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REVIEW

The effects of exercise dose on patients with Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Objective The effects of different exercise doses on motor function, balance, mobility, and quality of life (QOL) in patients with Parkinson's disease (PD) were evaluated.

Method The exercise intervention dose was evaluated based on the recommendations of the American College of Sports Medicine (ACSM) for developing and maintaining cardiorespiratory health, muscle strength, and physical function for PD patients and classified into high ACSM compliance and low or uncertain ACSM compliance. The impact of ACSM compliance on Unified Parkinson's Disease Rating Scale, Part III (UPDRS-III), Berg Balance Scale (BBS), Timed Up and Go (TUG), and 39-item Parkinson's Disease Questionnaire (PDQ-39) in patients with PD was compared using the standardized mean difference (SMD) along with the corresponding 95% confidence interval (95% CI).

Results A total of 26 articles were included, comprising 32 studies. Twenty-one studies were classified as high ACSM compliance, and 11 studies were classified as low or uncertain ACSM compliance. For the four outcome measures, the SMD ratio of exercise interventions with high ACSM compliance to those with low or uncertain ACSM compliance was as follows: UPDRS-III (− 0.74: − 0.17), TUG (− 0.62: − 0.17), PDQ-39 (− 0.58: − 0.31), and BBS (0.51: 0.52).

Conclusion The results suggest that compared with exercise interventions with low or uncertain ACSM compliance, exercise interventions with high ACSM compliance had a more significant improvement effect on motor function, mobility, and QOL in PD patients. However, the effect on balance was not as pronounced, and further research is needed to validate these findings.

Keywords Parkinson's disease · Exercise · ACSM · Dose · Meta-analysis

Introduction

Parkinson's disease (PD) is one of the most prevalent neurodegenerative disorders, characterized by motor and non-motor symptoms [1–3]. Due to the impairment in the motor system and motor function, PD is typically classified as a movement disorder [4]. The clinical features of PD mainly include resting tremors, bradykinesia, rigidity, postural instability, gait abnormalities, and gradually worsening symptoms over time [4–7]. In addition to motor symptoms, PD patients experience other non-motor symptoms such as cognitive and sensory impairments, insomnia, and depression [1, 8]. The World Health Organization (WHO) has stated that globally, the rate of disability and death attributed to PD is growing faster than any other neurological disorder. In 2015, there were over 6 million PD patients, with a mortality rate exceeding 100,000, representing a doubling since 1990, and this figure is projected to exceed 12 million in 2040 due to an aging population [9–11]. Therefore, we must strive to explore practical measures to alleviate the symptoms of PD patients.

The exact cause of Parkinson's disease is still unclear, but it is widely believed to be caused by genetic susceptibility, environmental factors, and abnormal immune system activity [2, 12]. The motor symptoms of PD are caused by

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damage to the nigrostriatal pathway in the midbrain, leading to a reduction in the neurotransmitter dopamine [12, 13]. PD prevalence leads to a significant decline in the quality of life for patients and their families, as well as an increased social burden. Currently, technological medical methods cannot cure PD, and we can only prevent or alleviate the clinical symptoms of PD through some therapeutic measures [3]. The treatment of PD includes drug therapy and non-pharmacological therapy. Levodopa is the most effective drug for treating PD, but its effect can only last for about 10 years [14]. Long-term use of levodopa or other treatment drugs by patients can lead to complications such as motor fluctuations and movement difficulties, as well as side effects such as insomnia and orthostatic hypotension [1]. Non-pharmacological treatments have received increased attention in recent years. In non-pharmacological therapy, exercise is an important auxiliary method for treating PD [15]. PD is a chronic progressive disease, and regular exercise can alleviate the skeletal muscle and cardiovascular problems that PD patients develop due to reduced physical activity [16, 17].

The previous studies have discussed the role of exercise as a neuroprotective intervention in PD and neurodegenerative disorders. Exercise has been found to directly or indirectly support synaptic health in the brain and can even have a direct impact on areas primarily affected by synapses in PD, providing neuroprotection. Furthermore, exercise may hinder neurodegeneration through various mechanisms such as improving serotonergic signaling, enhancing neurotrophic factor expression, and improving mitochondrial bioenergetics [18]. Therefore, theoretical research supports exercise intervention as a viable strategy for preventing and counteracting the progression of such diseases.

Practical studies have demonstrated that exercise intervention can improve gait, reduce the frequency of falls, and improve quality of life and aerobic capacity in PD patients [19, 20]. Currently, a large number of exercise intervention experiments have verified the preventive and therapeutic effects of different exercise programs on PD [21–23] as well as the effects of exercise on the clinical symptom manifestations of PD patients [22, 24, 25]. In recent years, multiple meta-analyses have compared the effects of different exercise interventions on the motor function of PD patients. Hao ZK and colleagues' study showed that dance, yoga, virtual reality training, and resistance training have more advantages than other exercise modes [26]. Mustafaoglu R et al. pointed out that different exercise interventions have varying effects depending on functional performance areas, and that dance is an effective exercise to improve the quality of life of PD patients [27]. Zhou X et al. compared the effects of different intensities and cycles of aerobic and resistance training on PD patients [28]. Numerous studies have proven the preventive and therapeutic effects of exercise as a non-pharmacological therapy for PD patients, but research on the exercise dose during exercise intervention is relatively lacking. Therefore, the purpose of this paper is to explore the optimal exercise dose for treating and preventing PD.

The American College of Sports Medicine (ACSM) has developed recommended exercise prescriptions for PD patients, which involve aspects of flexibility, cardiovascular endurance, muscle strength, functional training, and motor control [29]. However, it is not currently clear whether exercise interventions based on ACSM guidelines have a greater impact on PD patients compared to interventions with lower compliance rates to these recommendations. The aim of this systematic review is to compare the effects of high compliance to ACSM guidelines versus low or uncertain compliance exercise interventions on PD patients.

Materials and methods

This systematic review and meta-analysis was reported following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and was registered in PROSPERO (CRD42023426987).

Search strategy

We searched PubMed, Embase, Web of Science, and Cochrane databases from the date of establishment to March 12, 2023. The search strategy followed the PICOS principle and focused on research participants, interventions, and research methods. The search included the following subject headings and keywords: ("Parkinson Disease" or "Idiopathic Parkinson's Disease" or "Lewy Body Parkinson's Disease" or "Parkinson's Disease, Idiopathic" or "Parkinson's Disease, Lewy Body" or "Parkinson Disease, Idiopathic" or "Parkinson's Disease" or "Idiopathic Parkinson Disease" or "Lewy Body Parkinson Disease" or "Primary Parkinsonism" or "Parkinsonism, Primary" or "Paralysis Agitans") AND ("Exercise" or "Exercises" or "Sports" or "Physical Activity" or "Motor Activity" or "Training" or "endurance training" or "Tai Chi" or "yoga" or "Balance" or "Resistance" or "Flexibility" or "Cardiovascular" or "Aerobic") AND ("Randomized controlled trial" or "controlled clinical trial" or "randomized" or "placebo" or "randomly"). The specific search strategy is provided in Appendix 1. We also hand-searched the references of relevant review articles and retrieved articles for supplementary studies. If necessary, we contacted study authors to obtain additional information.

Criteria for selection of studies

If studies met the following criteria, they were included: (a) published randomized controlled trials; (b) study subjects were PD patients; (c) the experimental group intervention

could be any type of exercise, such as resistance training, aerobic exercise, flexibility exercise, etc.; (d) control interventions could be no treatment or any treatment not related to exercise, such as conventional physical therapy, family education, psychotherapy, etc.; and (e) outcome measures in the study included Unified Parkinson's Disease Rating Scale, Part III (UPDRS-III) or Movement Disorder Society Unified Parkinson's Disease Rating Scale, Part III (MDS-UPDRS- III), Berg Balance Scale (BBS), Timed Up and Go (TUG) test, and 39-item Parkinson's Disease Questionnaire (PDQ-39).

The following studies were excluded: (a) Studies reported as conference abstracts, review articles, or editorials; (b) studies with exercise or no standard therapy as the control group; (c) studies involving patients with other cardiovascular or metabolic diseases; (d) studies that administered special drug treatment during the exercise intervention; and (e) duplicate publications reporting the same experimental data from a single study.

Two authors (WLC and DL) independently screened the titles and abstracts of the retrieved literature for eligibility. If either author deemed a study potentially eligible, the full text of the article was obtained. The two authors then independently assessed the full text for eligibility. In cases of disagreement, a third author (JX) provided a final decision through discussion until a consensus was reached. There were no restrictions on the age, sex, body mass index, publication date, or language of the study participants.

