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Are movement-based mindful exercises (QIGONG, TAI CHI, AND YOGA) beneficial for stroke and Parkinson's disease? A scoping review



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ARTICLE INFO	A B S T R A C T
Keywords: Stroke Parkinson's Disease Meta-analysis QiQong Yoga Tai Chi	Objective: To synthesize evidence from systematic reviews on the effects of qigong, tai chi, and yoga in people with neurological diseases. Methods: A systematic search was conducted in PubMed, PsycINFO, Embase, CINAHL and Cochrane Library until September 2022. Methodological quality was assessed using the AMSTAR 2 tool. A qualitative synthesis of included reviews and meta-analyses was performed. Citation matrices and the corrected covered area were used to explore the overlap of randomized controlled trials among reviews. Results: Nineteen systematic reviews (containing 74 trials and 80 meta-analyses) in people with Parkinson's disease (PD) or stroke were included. The critical domains of the AMSTAR 2 were not satisfied in more than half of the reviews, and only 4 evaluated the certainty of the evidence. The overlap was very high (21.7%) and high (11%) for tai chi studies in PD and stroke, respectively. In people with PD, qigong, yoga, and tai chi can improve balance, with tai chi being beneficial to increase functional mobility. For stroke patients, tai chi was better than controls to enhance motor function and independence, but not for health-related quality of life and quality of sleep. Findings on balance, walking ability and depression were inconclusive in stroke population. <i>Conclusions:</i> Qigong, tai chi, and yoga appear to be effective to improve balance performance in people with PD. Tai chi practice enhances motor function and independency in stroke patients.

1. Introduction

There is an urgent need to face the increasing demand for neurorehabilitation ¹, with stroke as the leading cause of disability globally ², and Parkinson's disease (PD) as the fastest growing neurological condition ³. Dealing with uncertainty is the rule in neurologic diseases ⁴. These have a long and variable course ⁵, and frequently lead to complex and diverse motor and nonmotor symptoms, such as spasticity, tremor, or mobility restrictions ⁶, which ultimately compromise well-being and quality of life ⁷.

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Clinical guidelines suggest different approaches to prevent sensorimotor impairments and enhance the behavioural and emotional state in people with PD ⁸ or stroke ⁹. Patient active engagement should be inherent to clinical care in neurology ¹⁰. The use of coping strategies during rehabilitation, i.e., self-management interventions, contribute to a better adaption to long-term disability ¹¹ and can promote recovery ^{12–15}. Different forms of physical exercise, as a key domain for self-management ¹², are highly recommended to improve health-related outcomes in adults with neurological diseases ^{8,9}. Among these, movement-based mindful exercises, i.e., qigong, tai chi, and yoga, that

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combine gentle movements with conscious breathing and awareness, have emerged as safe, patient-centred, and cost-effective adjuvant treatments for chronic disorders ^{16,17}. Practice of mindful exercises helps to empower patients to adopt healthy behaviours ^{17,18}, and has an impact on brain functional activity ^{19,20}, thus they can be particularly beneficial for both physical and mental health ^{18,21}. In people with PD or stroke, these therapies have proven effective for physical and psycho-^{2,23}. In logical measures, although better quality evidence is warranted 2 addition, because of the rise of systematic reviews about this research topic an umbrella review is needed to analyse literature results. The aim of this umbrella review was to synthesize and analyse scientific literature on the effects of movement-based mindful exercises on balance, walking parameter, psychological factors, motor function and health-related outcomes in individuals with neurological diseases to determine the most beneficial approach when compared to other types of therapies and/or with usual care.

2. Methods

2.1. Protocol and registration

The umbrella review was conducted following the guidelines of the Preferred Reporting Items for Overviews of Systematic Reviews (PRIOharms) ²⁴. The review protocol was registered at Open Science Framework Registry (DOI: 10.17605/OSF.IO/MQW4U) prior to the selection of systematic reviews and data extraction processes.

2.2. Data sources and search strategy

A researcher (PGG) conducted the search in PubMed, PsycINFO (via ProQuest), Embase, CINAHL (via EBSCOhost) and Cochrane Library from database inception to September 2022. We used Medical Subject Heading (MeSH) terms related to mindful exercises (qigong, tai chi, and yoga,) and the study design of interest (systematic review). No terms describing specific neurological conditions were included in the search strategies to avoid limitations of potentially eligible records (Supplementary File A).

2.3. Eligibility criteria and outcomes of interest

The PICO framework ²⁵ (Patient, Intervention, Comparison, Outcome) was followed to determine the eligibility criteria.

The inclusion criteria were:

- I) Studies: Systematic reviews with meta-analysis.
- II) Patients: adults with any neurological disease, e.g., stroke, PD, multiple sclerosis.
- III) Intervention: qigong, tai chi, and yoga.
- IV) Comparisons: any type of control group, e.g., active controls or waitlist.
- V) Outcomes: balance (e.g. centre of pressure, static or dynamic balance), walking parameters (e.g. velocity, cadence, stride length), psychological factors (e.g. depression, anxiety, stress), motor function, and health-related outcomes.

