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Effects of aerobic exercise on the symptoms of people with Parkinson's Disease at different stages: A Systematic Review

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Effects of aerobic exercise on the symptoms of people with Parkinson's Disease at different stages: A Systematic Review

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Resumo

Introdução: O exercício tem sido identificado como benéfico na melhoria da capacidade funcional com ênfase na atividade de marcha, controle postural e produção vs/manutenção de força, tendo impacto também na qualidade de vida de pacientes com doença de Parkinson (DP). Dos diferentes tipos de programas de exercícios, o exercício aeróbio é o mais estudado e já demonstrou efeitos positivos a nível motor, qualidade de vida, cognição e emoção. Esta revisão sistemática teve como objetivo identificar os efeitos do exercício aeróbico nos sintomas de pessoas com doença de Parkinson (DP) em diferentes estadios.

Métodos: PubMed (Medline), Cochrane Central Library, Physiotherapy Evidence Database (PEDro) e Web of Science (Core Colection) foram todos pesquisados. A ferramenta Cochrane Risk-of-Bias para ensaios randomizados, versão 2 (RoB 2), também foi utilizada para avaliar a qualidade metodológica e o risco de viés dos estudos.

Resultados: Um total de 14 estudos envolvendo 729 pacientes com DP foram incluídos. O exercício aeróbio melhorou os sintomas motores e não motores, como a mobilidade funcional, equilíbrio, velocidade da marcha, função motora global, ansiedade, depressão, fadiga, qualidade do sono e cognição em todos os estadios da DP.

Conclusão: O exercício aeróbico é uma abordagem não farmacológica eficaz para melhorar os sintomas motores e não motores em indivíduos com DP, independentemente do estadio da DP em que se encontrem. Além disso, para a dose mínima de exercício aeróbico, recomendamos que o período de exercício seja não menos de 3 vezes por semana, com duração de 60 minutos por sessão e intensidade mínima de 60% da Frequência cardíaca de reserva (FCR).

Palavras-chave: Exercício aeróbio, Sintomas motores, Sintomas não motores, Doença de Parkinson, Revisão Sistemática

Abstract

Introduction: Exercise has been identified as beneficial in improving functional capacity with an emphasis on gait activity, postural control and production vs/maintenance of strength, also impacting the quality of life of Parkinson's disease (PD) patients. Among the different types of exercise programs, aerobic exercise is the most widely studied and has already shown positive effects at motor, quality of life, cognition and emotion levels. This systematic review aimed to examine the effects of aerobic exercise on the symptoms of people with Parkinson's disease (PD) at different stages.

Methods: PubMed (Medline), Cochrane Central Library, Physiotherapy Evidence Database (PEDro) and Web of Science (Core Colection) were all searched. The Cochrane Risk-of-Bias tool for randomized trials, Version 2 (RoB 2), was also used to assess the methodological quality and risk of bias of studies.

Results: A total of 14 studies involving 729 PD patients were included. Aerobic exercise improved motor and non-motor symptoms such as functional mobility, balance, gait velocity, global motor function, anxiety, depression, fatigue, sleep quality and cognition across all PD stages.

Conclusion: Aerobic exercise is an effective non-pharmacological approach for improving motor and non-motor symptoms in individuals with PD, regardless of the PD stage they are in. In addition, for the minimum dose of aerobic exercise, we recommend that the exercise period is no less than 3 times per week, with a duration of 60 min per training session and a minimum intensity of 60% of HRR.

Keywords: Aerobic exercise, Motor symptoms, Non-motor symptoms, Parkinson's Disease, Systematic review

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List of abbreviations

PD – Parkinson's Disease

FITT– Frequency, Intensity, Type and Time

APTA – American Physical Therapy Association

JBI – Joanna Briggs Institute

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO – Prospective Register of Systematic Reviews

NA – Not Applicable

RCTs – Randomized Controlled Trials

PEDro – Physiotherapy Evidence Database

MeSH – Medical Subject Headings

H&Y – Hoehn and Yahr

RoB2 – Version 2 of the Cochrane Risk-of-Bias tool for randomized trials

BWSTT – Body Weight-Supported Treadmill Training

RAGT – Robotic-Assisted Gait Training

HRmax – Maximum Heart Rate

HRR – Heart Rate Reserve

ACSM – American College of Sports Medicine

UPDRS-III – Unified Parkinson's Disease Rating Scale III

MDS-UPDRS – Movement Disorders Society – Unified Parkinson's Disease Rating Scale III

TUG – Time up and Go

BBS – Berg Balance Scale

6MWT – Six Minute Walk Test

NMSS – Non-Motor Symptom Scale

BDI – Beck Depression Inventory

GDS-15 – Geriatric Depression Scale–15 items

Ham-A – Hamilton Anxiety Rating Scale

HADS – Hospital Anxiety and Depression Scale

MoCA – Montreal Cognitive Assessment

ST – Stroop Test

PFS-16 – Parkinson's Disease Fatigue Scale

FSS – Fatigue Severity Scale

FIS – Fatigue Impact Scale

PSQI – Pittsburgh Sleep Quality Index

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1. Introduction

Parkinson's Disease (PD), characterized by progressive loss of dopamine-producing neurons in the pars compacta region of the substantia nigra (1), results from dysfunction in the corticostriatal pathways, essential for the control of movement and cognition (2). Considered as a movement disease (3), in addition to motor changes, patients with PD may also display non-motor symptoms, such as cognitive and sensory deficits, insomnia and depression, with a strong impact on functional activities (4). All these changes cause progressive difficulties in their daily lives, greater dependence and social isolation, significantly affecting their quality of life and that of their families (5).

Along with a pharmacological approach, based on levodopa and dopaminergic agonists (6), it is recommended that patients with PD be integrated into multidisciplinary teams (1). In this team, the physiotherapist is responsible for developing, maintaining and restoring maximum movement and functional capacity throughout life, also emphasizing the importance of physical activity and exercise (7).

Physical exercise is defined as a planned, structured and repetitive physical activity, the ultimate objective of which is to improve and/or maintain one or more components of physical fitness (8). This practice highlights numerous benefits, such as increased neurogenesis, decreased blood pressure levels, improved respiratory function or increased muscle function (9). To obtain the benefits of exercise and simultaneously prevent potential injuries, the FITT (Frequency, Intensity, Type and Time) principle of exercise prescription must be followed (10).