Data synthesis and analysis

The data extraction process was conducted independently by two authors (WLC and LJY). The primary outcomes considered in this study were UPDRS-III, BBS, TUG, and PDQ-39. An Excel spreadsheet was designed in advance to extract relevant data, including publication characteristics (title, author names, publication year, and country), methodological characteristics (number of study groups, group designs, interventions, and sample sizes), participant characteristics (age, sex ratio, disease duration, and Parkinson's disease Hoehn and Yahr staging), exercise characteristics (intervention frequency, exercise intensity, exercise duration, repetition numbers, and set numbers), and risk assessment and outcome features.

When extracting outcome data, if the data were presented graphically without clear textual descriptions, Engauge Digitizer software was used for data extraction. For studies with multiple follow-ups, only the data immediately assessed after the intervention were extracted.

After data extraction, the exercise intervention dose and compliance were evaluated. The exercise intervention dose in the included studies was evaluated based on the recommendations of the American College of Sports Medicine for developing and maintaining cardiopulmonary and neuromotor function in PD patients [29]. Two authors (WLC and JX) independently scored each aspect (including frequency, intensity, duration, etc.) of the exercise intervention in each study according to the different criteria defined by the ACSM recommended dose, in order to assess exercise dose compliance (Table 1).

The scoring range for each exercise indicator was from 0 to 2 points. A score of 2 points indicated compliance with the criteria; a score of 1 point indicated uncertainty; and a score of 0 points indicated non-compliance. In cases of disagreement between the two authors, a discussion was held with the third author to reach a consensus. Based on this scoring system, we calculated the proportion of exercise dose compliance in each study according to the ACSM recommended dose. When the proportion was $\geq 70\%$, it was classified as high compliance to ACSM recommendations, and when the proportion was $< 70\%$, it was classified as low or uncertain compliance to ACSM recommendations.

Statistical analysis

Meta-analysis was performed using STATA 16.0 to compare the results of the included studies. The studies were divided into two groups in the meta-analysis based on high and low or uncertain compliance to ACSM recommendations. The heterogeneity between studies of each subgroup was assessed using the Higgins I^2 statistic and interpreted according to the recommendations of the Cochrane Handbook [30]. In the

Table 1 ACSM exercise recommendations for PD patients

Exercise dose	Cardiorespiratory exercise	Resistance exercise	Flexibility exercise
Frequency	3 days per week	2–3 days per week	More effective on ≥ 2–3 days per week, daily
Intensity/workload	40–60% VO^2R or HRR; RPE of 12–13 on a 6–20 scale	Start with 40–50% 1RM, more capable with 60–70% 1RM	Full range of flexion, extension and rotation, or stretching to minor discomfort
Duration	Continuous or cumulative 30 min	≥ 1 group, 8–12 repetitions; adult Parkinson's patients started with 10–15 repetitions	Keep static pulling for 10–30 s; repeat 2–4 times

HRR heart rate reserve, *VO^2R* oxygen uptake reserve, *RPE* rating of perceived exertion, *1RM* one repetition maximum

heterogeneity test, a fixed effect model was used to test the effect size if $I^2 \leq 50\%$, while a random effect model was used if $I^2 > 50\%$, and the effect size was represented by the standardized mean difference (SMD) combined with a 95% confidence interval (95% CI). The possibility of publication bias was evaluated by constructing a funnel plot for each study's effect size relative to standard error. The Begg's rank correlation method and Egger's linear regression method were used to test the asymmetry of the funnel plot, and $P < 0.05$ was considered statistically significant. Sensitivity analysis was also performed by iteratively excluding studies to test the robustness of the results.

Quality appraisal

The quality of the included studies was assessed by two pairs of authors (LCW and JX, DL and LJY), according to the Cochrane Collaboration's recommended quality assessment criteria for randomized controlled trials [31]. All studies included in this review were randomized controlled trials. According to the Cochrane Handbook, when including randomized controlled trials, the recommended tool is the revised version of the Cochrane tool, called the risk of bias tool (Rob 2) [32]. The Rob 2 tool provides a framework for assessing the risk of bias in individual outcomes in any type of randomized trial. The evaluation indicators include random sequence generation, allocation concealment, blinding of participants and researchers, blinding of outcome assessments, incomplete outcomes, selective reporting, and other biases. Reviewers scored different studies based on the Cochrane Handbook, with the risk of bias in each domain classified into three levels: "low risk," "some concerns," and "high risk." If the risk of bias evaluation results in all domains is low risk, then the overall risk of bias is low; if some domains are evaluated as "some concerns," and there is no domain with high risk, then the overall risk of bias is "some concerns"; and if the risk of bias assessment result for any one domain is "high risk," then the overall risk of bias is "high risk" [33].

Results

Study selection

A total of 9300 literature were retrieved from four databases, PubMed ($n = 1386$), Embase ($n = 1728$), Web of Science ($n = 2532$), and Cochrane ($n = 3654$). After removal of duplicates, 6342 records remained. Following a thorough review of the titles and abstracts, 158 articles were considered as potential candidates for inclusion. Finally, after a comprehensive reading of the full texts, 26 relevant articles were incorporated [34–59] (Fig. 1).

Study characteristics

The 26 included articles covered 32 comparative research studies, with six articles reporting on two exercise intervention groups. A total of 1177 participants were included in the 32 studies, with 607 participants in the intervention group and 570 participants in the control group. In terms of gender ratio, except for three studies that did not report the proportion of gender, the intervention group included 341 males and 239 females, while the control group included 345 males and 206 females. The age of the participants ranged from 46 to 83 years old, with the intervention group ranging from 49 to 79 years old and the control group ranging from 46 to 83 years old. Two studies did not report the duration of the disease among the participants. After excluding these two studies, the disease duration of the intervention group ranged from 0.59 to 24.6 years, and that of the control group ranged from 0.58 to 31 years. Eleven studies did not report Hoehn and Yahr stage scores, with the Hoehn and Yahr stage scores of the intervention group ranging from 0.5 to 4 and those of the control group from 1 to 4. With regard to geographic distribution, eight studies were from Brazil, five from the US, four from China, three from Turkey, and two each from Sweden, Belgium, India, and South Korea, while Thailand, the UK, Iran, and Italy each had one study. In terms of participant recruitment, the participants were primarily recruited through hospital clinics, communities, and advertising media (Table 2).

Looking at the outcome measures included in the studies, UPDRS III was included in 16 studies, involving 731 participants, including 375 in the intervention group and 356 in the control group. BBS was included in 12 studies, involving 357 participants, including 180 in the intervention group and 177 in the control group. TUG was included in 18 studies, involving 631 participants, including 323 in the intervention group and 308 in the control group. PDQ-39 measures were included in 14 studies, involving 507 participants, including 258 in the intervention group and 249 in the control group.

The duration of the interventions in the 32 studies ranged from 6 weeks to 16 months, with exercise frequency ranging from 2 times per week to 7 times per week. All studies included supervised exercise or home-based exercise interventions. Among the 32 studies, six interventions involved resistance training, two involved aerobic exercise, and three each involved balance training, treadmill training, and Tai Chi exercise. One study involved aquatic-based exercise, while other interventions included exercise based on virtual reality, Pilates, Nordic walking, and more. Based on the ACSM recommendations, 25 studies involved aerobic exercise dose, 12 studies involved resistance exercise dose, and 16 studies involved flexibility exercise dose (Table 3).

