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Review Article

Evidence-Based Physiotherapeutic Interventions Enhancing Hand Dexterity, Activities of Daily Living and Quality of Life of Parkinson's Disease Patients: A Systematic Review

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ABSTRACT: ***Objectives:*** This systematic review primarily aims to identify the optimal physiotherapeutic intervention to improve hand dexterity in Parkinson's Disease (PD) patients. The secondary objectives were to identify the hand dexterity physiotherapeutic interventions available for PD patients, and to determine the quality of these interventions. ***Review Methods:*** Eight electronic databases were systematically searched to identify relevant randomized controlled trial full-text articles using the established search strategy. The primary outcomes of interest were measurements for hand dexterity and activities of daily living (ADL). ***Results:*** A total of 11 studies comprising 647 participants with PD were included. Most studies had a high risk of performance bias and an unclear risk of selection bias. The intervention training period ranged from a single session to 12 weeks. Compared to their respective control group, eight out of 11 studies revealed significant results in hand dexterity, two out of three studies reported positive effects on ADL, four of seven studies showed significant improvements in upper limb motor performance, and two studies perceived positive benefits in terms of overall quality of life. Five out of 11 studies that recorded the occurrence of adverse events reported no adverse events post-intervention. ***Conclusion:*** The dearth of evidence made it difficult to support any one intervention as the best intervention when compared to the other PD treatments in upper limb rehabilitation. Regardless, a home-based dexterity rehabilitation programme is still a promising approach to enhance dexterity-related functional abilities.

RÉSUMÉ : Interventions en physiothérapie fondées sur des données probantes, susceptibles d'améliorer la dextérité, les activités de la vie quotidienne et la qualité de vie chez des patients atteints de la maladie de Parkinson : résultats d'une revue systématique. ***Objectifs :*** Cette revue systématique visait, tout d'abord, à discerner la meilleure intervention possible de physiothérapie susceptible d'améliorer la dextérité chez des patients atteints de la maladie de Parkinson (MP). L'étude visait, en second lieu, à relever les exercices physiothérapeutiques de dextérité convenant aux personnes atteintes de la MP et à déterminer la qualité de ces interventions. ***Méthode de recherche :*** L'équipe a entrepris une recherche systématique dans huit bases de données afin de relever des articles complets sur des essais comparatifs et à répartition aléatoire pertinents à l'aide d'une démarche préétablie de travail. Les principaux critères d'évaluation étaient les mesures de la dextérité et les activités de la vie quotidienne (AVQ). ***Résultats :*** Au total, 11 études, totalisant 647 sujets atteints de la MP, ont été incluses dans l'analyse. La plupart des études retenues présentaient un risque élevé de biais de performance et un risque incertain de biais de sélection. La durée des périodes d'intervention variait de 1 séance à 12 semaines de formation. Comparativement aux groupes témoins respectifs, des résultats notables relatifs à la dextérité ont été enregistrés dans 8 études sur 11; des effets favorables sur les AVQ, dans 2 études sur 3; une amélioration sensible de la performance motrice des membres supérieurs, dans 4 études sur 7; et la perception d'effets bénéfiques sur la qualité de vie en général, dans 2 études. Enfin, la manifestation d'événements indésirables avait été consignée dans 5 études sur 11, et il n'est fait aucune mention d'événement défavorable après les interventions. ***Conclusion :*** L'insuffisance marquée de données probantes a rendu difficile la sélection de la meilleure intervention qui soit, comparativement aux autres traitements de réadaptation des membres supérieurs adaptés au contexte de la MP. Néanmoins, un programme de réadaptation de la dextérité à domicile se révèle une approche pleine de promesse quant à l'amélioration de la capacité fonctionnelle liée à la dextérité.

Keywords: manual dexterity; Parkinson's disease; physiotherapeutic intervention

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Introduction

Parkinson's disease (PD) is the most common movement disorder, and it is chronic and progressive in nature.[1] The prevalence of PD in the general population is approximately 0.3% of the entire population and 1% of those over 60 years old.[2] Furthermore, the crude prevalence rate in Asian countries specifically ranges from 15 to 328 per 100,000 individuals.[3,4]

Upper extremity disorders are frequently reported in PD as well, especially the hand dysfunction, is a common presentation of PD.[5] It affects the functionality of the hand, which results in impaired manual dexterity, fine motor skills deficits, poor grip force control and inability to perform coordinated movements in early stages due to unilateral tremor, mild hypokinesia and rigidity. Some common issues encountered include reduced movement speed and amplitude, poor sequential task performance, disordered fine manipulation of hand involving reach-to-grasp movements, and gripping and manipulating objects using assistive devices, such as crutches and wheelchairs. Furthermore, dexterity difficulties are the second contributor to PD's impairment following ambulation, making it a burden to the disease.[5–6] Additionally, during their middle stages, participants encountered heightened challenges in self-care activities due to bilateral bradykinesia, axial and distal rigidity, poor synchronisation and torque modulation, rendering their activity limitations more complex. These impairments make them highly dependent on assistive devices and caregiver assistance. In the late stage of PD, limited functional activities and poor structural abilities have been observed due to severe rigidity and joint stiffness, eventually leading to difficulties in daily and self-care activities, in addition to the loss of independence and reduced quality of life (QoL) throughout the illness.[7,20]

As dexterity performance is slowly deteriorating, several management protocols and interventions have been considered for use in PD rehabilitation programmes that focus on improving hand functionality. However, based on the evidence, majority of the treatment protocols are aimed to improve the gait and lower limb functions.

To date, no evidence on which intervention could best enhance hand dexterity in PD individuals has been investigated. Therefore, this research aimed to determine the best treatment available to improve hand dexterity in patients with PD, by comparing different types of interventions needed to enhance their QoL and well-being, while allowing them to perform functional tasks as independently as possible. This systematic review also aimed to provide better hand dexterity improvement options in individuals with PD in the near future. All in all, the primary objective of this systematic review was to identify the best physiotherapy intervention to improve hand dexterity in PD patients. The secondary objectives were to identify the hand dexterity interventions available for PD patients and determine the quality of these interventions.

Research methodology

Search protocol and registration

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. Following the PRISMA guideline ensures that a systematic review or a meta-analysis is better documented in the way of transparency and accuracy. This systematic review was registered with PROSPERO (CRD42020219788).