In this context, exercise has been identified as beneficial in improving functional capacity with an emphasis on gait activity, postural control and production vs/maintenance of strength (11), also impacting the quality of life of these patients (12). This benefits seem to be related to changes in the dopaminergic system, since individuals who regularly exercise demonstrate differences regarding 1) the release of dopamine in the caudate, 2) the activation of the ventral striatum during reward anticipation and 3) improvements in apathy and mood, compared to sedentary individuals (13). It also alters synaptogenesis, increases regional cerebral blood flow, as well as endogenous cerebral neurotrophic levels, which attenuate the loss of striatal dopamine (14).

Epidemiological evidence suggests that exercise, of moderate to vigorous intensities, may be associated with a lower risk of PD, when integrated at an early stage of life, or attenuate its progression (14,15), improving motor and non-motor deficits (16).

Among the different types of exercise programs, aerobic exercise is the most widely studied being the most common in the PD population, cycling on a stationary bicycle and walking on a treadmill (17).

Aerobic exercise is a type of exercise that increases heart rate while using large muscles groups repetitively and rhytmically (18) and has already shown some positive effects in PD at motor, quality of life, cognition and emotional levels (16).

However there is insufficient evidence about the effecst of aerobic exercise on gait, balance, falls, and functional mobility, as well as on cognition, depression, sleep, and anxiety (19).

Thus, questions about the benefits of aerobic exercise on motor and non-motor symptoms at different stages of PD, as well as more specific recommendations for the prescription of aerobic exercise, such as intensity, frequency and time still remain unanswered. Therefore, the present study aims to summarize and identify the benefits of aerobic exercise on motor and non-motor symptoms in patients with PD at different stages.

1.1. Review questions

1. What are the reported benefits of aerobic exercise on motor and non-motor symptoms in people with PD?
2. Are there differences depending on the clinical condition (mild, moderate, severe) based on the identified benefits?
3. What dosages (intensity, frequency and time) are prescribed for aerobic exercise and what factors influence the choice?

2. Methods

This systematic review was developed according to the Joanna Briggs Institute (JBI) guidelines (20). All report and preparation **processes** followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (21). The protocol for the construction stages of this review was registered in the International Prospective Register of Systematic Reviews (PROSPERO), under the registration number CRD42024547874 (Appendix 1).

2.1 Eligibility criteria

The inclusion and exclusion criteria were definied according to PICO (22), described on table 1.

Table 1 – Inclusion and exclusion criteria according to PICO strategy

Population	Adults (≥ 18 years) with a confirmed diagnosis of PD
Intervention	Aerobic exercise
Comparison	NA
Outcome	Motor and non-motor symptoms
Type of study	Randomized Controlled Trials (RCTs)

Not Applicable

Studies were included if they met the following criteria: (1) RCTs published on the last 5 years till the 22nd of March , (2) only studies written in English were considered for inclusion and (3) without excluding any geographical area.

2.2 Search strategy

A literature search was conducted from March 10th to March 22nd, 2024, in the following electronic databases: PubMed (Medline), Cochrane Central Library, Physiotherapy Evidence Database (PEDro) and Web of Science (Core Colection). The key terms were selected according to the Medical Subject Headings (MeSH) terms adapted to each database and were the following: "parkinson's disease", "aerobic exercise", "symptomatology". The key terms were combined in the different databases with the Boolean operators "OR" and/or "AND" (Appendix 2).

2.3 Study selection

The searches were conducted by two of the researchers (AP; LP) using the previously mentioned search strategy.

Its results were exported to reference management software (Mendeley) and duplicates were automatically removed.

Titles and respective abstracts of the studies were evaluated by the main researcher (AP), and were subsequently reviewed by a second and third researcher (AS; LP), independently.

The full text of each relevant study was selected for full reading and analysis in order to assess its eligibility. The included studies were subsequently independently verified by the researchers (AS; LP).

In case of disagreement, or when it was not clear whether or not the study should be included, consensus was reached through discussion between all investigators (AP; AS and LP).

2.4 Data extraction

Data from each eligible study were extracted using a standardized form specifically designed for data extraction by the principal investigator (AP) and verified by the remaining investigators (AS; LP).

The data that was obtained consisted of various study characteristics, such as the name of the first author and the year of publication. Additionally, population characteristics, including sample size and Hoehn and Yahr (H&Y) classification were also included. Detailed information regarding the intervention, such as it's type, intensity, duration, and frequency, was recorded. Furthermore, outcome measures and the corresponding results were documented as part of the extracted data.

2.5 Quality assessment and publication bias

The methodological quality and risk of bias for each individual study was assessed using the Version 2 of the Cochrane Risk-of-Bias tool for Randomized Trials (RoB 2) (23).

The tool evaluates five domains of bias, which encompass the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each item was categorized as having a "Low risk," "Some concerns," or "High risk" of bias, according to the RoB 2 guidance. The assessment of bias was conducted by the main researcher (AP) and independently reviewed by the other researchers (AS;LP). Any disagreements or discrepancies were resolved through dialogue.