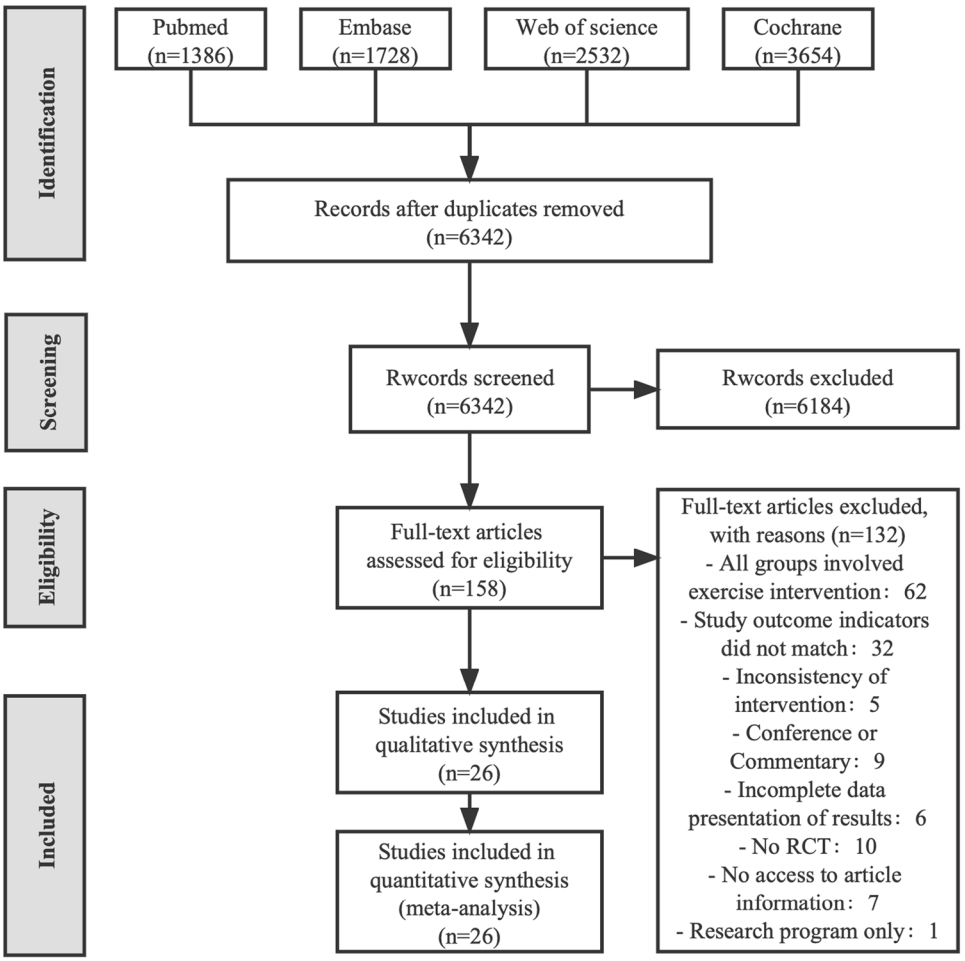

Fig. 1 PRISMA study flow diagram

Risk of bias

All studies found that the risk of bias in random sequence generation was low. Among the included 26 studies, 12 were considered to have low risk of allocation concealment bias, 14 did not report the allocation method, and were, therefore, considered to have an uncertain risk. The blinding of both researchers and participants was associated with a higher risk of bias because exercise interventions were difficult to implement in a double-blind manner. Therefore, the overall risk of bias in this category was relatively high. Regarding outcome assessment blinding, 15 studies used random testing or blinded assessors, resulting in low risk; 10 studies did not mention the outcome assessment method and had some concerns; and one study did not guarantee outcome blinding, thus considered to have high risk. Among the 15 studies with incomplete outcome reporting, the number of subjects after the intervention was consistent or mostly consistent with baseline, so they were considered to have low risk. In five studies, the number of dropouts was small (5–10 individuals), resulting in some concerns, while four studies had a significant difference in the number of subjects before and after the intervention (≥ 10 individuals), resulting in high risk. The risk of selective reporting bias was low in 20 studies, and there were some concerns in six studies due to failure to report pre-registered plans or provide detailed explanations for subject dropouts. Five studies were at high risk of other biases (Fig. 2).

Compliance with the ACSM recommendations

Compliance with the ACSM recommendations was ≥ 70% in 21 of the 32 studies, while in 11 studies, compliance with ACSM was less than 70%. The reasons for low compliance were the mismatch between exercise intervention dose and the ACSM recommendations, as well as insufficient information on exercise prescription for appropriate evaluation.

From the perspective of outcome measures, compliance proportions were analyzed as follows: For studies with UPDRS-III as the outcome measure, 12 studies had high ACSM compliance, while four studies had low or uncertain ACSM compliance. For studies with BBS as the outcome measure, seven studies had high ACSM compliance, while five studies had low or uncertain ACSM compliance. For

Table 2 Basic characteristics of the study

References	Country	Initial sample size (n)		Gender ratio				Age (years)		Duration of disease		Hoehn and Yahr	
		Ig	Cg	Ig(M)	Ig(F)	Ig(M)	Cg(F)	Ig	Cg	Ig	Cg	Ig	Cg
Liao [40]	China	12	12	6	6	5	7	67.3 ± 7.1	64.6 ± 8.6	7.9 ± 2.7	6.4 ± 3.0	2.0 ± 0.7	1.9 ± 0.8
Liao [40]	China	12	12	6	6	5	7	65.1 ± 6.7	64.6 ± 8.6	6.9 ± 2.8	6.4 ± 3.0	2.0 ± 0.8	1.9 ± 0.8
Conradsson [38]	Sweden	47	44	28	19	22	22	72.9 ± 6.0	73.6 ± 5.3	6.0 ± 5.1	5.6 ± 5.0	NR	NR
Khobkhun [58]	Thailand	10	8	6	4	4	4	68.60 ± 6.67	68.88 ± 6.73	5.08	4.8	2.6	2.58
Amano [36]	US	15	9	7	8	7	2	66 ± 11	66 ± 7	8 ± 5	5 ± 3	2.4 ± 0.6)	2.4 ± 0.4
Ferreira [45]	Brazilian	18	17	NR	NR	NR	NR	64.1 ± 7.0	67.6 ± 8.9	6.4 ± 2.7	4.5 ± 4.0	1.5 ± 0.5	1.5 ± 0.5
Fisher [34]	US	10	10	6	4	8	2	64.0 ± 14.5	63.1 ± 11.5	14.7 ± 9.9	17.7 ± 13.3	1.9 ± 0.5	1.9 ± 0.3
de Lima [48]	Brazilian	18	15	NR	NR	NR	NR	66.2 ± 5.5	67.2 ± 5.2	NR	NR	NR	NR
Ni [41]	US	14	10	9	5	4	6	71.6 ± 6.6	74.9 ± 8.3	6.6 ± 4.4	5.9 ± 6.2	2.2 ± 0.6	2.1 ± 0.7
Collett [42]	UK	54	51	31	23	30	21	66 ± 9	67 ± 7	4.8 ± 4.1	5.3 ± 4.1	NR	NR
Leavy [53]	Sweden	61	56	28	33	34	22	70 ± 8.5	70 ± 6.5	6.6 ± 5.1	8 ± 5.8	NR	NR
Peloggia Cursino [46]	Brazilian	7	7	NR	NR	NR	NR	63.29 ± 11.06	72 ± 10.52	2.86 ± 1.57	6.29 ± 3.35	2 ± 0.82	2.29 ± 0.95
Youm [54]	South Korea	10	7	6	4	4	3	68.0 ± 6.8	72.1 ± 6.0	6.4 ± 3.6	8.0 ± 4.0	NR	NR
Schenkman [35]	US	31	31	26	15	26	15	63.4 ± 11.2	66.3 ± 10.1	3.9 ± 4.2	4.5 ± 3.8	2.2 ± 0.5	2.3 ± 0.4
Schenkman [35]	US	33	31	24	15	26	15	64.5 ± 10.0	66.3 ± 10.1	4.9 ± 3.7	4.5 ± 3.8	2.3 ± 0.4	2.3 ± 0.4
Santos [49]	Brazilian	13	14	11	2	11	3	61.7 ± 7.3	64.5 ± 9.8	7.0 ± 2.8	6.5 ± 2.0	1.4 ± 0.6	1.3 ± 0.3
Demonceau [43]	Belgium	16	15	12	4	10	5	65 ± 8	63.3 ± 6	5 ± 3	5 ± 2	1.75 ± 0.75	1.75 ± 0.25
Demonceau [43]	Belgium	15	15	8	7	10	5	67 ± 10	63.3 ± 6	7 ± 3	5 ± 2	1.75 ± 0.75	1.75 ± 0.25
Arfa-Fatollahkhani [47]	Iran	11	9	8	3	7	2	60.63 ± 9.36	61.55 ± 8.57	8.89 ± 5.14	8.50 ± 6.34	2.13 ± 0.32	2.0 ± 0.35
Gao [37]	China	37	39	23	14	27	12	69.54 ± 7.32	68.28 ± 8.53	9.15 ± 8.58	8.37 ± 8.24	NR	NR
Chen [55]	Brazilian	23	25	17	6	18	7	63.4 ± 6.9	63.6 ± 7	7.6 ± 6	9.6 ± 4.8	NR	NR
Chen [55]	Brazilian	26	25	18	8	18	7	63.2 ± 6.4	63.6 ± 7	8.4 ± 5.9	9.6 ± 4.8	NR	NR
Goz [57]	Turkey	6	6	0	6	3	3	64 ± 15	61 ± 15	4.21 ± 0.96	5.5 ± 4.5	1.75 ± 0.25	1.5 ± 0.5
Goz [57]	Turkey	8	6	2	6	3	3	65 ± 13	61 ± 15	2.57 ± 2.44	5.5 ± 4.5	1 ± 0.5	1.5 ± 0.5
Silva [50]	Brazilian	14	11	8	6	6	5	63.12 ± 13.61	64.23 ± 13.45	NR	NR	3 ± 1	3 ± 1
Moon [52]	South Korea	8	7	5	3	5	2	63.38 ± 5.37	62.14 ± 5.55	0.95 ± 0.36	0.96 ± 0.38	2.63 ± 0.52	2.71 ± 0.49
Cugusi [39]	Italy	10	10	8	2	8	2	68.1 ± 8.7	66.6 ± 7.3	7 ± 2	7 ± 4	2.4 ± 0.8	2.3 ± 0.5
Ribas [44]	Brazilian	10	10	4	6	4	6	61.70 ± 6.83	60.20 ± 11.29	6.5 ± 4	7 ± 2.79	1.5 ± 0.5	1.75 ± 0.25
Khuzema [51]	India	9	9	6	3	7	2	72 ± 5.22	70.89 ± 6.01	5.67 ± 2.33	5.23 ± 3.12	NR	NR
Khuzema [51]	India	9	9	6	3	7	2	68.11 ± 4.23	70.89 ± 6.01	6.2 ± 1.67	5.23 ± 3.12	NR	NR
Coban [56]	Turkey	20	20	9	11	10	10	58.85 ± 8.09	60.75 ± 7.62	5.32 ± 6.23	5.35 ± 3.33	2.05	2.3
Li [59]	China	20	20	13	7	16	4	67.57 ± 3.95	70 ± 5.59	6.83 ± 4.09	7.76 ± 4.55	NR	NR