Search strategy

The development of the search strategy, which was in accordance with the Problem/Population, Intervention, Comparison, Outcome (PICO) format, was discussed among three reviewers (LMH, CPK and FWH). The developed search strategies were adapted for use in all the selected databases, summarises in Table 1. The relevant keywords and search terms were decided, summarises in Table 2, which are (1) Parkinson*; (2) "hand dexterity" OR "manual dexterity"; (3) physiotherapy; (4) physiotherapy intervention OR technique OR management OR rehabilitation. Formal searching of the databases was started once the consistency within the search process was achieved. The most relevant articles were identified by searching through the following databases: Clinical Key; Cochrane Library; Ovid; Physiotherapy Evidence Database (PEDro); PubMed; PubMed Central; Science Direct; Scopus. These databases were selected because they are related to healthcare services and rehabilitation provisions, and contain predominantly peer-reviewed journal articles, where studies relevant to the objectives of this systematic review could be easily identified. Grey literature search (Google Scholar) was undertaken with the first ten pages of the results reviewed. Hand searching through the reference list of all identified and relevant articles were also performed. All searches were performed between July 2020 and November 6, 2020.

Study design

Only randomised controlled trials (RCTs) were included in this review.

Population

Studies were included if the subjects fulfilled the following criteria: (1) adults aged 18 and over; (2) clinically diagnosed with PD with no exclusion based on type. Studies including a mixed sample of participants, such as patients with conditions other than PD, were excluded. No restrictions were made in relation to gender, disease duration and disease severity.

Intervention

A variety of hand dexterity rehabilitation programmes and interventions based on physiotherapy practice were included to gain a comprehensive overview of current approaches. The interventions were directed to the PD patient themselves. The type of treatment was not limited to a specific mode as all treatments were included.

Outcome measures

Primary outcomes of interest were hand dexterity and ADL. Secondary outcomes of interest were upper limb motor function, QoL, adverse events, adherence and compliance and quality of intervention.

Study selection

Following the search through the databases, the initial result was finalised, and the title, abstract and full text of all studies were independently screened by three reviewers (LMH, CPK and FWH) to identify studies for possible inclusion in the review, as well as removing duplicate articles. The inclusion criteria for study selection were (1) studies that included adult participants

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Table 1. Boolean operators SEARCH STRATEGY

NO	Clinical Key search strategy	Cochrane Library search strategy	Ovid search strategy	PEDro	PubMed search strategy	PubMed Central search strategy	Scopus search strategy
1	Parkinson Disease	Parkinson Disease	Parkinson	Parkinson	Parkinson	Parkinson	Parkinson
2	"Hand dexterity"	"Hand dexterity"	"Hand dexterity"	"Hand dexterity"	"Hand dexterity"	"Hand dexterity"	"Hand dexterity"
3	"Manual dexterity"	"Manual dexterity"	"Manual dexterity"	"Manual dexterity"	"Manual dexterity"	"Manual dexterity"	"Manual dexterity"
4	Physiotherapy	2 OR 3	2 OR 3	2 OR 3	2 OR 3	Physiotherapy	Physiotherapy
5	Intervention	1 AND 4	1 AND 4	1 AND 4	1 AND 4	Intervention	Intervention
6	Technique					Technique	Technique
7	Management					Management	Management
8	Rehabilitation					Rehabilitation	Rehabilitation
9	2 OR 3					2 OR 3	2 OR 3
10	5 OR 6 OR 7 OR 8					5 OR 6 OR 7 OR 8	5 OR 6 OR 7 OR 8
11	1 AND 4 AND 9 AND 10					1 AND 4 AND 9 AND 10	1 AND 4 AND 9 AND 10

Table 2. PICO table

PICO element	Keywords	Search Items	Search strategies
P(Patient population)	Parkinson Disease	Parkinson Disease	Parkinson Disease
I (Intervention)	Physiotherapy interventions	Physiotherapy interventions	Physiotherapy interventions
C(Comparison)	Physiotherapy interventions		
O (Outcome)	Primary – Hand dexterity Secondary- Upper Limb Motor Function and quality of life	Hand dexterity, Physiotherapy technique OR management OR rehabilitation Upper Limb Motor Function and quality of life	Hand dexterity, Physiotherapy technique OR management OR rehabilitation Upper Limb Motor Function and quality of life

diagnosed with PD, (2) RCTs that evaluated the effects of physiotherapeutic interventions in improving hand dexterity, and (3) full-text studies published in English between 2010 and 2020. Papers that did not meet the inclusion criteria were excluded. Disagreements that arose were resolved through discussion or with the help of an experienced external reviewer (DTV) to provide an independent decision when necessary.

Methodological quality

The modified McMaster Critical Appraisal Tool[8] was used to assess the methodological quality of the eligible studies. The tool scoring used a dichotomous rating scale of yes/no options to rate the methodological quality of the study where Yes = 1 and No = 0, with a maximum score of 14.

The risk of bias for every study was also determined. The Cochrane Risk of Bias tool[9] was used to identify the risk of bias for every study. The risk of bias of each study was classified as either high, low or unclear risk. Articles that fulfilled at least four of the six criteria were considered to be at low risk of bias.

The evidence hierarchy from the National Health and Medical Research Council (NHMRC)[10] Designation of Levels of Evidence was used to measure the level of evidence of the individual paper. The study design of each selected study was assessed according to its rank in the hierarchy system, which classified the body of evidence into four levels (Level I, Level II, Level III-1, Level III-2, Level III-3, Level IV). The grades of recommendations from the NHMRC guideline were used to assess the individual components of the studies. Four components were graded, namely study quality, findings consistency, clinical impact and results generalisability, with "Excellent," "Good," "Satisfactory" or "Poor." Any disagreements were resolved through discussion or with the help of an experienced external reviewer (DTV) only when necessary.

Data extraction

Customised data extraction tables were constructed and developed for this review to organise and summarise information from the studies. Data from the studies were then extracted onto the tables for data collection purposes. The data extraction tables contained information such as study characteristics, participants details, outcome measures, intervention outlines and study results. Any disagreements or conflicts were resolved through discussion or with the help of an external reviewer (DTV) when the group could not come to an agreement. Study authors of the articles were contacted for additional information when necessary.

