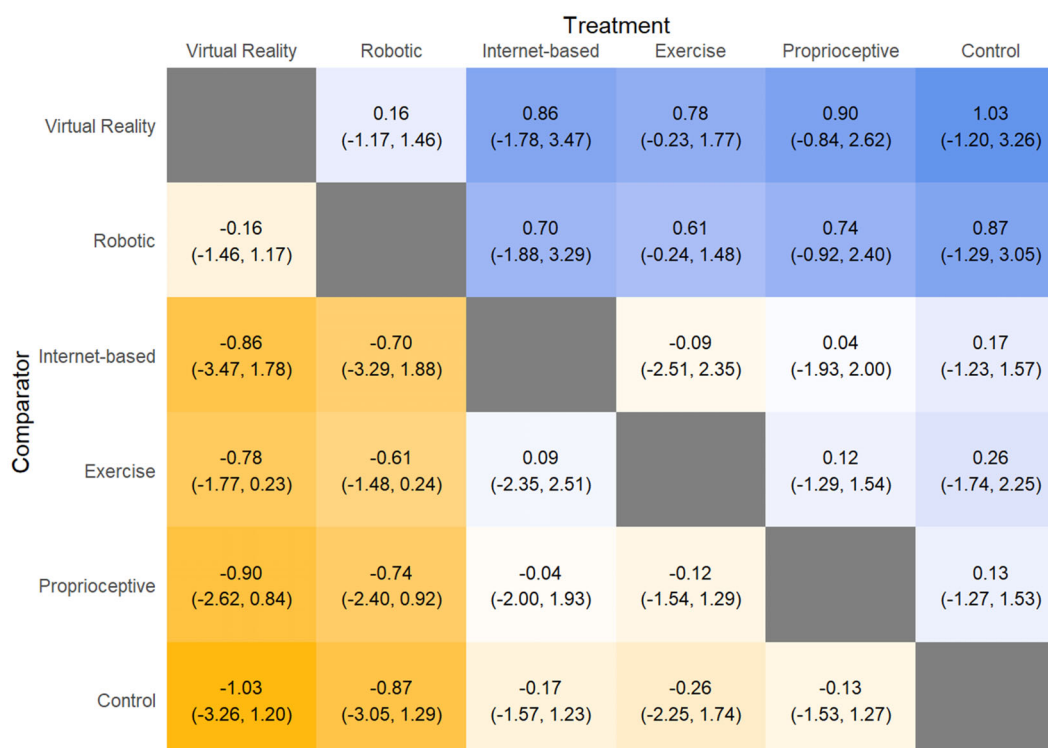
Discussion

This network meta-analysis of 2095 patients investigated the role of four technology-based interventions ((i) Internet-based, (ii) proprioceptive, (iii) robot, and (iv)

Table 1. Surface under the cumulative ranking scores for respective outcomes.

	Control	Exercise	Internet-based	Proprioceptive	Robotic	Virtual reality
UPDRS	31.75	36.87	42.53	36.26	72.95	79.63
TUG timing	4.87	46.03		43.66	75.93	79.51
Stride length	8.99	51.17		75.17	45.87	68.79
10MWT speed	14.23	43.05	51.44	66.01	77.78	47.51
Balance scale scores	15.37	43.26	45.03	40.66	68.66	87
Quality-of-life measures	5.64	76.79	27.9	36.73	62.69	90.24

UPDRS, Unified Parkinson's Disease Rating Scale; TUG, Timed up and go.

**Figure 2.** League table heat plot comparing changes in Unified Parkinson's Disease Rating Scale scores. A blue cell indicates a positive value, and a yellow cell indicates a negative value. A negative value indicates an improvement in the outcome (favoring the treatment arm).

VR) in improving the physical rehabilitation and quality of life of patients afflicted with PD. Our findings highlighted that the different interventions are well-suited for improving different aspects of motor function.

Virtual reality intervention, through mediums such as Xbox Kinect or full audio-visual sensory immersion, fares the best in terms of improving overall motor function as measured by the UPDRS motor outcome. Robotic intervention improves 10MWT results the most as measured by the SUCRA score. Virtual reality intervention improves TUG scores,⁸⁴ a measure of functional mobility and fall

risk, and balance scale scores. Several interventions improve mobility to differing degrees as measured by the outcome measures stride length and 10 MWT. Virtual reality intervention improved QoL the most significantly. While there have been previous meta-analyses investigating the effects of exercise, VR, Internet-based, and robotic interventions on PD patients, there has been no network meta-analysis that compares these interventions directly, nor has there been any form of meta-analysis aggregating the effects of proprioceptive interventions such as peripheral stimulation.