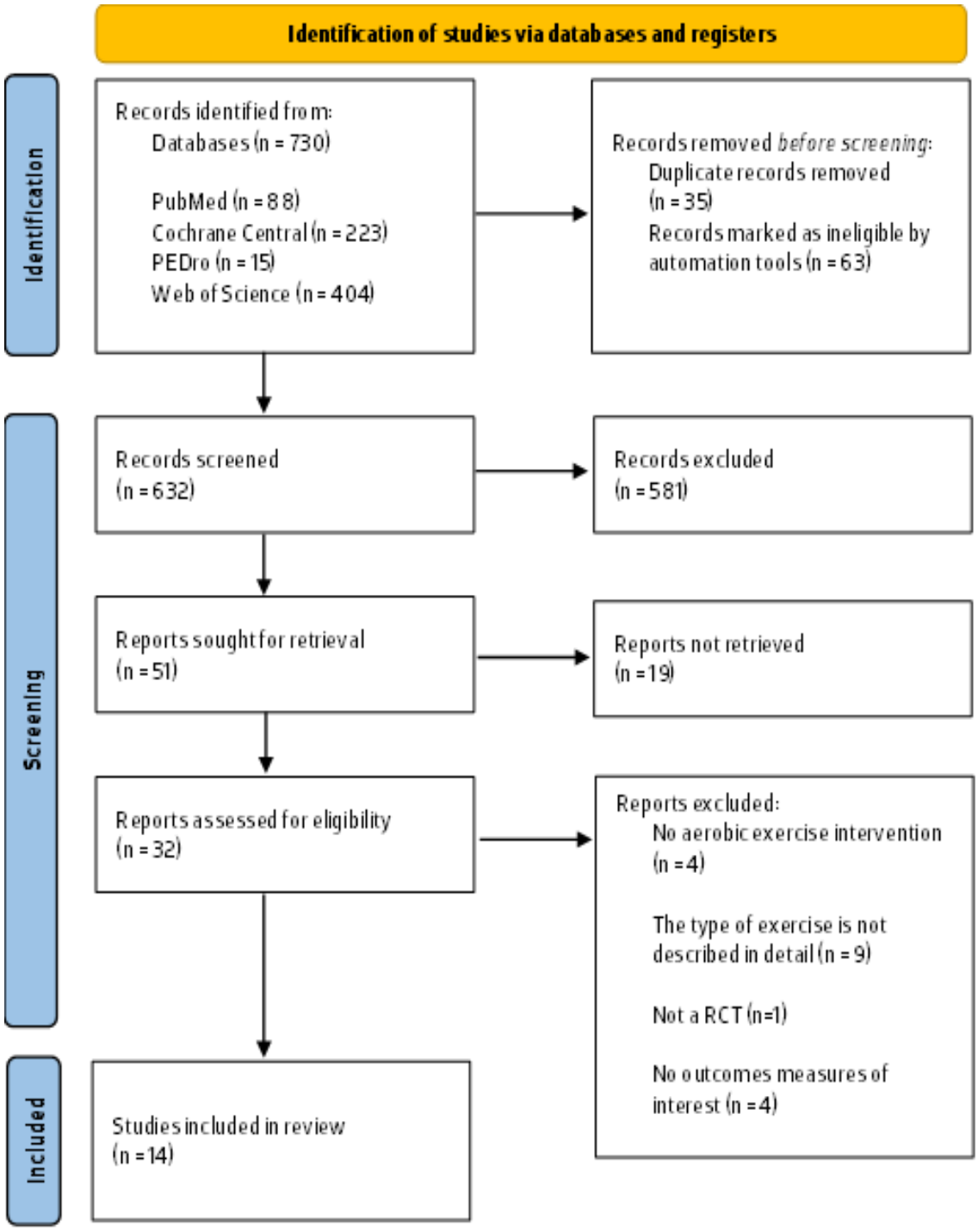
3. Results

3.1 Study selection

The literature search retrieved 730 studies, 632 remained after duplicates were removed. Titles and abstracts were read and 581 were excluded. The remaining 51 studies were fully read. 19 studies were removed because access to the full text was not possible. 32 studies were assessed

for eligibility, of which results 14 studies included in this review. Figure 1 shows the PRISMA flowchart with the study selection procedure.

Figure 1 – PRISMA 2020 flow diagram



3.2 Studies characteristics

A general study information, age groups, genre distribution, H&Y classification and outcomes measures are presented in table 2.

The studies were conducted in Asia – Turkey (n=2) (24,25), Iran (n=1) (26), Taiwan (n=1) (27), China (n=1) (28) –; Europe – Italy (n=3) (29–31), Poland (n=1) (32), Hungary (n=1) (33), Netherlands (n=1)(34) –; North America – USA (n=2) [35,36] –; South America – Brazil (n=1) (37).

The participants of the studies were recruited from clinical health centers at universities (n=4) (24,25,32,34), hospitals (n=4) (27,29,33,37), associations (n=2) (28,36), clinics (n=3) (26,30,35) and at 3 neurorehabilitation facilities (n=1) (31) in several countries.The total number of individuals participating in all articles selected was 720 (391 males and 329 females) . Sample sizes ranged between 16 (36) and 130 participants (34), mean average age was 66 years and ranged across studies from 18 (27)and 80 years (31).

Of the 14 studies, only 3 assessed outcomes measures in OFF medication state(32,34,35).

Each study included aerobic exercise protocols in different modalities. 5 used stationary cycling training [32,33,35,36], 3 used different aerobic exercise programs (25,27,29), 2 used Nordic walking (30,37), 1 used treadmill training (26), 1 used Body Weight-Supported Treadmill Training (BWSTT) (24), 1 used Robotic-Assisted Gait Training (RAGT) (31) and 1 brisk walking (28). The majority of studies did not include a home-based component in the exercise intervention, except 2 studies (27,34).

A total of 8 studies used Maximum Heart Rate (HRmax) to assess intensity (24,25,27,31–33,36,37) and 6 studies used Heart Rate Reserve (HRR) (26,28–30,34,35). Three of the studies (26,33,37) also measured the training intensity with the Borg Rating of Perceived Exertion scale (38), in which 11 represents "light" intensity, 13 "somewhat hard" and 17 "very hard".

Training intensities < 40% of HRR or < 55% of HRmax, 40-59% of HRR or 55-69% of HRmax, and ≥ 60% of HRR or ≥ 70% of HRmax were considered as low, moderate, and high intensities, respectively, following American College of Sports Medicine (ACSM) guidelines for adult individuals (8). Moderate was used in 2 studies (28,36), high-intensity was used in 7 studies (24,26,29–31,33,35) and moderate to high intensity was used in 5 studies (25,27,32,34,37).

The training period length varied widely across the 15 studies: 5 studies had 8 weeks of training with 2/3 sessions per week (25,30,32,35,36). 2 studies used 6 weeks of training (24,37) and 2 used 4 weeks (29,31), 26 weeks (28), 24 weeks (34), 10 weeks (26), 5 weeks (33) and 2 weeks

(36). The average weekly frequency ranged from two (26,30,37) to five days (24,29,31,33), and session duration ranged from 30 (24–27,34) to 75 (30) minutes of training.

The majority of studies had an active control group, except 4 studies who performed only usual care (26,27,32,33).

The intervention characteristics are described in Table 3.

3.3 Effects of aerobic exercise on motor symptoms

This systematic review focused on several motor symptom outcomes, including the Unified Parkinson's Disease Rating Scale III (UPDRS-III) or the revised Movement Disorders Society – Unified Parkinson's Disease Rating Scale III (MDS-UPDRS III), Time up and Go (TUG) test, Berg Balance Scale (BBS) and Six Minute Walk Test (6MWT).

A total of 12 studies analyzed the impact of aerobic exercise on global motor function using the UPDRS-III (24,25,27,29–32,36,37) or the MDS-UPDRS III (28,34,35) and all reported significant improvements after engaging in aerobic exercise.