Data synthesis

Descriptive data synthesis of narrative summary and tabulation was used in this review due to the disparate outcome measures and interventions employed in each selected study. A general descriptive discussion of the research findings gave an overview of the study results and its importance. The characteristics of the studies were presented in multiple tables. This allows a comparison of results to be made between studies, and the reviewer's views about the research can then be formulated. For studies that included effect size in its result, the following range of effect size was used as a standard in this review: 0.2 to 0.49 was considered to

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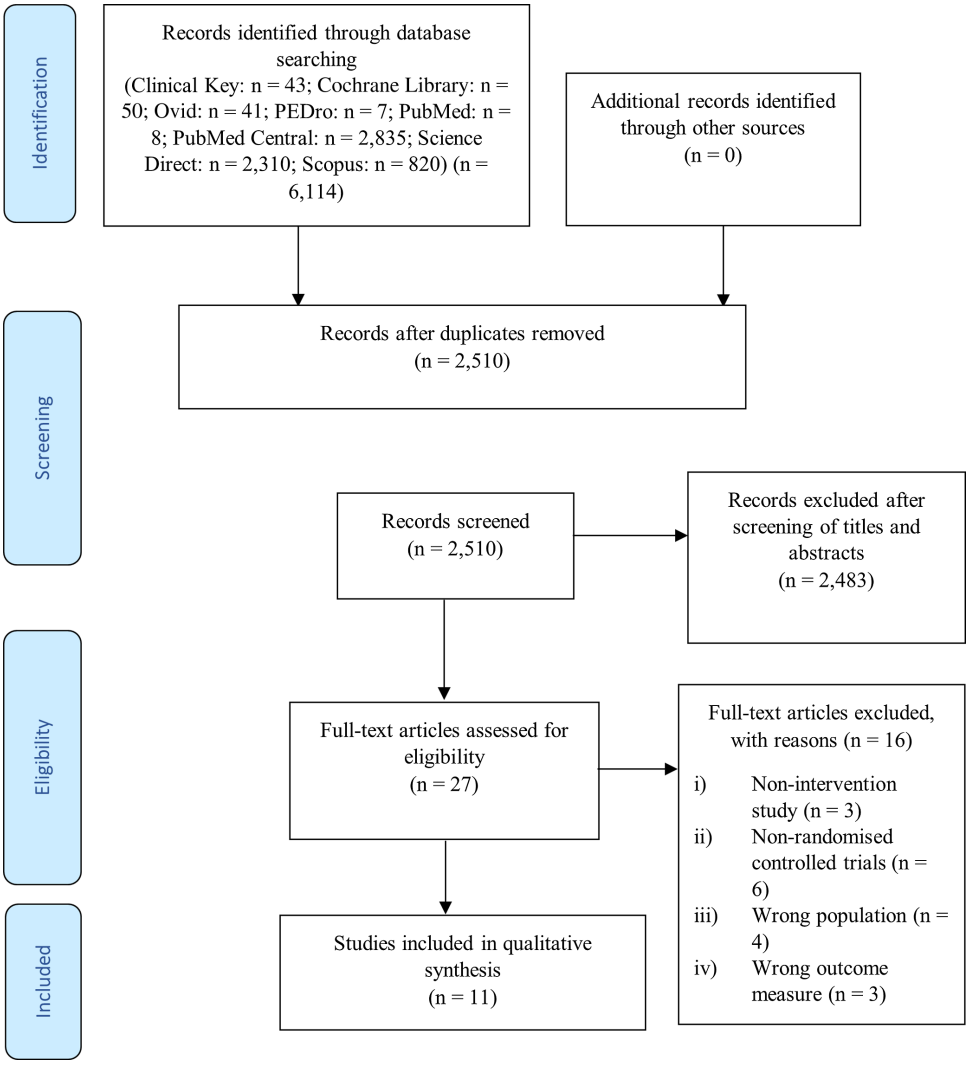

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.

be small, 0.5 to 0.79 was considered to be medium, and 0.8 or above was considered to be large.[11]

Results

Search results

A total of 6,114 studies were identified through initial database searches using the search strategy. Titles and abstracts of 2,510 studies were screened based on the established criteria. Studies that did not meet the predefined inclusion criteria were excluded. From these, 27 full-text articles were evaluated for eligibility. Following a thorough final screening, 11 full-text studies were eligible for inclusion in this systematic review,[12,13,14,21–22] while 16 full-text articles were excluded for not meeting the inclusion criteria. The reasons for exclusion included other focus of study (n = 3), other study design ($n = 6$), other study population ($n = 4$) and other outcome measure ($n = 3$). A PRISMA flow diagram that presents the study selection process for searches is outlined in Figure 1.

Study characteristics

All studies were published between 2011 and 2020. Of the 11 articles included in this review, a plurality was conducted in Spain,[13,15,19] whereas the others came from Korea,[18] Slovenia,[14] Australia,[12] Thailand,[22] Italy,[16] Switzerland,[21] Iran,[20] and the USA.[17]

Sample characteristics

A total of 11 studies involving 647 participants with PD were included for analysis in this review. Of the 11 studies, 399 males (59%) and 272 females (41%) were reported on baseline, with mean ages ranging from 59.15 ± 11.26 years to 83.0 ± 7.6 years. Study sample sizes varied from 20 to 234, and mean disease duration reported in most samples was more than six years. Disease severity of the included participants ranged from stages I to IV on the Hoehn and Yahr scale, with no study recruiting patients with stage-V PD. The participant characteristics during the baseline assessments are summarised in Table 3.

Methodological quality

A summary of critical appraisal scores using the modified McMaster Critical Appraisal Tool for all study methodologies are given in Table 4.