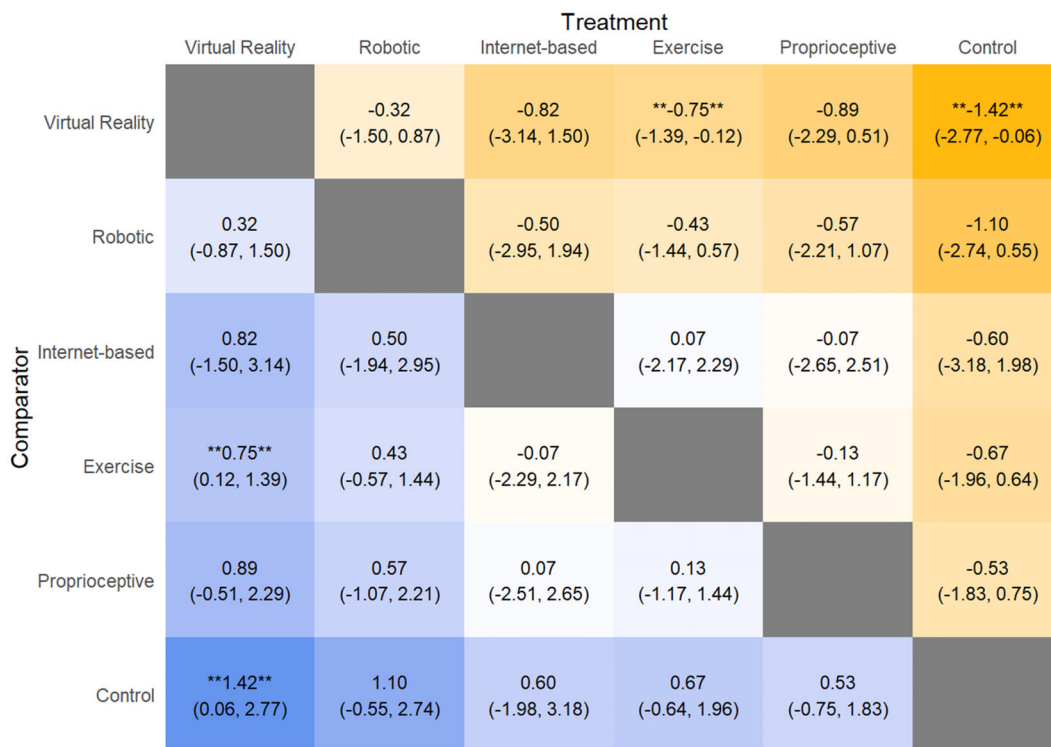
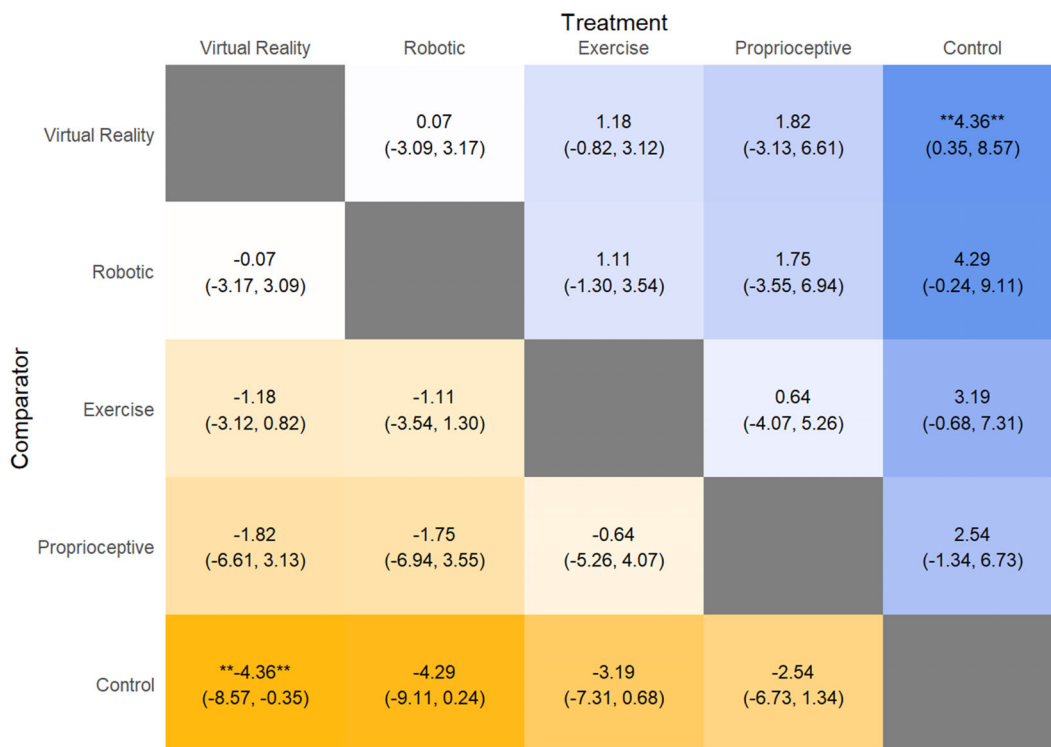


Figure 3. League table heat plot comparing changes in timed up-and-go test timings (above) and balance scale scores (below). A blue cell indicates a positive value, and a yellow cell indicates a negative value. A negative value (above) and a positive value (below) indicates an improvement in the outcome (favoring the treatment arm).

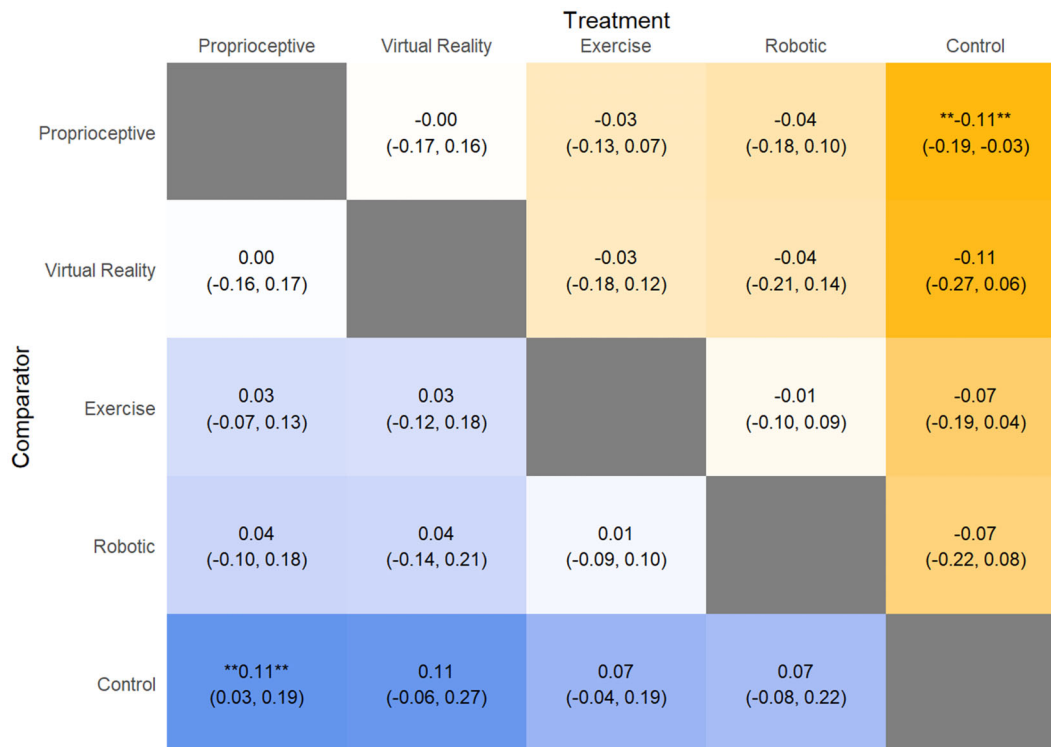


Figure 4. League table heat plot comparing changes in stride length. A blue cell indicates a positive value, and a yellow cell indicates a negative value. A positive value indicates an improvement in the outcome (favoring the treatment arm).