The exclusion criteria were:

- I) Meta-analyses including study designs different from randomized controlled trials (RCTs).
- II) Meta-analyses where movement-based mindful exercises were analysed together with other experimental interventions.
- III) Meta-analyses based on the use of odds ratio.
- IV) Outcome measures not included in at least two different reviews.
- V) Reviews where neurological diseases were analysed along with other chronic conditions, e.g., cancer, or cardiorespiratory diseases.

- VI) Full text was unavailable.
- VII) Systematic reviews not written in English or Spanish.
- VIII) Studies not indexed in journals.
 - IX) Reviews studying neurological conditions not considered movement disorders or cerebrovascular/motor neuron diseases such as epilepsy, headache or peripherical nerves disorders (according to the International Classifications of Diseases).

2.4. Data management and selection process

Data management was performed using the Mendeley desktop v1.19.8. First, record duplicates were automatically removed by the software. Then, a researcher (CGM) screened retrieved results by title and abstract and examined the full text of eligible systematic reviews. When necessary, consensus for any query of search, inclusion or data management was reached between three of the research team members (CGM, PGG, AMHR).

2.5. Assessment of methodological quality

The methodological quality of the reviews was assessed by two independent researchers (MJCH, JMC) using the A MeaSurement Tool to Assess systematic Reviews-2 (AMSTAR-2) ²⁶ Any disagreement was solved with a third reviewer (AMHR). The AMSTAR 2 is not intended to generate an overall score, but rather to interpret the potential impact of an inadequate rating in the different domains, especially those considered as critical (items 2, 4, 7, 9, 11, 13, and 15) ²⁶.

2.6. Data extraction and synthesis

For the narrative synthesis, data were extracted in a standardized manner including: first author (year of publication); number of analysed RCTs; sample of the included RCTs; interventions, with exercise characteristics (i.e., style and delivery format) and duration; outcomes, including assessment tools; and effect size (overall or subgroups analysis). For effect size data, we consider the overall results of the metaanalyses for each outcome of interest. When an overall analysis was not available or does not meet our mentioned criteria, findings for subgroup analyses were reported. Data extraction process was divided by neurological diseases.

To detect the potential overlap among the included reviews, we used citation matrices to calculate the "Corrected Covered Area" (CCA) ²⁷ where the overlap is defined as slight (CCA < 6%), moderate (6–10%), high (11–15%), or very high (CCA > 15%) ²⁷. A co-occurrence analysis and bibliometric mapping were performed with the software VOS Viewer v. 1.6.18.

2.7. Protocol deviation

Compared to the registered protocol, we have included additional information from the primary studies (number of participants and countries where the studies were conducted). We have also added the co-occurrence and bibliometric analyses.

3. Results

The initial search retrieved 7702 records. After removing duplicates, 2530 records were screened by title and abstract. Finally, we assessed for eligibility 72 full texts, of which a total of 19 reviews, containing 80 meta-analyses, were included in the qualitative synthesis (Fig. 1). All excluded reports (n = 53) are listed in the Supplementary File B.

After the screening process, only reviews focused on stroke or PD met our eligibility criteria. Eight systematic reviews, that contained 30 primary trials, were in adults with PD $^{23,28-32,34,35}$, 10 reviews assessed patients after stroke and retrieved information from 42 studies $^{22,36-44}$, and one review included participants with PD or stroke and contained

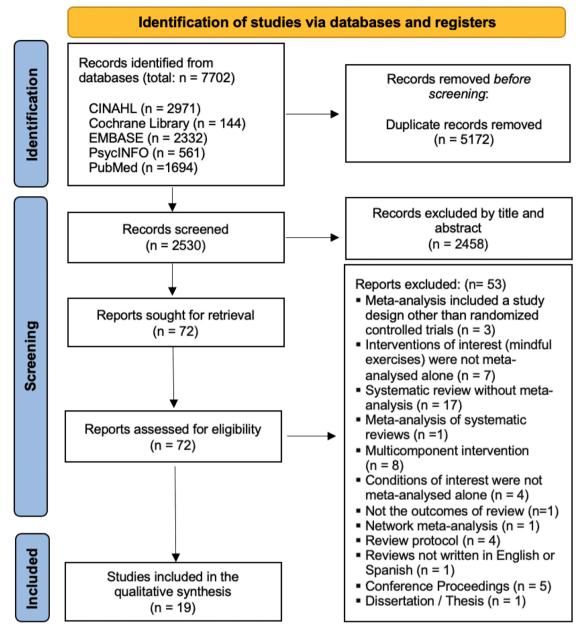


Fig. 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.

two additional primary studies ³³. The samples' characteristics, types of intervention and control groups, study outcomes, and main results (with effect size), are shown in Table 1 for reviews in PD and Table 2 for stroke. Data from the systematic review including patients with PD or stroke ³³ are listed separately in both tables. As supplementary file C we provide the reasons to exclude some meta-analyses.

Ten reviews used the Cochrane Risk of Bias tool or followed the guidelines of the Cochrane Handbook for systematic reviews of interventions to assess the methodological quality of primary research ^{22, 23,32,34,36–39,43,44}, with an additional 5 reviews using the Physiotherapy Evidence Database (PEDro) scale ^{28,30,33,35,40}. Only 4 of the systematic reviews (21%) evaluated the certainty of the evidence with the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach ^{22,33,37,39}.