IG intervention group, *CG* control group, *M* male, *F* female, *NR* no report

Table 3 Study intervention and outcome reporting characteristics

References	Interventions	Length of intervention	UPDRS-III	BBS	TUG	PDQ-39
Liao [40]	Virtual reality-based Wii Fit exercise	6 weeks			√	√
Liao [40]	Traditional exercise	6 weeks			√	√
Conradsson [38]	HiBalance program	10 weeks	√			
Khobkhun [58]	Home-based exercise program	10 weeks	√		√	
Amano [36]	Tai Chi exercise	16 weeks	√			
Ferreira [45]	Resistance training	24 weeks	√			√
Fisher [34]	Body weight-supported treadmill training	8 weeks	√			
de Lima [48]	Resistance training	20 weeks	√		√	√
Ni [41]	Power-based resistance training	3 months				√
Collett [42]	Aerobic and resistance training	12 months	√			
Leavy [53]	HiBalance program	10 weeks			√	
Peloggia Cursino [46]	Body weight-supported treadmill training	6 weeks				√
Youm [54]	Trunk resistance and stretching exercise	12 weeks	√		√	
Schenkman [35]	Aerobic exercise	16 months	√			√
Schenkman [35]	Flexibility/balance/function exercise	16 months	√			√
Santos [49]	Nintendo Wii	2 months	√		√	√
Demonceau [43]	Aerobic training	12 weeks				√
Demonceau [43]	Strength training	12 weeks				√
Arfa-Fatollahkhani [47]	Treadmill training	10 weeks			√	
Gao [37]	24-form Yang style Tai Chi exercise	12 weeks	√	√	√	
Chen [55]	Resistance training (using weightlifting machines at a gym)	3 months	√	√	√	√
Chen [55]	Resistance training (using free weights and elastic bands)	3 months	√	√	√	√
Goz [57]	Pilates exercise	6 weeks		√		
Goz [57]	Elastic taping exercise	6 weeks		√		
Silva [50]	Dual-task aquatic exercise	10 weeks		√	√	
Moon [52]	Balance training	8 weeks		√	√	
Cugusi [39]	Nordic walking	12 weeks	√	√	√	
Ribas [44]	Exergaming	12 weeks		√		
Khuzema [51]	Tai Chi exercise	8 weeks		√	√	
Khuzema [51]	Yoga exercise	8 weeks		√	√	
Coban [56]	Pilates exercise	8 weeks		√	√	
Li [59]	Wuqinxi Qigong exercise	12 weeks	√		√	√

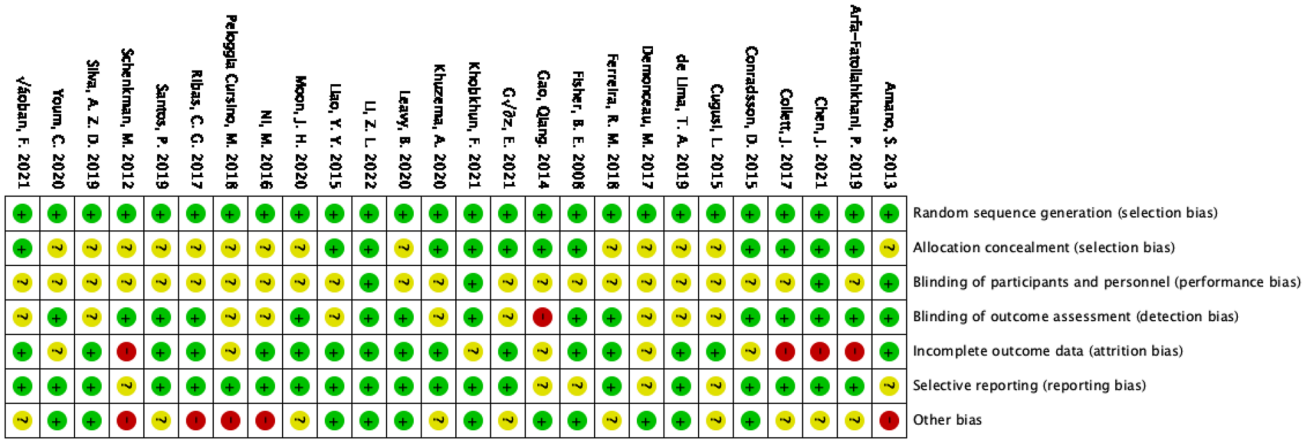

Fig. 2 Risk of bias summary: The review author's judgment of the risk of bias of each included study

studies with TUG as the outcome measure, 12 studies had high ACSM compliance, while six studies had low or uncertain ACSM compliance. For studies with PDQ-39 as the outcome measure, 11 studies had high ACSM compliance, while three studies had low or uncertain ACSM compliance.

Meta-analysis

Motor function

In our analysis of 16 studies involving 731 participants with UPDRS-III as the outcome measure, we first performed a heterogeneity test and found an I^2 greater than 50% ($I^2 = 87.4\%$, $P = 0.000$); thus, we used a random effects model for statistical analysis. Our analysis found a total combined SMD of − 0.6 (95% CI − 1.05, − 0.15), indicating the beneficial effect of exercise intervention on UPDRS-III in PD patients. In subgroup analysis, we grouped studies according to the proportion of compliance with ACSM recommendations. The combined SMD for the subgroup with high ACSM compliance was -0.74 (95% CI − 1.26, − 0.22). For the subgroup with low or uncertain ACSM compliance, the combined SMD was − 0.17 (95% CI − 1.16, 0.82). Subgroup difference analysis showed a significant difference between exercise interventions with high ACSM compliance and those with low or uncertain ACSM compliance (Fig. 3). Therefore, we conclude that exercise interventions with high ACSM compliance have better therapeutic effects on UPDRS-III in PD patients than those with low or uncertain ACSM compliance.

In the subgroup with high ACSM compliance, individual study heterogeneity in the outcome measure UPDRS-III was 88.5%. In the subgroup with low or uncertain ACSM compliance, the heterogeneity was 85.3%. Visual inspection of the funnel plot (Fig. 7A) showed approximate symmetry on both sides, indicating no obvious publication bias. Furthermore, Begger's test ($P = 0.719$) and Egger's test ($P = 0.484$) confirmed the absence of significant publication bias. In sensitivity analysis (Fig. 8A), we found that no single study had a significant impact on the overall results, demonstrating the robustness of our findings.