The highly significant improvements to TUG scores and balance scale scores after VR intervention are supported by existing literature, which indicate that VR intervention improves dynamic balance.^{85,86} Balance is achieved and sustained through a complex influx of sensory inputs, involving different modalities (e.g., vestibular, audio, and vision). These inputs are integrated, and they interact with motor planning to finally give a motor output. It is hypothesized that VR rehabilitation most significantly improves balance as it is a global intervention that stimulates many senses at once and hence, when integrated, improve balance tremendously.⁶⁷ PD patients are twice as likely to have falls and fractures as non-PD subjects.⁸⁷ Thus, restoring balance and postural stability is vital.

The improvement to 10MWT results after robotic intervention could be explained through a variety of mechanisms. It is hypothesized that robotic gait training improves gait parameters and walking capacity by facilitating repetitive gait-like movements, synchronizing the walking pattern and strengthening the neuronal circuits contributing to gait pacing.⁵⁹ Proprioceptive interventions via biofeedback and peripheral stimulation improve the amount of proprioceptive sensory input, which has been demonstrated to play a vital part in the production and coordination of movements.⁸⁸ Proprioceptive

interventions through pressure or vibratory stimulation may be crucial in patients in the most advanced stages of the disease. In that stage, patients may be severely compromised cognitively and can no longer undergo treatments which involve explicit learning strategies (e.g., cueing and decomposition of movements).⁴⁷

Current therapeutic options such as pharmacotherapy and deep brains stimulation have proven sub-optimal in improving motor outcomes such as postural abnormality. Pharmacological interventions can even aggravate nonmotor parkinsonian symptoms such as hallucinations and orthostatic hypotension.

In terms of cost, Internet-based interventions have been shown to be largely cost-effective in various settings,⁸⁹ and with increased Internet connectivity, it is expected to be increasingly utilized at low cost. Carpino et al.⁹⁰ have demonstrated that robotic interventions using operational machines such as the ones studied in the included studies^{57–59} cost the same as conventional rehabilitation. The cost-effectiveness of VR rehabilitation is still being investigated, with studies estimating that VR incurs extra cost, but this increase may be counterbalanced when time for therapist supervision is reduced.⁹¹ For proprioceptive interventions, few studies have estimated their cost-effectiveness. However, with 3D printing, it is predicted

		Treatment					
		Robotic	Proprioceptive	Internet-based	Virtual Reality	Exercise	Control
Comparator	Robotic		-0.02 (-0.24, 0.20)	-0.05 (-0.23, 0.14)	-0.05 (-0.20, 0.09)	-0.06 (-0.13, 0.01)	-0.15 (-0.39, 0.08)
	Proprioceptive	0.02 (-0.20, 0.24)		-0.03 (-0.29, 0.24)	-0.04 (-0.28, 0.21)	-0.04 (-0.25, 0.17)	**0.14** (-0.22, -0.05)
	Internet-based	0.05 (-0.14, 0.23)	0.03 (-0.24, 0.29)		-0.01 (-0.22, 0.20)	-0.01 (-0.18, 0.16)	-0.11 (-0.39, 0.17)
	Virtual Reality	0.05 (-0.09, 0.20)	0.04 (-0.21, 0.28)	0.01 (-0.20, 0.22)		-0.00 (-0.13, 0.12)	-0.10 (-0.36, 0.15)
	Exercise	0.06 (-0.01, 0.13)	0.04 (-0.17, 0.25)	0.01 (-0.16, 0.18)	0.00 (-0.12, 0.13)		-0.10 (-0.32, 0.12)
	Control	0.15 (-0.08, 0.39)	**0.14** (0.05, 0.22)	0.11 (-0.17, 0.39)	0.10 (-0.15, 0.36)	0.10 (-0.12, 0.32)	

Figure 5. League table heat plot comparing changes in 10-meter walk test. A blue cell indicates a positive value, and a yellow cell indicates a negative value. A positive value indicates an improvement in the outcome (favoring the treatment arm).

that interventions utilizing plantar stimulation will have greatly reduced cost.⁹² Safety profiles of these interventions are nascent, but preliminary findings for VR interventions indicate that it is feasible and safe.⁹³ As for robotic interventions, ensuring safety is a great challenge. A mismatch in the positioning of the patient and the machine may cause unintended, unsafe interaction forces at the patient's joints.⁹⁴ In terms of wearable robots, translation from controlled laboratory settings to uncontrolled environments such as a patient's home proves challenging.⁹⁵

Conventional rehabilitation is considered an adjuvant to medical interventions, such as medications and surgeries, in PD treatment as it can attenuate the symptoms or even delay the disease progression.⁹⁶ This network meta-analysis has given credence to the idea that a neurorehabilitation program, utilizing a mix of interventions that most effectively target and improve various QoL, gait, and balance parameters, would be ideal. It should be cautioned that with the relative nascence of the field, provider experience is limited. Despite this, and the possibly high start-up cost of setting up such programs, more research should be done utilizing these interventions and observing how these programs can be safely implemented at a low cost and monitored virtually. More cohort studies should be done to combine these approaches with

traditional pharmacological approaches and establish the long-term effects of these interventions on QoL, gait, and balance parameters of PD patients.

Strength and limitations

This network meta-analysis is the first to compare four technology-based interventions: (i) Internet-based, (ii) proprioceptive, (iii) robot, and (iv) VR. The results provide information on how the four interventions fare against active and inactive controls. The recent safety and cost-effectiveness studies suggest that these four interventions may be implemented at scale. However, more thorough safety protocols when designing and testing the interventions are required. It is noteworthy that with increasing Internet connectivity, reduced cost of 3D printed proprioceptive interventions and highly portable VR setups, a home-based rehabilitative approach might be viable for PD, further increasing their convenience and reducing barriers to healthcare access. However, the reliability of this study is affected by a few factors: (i) There are few nonproprioceptive studies that utilize inactive controls (ii) included studies of the same intervention do not always use the same set of outcome measures, reducing the amount of data points that can be aggregated per outcome (iii) heterogeneity was