3.1. Co-occurrence analysis

The use of VOS viewer maps to reflect network and density

visualization analyses could not detect a clear pattern, probably because 8 reviews (40%) ^{23,30,32,34,35,37,40,44} did not include key words (Figs. 2 and 3). The most commonly used terms were balance, gait, motor impairment, rehabilitation, and complementary therapies.

3.2. Overlapping

Systematic reviews returned 149 trials, including double counting. Of these, 74 reports were original studies. Those publications included in more than one review are listed in the citation matrix for reviews in PD (supplementary material D) or stroke (supplementary material E). The review with studies in people with PD or stroke ³³ is cited in both. Three of the studies analysed by Wu et al. ⁴² could not be retrieved due to insufficient information and lack of response from the corresponding author of the review. The corrected covered area (CCA) was calculated to determine the degree of overlap across reviews ²⁷. For reviews in patients with PD, the CCA indicated no overlap (0%) for controlled trials of qigong and yoga, and a very high overlap (21.7%) for trials about tai

Table 1

Included systematic reviews in people with Parkinson's disease.

Study	RCTs included in this umbrella	Sample of included RCTs, (mean age, sex)	Interventions; weeks of duration	Outcomes of interest	Effect size (overall or subgroup analysis)
Chen et al. 2020	China (3), Germany (1), Italy (1), Korea (1), USA (1) Total: 7	Qigong group (N/S) Total: 325 (64.1 yrs., 145 women)	Qigong group: Qigong styles (Guolin, Baduanjin, Wuqinxi); 7–48 wks. CG: aerobic training, walking, or no intervention; 7–24 wks.	Balance: BBS Motor function: UPDRS III Walking ability (endurance): 6MWT,10MWT	 Balance (overall, 5 studies) SMD: 0.72 (0.23–1.20), P < 0.001 I² = N/S Motor function (overall, 7 studies) SMD: 0.59 (0.24–0.93), P < 0.0001, I² = N/S Walking endurance (overall, 4 studies) SMD: 0.78 (0.10–1.47), P = 0.03, 2
Chen et al. 2020 Kwok et al. 2016 Liu et al. 2019 Monteiro- Mazzarin et al. 2017 Ni et al. 2014	USA (2) Total: 2	Yoga group (23) Total: 40 (67 yrs., sex N/ S)	Yoga group: Yoga styles (Iyengar Hatha or Vinyasa); 12 wks. CG: no intervention or education; N/S to 12 wks.	Balance: BBS Motor function: UPDRS III	$I^{2} = N/S$ • Balance (overall, 2 studies) SMD: 1.22 (0.25–2.20), P = 0.01, I^{2} = 40% • Motor function (overall, 1 studies) SMD: - 2.35 (-3.21 to -1.50), P < 0.0001, I^{2} = 0%
	China (1), Korea (1), USA (2) Total: 4	TC group (83) Total: 159 (65.3 yrs., sex N/S)	TC group: TC styles (8-form Yang, 24- form, Cheng Manching short); 10–16 wks. CG: no intervention or no exercise; N/S	Balance: BBS Functional mobility: TUG Motor function: UPDRS III Walking ability (endurance): 6MWT	• Balance (overall, 2 studies) SMD: 1.22 (0.80–1.65), $P < 0.0001, I^2 = 0\%$ • Functional mobility (overall, 3 studies) SMD: $-0.82 (-1.32 to -0.32),$ $P = 0.001, I^2 = 65\%$ • Motor function (TC at high dose, 3 studies) SMD: $-0.37 (-1.31 to 0.57),$ $P = 0.44, I^2 = 80\%$ • Walking endurance (overall, 2 studies) SMD: 0.82 (0.21–1.42), $P = 0.009$ $I^2 = 0\%$
.iu et al. 2019	(1), USA (2) Total: 355 (mean age Total: 5 and sex N/S) eiro- Country (N/S) TC group (86) zzarin et al. Total: 2 Total: 240 (67.1 yrs., sex N/S)		TC group: TC styles (Yang, Yang short, or N/S); 4–24 wks. CG: resistance or stretching training, walking, or no intervention; 4–24 wks.	Balance: BBS Functional mobility: TUG	 Balance (overall, 3 studies) MD: 3.47 (2.11-4.83), P < 0.0001 I² = 0% Functional mobility (overall, 4 studies) MD: - 1.06 (-1.61 to -0.51), P = 0.0002, I² = 30%
Mazzarin et al.		Total: 240 (67.1 yrs., sex	TC group: TC styles N/S; N/S CG: Qigong, resistance or stretching training, or no exercises; N/S	Motor function: UPDRS III	 Motor function (overall, studies) SMD: - 0.47 (-0.78 to -0.16), P = 0.003, I² = N/S
vi et al. 2014	(1), USA (4)	Total. 347 (65.7 yrs., 130 women). Sex N/S, 1	TC group: TC styles (short-form Yang, 8- form Yang, 24-form); 4–24 wks. CG: medication, walking, physical exercise, resistance or stretching training; N/S	Balance: BBS Functional mobility: TUG Health-related QoL: PDQ-39, PDQ-39SI Motor function: UPDRS III Walking ability (step length, speed): N/S	P = 0.003, 1 = 17/3 • Balance (TC + med., 3 studies) MD: 4.25 (2.83–5.66), P < 0.0001 I ² = 53% • Functional mobility (TC - med., 3 studies) MD: - 0.75 (-1.30 to -0.21), P = 0.007, I ² = 42% • Health-related QoL (TC - med., 3 studies) SMD: - 1.10 (-1.81 to -0.39), P = 0.002, I ² = 82% • Motor function (TC + med., 5 studies) MD: - 4.34 (-6.67 to -2.01), P = 0.0003, I ² = 91% • Walking speed (TC + med., 2 studies) SMD: 0.41 (-0.37 to 1.19), P = 0.30, I ² = 85% • Walking step length (TC - med., 2 studies)