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Table 3. Participants baseline characteristic

	Demographic characteristics				Disease-related characteristics						
	Age (years) (mean ± SD)				Disease duration (years) (mean ± SD)		Levodopa (mg) (mean ± SD)		H&Y (mean ± SD)		
Author, year	EG	CG	Male (n)	Female (n)	EG	CG	EG	CG	H&Y stage	EG	CG
Allen et al., 2017[12]	67.5 ± 7.3	68.4 ± 8.5	23	15	7.9 ± 3.9	8.7 ± 6.1	939 ± 531	711 ± 703	NAD	NAD	NAD
Cabrera-Martos et al., 2019[13]	69.45 ± 12.32	71.78 ± 5.80	31	19	6.24 ± 2.62	7.17 ± 2.03	765.46 ± 333.27	901.90 ± 352.82	II - III	NAD	NAD
Cikajlo & Peterlin Potisk, 2019[14]	67.7 ± 7.6	71.3 ± 8.4	9	11	NAD	NAD	NAD	NAD	II - III	NAD	NAD
Fernández-González et al., 2019[15]	65.77 ± 7.67	67.36 ± 12.12	11	12	NAD	NAD	NAD	NAD	II - IV	NAD	NAD
Ferrazzoli et al., 2018[16]	66.5 ± 8.6	66.9 ± 10.5	136	98	9.0 ± 5.6	7.4 ± 5.3	583 ± 327	N/A	II - IV	2.6 ± 0.5	2.6 ± 0.6
Horin et al., 2019[17]	63.2 ± 9.3	64.9 ± 8.4	24	13	6.7 ± 5.6	6.0 ± 4.3	1087.0 ± 730.6	937.2 ± 395.5	II - III	2 (2, 3)	2 (2, 2)
Lee et al., 2011[18]	83.0 ± 7.6	77.9 ± 5.5	4	16	NAD	NAD	387.5 ± 153.6	330 ± 148.7	II - III	NAD	NAD
Mateos-Toset et al., 2016[19]	72.60 ± 8.86	69.97 ± 9.59	38	22	6.60 ± 4.15	7.10 ± 3.44	NAD	NAD	II - III	NAD	NAD
Taghizadeh et al., 2018[21]	61.05 ± 13.9	59.15 ± 11.26	35	5	7.8 ± 5.88	8.7 ± 5.33	NAD	NAD	I - III	NAD	NAD
Vanbellingen et al., 2017[22]	67.15 ± 7.94	68.16 ± 7.38	63	40	6.12 ± 3.52	6.35 ± 3.99	741.63 ± 471.8	745.43 ± 502.69	I - IV	1.94 ± 0.90	2.00 ± 0.82
Vorasoot et al., 2020[23]	66.74 ± 10.82	69.52 ± 10.31	25	21	4.41 ± 4.23	3.37 ± 2.36	370.79 ± 252.31	512.96 ± 339.33	I - III	2 (2, 2.5)	2 (2, 2.5)

SD = Standard Deviation; H&Y = Hoehn and Yahr; EG = experimental group; CG = control group; NAD = not addressed.

Table 4. Methodological quality

Author & year	1	2	3	4a	4b	4c	5a	5b	6a	6b	6c	7a	7b	7c	7d	8	Total /14 (%)
Allen et al., 2017[12]	Y	Y	RCT – II	37	Y	Y	Y	Y	Y	Y	NAD	Y	Y	Y	Y	Y	13 (93)
Cabrera-Martos et al., 2019[13]	Y	Y	RCT – II	50	Y	Y	Y	Y	Y	Y	NAD	Y	Y	Y	Y	Y	13 (93)
Cikajlo & Peterlin Potisk, 2019[14]	Y	Y	RCT – II	20	Y	N	Y	Y	Y	Y	NAD	N	Y	Y	N	Y	10 (71)
Fernández-González et al., 2019[15]	Y	Y	RCT – II	23	Y	N	Y	Y	Y	Y	NAD	Y	Y	Y	N	Y	11 (79)
Ferrazzoli et al., 2018[16]	Y	Y	RCT – II	234	Y	Y	Y	Y	Y	Y	NAD	Y	Y	Y	Y	Y	13 (93)
Horin et al., 2019[17]	Y	N	RCT – II	37	Y	N	Y	Y	Y	Y	NAD	Y	Y	N	Y	Y	10 (71)
Lee et al., 2011[18]	Y	Y	RCT – II	20	Y	N	Y	Y	N	Y	NAD	Y	Y	Y	Y	Y	11 (79)
Mateos-Toset et al., 2016[19]	Y	Y	RCT – II	60	Y	Y	Y	Y	Y	Y	NAD	Y	Y	N	N	Y	11 (79)
Taghizadeh et al., 2018[21]	Y	Y	RCT – II	40	Y	N	Y	Y	N	Y	NAD	Y	Y	Y	N	Y	10 (71)
Vanbellingen et al., 2017[22]	Y	N	RCT – II	103	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13 (93)
Vorasoot et al., 2020[23]	Y	N	RCT – II	46	Y	Y	N	N	Y	Y	NAD	Y	Y	Y	Y	Y	10 (71)

1. A clearly stated study purpose; 2. Sufficient background literature; 3. Study design; 4a. Sample size; 4b. Detailed sample description; 4c. Sample size justification; 5a. Use of reliable outcome measures; 5b. Use of valid outcome measures; 6a. Detailed intervention description; 6b. Absence of contamination; 6c. Absence of cointervention; 7a. Statistical significance reported; 7b. Appropriate analysis methods; 7c. Clinical importance reported; 7d. Dropouts reported; 8. Appropriate conclusion.
Y = yes; *N* = no; NAD = not addressed; RCT = randomised controlled trial.

Table 5. Risk of bias

	Random sequence generation	Allocation concealment	Blinded participants and personnel	Blinded assessor	Incomplete data	Selective reporting
Allen et al., 2017[12]	Low	Low	High	Low	High	Low
Cabrera-Martos et al., 2019[13]	Low	Low	Low	Low	Low	Low
Cikajlo & Peterlin Potisk, 2019[14]	High	Unclear	High	Unclear	Unclear	Low
Fernández-González et al., 2019[15]	Unclear	Unclear	High	Unclear	Unclear	Low
Ferrazzoli et al., 2018[16]	Low	Low	High	High	Unclear	High
Horin et al., 2019[17]	Unclear	Unclear	High	High	Unclear	Low
Lee et al., 2011[18]	Unclear	Unclear	High	Unclear	Unclear	Low
Mateos-Toset et al., 2016[19]	Low	Low	Unclear	Low	Unclear	Low
Taghizadeh et al., 2018[21]	Unclear	Unclear	High	Low	Unclear	Low
Vanbellingen et al., 2017[22]	Low	Low	Low	Low	High	Low
Vorasoot et al., 2020[23]	Low	Unclear	High	Unclear	Low	Low

Four studies[12,13,16,21] have scored 13 out of 14 for their relatively good methodology quality following the methodological quality assessment. The remaining seven studies achieved a moderate methodological quality rating, with scores ranging from 10 to 11.