8 studies (25,26,28–31,34,36) used the TUG test to analyzed the impact of aerobic exercise on functional mobility and all showed significant improvements except two (31,34).

Balance assessed by the BBS was used by 4 studies (24,25,29,33). They all reported significant results, although, in this studies, the experimental group had similarly improvements compared to control groups.

Finally, the impact of aerobic exercise on gait velocity was analyzed in 9 studies (24–26,28–31,33,34) by 6MWT, showing significant results in all of them. However, only 3 showed between-group differences (24,26,28).

3.4 Effects of aerobic exercise on non-motor symptoms

We also focused our systematic review on non motor symptoms outcomes, such as depression, cognition, fatigue and sleep.

Non-motor Symptom scale (NMSS) was used to measure the non-motor symptoms in general in only 1 study (30) reporting significant improvements in the experimental group, but differences between groups were not significant.

Depression was measured using the Beck Depression Inventory (BDI) (n=2) (30,33) the Geriatric depression Scale–15 items (GDS-15) (n=2) (27,37), the Hamilton Anxiety Rating Scale (Ham-A) (n=1) (30) and the Hospital Anxiety and Depression Scale (HADS) (n=1) (34). They all reported

significant improvements, although similarly in both groups, except 1 (27) that reported significant differences between the groups.

Cognition was evaluated using the Montreal Cognitive Assessment (MoCA) (n=2) (34,37) and Stroop Test (ST) (n=1) (32). Both studies that used MoCA (34,37) revelead no between-group differences, but the 1 that used ST (32) showed an increase in performance following aerobic exercise.

Fatigue was analyzed using the 16-item Parkinson's Disease Fatigue Scale (PFS-16) (n=1) (30), Fatigue Severity Scale (FSS) (n=2) (24,27) and Fatigue Impact Scale (FIS) (n=1) (24). Only FSS and FIS revealed significant improvements in the experimental groups.

To conclude, sleep quality was also assessed by the Pittsburgh Sleep Quality Index (PSQI) in 1 study (27) reporting significant improvements in the exercise group compared to the control group.

3.5 Effects of aerobic exercise across H&Y stages

The stages of Parkinson's disease, attributed by the H&Y classification (39) varied with 3 studies including patients at mild stage (27,34,35), 9 at mild to moderate (25,26,28–30,32,33,36,37) and 2 at moderate to severe (24,31).

The main motor outcomes were similar over the initial stages with improvements in gait, balance and mobility. In the most advanced stages the enhancement was essentially in gait parameters.

The main non-motor outcomes differ in the initial stages only in the quality of sleep, improved at mild stages and at the moderate to severe stages were only observed changes in fatigue.

The effects of aerobic exercise across the H&Y stages are described in Table 4.

3.6 Risk of bias in included studies

As shown in Figure 2 , the risk of bias of all the included studies was found as follows: 8 studies were classified as low risk of bias for randomization process (25,27,29,31–34,37) and 6 with some concerns(24,26,28,30,35,36), since they don't described the allocation concealment; 6 studies were graded as some concerns for deviations from the intended interventions (28,30–32,36,37); all studies (n=14) were classified as low risk of bias for missing outcome data since data for the outcomes were available for all, or nearly all, participants randomized; 2 studies had a high risk of bias for measurement of the outcome since the outcome assessors were aware of the intervention received by study participants (32,35); lastly all studies (n=14) had low risk of

bias for the reported result. Overall, 4 studies had a low risk of bias (25,29,33,34), 8 were classified with some concerns (24,26–28,30,31,36,37) and two with high risk of bias(32,35).