 $I^2 = 67\%$ (continued on next page)

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Table 1 (continued)

Study	RCTs included in this umbrella	Sample of included RCTs, (mean age, sex)	Interventions; weeks of duration	Outcomes of interest	Effect size (overall or subgroup analysis)
Winser et al., 2018	China (3), Korea (1), USA (3) Total: 7	TC group (N/S) Total: 414 (age N/S, 142 women) Sex N/S, 1 study	TC group: TC styles (24-form Yang, short- form Yang, 6-form); 4–24 wks. CG: multimodal exercise, walking, resistance or stretching training, or no treatment; 4–24 wks.	Balance: BBS Functional mobility: TUG	 Balance (vs. active control, 3 studies) WMD: 4.21 (-1.98 to 10.39), P = 0.18, I² = N/S Balance (vs. no intervention, 2 studies) WMD: 1.55 (-0.80 to 3.90), P = 0.20, I² = N/S Functional mobility (vs. active control, 2 studies) WMD: - 0.19 (-1.74 to 1.35),
Yang et al., 2014	China (3), USA (4) Total: 7	TC group (196) Total: 447 (66.1 yrs., sex N/S)	TC group: TC styles (Yang, 24-short form, 6-form, or N/S); 4–24 wks. CG: walking, Qigong, resistance or stretching training, or no intervention; N/ S	Balance: BBS, FRT, OLST, TST Functional mobility: TUG Walking ability (endurance): 6MWT Walking ability (step length, speed): N/S	$\begin{split} P &= 0.0002, \ l^2 &= N/S \\ &= \ Balance (vs. active \ control, 3 studies) \\ SMD: 0.74 (0.38-1.10), \\ P &< 0.0001, \ l^2 &= 35\% \\ &= \ Balance, BBS (vs. no \ intervention, 2 studies) \\ SMD: 1.22 (0.80-1.65), \\ P &< 0.0001, \ l^2 &= 0\% \\ &= \ Balance, BBS (vs. no \ intervention, 2 studies) \\ SMD: 1.22 (0.80-1.65), \\ P &< 0.0001, \ l^2 &= 0\% \\ &= \ Balance, OLST (vs. no \ intervention, 2 studies) \\ SMD: 0.48 (-0.49 to 1.46), \\ P &= 0.33, \ l^2 &= 61\% \\ &= \ Balance, TST (vs. no \ intervention, 2 studies) \\ SMD: 0.48 (-0.64 to 1.50), \\ P &= 0.43, \ l^2 &= 68\% \\ &= \ Functional mobility (vs. no \ intervention, 3 studies) \\ SMD: 1.06 (0.68-1.44), \\ P &< 0.0001, \ l^2 &= 0\% \\ &= \ Walking speed (vs. active \ control, 2 studies) \\ SMD: 0.27 (-0.01 to 0.55), \\ P &= 0.06, \ l^2 &= 0\% \\ &= \ Walking step length (vs. active \ control, 2 studies) \\ SMD: 0.28 (-0.21 to 0.77), \\ P &= 0.27, \ l^2 &= 35\% \\ &= \ Walking step length (vs. no \ intervention, 2 studies) \\ SMD: -0.00 (-0.57 to 0.56), \\ P &= 0.99, \ l^2 &= 0\% \\ &= \ Walking step length (vs. no \ intervention, 2 studies) \\ SMD: -0.00 (-0.57 to 0.56), \\ P &= 0.99, \ l^2 &= 0\% \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ SMD: -0.00 (-0.57 to 0.56), \\ P &= 0.99, \ l^2 &= 0\% \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ SMD: -0.00 (-0.57 to 0.56), \\ P &= 0.99, \ l^2 &= 0\% \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ SMD: -0.00 (-0.57 to 0.56), \\ P &= 0.99, \ l^2 &= 0\% \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ SMD: -0.00 (-0.57 to 0.56), \\ P &= 0.99, \ l^2 &= 0\% \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ SMD: -0.00 (-0.57 to 0.56), \\ P &= 0.99, \ l^2 &= 0\% \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ &= \ Walking endurance (vs. no \ intervention, 2 studies) \\ &= \ Walking endurance (vs. n$
Yu et al., 2021	Country (N/S) Total: 17	TC group (455) Total: 951 (65.5 yrs., 332 women) Mean age or sex N/S, 3 studies	TC group: TC styles N/S; 8–24 wks. CG: Qigong, walking, usual care, resistance or stretching training, routine exercise; N/S	Balance: BBS Functional mobility: TUG Health-related QoL: PDQ-39 Motor function: UPDRS III Walking ability (speed): N/S	SMD: 0.53 (-0.07 to 1.12), P = 0.08, $I^2 = 0\%$ • Balance (overall, 10 studies) MD: 2.74 (2.14-3.34), P < 0.0001 $I^2 = 40\%$ • Functional mobility (overall, 5 studies) MD: - 1.05 (-2.06 to -0.05), P = 0.04, $I^2 = 59\%$ • Health-related QoL (overall, 4 studies) MD: - 5.59 (-11.39 to 0.21), P = 0.06, $I^2 = 69\%$ • Motor function (overall, 10 studies) MD: - 1.58 (-3.60 to 0.43), P = 0.12, $I^2 = 75\%$ • Walking speed (overall, 6 studies)