		Treatment					
		Virtual Reality	Exercise	Robot	Proprioceptive	Internet-based	Control
Comparator	Virtual Reality		0.13 (-0.24, 0.50)	0.27 (-0.45, 0.95)	0.58 (-0.03, 1.22)	**0.70** (0.04, 1.38)	**0.95** (0.52, 1.43)
	Exercise	-0.13 (-0.50, 0.24)		0.14 (-0.47, 0.71)	0.45 (-0.10, 1.03)	0.57 (-0.04, 1.20)	**0.82** (0.40, 1.28)
	Robot	-0.27 (-0.95, 0.45)	-0.14 (-0.71, 0.47)		0.32 (-0.47, 1.16)	0.43 (-0.40, 1.32)	0.69 (-0.01, 1.47)
	Proprioceptive	-0.58 (-1.22, 0.03)	-0.45 (-1.03, 0.10)	-0.32 (-1.16, 0.47)		0.11 (-0.64, 0.87)	0.37 (-0.18, 0.94)
	Internet-based	**0.70** (-1.38, -0.04)	-0.57 (-1.20, 0.04)	-0.43 (-1.32, 0.40)	-0.11 (-0.87, 0.64)		0.25 (-0.30, 0.84)
	Control	**0.95** (-1.43, -0.52)	**0.82** (-1.28, -0.40)	-0.69 (-1.47, 0.01)	-0.37 (-0.94, 0.18)	-0.25 (-0.84, 0.30)	

Figure 6. League table heat plot comparing changes in quality-of-life measures. A blue cell indicates a positive value, and a yellow cell indicates a negative value. A negative value indicates an improvement in the outcome (favoring the treatment arm).

introduced due to the different final timepoints and follow-up durations for the included studies. In some studies, it was noticed that the effects of the interventions subside after a longer time-period, causing effect sizes to be insignificant. More cohort studies can be done to investigate the changes in effect size with time (iv) patients were aware of the intervention that they received in most studies, and this could have led them to adopt behaviors (health-related or otherwise) that could influence the relatively subjective measurements of QoL. Future studies should track longitudinally if the effects of these technology-based interventions persist after the intervention has stopped. Future studies can investigate if there exists a synergistic effect between conventional therapies and the technology-based interventions outlined here. Lastly, future work should include studies on the impact of various technology-based interventions on cognitive outcomes, in view of the potential of integrated motor-cognitive methods for PD rehabilitation.

Conclusion

This Bayesian network meta-analysis demonstrated that four technology-based interventions (Internet-based, proprioceptive, robotic, and VR) can significantly improve QoL, gait, and balance parameters in PD patients, with

each intervention being the most effective in different outcome measures. The results suggest that with current technology, a multi-modality rehabilitative approach using a combination of conventional therapies (e.g., pharmacotherapy) and the four technology-based interventions should be explored. With the proliferation of telemedicine technology, perhaps future studies can also investigate implementing these approaches at home to improve outcomes while increasing patient convenience and satisfaction. Research looking into the longer-term effects of these technology-based interventions and their interactions with conventional therapies can facilitate individualized management specific to different motor subtypes of PD.

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Conflict of Interest

The authors do not have any competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author Contributions

CE Yau, ECK Ho, NY Ong, CJK Loh, AS Mai, and Professor E-K Tan contributed to (1) the conception and design of this project; (2) acquisition, analysis, and interpretation of data; (3) drafting and revising it critically for important intellectual content. All authors gave their final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

References

- Hirsch L, Jette N, Frolkis A, Steeves T, Pringsheim T. The incidence of Parkinson's disease: a systematic review and meta-analysis. *Neuroepidemiology*. 2016;46(4):292-300. doi:10.1159/000445751
- Schapiro AHV. Neurobiology and treatment of Parkinson's disease. *Trends Pharmacol Sci*. 2009;30(1):41-47. doi:10.1016/j.tips.2008.10.005
- Ou Z, Pan J, Tang S, et al. Global trends in the incidence, prevalence, and years lived with disability of Parkinson's disease in 204 countries/territories from 1990 to 2019. *Front Public Health*. 2021;9:776847. doi:10.3389/fpubh.2021.776847
- Feigin VL, Nichols E, Alam T, et al. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol*. 2019;18(5):459-480. doi:10.1016/S1474-4422(18)30499-X
- Moustafa AA, Chakravarthy S, Phillips JR, et al. Motor symptoms in Parkinson's disease: a unified framework. *Neurosci Biobehav Rev*. 2016;68:727-740. doi:10.1016/j.neubiorev.2016.07.010
- Schapiro AHV, Bezdard E, Brotchie J, et al. Novel pharmacological targets for the treatment of Parkinson's disease. *Nat Rev Drug Discov*. 2006;5(10):845-854. doi:10.1038/nrd2087
- Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord*. 2015;30(12):1591-1601. doi:10.1002/mds.26424
- Marsili L, Rizzo G, Colosimo C. Diagnostic criteria for Parkinson's disease: from James Parkinson to the concept of prodromal disease. *Front Neurol*. 2018;9:156. doi:10.3389/fneur.2018.00156
- Kuopio A-M, Marttila RJ, Helenius H, Toivonen M, Rinne UK. The quality of life in Parkinson's disease. *Mov Disord*. 2000;15(2):216-223. doi:10.1002/1531-8257(200003)15:2<216::AID-MDS1003>3.0.CO;2-#
- Stamford JA, Schmidt PN, Friedl KE. What engineering technology could do for quality of life in Parkinson's disease: a review of current needs and opportunities. *IEEE J Biomed Health Inform*. 2015;19(6):1862-1872. doi:10.1109/JBHI.2015.2464354
- Abbruzzese G, Marchese R, Avanzino L, Pelosin E. Rehabilitation for Parkinson's disease: current outlook and future challenges. *Parkinsonism Relat Disord*. 2016;22:S60-S64. doi:10.1016/j.parkreldis.2015.09.005
- Rascol O, Payoux P, Ory F, Ferreira JJ, Brefel-Courbon C, Montastruc J-L. Limitations of current Parkinson's disease therapy. *Ann Neurol*. 2003;53(S3):S3-S15. doi:10.1002/ana.10513
- Fasano A, Aquino CC, Krauss JK, Honey CR, Bloem BR. Axial disability and deep brain stimulation in patients with Parkinson disease. *Nat Rev Neurol*. 2015;11(2):98-110. doi:10.1038/nrneurol.2014.252
- Tsuboi T, Watanabe H, Tanaka Y, et al. Distinct phenotypes of speech and voice disorders in Parkinson's disease after subthalamic nucleus deep brain stimulation. *J Neurol Neurosurg Psychiatry*. 2015;86(8):856-864. doi:10.1136/jnnp-2014-308043
- Rogers MW. Disorders of posture, balance, and gait in Parkinson's disease. *Clin Geriatr Med*. 1996;12(4):825-845. doi:10.1016/S0749-0690(18)30203-9
- Dockx K, Bekkers EMJ, Van den Bergh V, et al. Virtual reality for rehabilitation in Parkinson's disease. *Cochrane Database Syst Rev*. 2016;2016:CD010760. doi:10.1002/14651858.CD010760.pub2
- Sale P, De Pandis MF, Domenica LP, et al. Robot-assisted walking training for individuals with Parkinson's disease: a pilot randomized controlled trial. *BMC Neurol*. 2013;13:50. doi:10.1186/1471-2377-13-50
- Kleiner AFR, Souza Pagnussat A, Pinto C, Redivo Marchese R, Salazar AP, Galli M. Automated mechanical peripheral stimulation effects on gait variability in individuals with Parkinson disease and freezing of gait: a double-blind, randomized controlled trial. *Arch Phys Med Rehabil*. 2018;99(12):2420-2429. doi:10.1016/j.apmr.2018.05.009
- Achey M, Aldred JL, Aljehani N, et al. The past, present, and future of telemedicine for Parkinson's disease: telemedicine for Parkinson's disease. *Mov Disord*. 2014;29(7):871-883. doi:10.1002/mds.25903
- Lee HS, Park YJ, Park SW. The effects of virtual reality training on function in chronic stroke patients: a