Balance

In the 12 studies with 357 participants that used BBS as the outcome measure, we first performed a heterogeneity test and found an I^2 less than 50% ($I^2 = 30.4\%$, $P = 0.149$); thus, we used a fixed effects model for statistical analysis. Our analysis found a total combined SMD of 0.51 (95% CI 0.30, 0.73), indicating the beneficial effect of exercise intervention on BBS in PD patients. In subgroup analysis, we grouped studies according to the proportion of compliance with ACSM recommendations. The combined SMD for the subgroup with high ACSM compliance was 0.51 (95% CI

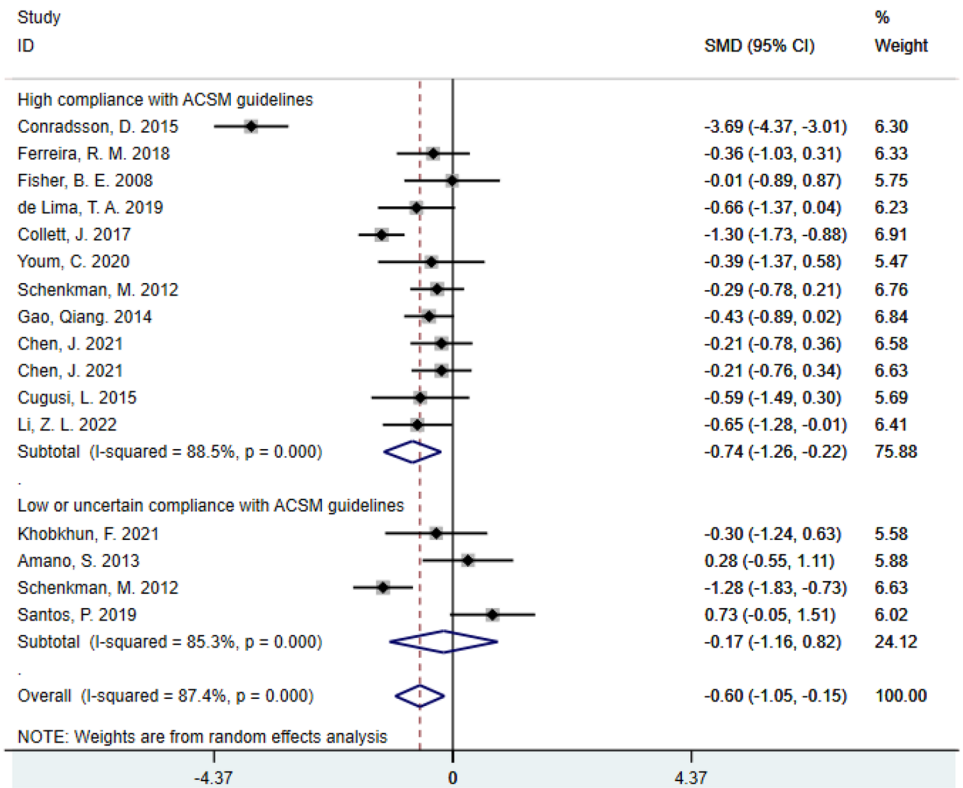

Fig. 3 Forest plot of meta-analysis on the effect of exercise dose on UPDRS-III in PD patients

0.26, 0.76), while for the subgroup with low or uncertain ACSM compliance, the combined SMD was 0.52 (95% CI 0.12, 0.92). Subgroup difference analysis showed no significant difference between exercise interventions with high ACSM compliance and those with low or uncertain ACSM compliance (Fig. 4). Therefore, we conclude that exercise interventions with high ACSM compliance are not superior to those with low or uncertain ACSM compliance in terms of the therapeutic effect on BBS in PD patients.

In the subgroup with high ACSM compliance, the individual study heterogeneity for BBS was 56.3%. In the subgroup with low or uncertain ACSM compliance, the individual study heterogeneity was 0.0%. The funnel plot analysis (Fig. 7B) showed approximate symmetry on both sides, indicating no obvious publication bias. Furthermore, Begger's test ($P = 0.217$) and Egger's test ($P = 0.102$) confirmed the absence of significant publication bias. In sensitivity analysis (Fig. 8B), we found that no single study had a significant impact on the overall results, demonstrating the robustness of our findings.

Mobility

When analyzing the results for the Timed Up and Go test, we included a total of 631 participants from 18 studies. We first performed a heterogeneity test and found I^2 to be less than 50% ($I^2 = 29.2\%$, $P = 0.120$); thus, we used a fixed effects model for statistical analysis. Our analysis found a total combined SMD of − 0.44 (95% CI − 0.60, − 0.28), indicating the beneficial effect of exercise intervention on TUG in PD patients. In subgroup analysis, we grouped studies according to the proportion of compliance with ACSM recommendations. The combined SMD for the subgroup with high ACSM compliance was − 0.62 (95% CI − 0.82, − 0.41), while for the subgroup with low or uncertain ACSM compliance, the combined SMD was − 0.17 (95% CI − 0.43, − 0.08). Subgroup difference analysis showed a significant difference between exercise interventions with high ACSM compliance and those with low or uncertain ACSM compliance (Fig. 5). Therefore, we conclude that exercise interventions with high ACSM compliance have better therapeutic effects on TUG in PD patients than those with low or uncertain ACSM compliance.

In the subgroup with high compliance, the individual studies measuring TUG showed a heterogeneity of 17.7%. In the low or uncertain compliance subgroup, heterogeneity was 0.0%. Funnel plot inspection (Fig. 7C) showed approximate symmetry on both sides, indicating no obvious publication bias. Furthermore, Begger's test ($P = 0.677$) and Egger's test ($P = 0.649$) confirmed the absence of significant publication bias. In sensitivity analysis (Fig. 8C), we found that no single study had a significant impact on the overall results, demonstrating the robustness of our findings.

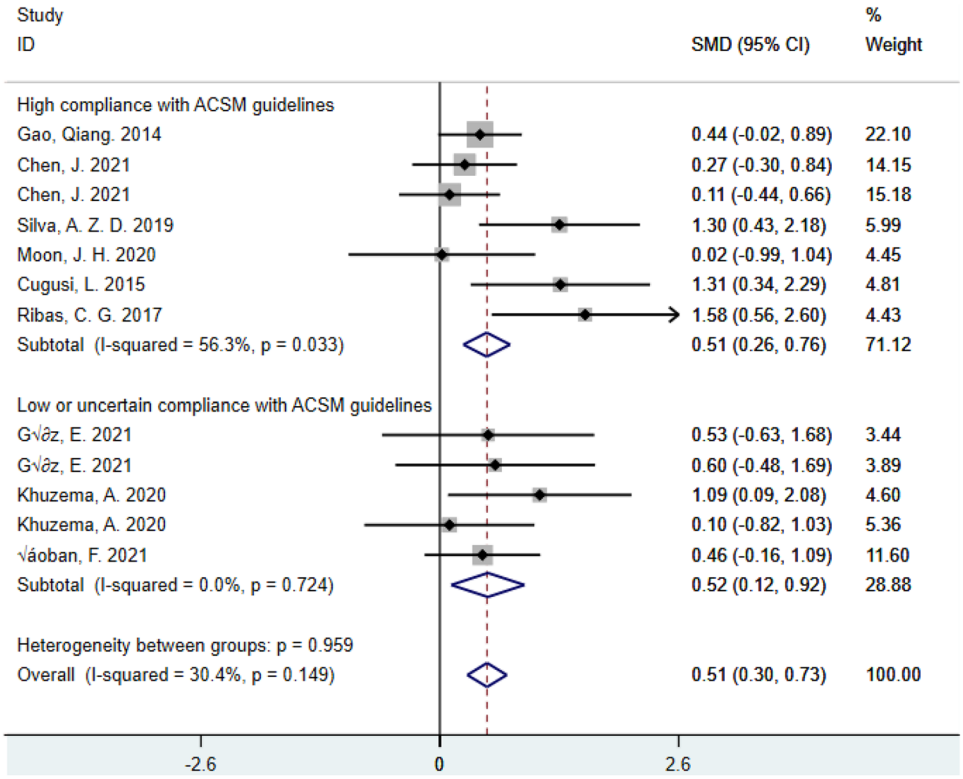

Fig. 4 Forest plot of meta-analysis on the effect of exercise dose on BBS in PD patients