Table 1 (continued)

Study	RCTs included in this umbrella	Sample of included RCTs, (mean age, sex)	Interventions; weeks of duration	Outcomes of interest	Effect size (overall or subgroup analysis)
					SMD: 0.47 (0.12–0.83), $P = 0.009$, $I^2 = 74\%$
Zhou et al., 2015	China (3), USA (6) Total: 9	TC group (N/S) Total: 569 (66.2 yrs., sex N/S)	TC group: Yang-style or N/S; 4–24 wks. CG: dance, walking, Qigong, resistance or stretching training, or no intervention; N/ S	Balance: BBS, OLST, FRT Functional mobility: TUG Health-related QoL: PDQ-39 Motor function: UPDRS III Walking ability (endurance): 6MWT Walking ability (speed, step length): N/S	• Balance (overall, 6 studies) SMD: 0.85 (0.51–1.20), P < 0.0001, $I^2 = 52\%$ • Functional mobility (overall, 4 studies) SMD: - 0.73 (-1.35 to -0.10), P = 0.002, $I^2 = 79\%$ • Health-related QoL (overall, 4 studies) SMD: - 0.49 (-1.64 to 0.66), P = 0.40, $I^2 = 87\%$ • Motor function (overall, 7 studies) SMD: - 0.75 (-1.22 to -0.28), P = 0.002, $I^2 = 78\%$ • Walking endurance (overall, 2 studies) SMD: - 0.53 (-1.12 to 0.07), P = 0.08, $I^2 = 0\%$ • Walking speed (overall, 3 studies) SMD: 0.21 (-0.04 to 0.46), P = 0.11, $I^2 = 0\%$ • Walking step length (overall, 3 studies) SMD: 0.22 (-0.13 to 0.57), P = 0.21, $I^2 = 29\%$

Effect size data are reported as mean difference, standardized or weighted mean difference, with (95% confidence interval). I2 index statistic indicates the level of heterogeneity. Effect size consider the overall information of the meta-analysis for the outcomes of interest. Subgroup analyses are included when an overall meta-analysis was not available. Age and sex data are included when reported in more than half of the studies.

Abbreviations: BBS, Berg balance scale; CG, control group; FRT, Functional reach test; med., medication; MD, mean difference; N/S, non-specified; OLST, one leg stance test; PDQ-39, Parkinson's disease questionnaire-39; PDQ-39SI, PDQ-39 summary index; QoL, quality of life; RCT, randomized controlled trial; SMD, stan-dardized mean difference; TC, Tai-Chi; TST, Tandem stand test; TUG, Timed-up and go test; UPDRS III, Movement Disorders Society-Unified Parkinson's disease rating scale part III; wks., weeks; WMD, weighted mean difference; yrs., years; 6MWT, 6-minute walk test; 10MWT, 10-minute walk test.

chi. In reviews about stroke, the CCA was 0% for yoga and 11% for tai chi studies, denoting a high overlap.

3.3. Methodological quality

The data for risk of bias is shown in Table 3. The items with the highest concerns for methodological quality were: a) lack of a comprehensive search strategy or explanation of the selection of the study designs; b) absence of a list of excluded studies; c) no report on the sources of funding for the individual studies; and d) no assessment of the impact of the risk of bias in individual studies on the review results. Among the seven domains identified as critical in the AMSTAR 2²⁶, only the item 9 (use of a satisfactory technique to evaluate the studies' risk of bias) scored 'Yes' in more than 50% of the assessed reviews ^{22,23,28,30,32–40,43, 44}.