Figure 2 – Risk of bias evaluation of the RCTs using the ROB 2 tool

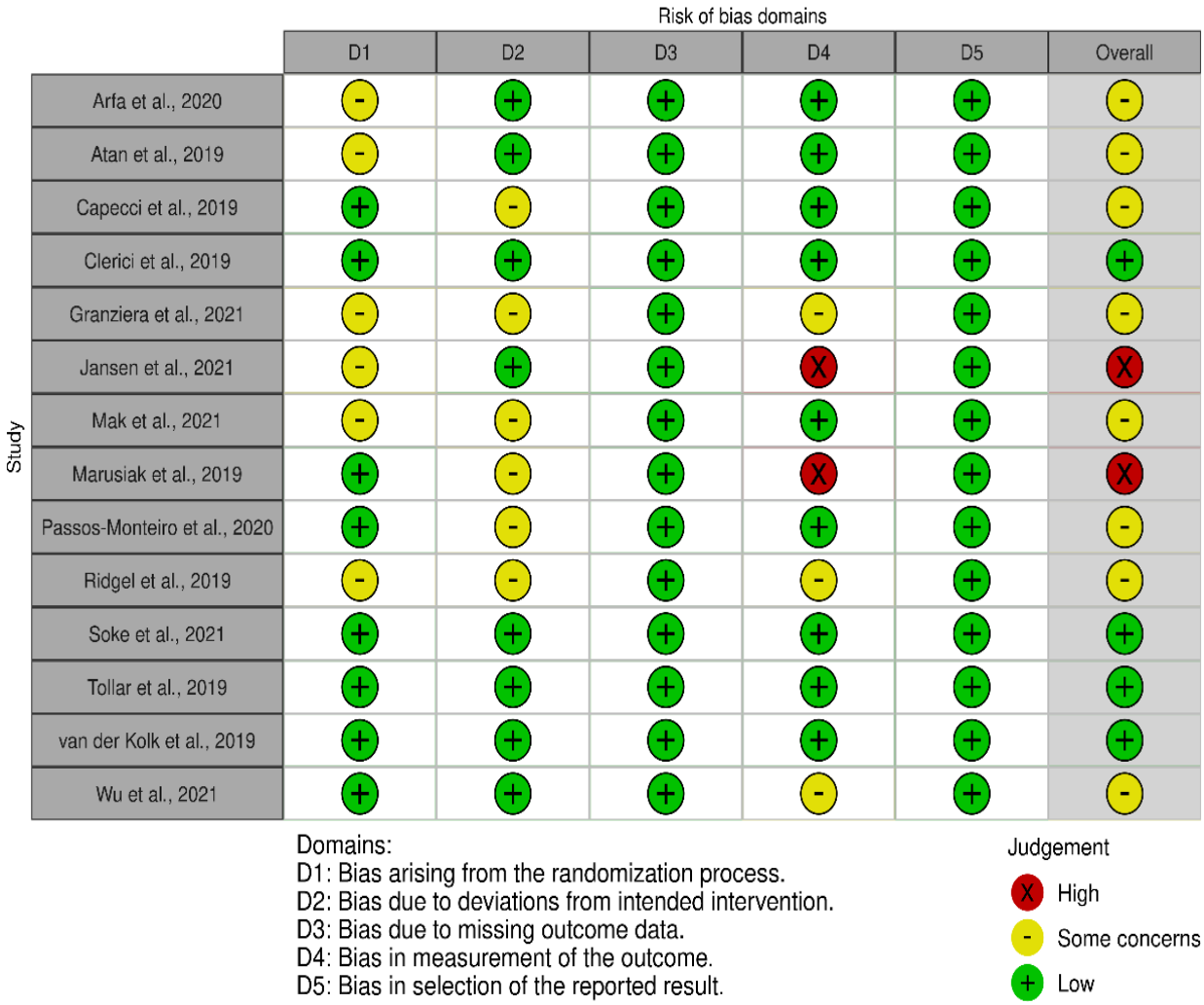


Table 2 – Study characteristics

Reference	Country	n	H&Y classification	Outcome measures
(Arfa et al., 2020)	Iran	**Experimental:** 11 (8 males) 60.63±9.36 years **Control:** 9 (7 males) 61.55±8.57 years	1,5–2,5	ON medication Primary: SF–8, 6MWT, TUG
(Atan et al., 2019)	Turkey	**Experimental:** 10 (4 males) 72.2±7.9 years 10 (4 males) 68.6±8.2 **Control:** 10 (3 males) 69.7±8.0 years	2–4	ON medication Primary: 6MWT Secondary: UPDRS, BBS, NHP, FIS and FSS
(Capecci et al., 2019)	Italy	**Experimental:** 48 (19 males) 68.1 ± 9.8 years **Control:** 48 (24 males) 67.0 ± 7.6 years	2–5	ON medication Primary: 6MWT, TUG, 10MWT, FOG–Q, UPDRS II item 14 Secondary: FOG–Q, UPDRS II item 14, WHS, UPDRS (total, II and III), PDQ–39

Table 3 – Study characteristics

Reference	Country	n	H&Y classification	Outcome measures
(Clerici et al., 2019)	Italy	**Experimental:** 27 (19 males) 67 ± 8 years **Control:** 25 (20 males) 67 ± 11 years	2-3	ON medication Primary: FOG-Q Secondary: UPDRS (total, II and III), BBS, TUG, 6MWT
~ (Granziera et al., 2021)	Italy	**Experimental:** 16 (10 males) 68.8 ± 10.2 years **Control:** 16 (11 males) 68.3 ± 6.2 years	2-3	ON medication Primary: UPDRS III Secondary: 6MWT, 10MWT, POMA T, TUG, PDQ-39, PFS-16, BDI, HAM-A, NMSS
(Jansen et al., 2021)	USA	**Experimental:** 14 (6 males) 63.50±6.31 years **Control:** 15 (8 males) 62.07±12.19 years	1-2	OFF medication Primary: MDS-UPDRS III

Table 4 – Study characteristics

Reference	Country	n	H&Y classification	Outcome measures
(Mak et al., 2021)	China	**Experimental:** 33 (11 males) 61.9 ± 6.4 years **Control:** 31 (9 males) 62.7 ± 7.2 years	1-5	ON medication Primary: MDS-UPDRS Secondary: FGS, TUG, 6MWT, Mini-BEST
(Marusiak et al., 2019)	Poland	**Experimental:** 10 (6 males) 72±10 years **Control:** 10 (3 males) 74±9 years	1,5 – 3	OFF medication Primary: TMT (parts A and B), ST (parts I and II) Secondary: H&Y, UPDRS, SE-ADL
(Passos-Monteiro et al., 2020)	Brazil	**Experimental:** 16 (13 males) 64.9±10.2 years **Control:** 17 (7 males) 70.5±5.8 years	1 – 4	ON medication Primary: WHOQOL-BREF, WHOQOL-OLDL Secondary: MoCA, GDS-15, UPDRS-III, H&Y

Table 5 – Study characteristics

Reference	Country	n	H&Y classification	Outcome measures
(Ridgel et al., 2019)	USA	**Experimental:** 8 (4 males) 69.9±7.4 years **Control:** 8 (5 males) 70.0±6.4 years	1-3	ON medication Primary: UPDRS-III, TUG
(Soke et al., 2021)	Turkey	**Experimental:** 14 (10 males) 57.7 ± 8.1 years **Control:** 12 (8 males) 56.2 ± 8.7 years	1-3	ON medication Primary: BBS, PST, LOS, PT, 6MWT, TUG Secondary: ABC, UPDRS (total, II and III) and PDQ-8
(Tollar et al., 2019)	Hungary	**Experimental:** 25 (12 males) 70.0±4.69 years 25 (11 males) 70.6±4.10 years **Control:** 24 (13 males) 67.5±4.28 years	2-3	ON medication Primary: UPDRS II score Secondary Outcomes: PDQ-39, BDI, SE-ADL, EQ-5D, BBS, BESTest, TAT, DGI, 6MWT

Table 6 – Study characteristics

Reference	Country	n	H&Y classification	Outcome measures
(van der Kolk et al., 2019)	Netherlands	**Experimental:** 65 (42 males) 59.3 ± 8.3 years **Control:** 65 (38 males) 59.4 ± 9.3 years	1-2	OFF medication Primary: MDS-UPDRS Secondary: MDS-UPDRS-IV, Mini- BEST, TUG, 6MWT, HADS, SCOPA, MoCA, TMT, TAP, PDQ-39, VO_2 max
(Wu et al., 2021)	Taiwan	**Experimental:** 49 (26 males) 63.65±6.02 years **Control:** 49 (30 males) 66.59±8.61 years	1-2	ON medication Primary: PDQ-8, GDS-15 Secondary: UPDRS (II and III), FSS, PSQI, HAS