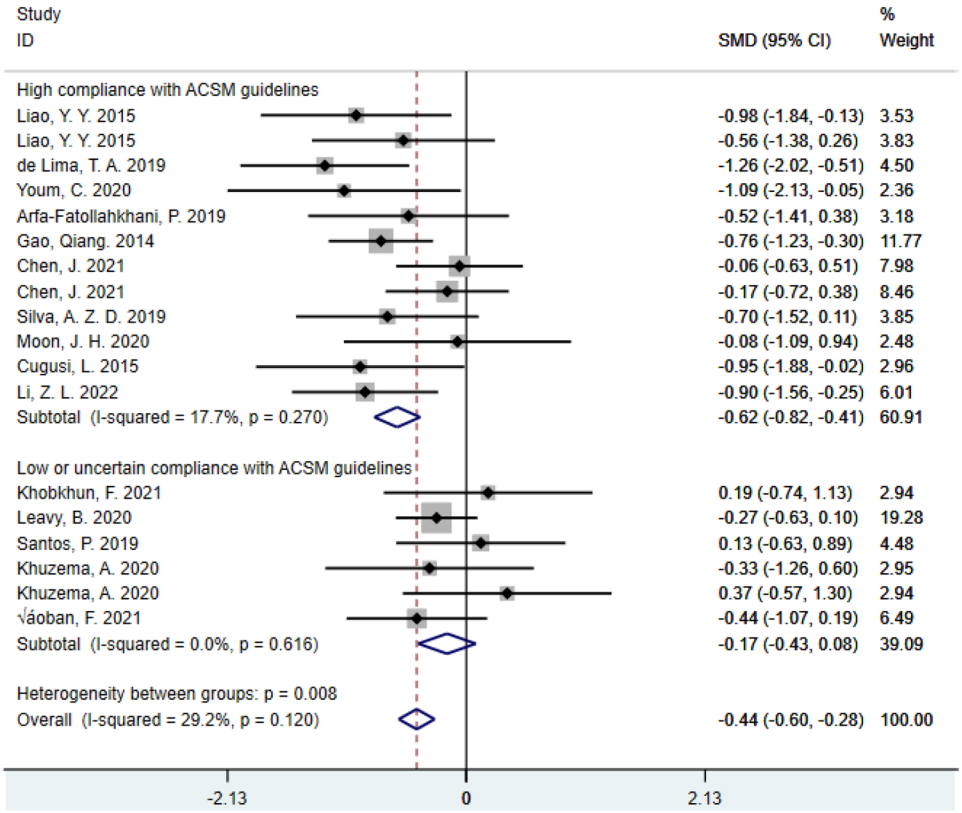

Fig. 5 Forest plot of meta-analysis on the effect of exercise dose on TUG in PD patients

Quality of life

When the outcome was PDQ-39, we analyzed 507 participants from 14 studies. First, we found significant heterogeneity ($I^2 = 80.0\%$, $P = 0.000$) through heterogeneity testing, and thus, a random effects model was adopted for statistical analysis. Our analysis found a total combined SMD of − 0.54 (95% CI − 0.96, − 0.12), indicating the beneficial effect of exercise intervention on the PDQ-39 of PD patients. In subgroup analysis, we grouped studies according to the proportion of compliance with ACSM recommendations. The combined SMD for the subgroup with high ACSM compliance was -0.58 (95% CI − 0.99, − 0.18), while for the subgroup with low or uncertain ACSM compliance, the combined SMD was -0.31 (95% CI − 1.83, 1.21). Subgroup difference analysis showed a significant difference between exercise interventions with high ACSM compliance and those with low or uncertain ACSM compliance (Fig. 6). Therefore, we conclude that exercise interventions with high ACSM compliance have better therapeutic effects on the PDQ-39 of PD patients than those with low or uncertain ACSM compliance.

In the subgroup with high ACSM compliance, the individual study heterogeneity in measuring PDQ-39 was 71.8%. In the subgroup with low or uncertain ACSM compliance, the heterogeneity was 93.2%. Inspection of the funnel plot (Fig. 7D) revealed approximate symmetry on both sides, indicating no obvious publication bias. Furthermore, Begger's test ($P = 0.870$) and Egger's test ($P = 0.913$) confirmed the absence of significant publication bias. In sensitivity analysis (Fig. 8D), we found that no single study had a significant impact on the overall results, demonstrating the robustness of our findings.

Discussion

This system review and meta-analysis synthesize various exercise modes, intensity levels, exercise duration, and other indicators used in the previous research to verify the influence of exercise dose on improving PD patients grouped according to ACSM compliance. To our knowledge, no other reviews currently ascertain the influence of exercise dose on PD patients using ACSM compliance as a standard.

In the previous studies, LO Lima et al. [60] and Lamotte G et al. [61] researched on the effects of progressive resistance and endurance exercise on PD patients, analyzing strength, fitness, and physical condition (maximum oxygen uptake and gait) as outcome measures. The authors concluded that resistance exercise could improve strength performance and physical condition. Still, both review analyses had limitations of limited data, and the objectivity of the results needed to be verified. Therefore, based on many randomized controlled trials, this study used UPDRS-III,

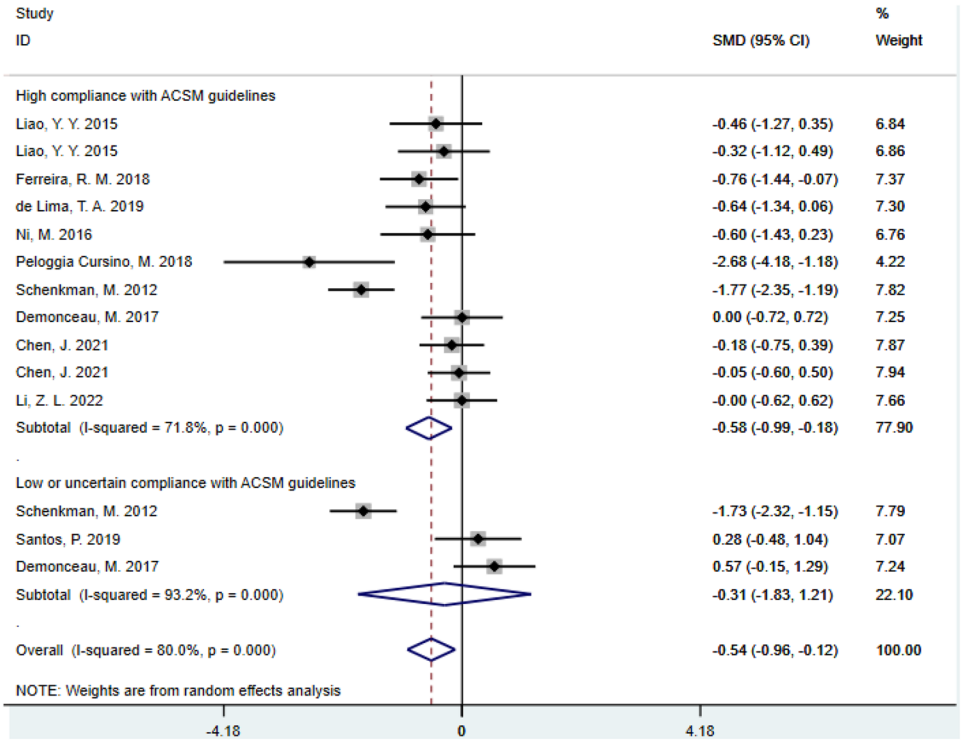

Fig. 6 Forest plot of meta-analysis on the effect of exercise dose on PDQ-39 in PD patients

BBS, TUG, and PDQ-39 as outcome measures to ensure the objectivity of the results as much as possible. Yang Y et al.'s meta-analysis also found that Tai Chi improved motor function and balance [62], consistent with our conclusions. We also found that the SMD of UPDRS-III was slightly higher than that reported in this study's review (SMD: -0.74 vs. -0.57) in the meta-analysis of exercise interventions that highly adhered to ACSM recommendations, which may have benefited our review results, indicating that an appropriate exercise dose would have more favorable effects on participants. After reviewing previous meta-analyses and relevant studies, we found that meta-analyses on PD patients focused more on a specific exercise program (Tai Chi [63], dance [64], yoga [65], treadmill [66], etc.) or a comparison between different types of exercise (aerobic exercise [67], resistance exercise [68], endurance exercise [69], etc.) and a network meta-analyses [26, 70]. Therefore, we can only infer that exercise can improve UPDRS-III, BBS, TUG, and PDQ-39 in PD patients, and no specific exercise program has been proven superior to others.

Currently, clinical physical interventions for the prevention and treatment of PD include deep brain stimulation, transcranial direct current stimulation, whole-body vibration, VR-assisted training, and interventions using wearable devices. These interventions have been applied in PD rehabilitation or are being investigated in clinical trials. Due to variations in intervention dosage and participant characteristics, experimental results have shown some differences, but the majority of published intervention studies have demonstrated positive outcomes [71–73]. Furthermore, through summarizing published experiments and unpublished clinical trials registered in multiple national clinical trial registries, it has been observed that there is diversity in the interventions used for PD treatment, but the extracted outcome measures are highly similar. Non-pharmacological interventions primarily focus on outcome measures related to motor function, gait, and quality of life in PD patients. Accordingly, our study also focuses on outcome measures related to motor function and quality of life in PD patients. Lastly, in addition to outcome measure extraction, we have also noted the combination of exercise interventions with the aforementioned physical treatment methods, such as utilizing VR-assisted technology for exercise [40]. From the currently published experimental results, the combination of these interventions has shown greater effectiveness compared to traditional single-mode exercise interventions or physical treatments alone [40, 49]. Comprehensive rehabilitation approaches such as intensive rehabilitation therapy and multimodal rehabilitation therapy [74, 75] that combine pharmacological and non-pharmacological treatments are also crucial. Existing research has demonstrated positive effects of comprehensive rehabilitation therapy on various aspects of PD patients, such as improving bradykinesia and motor learning abilities. However, it should be noted that different patients may benefit from different treatments depending on their physical condition, age, and comorbidities.