3.4. Main results

3.4.1. Parkinson's disease

A single review ²⁸ explored the impact of qigong in adults with PD. Qigong was more beneficial than controls to improve balance, motor function, and walking endurance. A positive impact on balance and motor function was also observed when comparing Yoga with education or no intervention ²⁹. A total of 8 reviews ^{23,29–35} studied the effects of different tai chi styles in people with PD. Most of them showed ^{23,29–32,35} that tai chi was superior to control interventions to increase balance, with conflicting results depending on the measurement tool ³⁴. Functional mobility, assessed with the timed-up and go test (TUG), was improved after regular tai chi practice ^{23,29,30,32,34,35}, with mixed

findings when analyses were subgrouped by the type of control (active vs. no intervention) ³³. Results were inconclusive for motor function and walking ability. Tai chi proved to be better than controls to enhance motor function in tree reviews ^{31,32,35}, whereas two found no differences between groups ^{23,29}. Similarly, three reviews concluded a positive impact on walking parameters favouring tai chi ^{23,29,32}, but this effect was not demonstrated in the other three reviews ^{32,34,35}. Finally, in only one ³² of the three reviews that investigated the effect of tai chi on health-related quality ^{23,32,35}, tai chi was superior to controls.

3.5. Stroke

The efficacy of yoga in stroke patients was investigated in one review that demonstrated a lack of positive effect on balance performance ³⁷. The remaining reviews included tai chi studies ^{22,33,36,38-44}. Overall, the impact of tai chi on balance was inconclusive. Two reviews found tai chi to be superior to controls ^{22,38}, whereas two observed no differences between groups ^{33,43}, and there were mixed results in another two depending on the measurement tool 42,44 . As regards motor function, tai chi appears to be more beneficial than control interventions ^{43,44}. Findings on walking ability were conflicting, with results recommending in favour of tai chi ^{22,43,44} or not ^{38,44}, depending on the walking parameter. Tai chi was better than usual care or rehabilitation to decrease the level of depression in two ^{36,39} out of three reviews ^{36,39,41}. Reviews also showed that tai chi was more effective than controls to avoid dependency in daily life activities ^{22,38}, but not to enhance health-related quality of life (physical or mental) ^{39,41} or the quality of sleep ^{38–40}.