Table 5 shows the risk of bias for each of the included studies. Four of the 11 studies were considered to be at low risk of bias.[12,13,19,21] The remaining 7 studies were considered as high or unclear risk of bias.

Table 6 summarises the ratings of the NHMRC Evidence Statement Form. The body of evidence showed that the interventions aimed to improve hand dexterity might be effective. However, the results should be interpreted with caution due to the varied outcome measures, and interventions used.

Interventions

The overview of the contents of the interventions including the quality of each intervention for both experimental and control groups is provided in Table 7. The intervention period varied between studies, with the total training period ranging from a 15-minute single session to 12 weeks of training. The intervention settings differed between studies, with only four studies taking place in a home-based setting,[12,13,17,22] rehabilitation centre,[14] Aparkan Association,[15] hospital,[16] laboratory,[19] and neurologic clinic.[23] Two studies did not specify the setting of the study.[18,21] The intervention quality varied in frequency from two times a week to daily sessions, and duration lasted from 15 minutes to 3 hours per session.

The selected study evaluated the effects of intervention such as Exergames,[12] a single hand-exercise session,[13] Immersive 3D virtual,[14] multidisciplinary, aerobic, motor-cognitive and intensive rehabilitation treatment (MIRT),[16] therapeutic putty exercises,[19] home-based dexterity programme,[21] handwriting exercise,[22] and one study used a smartphone application.[17] Majority of the study aimed to evaluate the effects on manual dexterity, hand grip, functional improvements, ADL performance as well as the levels of satisfaction, motivation aspects and compliance among patients in

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Table 6. National Health and Medical Research Council body of evidence

Component	Grade	Comments
1. Evidence base	A – more than two Level II studies with a low risk of bias	Number of studies: 11 studies
		Number of participants: 647 PD participants
		Level of evidence: Level II
2. Consistency	B – most studies are consistent	10 out of 11 studies reported statistical significanceStudy design: 11 RCTs
		Varied outcome measures and interventions
3. Clinical impact	B – substantial	Some studies included specifically designed games for their intervention groups
		No adverse effects reported
		9 out of 11 studies reported clinical importance
4. Generalisability	B – population studied in each study is similar to the target population for the review	Mean age ranged 59.15 ± 11.26 to 83.0 ± 7.6 years
		Studies conducted in 9 countries
Grade of recommendations	B – body of evidence can be trusted to guide practice in most situations	Most studies were of moderate methodological quality
		The current findings lack outcome homogeneity in evaluating effects of intervention for PD

PD = Parkinson's disease; RCT = randomised controlled trial.

Table 7. Contents of the interventions

			Experimental group			Control group		
Author & year	Intervention duration	Setting	Mode	Frequency (per week)	Duration (per session)	Mode	Frequency (per week)	Duration (per session)
Allen et al., 2017[12]	12 weeks	Home-based	Exergames	3 days	12 games	Usual care and activities	N/A	N/A
Cabrera-Martos et al., 2019[13]	4 weeks	Home-based	Individualised programme with specific goals	2 days	45 minutes	Standard intervention without specific goals	2 days	45 minutes
Cikajlo & Peterlin Potisk, 2019[14]	3 weeks	Rehabilitation centre	Immersive 3D virtual reality	10 sessions/3 week	30 minutes	Non-immersive 2D exergaming	10 sessions/3 week	30 minutes
Fernández-González et al., 2019[15]	6 weeks	Aparkan Association	UL treatment based on serious games designed using the LMC system	2 sessions	30 minutes	Specific UL intervention based on conventional physiotherapy	2 sessions	30 minutes
Ferrazzoli et al., 2018[16]	4 weeks	Hospital	MIRT	6 days	1 hour	Did nothing	N/A	N/A
Horin et al., 2019[17]	12 weeks	Home-based	Beats Medical Parkinsons Treatment App	Daily	30 minutes	Maintain normal routine	N/A	N/A
Lee et al., 2011[18]	4 weeks	NAD	Modified CIMT	5 days	3 hours	General UL exercises	5 days	3 hours
Mateos-Toset et al., 2016[19]	15 minutes	University laboratory	Individualised hand training session using therapeutic putty	N/A	15 minutes	Active UL ROM exercises	N/A	15 mins
Taghizadeh et al., 2018[21]	2 weeks	NAD	Current rehabilitation exercises and SMT	5 days	1 to 3 hours	Current rehabilitation interventions	N/A	N/A
Vanbellingen et al., 2017[22]	4 weeks	Home-based	HOMEDEXT	5 days	30 minutes	UL Theraband programme	5 days	30 minutes
Vorasoot et al., 2020[23]	4 weeks	Neurology clinic	Handwriting exercise	5 pages/ day	NAD	Did nothing	N/A	N/A

NAD = not addressed; N/A = not applicable; UL = upper limb; LMC = Leap Motion Controller; MIRT = Multidisciplinary Intensive Rehabilitation Treatment; CIMT = constraint-induced movement therapy; ROM = range of motion; SMT = sensory-motor training; HOMEDEXT = home-based dexterity programme.

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mild-to-moderate stages of the disease. The game-based study investigated the acceptability and feasibility of these games,[12,15] clinical effectiveness between immersive and non-immersive virtual reality exergaming.[14] The study used a mobile health smartphone application examined the effect of adherence and assessed usability of the mHealth application in addition to gait, speech and dexterity.[17]

Effects of interventions

An overview of the measures for dexterity, ADLs, upper limb motor function, QoL and other miscellaneous outcomes used for each study along with its main findings are presented in Tables 7 and 8.

Primary outcome – hand dexterity

A total of five[13,15,19,21,22] out of 11 studies[12–15,17–22] that measured hand dexterity using different outcome measures reported significant between-group results.