- systematic review and meta-analysis. *Biomed Res Int.* 2019;2019:7595639. doi:[10.1155/2019/7595639](https://doi.org/10.1155/2019/7595639)
21. Herman T, Giladi N, Hausdorff JM. Properties of the 'timed up and go' test: more than meets the eye. *Gerontology.* 2011;57(3):203-210. doi:[10.1159/000314963](https://doi.org/10.1159/000314963)
 22. Pelosin E, Cerulli C, Ogliastrro C, et al. A multimodal training modulates short afferent inhibition and improves complex walking in a cohort of faller older adults with an increased prevalence of Parkinson's disease. *J Gerontol A Biol Sci Med Sci.* 2020;75(4):722-728. doi:[10.1093/gerona/glz072](https://doi.org/10.1093/gerona/glz072)
 23. Ferrazzoli D, Ortelli P, Madeo G, Giladi N, Petzinger GM, Frazzitta G. Basal ganglia and beyond: the interplay between motor and cognitive aspects in Parkinson's disease rehabilitation. *Neurosci Biobehav Rev.* 2018;90:294-308. doi:[10.1016/j.neubiorev.2018.05.007](https://doi.org/10.1016/j.neubiorev.2018.05.007)
 24. Montero-Odasso M, Verghese J, Beauchet O, Hausdorff JM. Gait and cognition: a complementary approach to understanding brain function and the risk of falling. *J Am Geriatr Soc.* 2012;60(11):2127-2136. doi:[10.1111/j.1532-5415.2012.04209.x](https://doi.org/10.1111/j.1532-5415.2012.04209.x)
 25. Mirelman A, Rochester L, Reelick M, et al. V-TIME: a treadmill training program augmented by virtual reality to decrease fall risk in older adults: study design of a randomized controlled trial. *BMC Neurol.* 2013;13:15. doi:[10.1186/1471-2377-13-15](https://doi.org/10.1186/1471-2377-13-15)
 26. Cipriani A, Higgins JPT, Geddes JR, Salanti G. Conceptual and technical challenges in network meta-analysis. *Ann Intern Med.* 2013;159(2):130-137. doi:[10.7326/0003-4819-159-2-201307160-00008](https://doi.org/10.7326/0003-4819-159-2-201307160-00008)
 27. Spina S, Facciorusso S, Cinone N, et al. Effectiveness of robotic balance training on postural instability in patients with mild Parkinson's disease: a pilot, single blind, randomized controlled trial. *J Rehabil Med.* 2021;53(2):jrm00154. doi:[10.2340/16501977-2793](https://doi.org/10.2340/16501977-2793)
 28. Parsons TD, Gaggioli A, Riva G. Virtual reality for research in social neuroscience. *Brain Sci.* 2017;7(4):42. doi:[10.3390/brainsci7040042](https://doi.org/10.3390/brainsci7040042)
 29. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71. doi:[10.1136/bmj.n71](https://doi.org/10.1136/bmj.n71)
 30. Higgins JP, Li T, Deeks JJ. Choosing effect measures and computing estimates of effect. *Cochrane Handbook for Systematic Reviews of Interventions.* Wiley; 2019:143-176.
 31. Andrade C. Mean difference, standardized mean difference (SMD), and their use in meta-analysis: as simple as it gets. *J Clin Psychiatry.* 2020;81(5):20f13681. doi:[10.4088/JCP.20f13681](https://doi.org/10.4088/JCP.20f13681)
 32. Stocchi F, Sale P, Kleiner AFR, et al. Long-term effects of automated mechanical peripheral stimulation on gait patterns of patients with Parkinson's disease. *Int J Rehabil Res.* 2015;38(3):238-245. doi:[10.1097/MRR.000000000000120](https://doi.org/10.1097/MRR.000000000000120)
 33. Caudron S, Guerraz M, Eusebio A, Gros JP, Azulay JP, Vaugoyeau M. Evaluation of a visual biofeedback on the postural control in Parkinson's disease. *Neurophysiol Clin.* 2014;44(1):77-86. doi:[10.1016/j.neucli.2013.10.134](https://doi.org/10.1016/j.neucli.2013.10.134)
 34. Nanhoe-Mahabier W, Allum JH, Pasman EP, Overeem S, Bloem BR. The effects of vibrotactile biofeedback training on trunk sway in Parkinson's disease patients. *Parkinsonism Relat Disord.* 2012;18(9):1017-1021. doi:[10.1016/j.parkreldis.2012.05.018](https://doi.org/10.1016/j.parkreldis.2012.05.018)
 35. Volpe D, Giantin MG, Fasano A. A wearable proprioceptive stabilizer (Equistasi[®]) for rehabilitation of postural instability in Parkinson's disease: a phase II randomized double-blind, double-dummy, controlled study. *PLoS One.* 2014;9(11):e112065. doi:[10.1371/journal.pone.0112065](https://doi.org/10.1371/journal.pone.0112065)
 36. Carpinella I, Cattaneo D, Bonora G, et al. Wearable sensor-based biofeedback training for balance and gait in Parkinson disease: a pilot randomized controlled trial. *Arch Phys Med Rehabil.* 2017;98(4):622-630.e3. doi:[10.1016/j.apmr.2016.11.003](https://doi.org/10.1016/j.apmr.2016.11.003)
 37. van Valkenhoef G, Lu G, de Brock B, Hillege H, Ades AE, Welton NJ. Automating network meta-analysis. *Res Synth Methods.* 2012;3(4):285-299. doi:[10.1002/jrsm.1054](https://doi.org/10.1002/jrsm.1054)
 38. Béliveau A, Boyne DJ, Slater J, Brenner D, Arora P. BUGSnet: an R package to facilitate the conduct and reporting of Bayesian network meta-analyses. *BMC Med Res Methodol.* 2019;19(1):196. doi:[10.1186/s12874-019-0829-2](https://doi.org/10.1186/s12874-019-0829-2)
 39. Flynn A, Preston E, Dennis S, Canning CG, Allen NE. Home-based exercise monitored with telehealth is feasible and acceptable compared to centre-based exercise in Parkinson's disease: a randomised pilot study. *Clin Rehabil.* 2021;35(5):728-739. doi:[10.1177/0269215520976265](https://doi.org/10.1177/0269215520976265)
 40. Lai B, Bond K, Kim Y, Barstow B, Jovanov E, Bickel CS. Exploring the uptake and implementation of tele-monitored home-exercise programmes in adults with Parkinson's disease: a mixed-methods pilot study. *J Telemed Telecare.* 2020;26(1-2):53-63. doi:[10.1177/1357633X18794315](https://doi.org/10.1177/1357633X18794315)
 41. Beck CA, Beran DB, Biglan KM, et al. National randomized controlled trial of virtual house calls for Parkinson disease. *Neurology.* 2017;89(11):1152-1161. doi:[10.1212/WNL.0000000000004357](https://doi.org/10.1212/WNL.0000000000004357)
 42. Wilkinson JR, Spindler M, Wood SM, et al. High patient satisfaction with telehealth in Parkinson disease a randomized controlled study. *Neurology: Clinical Practice.* 2016;6(3):241-251. doi:[10.1212/CPJ.0000000000000252](https://doi.org/10.1212/CPJ.0000000000000252)
 43. Sekimoto S, Oyama G, Hatano T, et al. A randomized crossover pilot study of telemedicine delivered via iPads in Parkinson's disease. *Parkinsons Disease.* 2019;2019:1-7. doi:[10.1155/2019/9403295](https://doi.org/10.1155/2019/9403295)
 44. Ellis TD, Cavanaugh JT, DeAngelis T, et al. Comparative effectiveness of mHealth-supported exercise compared