Our research has found that exercise interventions could improve the scores of UPDRS-III (SMD = − 0.6; 95% CI

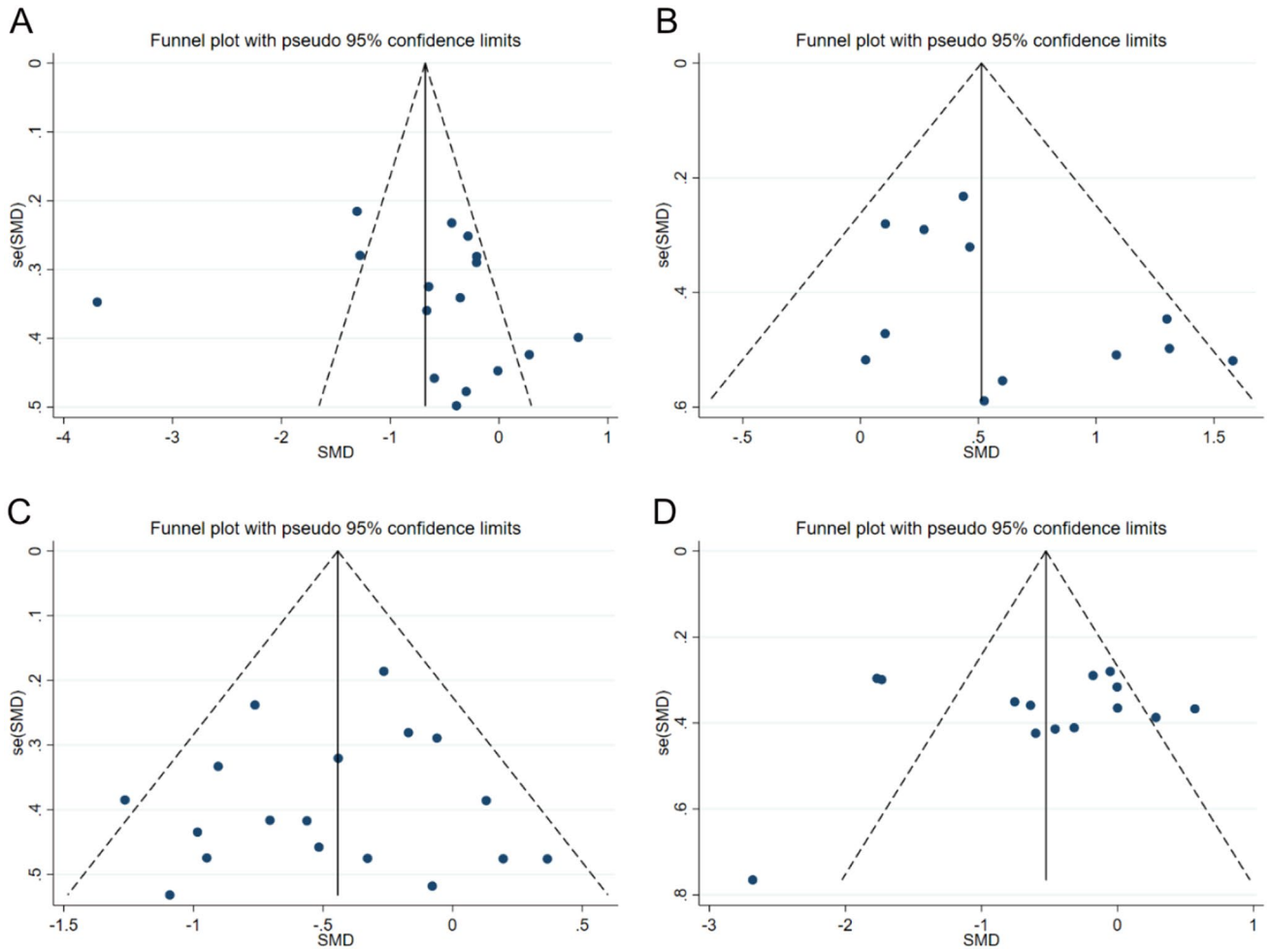

Fig. 7 Funnel plot of meta-analysis on the effect of exercise dose on UPDRS-III, BBS, TUG, and PDQ-39 in PD patients

− 1.05, − 0.15), BBS (SMD = 0.51; 95% CI 0.30, 0.73), TUG (SMD = − 0.44; 95% CI − 0.60, − 0.28), and PDQ-39 (SMD = − 0.54; 95% CI − 0.96, − 0.12) in PD patients, which is consistent with common knowledge and previous research conclusions [15, 76, 77] that exercise is an effective non-pharmacological treatment for PD patients. From the results of subgroup analysis, compared with exercise interventions with low or uncertain ACSM compliance, exercise interventions with high ACSM compliance had a better improvement effect on UPDRS-III (SMD − 0.74 vs. − 0.17), TUG (SMD − 0.62 vs. − 0.17), and PDQ-39 (SMD − 0.58 vs. − 0.31) in PD patients, but the improvement effect on BBS (SMD: 0.51 vs. 0.52) was not obvious. From the difference in effect size (SMD) comparison, exercise with high ACSM compliance had the most significant improvement effect on UPDRS-III (0.57), followed by TUG (0.45), and PDQ-39 (0.27), respectively.

One key point of this study is the interpretation of ACSM compliance. Exercise interventions recommended by ACSM include aerobic exercise, resistance exercise, and flexibility exercise, each with detailed descriptions of the recommended exercise dose. However, descriptions of exercise dose in randomized controlled trials for PD patients are not comprehensive or can only be attributed to one type of exercise intervention. For example, 11 studies only reported the exercise dose of aerobic exercise, four studies only reported the exercise dose of resistance exercise, and only five studies reported exercise dose that met the full classification recommended by ACSM. Additionally, some studies failed to report or inadequately reported the exercise intervention dose, such as only describing the dose as "individualized." This means that even if the exercise intervention dose is highly compliant with ACSM recommendations, it may be incorrectly classified as a low or uncertain compliance group. Similar to pharmacological treatments, detailed descriptions of the exercise prescription in intervention are essential for pinpointing the reasonable range of the exercise dose. Although we need to differentiate treatment for individuals during the specific