Six out of 11 studies had small effects size.[12,15,17,19–21] The study by Fernández-González et al.[15] and Taghizadeh et al.[20] produced both small and medium effect sizes in different outcomes. Four out of the 11 studies[12,13,17,22] were conducted in a home-based setting, had both medium and large effect sizes in the outcomes, while three studies[14,16,23] are conducted in hospital or clinic-based settings. Most of the studies had an average duration of 4–12 weeks and were administered with an average frequency of 3 days per week. The study by Lee et al.[18] involved a 4-week intervention which consisted of five sessions per week, each lasting for 3 hours demonstrated a significant large effect size.

Primary outcome – activities of daily living

Only two[16,22] out of three studies[12,16,22] that assessed ADL showed significant between-group results. Both the studies reported a small effect size in ADL. Out of these three studies two of them were received home-based exercise game[12,22] with an average frequency of 3 days per week.

Secondary outcome – upper limb motor function

Two[12,22] of the seven studies[12,14,16–18,21–22] that assessed upper limb motor function reported significant between-group results on motor function after the intervention. Two studies had small effect size[12,22] and a study by Allen et al.[12] also showed medium effect size. On the other hand, large effect size was reported by two studies.[14,18]

Secondary outcome – quality of life

Only[16] one of three studies[12,16,21] reported that assessed QoL shows significant between-groups improvement was perceived after their interventions in improving QoL. Also, two studies[16,21] had produced a small effect size.

Secondary outcome – miscellaneous

In the study conducted by Cabrera-Martos et al,[13] the between-groups result on Goal Attainment Scaling (GAS) reported a significant achievement with a large effect size.

The results of the study conducted by Cikajlo & Peterlin Potisk[14] on Intrinsic Motivation Inventory (IMI) reported significant differences in "perceived competence" and increased "effort/importance" in the experimental group. The between-group result revealed significant differences in "perceived competence."

The study by Fernández-González et al.[15] used Client Satisfaction Questionnaire (CSQ-8) for user satisfaction evaluation. The result for the experimental group and control group obtained a similar satisfaction score with no effect size.

Secondary outcome – adverse events

Two studies[12,15] have examined adverse side effects such as muscle soreness and undue fatigue. However, none of the participants reported experiencing adverse events following their participation in the intervention. To evaluate adverse side effects comprehensively, a follow-up assessment is necessary, and conducting more intensive dosage regimens is required to verify these results thoroughly.[15]

Secondary outcome – adherence and compliance

Nine studies[12–18,21,22] have assessed adherence and compliance, with five[12,16–18,21] reported dropouts due to personal reasons. In addition, the study conducted by Allen et al.[12] focused on exercise compliance, and participant feedback showed that the results in the experimental group were satisfying. The study conducted by Vanbellingen et al.[21] also required participants to document details of the interventions in a diary. The results showed that the experimental group has higher adherence than the control group. However, the protocol was deemed to bring patients fatigue and daily stress, and lack of motivation. Next, the study by Fernández-González et al.[15] and Vorasoot et al.[22] reported that all subjects showed excellent adherence and compliance to protocol. Finally, the adherence of the experimental group to the mHealth application dexterity exercises in the study conducted by Horin et al.[17] was lower than the other studies. The exit survey regarding the mHealth application completed by the subjects from the experimental group revealed that there is more negative feedback than positive feedback due to technical issues and repetitive exercises.

Discussion

This systematic review investigated the current intervention available to improve hand dexterity in PD patients, with the primary objective of identifying the best intervention in enhancing the dexterous hand function of PD patients. This review included 11 RCTs with moderate to excellent methodological quality. Quantitative meta-analysis was not carried out in this review due to the use of various outcome measures and diverse interventions. In addition, there were also several methodological flaws and risks of bias in the included studies following the methodological quality assessments. Hence, the dearth of evidence made it difficult to support any one intervention as the best intervention when compared to the other PD treatments.

Based on the data extracted, improvements in primary and secondary outcomes of interest were reported in each study. In terms of primary outcomes, eight studies[13–15,18–22] reported significant results on hand dexterity, and two studies[16,21] showed significant results on ADL. As for secondary outcomes, four studies [12,16,18,22] reported improvements in motor function, two studies[16,21] reported significant results in improving QoL, and two studies which were conducted by Cabrera-Martos et al.[13] and Cikajlo & Peterlin Potisk[14] showed significant results on Goal

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Table 8. Major findings

	Primary outcomes				Secondary outcomes					
	Hand dexterity		ADL		Upper limb motor function		QoL		Miscellaneous	
Author & year	**BW *p*-value**	**Cohen's *d***	**BW *p*-value**	**Cohen's *d***	**BW *p*-value**	**Cohen's *d***	**BW *p*-value**	**Cohen's *d***	**BW *p*-value**	**Cohen's *d***
Allen et al., 2017[12]	9-HPT: 0.840 CRT: 0.680 BBT: 0.440	0.18 0.10 0.28 (small)	MAM-36: 0.810	0.11	Horizontal tapping test (speed): 0.006* Horizontal tapping test (error): 0.020* Vertical tapping test (speed): 0.170 Vertical tapping test (error): 0.050* GPE: 0.800	0.55 (medium) 0.59 (medium) 0.40 (small) 0.54 (medium) 0.08	PDQ-39: 0.630	0.08	N/A	
Cabrera-Martos et al., 2019[13]	PPT: Most affected: <0.001* Least affected: 0.012* Bimanual: <0.001* Assembly task: 0.004*	1.10 (large) 0.78 (medium) 1.06 (large) 0.77 (medium)	N/A		N/A		N/A		GAS: <0.001*	1.91 (large)
Cikajlo & Peterlin Potisk, 2019[14]	BBT: Affected hand: 0.285	0.06	N/A		UPDRS-III: 0.2189	0.98 (large)	N/A		IMI "perceived competence": 0.037*	NIL
Fernández-González et al., 2019[15]	BBT: More affected: 0.381 Less affected: 0.518 PPT: More affected: 0.036* Less affected: 0.447 Both hands: 0.879 Assembly: 0.006*	0.09 0.00 0.42 (small) 0.29 (small) 0.23 (small) 0.75 (medium)	N/A		N/A		N/A		CSQ-8: high satisfaction NIL	0.03
Ferrazzoli et al., 2018[16]	N/A		ADL subscale of PDQ-39: Post-intervention: 0.016* Follow-up: NIL PDDS: Post-intervention & follow-up: NIL	0.20 (small) NIL NIL	Total UPDRS: Post-intervention & follow-up: NIL	NIL	PDQ-39: Post-intervention: <0.0001* Follow-up: NIL	0.33 (small) NIL	N/A	
Horin et al., 2019[17]	9-HPT: Dominant: NIL Non-dominant: NIL	0.37 (small) 0	N/A		MDS-UPDRS-III: NIL	0.10	N/A		N/A	
Lee et al., 2011[18]	BBT: Task limb: NIL Non-task limb: NIL	3.31 (large) NIL	N/A		FMA: Shoulder/arm/forearm: NIL Wrist: NIL Hand: NIL Coordination/speed: NIL ARAM: Grasp: NIL Grip: NIL Pinch: NIL Gross movement: NIL	4.30 (large) 2.23 (large) 2.32 (large) NIL 3.11 (large) 3.05 (large) 7.33 (large) 2.63 (large)	N/A		N/A	