SF-8 – Eight Item Short-Form Health Survey; 6MWT- Six Minute Walk Test; TUG – Timed Up and Go Test; UPDRS – Unified Parkinson's Disease Rating Scale; BBS – Berg Balance Scale; NHP – Nottingham Health Profile; FIS – Fatigue Impact Scale; FSS – Fatigue Severity Scale; 10MWT – Ten Minute Walking Test; FOGQ – Freezing of Gait Questionnaire; WHS – Walking Handicap Scale; PDQ-39 – Parkinson Disease Quality of Life Questionnaire test; POMA T – Tinetti Scale; PFS-16 – Parkinson's Disease Fatigue Scale; BDI – Beck Depression Inventory; HAM-A – Hamilton Anxiety Rating Scale; NMSS – Non-motor Symptom scale; MDS-UPDRS – Movement Disorder Society Unified Parkinson's Disease Rating Scale; FGS – fast gait speed; Mini-BEST – Mini-Balance Evaluation Systems Test; TMT – Trail Making Test; ST – Stroop Test; H&Y- Hoehn and Yahr scale; SE-ADL – Schwab and England Activities of Daily Living Scale; WHOQOL – World Health Organization Instrument for Quality of Life Assessment questionnaire; MoCA – Montreal Cognitive Assessment; GDS-15 – Geriatric Depression Scale–15 items; PST – Postural Stability Test; LOS – Limits of Stability Test; PT – Pull Test; ABC – Activities- specific Balance Confidence Scale; PDQ-8 – eight -item Parkinson' s Disease Questionnaire; EQ-5D – Euro-Quality of Life- 5 Dimensions; BESTest – Balance Evaluation Systems Test; TAT – Tinetti Assessment Tool; DGI – Dynamic gait index; HADS – Hamilton Anxiety and Depression Scale; SCOPA – Scales for Outcomes in Parkinson's disease; TAP – Test of Attentional Performance; VO2max – estimated maximal oxygen consumption; PSQI – Pittsburgh Sleep Quality Index; HAS – Hospital Anxiety Scale.

Table 7 – Characteristics of interventions

Reference	Intervention	Frequency (time/week)	Duration (min)	Intensity	Comparison	Main results
(Jansen et al., 2021)	Forced exercise (FE) on stationary semi-recumbent bicycle	3x/week for 8 weeks	50–60 min	60–80% of HRR	Voluntary exercise (VE) on stationary semi-recumbent bicycle	– Improvements in MDS-UPDRS Motor III by more than 4 points (~15%) for the FE and VE groups.
(Ridgel et al., 2019)	High-cadence cycling (recumbent stationary bicycle)	3x/week for 2 weeks	40 min	64% of HRmax	Stretching	– Improvements in UPDRS Motor III scores (2.5 pts, P=0.002) gait (P= 0.012) and TUG time (1.17 s, P=0.002).
(Atan et al., 2019)	BWSTT (10%) BWSTT (20%)	5x/week for 6 weeks	30 min	80% of HRmax	Treadmill training (0% BWSTT)	– Significant improvements in 6MWT in the experimental groups; – All groups showed significant increases in BBS; – UPDRS III scores decreased significantly in the 10% and 20% in supported groups (P = 0.012 and P = 0.005, respectively); – NHP decreased in the experimental groups (P = 0.003 and P = 0.002); – Significant improvements in both FIS and FSS scores (P = 0.005) in the experimental groups.
(Passos-Monteiro et al., 2020)	Nordic Walking	2x/week for 6 weeks	40–60 min	65 to 85% of HRmax Borg RPE: 13–17	Free walking	– Significant improvements in the overall, physical, psychological, social participation, and intimacy domains of quality of life, as well as in cognitive function and depressive symptoms for both groups; – Only the NW group showed improvement in the autonomy domain; – Similar enhancement of non-motor symptoms in both groups.

Table 8 – Characteristics of interventions

Reference	Intervention	Frequency (time/week)	Duration (min)	Intensity	Comparison	Main results
(Arfa-Fatollahkhani et al., 2020)	Treadmill training	2x/week for 10weeks	30 min	60% of HRR Borg RPE: 11 to 13	Usual care	– Balance and functional capacity were significantly improved in the case group after the intervention (TUG p-value: 0.003, 6MW p-value: 0.003) and for long-term; – Mental condition's scores of SF-8 in cases were not statistically different in short-term. P=0,016 for long-term.
(Wu et al., 2021)	Home-based exercise	3x/week for 8 weeks OR every day for 8 weeks	30–50 min OR 10–15 min per session every day	60-80% of HRmax	Usual care	– Significant improvements in depression, motor ability, fatigue, and sleep quality ($p < .05$), though not anxiety.
(Soke et al., 2021)	Task-oriented circuit training combined with aerobic training	3x/week for 8 weeks	30 min	60–80% of HRmax	Aerobic training	– Both groups showed an increase in functional mobility and balance confidence with improving balance and gait performance; – Both groups significantly improved UPDRS-II, UPDRS-III, UPDRS total, and PDQ-8 ($p< 0,05$).
(Mak et al., 2021)	Brisk walking and balance program (BW)	3x/week for 26 weeks	60 min – 150 min	40–60% of HRR	Upper limb training	– Significant decreases in MDS-UPDRS motor score after six weeks (–5.5 vs –1.6, $p < 0.001$) and 6 months (–6.0 vs –1.4, $p < 0.001$) of training; – Significant improvement for TUG time, FGS, 6MWT, and mini-BEST score (all $p < 0.05$).

Table 9 – Characteristics of interventions

Reference	Intervention	Frequency (time/week)	Duration (min)	Intensity	Comparison	Main results
(Clerici et al., 2019)	MIRT + Aquatic Therapy (AT)	MIRT: 5x/week (4 daily rehabilitative sessions) 1x/week physical exercise AT: 3x/week For 4 weeks	MIRT 60min AT 60 min	70% – 80% of HRR	MIRT	– Both groups had a substantial reduction in the FOGQ score; – Significant improvements in UPDRS, 6MWT and a significant reduction in time to complete the TUG.
(Granziera et al., 2021)	Nordic Walking (NW)	2x/week for 8 weeks	75 min	~ 60–80% of the HRR	Walking	– Improvements were observed in global motor outcome (p 0.001), dynamic and static balance ability (p 0.005; p 0.002), global non-motor symptoms outcome (p 0.003), fatigue (p 0.016), anxiety (p 0.043), and quality of life (p 0.003); – The NW failed to show any difference compared to the control group in all considered outcomes.
(Capecci et al., 2019)	RAGT	5 days/week for 4 weeks	45-min	80% of HRmax	Treadmill training	– Endurance and gait capacity were enhanced by 18% and 12%, in RAGT and treadmill training respectively; – Motor symptoms and quality of life were improved by 17% and 15%.
(Kolk et al., 2019)	Home-based stationary bike training	3x/week for 24 weeks	30 min	50- 80% of HRR	Stretching	– Only experimental group decreased MDS-UPDRSIII scores from pre-test to post-test.