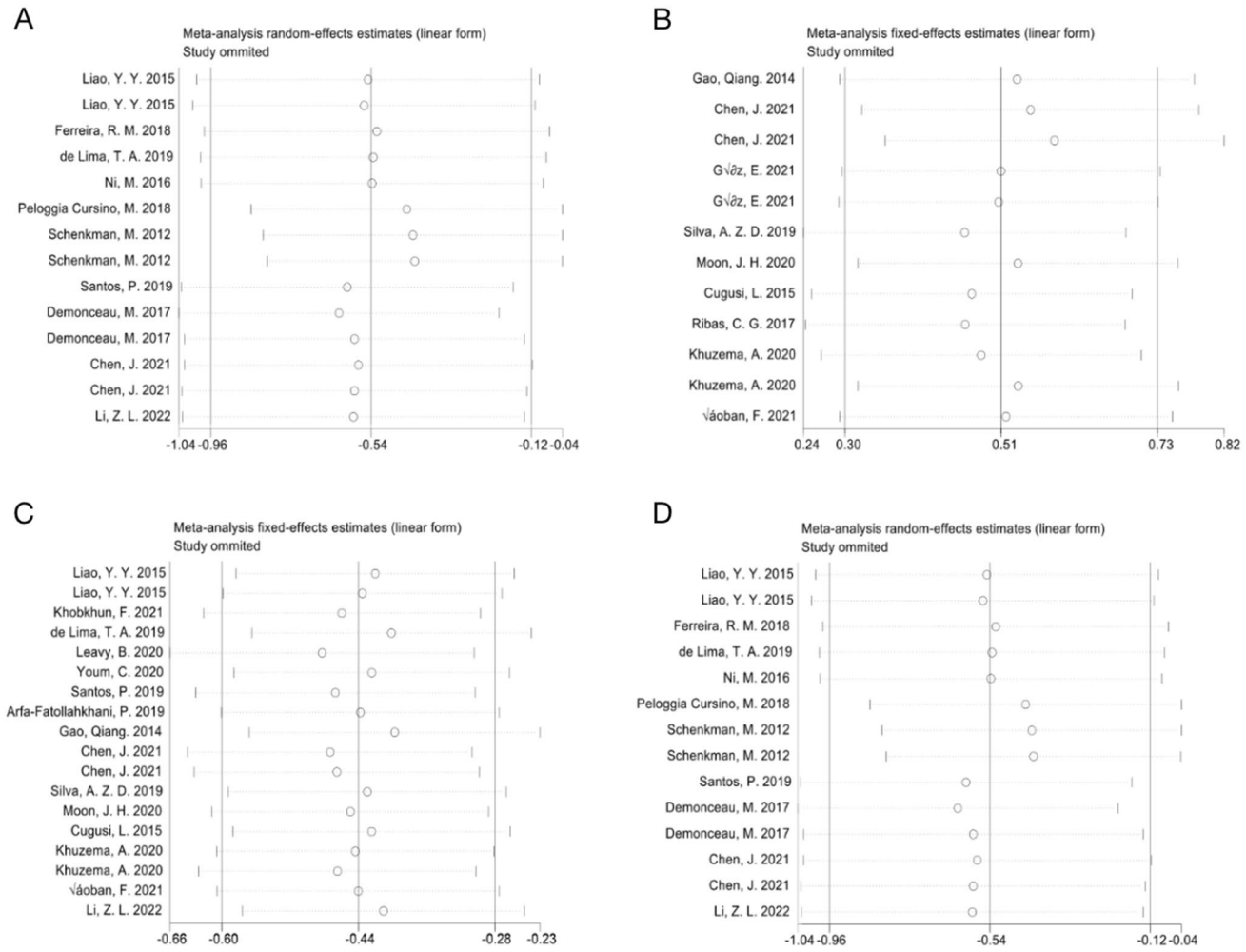

Fig. 8 Sensitivity analysis of meta-analysis on the effect of exercise dose on UPDRS-III, BBS, TUG, and PDQ-39 in PD patients

implementation process, we should also adjust within the range of reasonable exercise prescriptions.

This study also has certain limitations that may lead to bias in the results. The 21 highly ACSM-compliant exercise interventions included various types of exercise, such as virtual reality training, balance training, resistance training, flexibility training, water-based exercise, mind–body exercise, etc., which may have relatively high heterogeneity among studies. Secondly, the interventions provided varied in frequency, intensity, time, and so on, so it is difficult to compare and recommend general standards for the best exercise intervention. Previous meta-analysis and randomized controlled trials lacked comparative studies of exercise intensity and frequency, which made it difficult to determine and design the best exercise program for PD patients in terms of type, dose, and duration. Furthermore, there is a risk of potential bias in every study. Any unclear or high risk of bias factors in each study will increase the final estimate of the intervention effect. The overall bias of the results in this review may be more related to blinding of the interveners and participants, followed by blinding of allocation and output of results. Lastly, although the extraction of data from the figures and tables was minimized to reduce errors, it is inevitable (Table 4).

Conclusion

This review supports the recommendation that exercise is an effective measure for improving clinical symptoms in PD patients, and our results confirm this conclusion once again. In the process of analyzing the best exercise dose for PD patients, we found that compared with exercise interventions with low or uncertain ACSM compliance, exercise interventions with high ACSM compliance had a more significant improvement effect on motor function, mobility, and QOL, but not on balance. Additionally, some studies did not

Table 4 Assessment of ACSM compliance

Author, year	Cardiorespiratory exercise						Resistance exercise									Flexibility exercise				ACSM compliance	
	Frequency (days/week)		Intensity/ workload		Duration (min)		Frequency (days/week)		Intensity/ workload		Repetition (times)		Sets (groups)		Frequency (days/week)		Intensity/ workload		Duration (min)		Points	Percent
Liao, Y. Y. 2015	2	☹	NR	😐	60	☺	2	☺	NR	😐	NR	😐	NR	😐	2	☺	Yoga practice intensity	☺	10	☺	14/20	70%
Liao, Y. Y. 2015	2	☹	NR	😐	60	☺	2	☺	NR	😐	10-15	☺	3	☺	2	☺	Gentle joint extension and flexion and trunk rotation	☺	10	☺	16/20	80%
Conradsson, D. 2015	3	☺	NR	😐	60	☺															5/6	83%
Khobkhun, F. 2021	7	☹	NR	😐	55	☺									7	☺	Segmented rotation exercises	☺	NR	😐	8/12	67%
Amano, S. 2013	2	☹	NR	😐	60	☺															3/6	50%
Ferreira, R. M. 2018							2	☺	ACSM	☺	8-12	☺	NR	😐							7/8	88%
Fisher, B. E. 2008	3	☺	ACSM	☺	45	☺															6/6	100%
de Lima, T. A. 2019							2	☺	ACSM	☺	8-12	☺	NR	😐							7/8	88%
Ni, M. 2016							2	☺	30-90% 1RM	😐	10-12	☺	NR	😐							6/8	75%
Collett, J. 2017	2	☹	55-85% HRmax	😐	30	☺	2	☺	NR	😐	10	☺	2	☺							10/14	71%
Leavy, B. 2020	2	☹	NR	😐	60	☺															3/6	50%
Peloggia Cursino, M. 2018	3	☺	NR	😐	30	☺															5/6	83%
Youm, C. 2020	3	☺	RPE: 2-6	☹	60-90	☺	3	☺	NR	😐	10-30	☺	1-3	☺	3	☺	Full body dynamic stretching	☺	0.5	☺	17/20	85%
Schenkman, M. 2012	3	☺	65-80% HRmax	☹	40-60	☺															4/6	67%
Schenkman, M. 2012															3	☺	Full-body flexibility training	☺	Ind.tail	😐	5/6	83%
Santos, P. 2019	2	☹	Ind.tail	😐	40	☺															3/6	50%
Demonceau, M. 2017	2-3	😐	40-80% PWL	😐	60-90	☺															4/6	67%
Demonceau, M. 2017							2-3	☺	50-90% 1RM	😐	5-15	😐	1-3	☺							6/8	75%
Arfa-Fatollahkhani, P. 2019	2-3	😐	60% HRR	☺	30	☺															5/6	83%
Gao, Qiang. 2014	3	☺	NR	😐	60	☺									3	☺	Full range of flexion	☺	Ind.tail	😐	10/12	83%
Chen, J. 2021							2	☺	60% 1RM	☺	8-12	☺	3	☺	2	☺	Multi-part stretching	☺	0.25	☺	14/14	100%
Chen, J. 2021							2	☺	ACSM	☺	8-12	☺	1-3	☺	2	☺	Multi-part stretching	☺	0.25	☺	14/14	100%
G√∂z, E. 2021	2	☹	NR	😐	60	☺									2	☺	Full range of flexion	☺	NR	😐	8/12	67%
G√∂z, E. 2021	2	☹	NR	😐	60	☺	2	☺	Ind.tail	😐	NR	😐	NR	😐	2	☺	Full range of flexion	☺	NR	😐	13/20	65%
Silva, A. Z. D. 2019	2	☹	Medium intensity	☺	40	☺									2	☺	Full range of extension and rotation	☺	NR	😐	9/12	75%
Moon, J. H. 2020	3	☺	NR	😐	30	☺															5/6	83%
Cugusi, L. 2015	2-3	😐	Medium intensity	☺	60	☺															5/6	83%
Ribas, C. G. 2017	2	☹	NR	😐	30	☺	2	☺	NR	😐	NR	😐	NR	😐	2	☺	Diagonal exercises for the torso, neck and extremities	☺	10	☺	14/20	70%
Khuzema, A. 2020	5	☹	RPE: 11-15	😐	30-40	☺									5	☺	Full range of flexion	☺	NR	😐	8/12	67%
Khuzema, A. 2020	5	☹	RPE: 11-15	😐	30-40	☺									5	☺	Full range of flexion	☺	NR	😐	8/12	67%
√áoban, F. 2021	2	☹	Ind.tail	😐	45	☺									2	☺	Full range of flexion	☺	Ind.tail	😐	8/12	67%
Li, Z. L. 2022	2	☹	60-70% HRmax	😐	90	☺									2	☺	Mild discomfort	☺	0.5	☺	9/12	75%

Happy/green face: Fulfills recommendation (2 points). Neutral/yellow face: Uncertain fulfillment (1 point). Unhappy/red face: Does not fulfill recommendation (0 points). ACSM: American College of Sports Medicine Recommendations

HRR heart rate reserve, *VO^2R* oxygen uptake reserve, *RPE* rating of perceived exertion, *HRmax* maximum heart rate, *PWL* peak work load, *1RM* one repetition maximum, *Ind. tail.* individually tailored, *NR* not reported

provide detailed exercise intervention plans, so this needs to be further validated in the future research.

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Author contributions WLC conceived and designed the study, and the screening of titles and abstracts was completed by WLC and DL, with disputes resolved by JX. Data inclusion was completed by WLC and LJY. WLC and JX independently scored the compliance of each exercise intervention with ACSM recommended dose. All authors participated in the quality assessment of the included literature. The initial draft of the manuscript was completed by WLC and DL, and all authors provided comments on the first few versions of the manuscript and approved the final version.

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Data Availability The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Declarations

Conflict of interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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