 Table 2

 Included systematic reviews in people after stroke

2022 (2), Japan (1) Total: P32 (63.3 yrs, sex studies form Taiji, 5-12 wis. HADD, HAMD, GHQ-D studies Lawren-ce et al., 2017 Total: 2 Yoga group (14) Yoga group (14) Yoga group (14) Pace, exercise training (rehab.); N/S Balance: BBS Balance: BBS Balance: BBS 2017 Total: 2 women) Total: 120 (59.3 yrs, sex Korea (1), 2017 TC group (613) TC group (153) TC group; TC styles (24-form Yang, 12-form balance, TG exercise); 4-46 wks. ADL: BI, modified BI, TS, SF-36 (physical state) balance: BS SMD : 2.38 (-1.4 P = 0.022, 1 ² = 0 2017 Japan (1), USA (2) TC group (13) TC group; TC styles (24-form Yang, 12-form balance, TG exercise); 4-46 wks. ADL: BI, modified BI, TS, SF-36 (physical state) balance: BS Balance: BS SMD : 1.21 (0.5 P = 0.0003, T ² • 0.0001, 1 ² • 0.00001, 1 ² • 0.0001, 1 ² • 0.0001, 1 ² • 0.0001, 1 ² • 0.0001, 1	all or subgrou
 Laver-ce Matriali (1), Voga group (48) voga group: Satyananda nidra, sasan, dygan, Justici (1), Voga group (48) vomen) 2017 Total: 2 2017 Total: 2 2017 Total: 2 2018 China (1), USA (2) studies Li et al., 2018 China (1), USA (2) studies Li et al., 2018 China (1), USA (2) studies Li et al., 2018 China (1), USA (2) studies Cina (2), Korea (1) (2), Sing (2) studies Cina (2), Korea (1) (2), Sing (2) studies Cina (2), Korea (1) (2), Sing (2) studies Cina (2), Sing (2) studies	0.67 to -0.18
i et al., 2017China (13), Japan (1)TC group (613) Total: 120 (53.3 yrs, sex studiesTC group: TC styles (24-form Yang, 12-form Hop-source, TC balance, TC exercise); 4-48 wks. GG: usual care, general rehab. exercise, rehab. usualing ability: FUG walking ability: Holden walking ability: H	e (overall, 2) 1 to 6.17),
1. Total: 17 walking scale, TUG, SPPB, or N/S studies . L Total: 17 walking scale, TUG, SPPB, or N/S studies . Guinty (N/S) TC group (133) TC group: TC styles (Yang, Sun) or N/S; 6-12 walking ability: TUG, SPPB, or N/S walking scale, TUG, SPPB, or N/S . Li et al., 2018 China (1), USA TC group (133) TC group: TC styles (Yang, Sun) or N/S; 6-12 Balance: FRT, DGI, SPPB walking ability: TUG, SPPB studies . Li et al., 2018 Country (N/S) TC group (133) TC group: TC styles (Yang, Sun) or N/S; 6-12 Balance: FRT, DGI, SPPB balance: SMD: - -0.03) . Lyu et al., 2018 Country (N/S) TC group (470) TC group: TC styles (Yang, balance, 6-form Yang, simplified 24 type, 12 type, 10 type, Yunshou; 2-24 wks. ADL: BI Balance: BBS . Synce N/S, 3 studies TC group: TC styles (Yang, balance, 6-form Yang, simplified 24 type, 12 type, 10 type, Yunshou; 2-24 wks. ADL: BI Balance: BBS . Synce N/S, 3 studies CG: conventional rehab, therapy, family rehab, therapy (phone guide), or N/S; N/S Making scale, TUG studies . ADL(T) studies S223 (342-7.05 studies S23 (342-7.05 . Balance Balance Balance S23 (342-7.05 S34 (332-156 <td>verall, 12) 5–1.85),</td>	verall, 12) 5–1.85),
Li et al., 2018China (1), USA (2), Korea (1)TC group (133) Total: 328 (64.7 yrs., sex N/S)TC group: TC styles (Yang, Sun) or N/S; 6-12 wks.Balance: FRT, DGI, SPPB Walking ability: TUG, SPPBBalance studies2018Total: 4N/S)CG: PT, breathing, stretching, or balance training, physical activity; N/S to 12 wks.SPPBSMD: 0.15 (-0. P = 0.475, 1 ² = - -0.033) = 0%.yu et al., 2018Country (N/S) Total: 15TC group (470) Total: 942 (57.5 yrs., 234 women). Mean age or sex N/S, 3 studiesTC group: TC styles (Yang, balance, 6-form Yang, simplified 24 type, 12 type, 10 type, therapy (phone guide), or N/S; N/SADL: BI Balance: BBSMD: 9.92 (6.82- Motor function: FMA walking ability: Holden walking scale, TUGMD: 9.92 (6.82- e e tudies.yu et al., 2018Country (N/S) Total: 15TC group (470) Total: 942 (57.5 yrs., 234 women). Mean age or sex N/S, 3 studiesTC group: TC styles (Yang, balance, 6-form Yang, simplified 24 type, 12 type, 10 type, therapy (phone guide), or N/S; N/SADL: BI Balance: BBS Walking ability: Holden walking scale, TUGMD: 9.92 (6.82- e e Balance studies.blance studiesBalance studiesBalance: BBS Balance: BBSMD: 10.10.10 (5.00) e e e e e balance studies.blance studiesBalance studiesBalance studiesBalance 	-12.19),
Lyu et al., 2018Country (N/S) Total: 15TC group (470) Total: 942 (57.5 yrs., 234 women). Mean age or sex N/S, 3 studiesTC group: TC group: TC gtyles (Yang, balance, 6-form Yang, simplified 24 type, 12 type, 10 type, Yunshou); 2-24 wks.ADL: BI Balance: BBS \bullet ADL (T Balance: BBS0.0001, $I^2 =$ therapy (phone guide), or N/S; N/SWolf function: FMA Walking scale, TUG $MD: 9.92$ (6.82- $0.0001, I^2 =$ $0.0001, I^2 =$ 	e (overall, 3) 27 to 0.58), 26.6%
$\begin{array}{c} (TC + n \\ MD: 4.49 \ (1.92 \\ P = 0.0006, 1^2 \\ = \\ \bullet \ Motor \\ limb \ (1 \\ studies \\ MD: 8.27 \ (4.69 \\ P < 0.0001, 1^2 \\ = \\ \bullet \ Motor \\ limb \ (1 \\ studies \\ MD: 2.75 \ (0.95 \\ P = 0.003, 1^2 \\ = \\ \bullet \ Walkin \\ Holden \\ MD: 0.61 \ (0.38 \\ P < 0.0001, 1^2 \\ \end{array}$	$\begin{array}{l} -13.02),\\ =0\%\\ C+rehab.,7\\)\\ >-15.28),\\ =93\%\\ e(TC alone,2)\\), P<0.0001,\\ e(TC +rehab.,2)\\), P<0.0001,\\ e(TC +rehab.,2 tudie),\\ +0, P<0.0001\\ function, 4 limi\\ ehab., 2 studie),\\ -7.06),\\ =0\%\\ function, uppe\\ C+rehab., 2,\\)\\ 11.84),\\ =7\%\\ function, lowe\\ C+rehab., 3\\)\\ +4.56),\\ 77\%\\ g ability,\\ (3 studies),\\ -0.85),\\ =0\%\\ g ability, TUG\\ ies) \end{array}$
2021Total: 6Total: 571 (66 yrs., 192Yang, modified 24-form); 4–24 wks.GHQ, HAMA, HAMDstudies	sion (overall, 6

(continued on next page)

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Table 2 (continued)