- with exercise alone for people with Parkinson disease: randomized controlled pilot study. *Phys Ther*. 2019;99(2):203-216. doi:10.1093/ptj/pzy131
45. Peppe A, Paravati S, Baldassarre MG, et al. Proprioceptive focal stimulation (Equistasi[®]) may improve the quality of gait in middle-moderate Parkinson's disease patients. Double-blind, double-dummy, randomized, crossover, Italian multicentric study. *Front Neurol*. 2019;10:10. doi:10.3389/fneur.2019.00998
 46. Pinto C, Pagnussat AS, Rozin Kleiner AF, et al. Automated mechanical peripheral stimulation improves gait parameters in subjects with Parkinson disease and freezing of gait: a randomized clinical trial. *Am J Phys Med Rehabil*. 2018;97(6):383-389. doi:10.1097/PHM.0000000000000890
 47. Galli M, Vicidomini C, Rozin Kleiner AF, et al. Peripheral neurostimulation breaks the shuffling steps patterns in parkinsonian gait: a double blind randomized longitudinal study with automated mechanical peripheral stimulation. *Eur J Phys Rehabil Med*. 2018;54(6):860-865. doi:10.23736/S1973-9087.18.05037-2
 48. El-Tamawy MS, Darwish MH, Khallaf ME. Effects of augmented proprioceptive cues on the parameters of gait of individuals with Parkinson's disease. *Ann Indian Acad Neurol*. 2012;15(4):267-272. doi:10.4103/0972-2327.104334
 49. Unterreiner M, Biedermann C, El-Fahem R, et al. Comparing computer-aided therapy with conventional physiotherapy in Parkinson's disease: an equivalence study. *Neurology Asia*. 2019;24(4):309-315.
 50. Ginis P, Nieuwboer A, Dorfman M, et al. Feasibility and effects of home-based smartphone-delivered automated feedback training for gait in people with Parkinson's disease: a pilot randomized controlled trial. *Parkinsonism Relat Disord*. 2016;22:28-34. doi:10.1016/j.parkreldis.2015.11.004
 51. Pagnussat AS, Kleiner AFR, Rieder CRM, et al. Plantar stimulation in parkinsonians: from biomarkers to mobility—randomized-controlled trial. *Restor Neurol Neurosci*. 2018;36(2):195-205. doi:10.3233/rnn-170744
 52. Subramanian L, Morris MB, Brosnan M, Turner DL, Morris HR, Linden DEJ. Functional magnetic resonance imaging neurofeedback-guided motor imagery training and motor training for Parkinson's disease: randomized trial. *Clinical trial*. *Front Behav Neurosci*. 2016;10:10. doi:10.3389/fnbeh.2016.00111
 53. Chang MC, Chun MH. The effect of balance training with tetra-ataxiometric posturography on balance function in patients with parkinsonism. *NeuroRehabilitation*. 2019;45(3):379-384. doi:10.3233/nre-192850
 54. Romanato M, Guiotto A, Spolaor F, et al. Changes of biomechanics induced by Equistasi[®] in Parkinson's disease: coupling between balance and lower limb joints kinematics. *Med Biol Eng Comput*. 2021;59(7):1403-1415. doi:10.1007/s11517-021-02373-3
 55. Shen X, Mak MKY. Balance and gait training with augmented feedback improves balance confidence in people with Parkinson's disease: a randomized controlled trial. *Neurorehabil Neural Repair*. 2014;28(6):524-535. doi:10.1177/1545968313517752
 56. Furnari A, Calabrò RS, De Cola MC, et al. Robotic-assisted gait training in Parkinson's disease: a three-month follow-up randomized clinical trial. *Int J Neurosci*. 2017;127(11):996-1004. doi:10.1080/00207454.2017.1288623
 57. Picelli A, Melotti C, Origano F, et al. Robot-assisted gait training is not superior to balance training for improving postural instability in patients with mild to moderate Parkinson's disease: a single-blind randomized controlled trial. *Clin Rehabil*. 2015;29(4):339-347. doi:10.1177/0269215514544041
 58. Picelli A, Melotti C, Origano F, Neri R, Waldner A, Smania N. Robot-assisted gait training versus equal intensity treadmill training in patients with mild to moderate Parkinson's disease: a randomized controlled trial. *Parkinsonism Relat Disord*. 2013;19(6):605-610. doi:10.1016/j.parkreldis.2013.02.010
 59. Picelli A, Melotti C, Origano F, et al. Robot-assisted gait training in patients with parkinson disease: a randomized controlled trial. *Neurorehabil Neural Repair*. 2012;26(4):353-361. doi:10.1177/1545968311424417
 60. Picelli A, Melotti C, Origano F, Waldner A, Gimigliano R, Smania N. Does robotic gait training improve balance in Parkinson's disease? A randomized controlled trial. *Parkinsonism Relat Disord*. 2012;18(8):990-993. doi:10.1016/j.parkreldis.2012.05.010
 61. Capecchi M, Pournajaf S, Galafate D, et al. Clinical effects of robot-assisted gait training and treadmill training for Parkinson's disease. A randomized controlled trial. *Ann Phys Rehabil Med*. 2019;62(5):303-312. doi:10.1016/j.rehab.2019.06.016
 62. Carda S, Invernizzi M, Baricich A, Comi C, Croquelois A, Cisari C. Robotic gait training is not superior to conventional treadmill training in parkinson disease: a single-blind randomized controlled trial. *Neurorehabil Neural Repair*. 2012;26(9):1027-1034. doi:10.1177/1545968312446753
 63. Galli M, Cimolin V, De Pandis MF, et al. Robot-assisted gait training versus treadmill training in patients with Parkinson's disease: a kinematic evaluation with gait profile score. *Funct Neurol*. 2016;31(3):163-170. doi:10.11138/fneur/2016.31.3.163
 64. Kim H, Kim E, Yun SJ, et al. Robot-assisted gait training with auditory and visual cues in Parkinson's disease: a randomized controlled trial. *Ann Phys Rehabil Med*. 2022;65(3):101620. doi:10.1016/j.rehab.2021.101620
 65. Kegelmeyer DA, Minarsch R, Kostyk SK, Kline D, Smith R, Kloos AD. Use of a robotic walking device for home and community mobility in Parkinson disease: a