(*Continued*)

Table 8. Major findings (*Continued*)

	Primary outcomes				Secondary outcomes					
	Hand dexterity		ADL		Upper limb motor function		QoL		Miscellaneous	
Author & year	BW *p*-value	Cohen's *d*	BW *p*-value	Cohen's *d*	BW *p*-value	Cohen's *d*	BW *p*-value	Cohen's *d*	BW *p*-value	Cohen's *d*
Mateos-Toset et al., 2016[19]	PPT: Dominant hand: 0.037* Nondominant hand: 0.037* Bimanual task: 0.023* Assembly task: 0.049* COTNAB: Dominant hand: 0.039* Nondominant hand: 0.037* Bimanual: 0.018*	0.23 (small) 0.21 (small) 0.25 (small) 0.17 0.18 0.31 (small) 0.36 (small)	N/A		N/A		N/A		N/A	
Taghizadeh et al., 2018[21]	BBT: Dominant hand: NIL Nondominant hand: NIL PPT: Dominant hand: NIL Nondominant hand: NIL Both hands: NIL Assembly: NIL	0.31 (small) 0.36 (small) 0.78 (medium) 0.21 (small) 0.47 (small) 0.12	N/A		N/A		N/A		N/A	
Vanbellingen et al., 2017[22]	9-HPT: Post-intervention: 0.006* Follow-up: 0.510 CRT: Post-intervention: 0.330 Follow-up: 0.980	0.47 (small) 0.08 0.12 0.07	ADL subscale of PDQ-39: Post-intervention: 0.080 Follow-up: 0.600 MDS-UPDRS-II: Post-intervention: 0.170 Follow-up: 0.690 DextQ-24: Post-intervention: 0.020* Follow-up: 0.16	0.26 (small) 0.04 0.27 (small) 0.07 0.48 (small) 0.33 (small)	MDS-UPDRS-III: Post-intervention: 0.570 Follow-up: 0.950	0.12 0.003	PDQ-39: Post-intervention: 0.190 Follow-up: 0.370	0.20 (small) 0.12	N/A	
Vorasoot et al., 2020[23]	Time taken to complete test: 0.015* Accuracy: 0.576 Subjective rating: <0.001*	0.70 (medium) 0.17 1.35 (large)	N/A		UPDRS-III: <0.322	0.30 (small)	N/A		N/A	

ND = no difference; N/A = not applicable; NIL = not in the list; BW = between-groups; Hand dexterity: 9-HPT = Nine-Hole Peg Test; CRT = coin rotation task; BBT = Box and Block Test; PPT = Purdue Pegboard Test; COTNAB = Chessington Occupational Therapy Neurologic Assessment Battery; ADL = Activities of daily living: MAM-36 = Manual Ability Measure-36 questionnaire; PDQ-39 Parkinson's Disease Questionnaire; PDDS = Parkinson's Disease Disability Scale; MDS-UPDRS = Movement Disorders Society Unified Parkinson's Disease Rating Scale; Upper limb motor function: GPE = Global Perceived Effect scale; UPDRS = Unified Parkinson's Disease Rating Scale; MDS-UPDRS = Movement Disorders Society Unified Parkinson's Disease Rating Scale; FMA = Fugl-Meyer Assessment; ARAM = Action Research Arm Test; QoL = Quality of life: PDQ-39 Parkinson's Disease Questionnaire Miscellaneous: GAS = Goal Attainment Scaling; IMI = Intrinsic Motivation Inventory; CSQ-8 = Client Satisfaction Questionnaire.
*= statistically significant ($p<0.05$).

Attainment Scaling and IMI under miscellaneous outcome measures, respectively.

In addition, no studies reported adverse events after the intervention, indicating that their interventions may be safe for individuals with PD. Among the nine studies[12–18,21,22] that reported dropouts during the study period, most reasons were unrelated to the intervention. However, there were subjects from the experimental group that discontinued participation[16,17,21] without providing specific reasons. In general, studies that showed high adherence or compliance, by way of dropout rate, total hour of training, or satisfaction, were Allen et al,[12], Cabrera-Martos et al, [13] Cikajlo & Peterlin Potisk,[14] Fernández-González et al,[15] Vanbellingen et al. [21] and Vorasoot et al.[22]

The study conducted by Horin et al.[17] did not provide any guidance from the therapist to the participants as they had to perform the exercises independently and depend solely on the mHealth application. The study results reported no improvements after the intervention and suggested that using the application alone was insufficient to significantly improve motor function in PD patients. This result was shown to be valid according to Keus et al,[23] who stated that supervised training in the short term typically produces a better result than non-supervised programmes. Dexterity deficits primarily affect the patients' daily activity and participation, which often occur within the community setting, particularly the home environment. Thus, rehabilitation focused on improving ADLs should be delivered in a real-world context as it is closer to the patients' daily environment.[23] Home-based rehabilitation allows patients to practice movements more comfortably and allows therapists to evaluate patient performance and intervention effect with ease.[13] In short, it is suggested that rehabilitation with minimal therapist supervision taking place in a home-based setting undoubtedly were more convenient to PD patients and produced a better result. The convenient home-based setting was employed by four of the 11 included studies.[12,13,17,21]

According to Ackerman et al,[25] a multidisciplinary rehabilitation service is effective and efficient as it ensures the continuity of care and maximises patient functional outcomes. However, it may also be inconvenient for patients and healthcare personnel to liaise with one another on the rehabilitation programme. For instance, although the study conducted by Ferrazzoli et al.[16] showed significant improvements in several aspects, it was multidisciplinary and involved different healthcare professions. At the end of the study period, it was reported that three participants each discontinued participation and did not attend the follow-up assessment without providing specific reasons. Hence, for outpatient rehabilitation, a multidisciplinary rehabilitation programme may not be feasible for mainstream care.