Table 10 – Characteristics of interventions

Reference	Intervention	Frequency (time/week)	Duration (min)	Intensity	Comparison	Main results
(Marusiak et al., 2019)	Stationary cycle ergometer aerobic interval training (AIT)	3x/week for 8 weeks	60 min	60–75% of HRmax	Usual care	– Amelioration of upper-extremity bradykinesia ($p = 0.015$); – Improvement in daily life manual functions ($p = 0.004$), mood, and intellectual function ($p = 0.005$).
(Tollar et al., 2019)	Agility exergaming (EXE) and stationary cycling (CYC)	5x/week for 5 weeks	60 min	80% of HRmax Borg RPE: 12–13	Usual care	– Both programs improved similarly. – Improvements in UPDRS-II; – The depression scores improved.

HRR – Heart rate reserve; RPE – Rating of perceived exertion; BWSTT – body weight-supported treadmill training; NHP- Nottingham Health Profile; MHR – Maximum heart rate; MIRT – Multidisciplinary, intensive, motor-cognitive rehabilitation treatment; RAGT – Robotic Assisted Gait Training

Table 11- Effects of aerobic exercise across H&Y stages

H&Y classification	Studies	Exercise Modalities	Main Motor Outcomes	Main Non-Motor Outcomes
Mild	(Jansen et al., 2021) (Wu et al., 2021) (van der Kolk et al., 2019)	Cycling Aerobic exercise program	Improved gait speed, balance and UPDRS scores	Improved sleep quality and cognitive function Reduced anxiety, depression and fatigue
Mild to moderate	(Ridgel et al., 2019) (Arfa-Fatollahkhani et al., 2020) (Soke et al., 2021) (Clerici et al., 2019) (Granziera et al., 2021) (Marusiak et al., 2019) (Tollar et al., 2019) (Passos-Monteiro et al., 2020) (Mak et al., 2021)	Cycling Treadmill Aerobic exercise program Nordic walking Brisk Walking	Enhanced gait parameters, balance, function capacity and mobility Improved UPDRS scores	Enhanced cognitive function and mood Reduced anxiety, depression and fatigue
Moderate to severe	(Atan et al., 2019) (Capecci et al., 2019)	Body weight support treadmill training Robotic-assisted Gait Training	Improved endurance and gait capacity	Reduced fatigue

4. Discussion

The aim of this systematic review was to analyze the benefits of aerobic exercise on motor and non-motor symptoms in individuals with PD and their differences depending on the clinical condition, but also identify the dosages for the aerobic exercise.

In this review we included 14 studies with 720 participants, with the male number (391) slightly higher than the female one (329), and the mean average age was 66 years. Both data are consistent with the current epidemiological knowledge, that shows that not only Parkinson's disease has a higher incidence in men compared to women, but also has a prevalence that increases with age, predominantly affecting people over 60 years old (40,41).

Regarding the intervention, the most common type of aerobic exercise adopted in the included studies was stationary cycling training, likely due to the reduced postural stability requirements. The individuals remain seated, allowing them to focus only on the desired lower extremity pedaling motion and facilitating higher levels of intensity through cadence or HR (42).

7 of the 14 studies revealed high aerobic exercise intensities, which can be explained by its positive impact on neuroplasticity. Studies suggest that vigorous exercise can stimulate the release of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), that promotes neuronal survival and can slow the progression of neurological degeneration typical of PD (43,44).

The frequency ranged from two to five days with 8-week period being the most frequent. This is considered the adequate period for significant improvements in physical fitness and motor function to begin to be noticed. In fact, one study (45) reported that 8 weeks of aerobic exercise altered various signaling pathways in the central nervous system, modulated cognitive or physiological processes. Shorter programs also tend to be more attractive to participants, especially those who may have difficulty committing to long-term interventions.

This review show that aerobic exercise significantly improved motor symptoms such as functional mobility, balance, gait velocity and overall global motor function.

TUG and BBS are commonly used to assess control and posture balance (46), which are essential characteristics due to the fact there is a high incidence of recurring falls in people with PD, ranging from 18% to 65% in a 1-year period (47,48). Our study provided evidence

that aerobic exercise improved BBS and TUG in PD patients, as well as enhanced falls prevention in daily life.

Gait impairments are common motor symptoms in PD and can significantly impact regular activities and QoL (49). Our analysis revealed significant improvements in gait velocity, resulting in a positive influence on gait function and potentially improve mobility and reduce fall risk.

Our findings also indicate a significant decrease on the UPDRS-III/MDS-UPDRS III, which measures global motor function in PD patients. According to a systematic review (50), regular intensive exercise therapy may reverse or attenuate the underlying neurodegenerative processes in PD ultimately leading to improved UPDRS scores.

The review also found that aerobic exercise positively impacted non-motor symptoms, such as depression, cognition, fatigue and sleep. Aerobic exercise reduced anxiety, depression and fatigue and improved sleep quality and cognitive function. These effects are likely mediated through the release of neurotrophic factors, improved cerebral blood flow, and the overall enhancement of brain health associated with aerobic activity (51).

The most recurrent non- motor symptom was depression, which can be explained since its one of the most common comorbidities associated with the disease, with around 40% to 60% of people suffering from it (52).

It was evident that was given greater focus to motor symptoms than non-motor symptoms in the included studies. Motor symptoms are more directly linked to dopaminergic system disfunction, which is the main target of therapeutic interventions, resulting in more immediate and noticeable effects in this area. On the other hand, non-motor symptoms involve other neurological systems and are multifactorial, which makes their response to treatment slower and less evident.

These benefits on motor and non-motor symptoms were pronounced across all stages of PD, though most in individuals at mild and mild to moderate stage of PD. In the earlier stages of PD, the brain's capacity for neuroplasticity is still relatively preserved, which means individuals in the early stages of PD can experience more noticeable improvements in motor function. The non-motor symptoms also tend to respond well to aerobic exercise in earlier stages, with reduced fatigue and improved sleep quality and mood, possibly due to its effects on neurotransmitters (53).

In moderate to severe PD stages, maintaining motor function becomes more challenging due to increased symptom severity and reduced mobility. The benefits on non-motor symptoms were less pronounced too, and it was only possible to perceive a reduction in fatigue. The most noticeable effects were on gait and fatigue because these symptoms become more altered and debilitating as the disease progresses.

Upon examining the aerobic training program implemented by the included studies, we may suggest that significant improvements require a minimum intensity of 60% of HRR, a frequency of three times per week and a duration of 60 min per training session. However, naturally, the aerobic exercise dosage can be personalized to accommodate the physical capabilities of the individuals.