- randomized controlled trial. *J Neurol Phys Ther.* 2024;48(2):102-111. doi:10.1097/npt.0000000000000467
66. Ribas CG, Alves da Silva L, Correa MR, Teive HG, Valderramas S. Effectiveness of exergaming in improving functional balance, fatigue and quality of life in Parkinson's disease: a pilot randomized controlled trial. *Parkinsonism Relat Disord.* 2017;38:13-18. doi:10.1016/j.parkreldis.2017.02.006
 67. Pazzaglia C, Imbimbo I, Tranchita E, et al. Comparison of virtual reality rehabilitation and conventional rehabilitation in Parkinson's disease: a randomised controlled trial. *Physiotherapy (United Kingdom).* 2020;106:36-42. doi:10.1016/j.physio.2019.12.007
 68. Ferraz DD, Trippo KV, Duarte GP, Neto MG, Bernardes Santos KO, Filho JO. The effects of functional training, bicycle exercise, and exergaming on walking capacity of elderly patients with Parkinson disease: a pilot randomized controlled single-blinded trial. *Arch Phys Med Rehabil.* 2018;99(5):826-833. doi:10.1016/j.apmr.2017.12.014
 69. Feng H, Li C, Liu J, et al. Virtual reality rehabilitation versus conventional physical therapy for improving balance and gait in parkinson's disease patients: a randomized controlled trial. *Med Sci Monit.* 2019;25:4186-4192. doi:10.12659/MSM.916455
 70. Pompeu JE, Mendes FADS, Silva KGD, et al. Effect of Nintendo Wii™ based motor and cognitive training on activities of daily living in patients with Parkinson's disease: a randomised clinical trial. *Physiotherapy (United Kingdom).* 2012;98(3):196-204. doi:10.1016/j.physio.2012.06.004
 71. Tollar J, Nagy F, Hortobágyi T. Vastly different exercise programs similarly improve parkinsonian symptoms: a randomized clinical trial. *Gerontology.* 2019;65(2):120-127. doi:10.1159/000493127
 72. Shih M-C, Wang R-Y, Cheng S-J, Yang Y-R. Effects of a balance-based exergaming intervention using the Kinect sensor on posture stability in individuals with Parkinson's disease: a single-blinded randomized controlled trial. *J Neuroeng Rehabil.* 2016;13(1):78. doi:10.1186/s12984-016-0185-y
 73. Gandolfi M, Geroïn C, Dimitrova E, et al. Virtual reality telerehabilitation for postural instability in Parkinson's disease: a multicenter, single-blind, randomized, controlled trial. *Biomed Res Int.* 2017;2017:1-11. doi:10.1155/2017/7962826
 74. Santos P, Machado T, Santos L, Ribeiro N, Melo A. Efficacy of the Nintendo Wii combination with conventional exercises in the rehabilitation of individuals with Parkinson's disease: a randomized clinical trial. *NeuroRehabilitation.* 2019;45(2):255-263. doi:10.3233/NRE-192771
 75. Yang WC, Wang HK, Wu RM, Lo CS, Lin KH. Home-based virtual reality balance training and conventional balance training in Parkinson's disease: a randomized controlled trial. *J Formos Med Assoc.* 2016;115(9):734-743. doi:10.1016/j.jfma.2015.07.012
 76. Liao YY, Yang YR, Wu YR, Wang RY. Virtual reality-based Wii fit training in improving muscle strength, sensory integration ability, and walking abilities in patients with Parkinson's disease: a randomized control trial. *Int J Gerontol.* 2015;9(4):190-195. doi:10.1016/j.ijge.2014.06.007
 77. Liao YY, Yang YR, Cheng SJ, Wu YR, Fuh JL, Wang RY. Virtual reality-based training to improve obstacle-crossing performance and dynamic balance in patients with Parkinson's disease. *Neurorehabil Neural Repair.* 2015;29(7):658-667. doi:10.1177/1545968314562111
 78. Tollár J, Nagy F, Kovács N, Hortobágyi T. A high-intensity multicomponent agility intervention improves Parkinson patients' clinical and motor symptoms. *Arch Phys Med Rehabil.* 2018;99(12):2478-2484.e1. doi:10.1016/j.apmr.2018.05.007
 79. van den Heuvel MRC, Kwakkel G, Beek PJ, Berendse HW, Daffertshofer A, van Wegen EEH. Effects of augmented visual feedback during balance training in Parkinson's disease: a pilot randomized clinical trial. *Parkinsonism Relat Disord.* 2014;20(12):1352-1358. doi:10.1016/j.parkreldis.2014.09.022
 80. Pedreira G, Prazeres A, Cruz D, Gomes I, Monteiro L, Melo A. Virtual games and quality of life in Parkinson's disease: a randomised controlled trial. *APD.* 2013;2(4):97-101. doi:10.4236/apd.2013.24018
 81. Kashif M, Ahmad A, Bandpei MAM, Gilani SA, Hanif A, Iram H. Combined effects of virtual reality techniques and motor imagery on balance, motor function and activities of daily living in patients with Parkinson's disease: a randomized controlled trial. *BMC Geriatr.* 2022;22(1):381. doi:10.1186/s12877-022-03035-1
 82. Kafle A, Rizvi SR. Effect of wii-based motor and cognitive training on activities of daily living in patients with Parkinson's disease. *Indian J Physiother Occupat Ther.* 2021;15:1-7.
 83. Goffredo M, Baglio F, De Icco R, et al. Efficacy of non-immersive virtual reality-based telerehabilitation on postural stability in Parkinson's disease: a multicenter randomized controlled trial. *Eur J Phys Rehabil Med.* 2023;59(6):689-696. doi:10.23736/s1973-9087.23.07954-6
 84. Barry E, Galvin R, Keogh C, Horgan F, Fahey T. Is the timed up and go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. *BMC Geriatr.* 2014;14:14. doi:10.1186/1471-2318-14-14
 85. Duque G, Boersma D, Loza-Diaz G, et al. Effects of balance training using a virtual-reality system in older fallers. *Clin Interv Aging.* 2013;8:257-263. doi:10.2147/CIA.S41453
 86. Cho KH, Lee KJ, Song CH. Virtual-reality balance training with a video-game system improves dynamic balance in