According to Abbruzzese et al,[26] significant improvements observed after physiotherapy interventions were usually not present after three months. This statement is supported by the two studies[16,22] in our review, showing that hand dexterity improvement were not sustained at follow-up. This suggested that an individualised long-term training might be needed to maintain the improvement in hand function.

This review aimed to suggest a feasible intervention protocol to improve hand dexterity in PD patients that could be incorporated into one's daily routine. The intervention protocol of the three studies by Ferrazzoli et al,[16] Lee et al.[18] and Taghizadeh et al.[21] had a duration of 1 to 3 hours per session for 5 to 6 days per week, which could be less suitable for integration into their routine. The European Physiotherapy Guideline for Parkinson's Disease[23] recommended that rehabilitation for complex motor sequences on gait and functional mobility should include three 30-minute sessions weekly for three weeks. It was also suggested that at least four weeks of training is needed to show significant improvements in patient functional abilities. The optimal parameter for a rehabilitation programme would be a minimum of 30 minutes duration, three sessions per week for three weeks based on the above recommendations. Studies with such parameters include Allen et al,[12] Cikajlo & Peterlin Potisk,[14] Vanbellingen et al,[22] and Vorasoot et al.[23]

Reach-to-grasp movements and object manipulation can be improved with the help of cueing strategies, provision of augmented feedback and by avoiding dual-tasking,[26] which is adopted for use by eight studies included in the review.[12–16,19,20,22]

Furthermore, the study by Cabrera-Martos et al.[13] that evaluated the effect of goal setting on an individualised programme had conveyed important information. The study results revealed that a goal-oriented intervention focusing on specific functional goals based on tasks and task components significantly improved manual dexterity and promoted goal achievement in PD subjects. The impact on participant motivation was also positively influenced, thereby increasing the attention of patients and exercise repetition. Therefore, this indicates that setting a set of specific functional goals before planning a treatment programme is essential in rehabilitation.

After thoroughly evaluating all the studies to identify the hand dexterity intervention that is most likely to produce the most significant results in PD patients, based on the aforementioned recommendations to be categorised as a good intervention, only one[21] out of the 11 studies had satisfied most of the suggestions. The study on HOMEDEXT programme focusing on the key components of dexterity had shown significant improvements in hand dexterity, ADL and QoL, with no adverse event reported, high adherence to the intervention, sufficient instruction given and the quality of the intervention protocol was not too long and not too frequent, and the intervention took place in a home-based setting. This suggested that the study intervention may have the potential and feasibility to improve the hand dexterity of PD patients in mainstream care.

Limitations

There are several other limitations in this review. Potential bias might have arisen in the review process. It was possible to overlook some promising and relevant studies despite the execution of an in-depth, extensive and comprehensive database search.

The sample age, disease stage and disease severity of the study population were not controlled in this review. Hand dexterity performance may deteriorate as people age or symptoms worsen. Thus, this might have influenced the study results, as younger patients with less severe PD would have yielded a better result.

Some studies did not provide information on their sample size calculation. Without information on the sample size justification, it was difficult to know if the power was sufficient with the given sample size. Next, the primary focus of the study with a small sample size was to examine the intervention usability. Hence, the result did not have sufficient power to evaluate the effectiveness of the intervention. These may predispose the study results to different types of error, thereby increasing the risk of bias and affecting the validity of a study result.

Most studies only evaluated the immediate effects of intervention within a short study period. The follow-up period

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for the included studies was either absent or short, up to only three months long. Nine out of a total of 11 studies did not observe whether the improvements have been sustained over time. They only assessed the performance of their participants at baseline and post-intervention.

A further limitation was the potential publication bias as this review only included English language full-text RCTs published within the last 10 years. High-quality studies might be available in papers with other types of study design and languages published beyond the past 10 years.

Future recommendations

Well-designed RCTs and a more extended follow-up period are needed to evaluate the efficacy, effectiveness and impact of treatments on PD subjects. Besides, the studies should also reflect the current practice of the rehabilitation field to allow for replication of interventions by the physiotherapists as well as other healthcare personnel. Methodological quality and reporting of a study should be improved to minimise the methodological flaws and risk of bias. More studies on the current topic are needed to determine the applicability of interventions in people with PD according to different characteristics of participants and disease. Detailed information on interventions, aimed to enhance dexterity function and the content and delivery of training, should be further studied to serve as a guideline for upper extremity rehabilitation. In essence, additional study is needed to verify our findings based on a firm body of evidence. Consider setting a cut-off score for the methodological quality assessment to avoid the inclusion of low-quality studies in the review only if necessary.

Conclusion

In conclusion, this systematic review provides valuable insights into interventions aimed at improving hand dexterity in Parkinson's disease (PD) patients. Despite the limitations and methodological flaws in the included studies, significant improvements in hand dexterity, activities of daily living (ADL) and quality of life (QoL) were reported across multiple studies. Importantly, no adverse events were reported, indicating the safety of these interventions for PD patients. Home-based rehabilitation programmes emerged as a promising approach, offering convenience and comfort for patients while allowing therapists to monitor progress effectively.

While more research is needed to establish the most effective interventions for improving hand dexterity in PD, the findings of this review provide valuable guidance for developing future rehabilitation programmes. By incorporating the recommended parameters, cueing strategies, goal-oriented approaches and considering the convenience and comfort of patients, clinicians can design interventions that enhance hand dexterity, ADL and QoL, ultimately improving the lives of individuals with Parkinson's disease.

Furthermore, it was difficult to draw a definite conclusion on the therapeutic applications of the current best intervention to improve hand dexterity in PD due to the limitations of this review discussed earlier, further investigation is needed before concluding an intervention is assuredly effective.

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