5. Study limitations and future suggestions

Despite our following of strict guidelines for this systematic review from the JBI and the PRISMA principles, there were several limitations that should be noted. Firstly, only English language literature was included in this study, omitted some articles published in other languages, which might have produced a publication bias.

Secondly, the sources of heterogeneity and bias cannot be completely controlled due to the large differences among the studies. In addition, the interventions provided varied widely from study to study, in duration, intensity, location and presence or absence of professional guidance and supervision. These factors may lead to heterogeneity and affect the accuracy of the results.

Furthermore, a relatively small number of studies were included, with only 14 papers reviewed, in-part due to the strict criterion.

Lastly, the methodological quality was also a limiting factor, with some publications showing some concerns or high risk of bias. The overall bias of the results in this review may be more related to randomization process, deviations from intended intervention and most of all with measurement of the outcomes.

It is important to continue further research to investigate the impact of aerobic exercise, especially studies including patients at severe stages of PD for better understanding.

6. Conclusion

In conclusion, this systematic review supports the recommendation that aerobic exercise is an effective non-pharmacological approach for improving motor and non-motor symptoms in individuals with PD, regardless of the PD stage they are in.

In addition, for the minimum dose of aerobic exercise, we recommend that the exercise period is no less than 3 times per week, with a duration of 60 min per training session and a minimum intensity of 60% of HRR.

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Appendixes

Appendix 1: PROSPERO prototocol

PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

A list of fields that can be edited in an update can be found here

1. * Review title.

Give the title of the review in English

Effects of aerobic exercise on the symptoms of people with Parkinson's at different stages: A Systematic Review

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

01/06/2023

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

02/09/2024

5. * Stage of review at time of this submission.

This field uses answers to initial screening questions. It cannot be edited until after registration.

Tick the boxes to show which review tasks have been started and which have been completed.

Update this field each time any amendments are made to a published record.

The review has not yet started: No

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Andreia Pita

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Miss Andreia

7. * Named contact email.

Give the electronic email address of the named contact.

10220143@ess.ipp.pt

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

School of Health - Polytechnic of Porto

Organisation web address:

https://www.ess.ipp.pt

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record. PLEASE USE AN INSTITUTIONAL EMAIL ADDRESS IF POSSIBLE.**

Miss Andreia Pita. School of Health - Polytechnic of Porto
Dr Augusta Silva. School of Health - Polytechnic of Porto
Mrs Liliana Pinho. CESPU

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

None

Grant number(s)

State the funder, grant or award number and the date of award

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

2) What are the benefits identified, and the evidence supporting the clinical symptoms (mild, moderate, severe)?

3) What dosages (intensity, frequency and time) are prescribed for aerobic exercise and what factors influence your choice?

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

The systematic review will be conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We will search PubMed (MEDLINE), Cochrane Central Register of Controlled Trials (CENTRAL), Physiotherapy Evidence Database (PEDro), and Web of Science (Core Collection) from the previous 5 years. We will use a Boolean search strategy with the operators AND, OR, and the search strategy will include terms describing or relating to intervention, participants, and outcomes.

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Parkinson's disease and aerobic exercise

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Adults (? 18 years) diagnosed with Parkinson's disease

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

Aerobic exercise

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Non applicable

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Include only randomized controlled trials

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Motor and non-motor symptoms (e.g. Unified Parkinson's Disease Rating Scale (UPDRS), Parkinson's Disease Quality of life scale-39)

Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Non applicable.

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

Non applicable

Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Non applicable.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

The data extraction will have various study characteristics, such as the name of first author and the year of publication. Additionally, participant characteristics, including sample size and H&Y stage will be also included. Detailed information regarding the intervention, such as it's type, intensity, duration, and

frequency, will be recorded. Furthermore, outcome measures and the corresponding results will be documented as part of the extracted data.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

The methodological quality and risk of bias for each individual study will be assessed using the Cochrane Risk of Bias tool for RCTs. The tool includes five domains of bias, which encompass the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each item was categorized as having a "Low risk," "Some concerns," or "High risk" of bias. The assessment of bias was conducted by the main reserarcher (AP) and independently reviewed by the other researchers (AS, LP). Any disagreements or discrepancies were resolved through dialogue.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

Aggregated data will be used and a narrative synthesis will be presented. In addition, a quantitative synthesis is planned.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

Non applicable.

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness

No

Diagnostic

No

Epidemiologic

No

Individual patient data (IPD) meta-analysis

No

Intervention

No

Living systematic review
No

Meta-analysis
No

Methodology
No

Narrative synthesis
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
No

Prospective meta-analysis (PMA)
No

Review of reviews
No

Service delivery
No

Synthesis of qualitative studies
No

Systematic review
Yes

Other
No

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer

No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

COVID-19
No

Crime and justice
No

Dental
No

Digestive system
No

Ear, nose and throat
No

Education
No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions

No

Musculoskeletal
No

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
Yes

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
No

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
No

Urological

No

Wounds, injuries and accidents

No

Violence and abuse

No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

Portugal

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.

Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information relevant to the registration of this review.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission). List authors, title and journal details preferably in Vancouver format.

Give the link to the published review or preprint.

Appendix 2: Search strategy

PubMed (Medline)	((Parkinson disease [MeSH Terms]) AND ((Exercise [MeSH Terms]) OR ("Aerobic Exercise" or "Endurance Training" or "Gait Training" or "Nordic Walking" or "Treadmill Training" or "Walking")) AND (Symptoms or symptomatology)) Article type: Randomized Controlled Trial Publication Date: 5 years	88
Cochrane Central	(Parkinson disease) in Title Abstract Keyword AND ("aerobic exercise" OR "walking" OR "endurance training" OR "nordic walking" OR "gait training" OR "treadmill training") in Title Abstract Keyword AND (Symptoms OR symptomatology) in Title Abstract Keyword – with Publication Year from 2019 to 2024, in Trials (Word variations have been searched)	223
PEDro	Parkinson disease AND aerobic exercise Method: Clinical Trial Published Since: 2019	15
Web of Science (Core Collection)	(TS=(Parkinson disease)) AND (TS=("Aerobic Exercise" or "Endurance Training" or "Gait Training" or "Nordic Walking" or "Treadmill Training" or "Walking")) AND (TS=(Symptoms or symptomatology)) Publication date: Last 5 Years Language: English	404