- chronic stroke patients. *Tohoku J Exp Med.* 2012;228(1):69-74. doi:[10.1620/tjem.228.69](https://doi.org/10.1620/tjem.228.69)
87. Kalilani L, Asgharnejad M, Palokangas T, Durgin T. Comparing the incidence of falls/fractures in Parkinson's disease patients in the US population. *PLoS One.* 2016;11(9):e0161689. doi:[10.1371/journal.pone.0161689](https://doi.org/10.1371/journal.pone.0161689)
88. Brognara L, Cauli O. Mechanical plantar foot stimulation in Parkinson's disease: a scoping review. *Diseases.* 2020;8(2):12. doi:[10.3390/diseases8020012](https://doi.org/10.3390/diseases8020012)
89. de la Torre-Díez I, López-Coronado M, Vaca C, Aguado JS, de Castro C. Cost-utility and cost-effectiveness studies of telemedicine, electronic, and mobile health systems in the literature: a systematic review. *Telemed J E Health.* 2015;21(2):81-85. doi:[10.1089/tmj.2014.0053](https://doi.org/10.1089/tmj.2014.0053)
90. Carpino G, Pezzola A, Urbano M, Guglielmelli E. Assessing effectiveness and costs in robot-mediated lower limbs rehabilitation: a meta-analysis and state of the art. *J Healthc Eng.* 2018;2018:7492024. doi:[10.1155/2018/7492024](https://doi.org/10.1155/2018/7492024)
91. Islam MK, Brunner I. Cost-analysis of virtual reality training based on the virtual reality for upper extremity in subacute stroke (VIRTUES) trial. *Int J Technol Assess Health Care.* 2019;35(5):373-378. doi:[10.1017/s026646231900059x](https://doi.org/10.1017/s026646231900059x)
92. Brognara L, Navarro-Flores E, Iachemet L, Serra-Catalá N, Cauli O. Beneficial effect of foot plantar stimulation in gait parameters in individuals with Parkinson's disease. *Brain Sci.* 2020;10(2):69. doi:[10.3390/brainsci10020069](https://doi.org/10.3390/brainsci10020069)
93. Norouzi-Gheidari N, Hernandez A, Archambault PS, Higgins J, Poissant L, Kairy D. Feasibility, safety and efficacy of a virtual reality exergame system to supplement upper extremity rehabilitation post-stroke: a pilot randomized clinical trial and proof of principle. *Int J Environ Res Public Health.* 2019;17(1):113. doi:[10.3390/ijerph17010113](https://doi.org/10.3390/ijerph17010113)
94. Rocon E, Ruiz AF, Raya R, et al. Human-robot physical interaction. In: Pons JL, ed. *Wearable Robots.* John Wiley & Sons, Ltd; 2008:127-163.
95. Bessler J, Prange-Lasonder GB, Schaake L, et al. Safety assessment of rehabilitation robots: a review identifying safety skills and current knowledge gaps. *Front Robot AI.* 2021;8:602878. doi:[10.3389/frobt.2021.602878](https://doi.org/10.3389/frobt.2021.602878)
96. Lu Y, Ge Y, Chen W, et al. The effectiveness of virtual reality for rehabilitation of Parkinson disease: an overview of systematic reviews with meta-analyses. *Syst Rev.* 2022;11(1):50. doi:[10.1186/s13643-022-01924-5](https://doi.org/10.1186/s13643-022-01924-5)

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1.