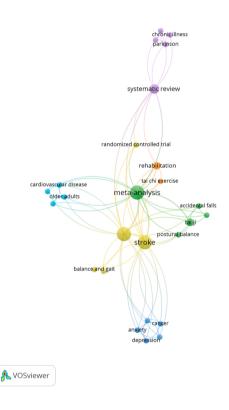
Study	RCTs included in this umbrella	Sample of included RCTs mean age, sex	Interventions; weeks of duration	Outcomes of interest	Effect size (overall or subgrou analysis)
		women). Mean age or sex N/S, 1 study	CG: usual rehab., regular care, family rehab. phone guide; N/S	Health-related QoL: SF- 36 Quality of sleep: PSQI	$\begin{array}{l} \text{SMD: } 0.36 \ (0.10-0.61), \\ \text{P} = 0.006, \ 1^2 = 47\% \\ & \bullet \ \text{Health-related QoL}, \\ & \text{mental (overall, 3 studies)} \\ \text{MD: } 6.15 \ (-3.05 \ to \ 15.36), \\ \text{P} = 0.19, \ 1^2 = 88\% \\ & \bullet \ \text{Quality of sleep} \\ & (\text{overall, 3 studies)} \\ \text{MD: } 0.33 \ (-1.15 \ to \ 1.81), \\ \text{P} = 0.66, \ 1^2 = 14\% \end{array}$
Si et al., 2020	Japan (1), USA (1) Total: 2	TC group (70) Total: 131 (mean age and sex N/S)	TC group: TC styles (Yang or TC easy); 12 wks. CG: rehab., usual care; 12 wks.	Quality of sleep: PSQI	P = 0.00, 1 = 14% • Quality of sleep (overall, 2 studies) SMD: 0.20 (-0.14 to 0.53), P = 0.258, $I^2 = 0\%$
Taylor-Piliae et al., 2020	Japan (1), Korea (1), USA (2) Total: 4	TC group (97) Total: 229 (67.2 yrs., 113 women)	TC group: TC styles (Yang, or N/S); 6–12 wks. CG: PT, usual care, aerobic or resistance training; N/S to 12 wks.	Depression: CES-D, GHQ- D Health-related QoL: GHQ, SF-36	 Depression (overall, 3 studies) Hedge's g = 0.45, P = 0.07, I² = 50.20% Health-related QoL, mental (overall, 3 studies) Hedge's g = 0.40, P = 0.15, I² = 54.76% Health-related QoL, physical (overall, 3 studies) Hedge's g = 0.34, P = 0.13, I²
Winser et al., 2018	China (1), Korea (1) Total: 2	TC group (N/S) Total: 158 (mean age N/S, 66 women)	TC group: TC styles (TC exercise, short-form Sun); 6–12 wks. CG: general PT, breathing + education + active mobilization; 6–12 wks.	Balance: TUG	 = 35.23% Balance (overall, 12 wks., 2 studies) WMD: - 0.45 (-3.43 to 2.54) P = 0.77, 1² = N/S Balance (overall, 18 wks., 2 studies) WMD: 1.81 (-5.39 to 9.02), P = 0.62, 1² = N/S
Wu et al., 2018	China, USA Total: 5	TC group (N/S) Total: 325 (mean age and sex N/S)	TC group: Yang style or N/S; N/S to 12 wks. CG: usual care, strength training, PT, community-based physical activity, acupuncture; N/S to 6 wks.	Balance: BBS, SPPB	P = 0.02, 1 - 10/3 = Balance (BBS, 3 studies) MD: 4.82 (2.14-7.50), P < 0.001, 1 ² = 99% = Balance (SPPB, 2 studies) MD: 0.29 (-0.09 to 0.68), P = 0.140, 1 ² = N/S
Zheng et al., 2021	China (16), USA (2), Korea (1), Total: 19	TC group (659) 1297 (59.2 yrs, sex N/S)	TC group: TC styles (N/S); N/S to 12 wks. CG: regular activity, health education, walking, conventional or comprehensive rehab., PT; N/S to 12 wks.	Balance: BBS, gravity swing test Motor function: FMA Walking ability: TUG, 6MWT, 10MWT	 Balance (BBS, 6 studies) MD: 7.67 (3.44–11.90), P = 0.0004, 1² = 99% Balance (SPPB, 2 studies) MD: - 0.22 (-1.00 to 0.56), P = 0.58, 1² = 0% Balance (swing area, studies) MD: - 0.79 (-1.48 to -0.10) P = 0.03, 1² = 83% Balance (swing lengt 3 studies) MD: - 0.79 (-2.05 to -1.49) P = 0.76, 1² = 97% Balance (swing speed 2 studies) MD: - 5.43 (-7.79 to -3.08) P < 0.0001, 1² = 0% Motor function (overall, 10 studies) MD: 4.15 (1.68–6.63), P = 0.001, 1² = 98% Walking ability (6MWT, 2 studies) MD: - 30.94 (-11.34 to 73.22) P = 0.15, 1² = 89%

Table 2 (continued)

Study	RCTs included in this umbrella	Sample of included RCTs mean age, sex	Interventions; weeks of duration	Outcomes of interest	Effect size (overall or subgroup analysis)
					 Walking ability (standing / walking test, 3 studies) MD: - 3.42 (-4.22 to -2.63), P < 0.0001, I² = 13%

Effect size data are reported as mean difference, standardized or weighted mean difference, or Hedge's g, with (95% confidence interval). I2 index statistic indicates the level of heterogeneity. Effect size consider the overall information of the meta-analysis for the outcomes of interest. Subgroup analyses are included when an overall meta-analysis was not available. Age and sex data are included when reported in more than half of the studies.

Abbreviations: ADL, activities of daily living; BBS, Berg balance scale; BDI, Beck depression inventory; BI, Barthel index; CES-D, Center for Epidemiologic Studies depression scale; CG, control group; CI, confidence interval; DGI, dynamic gait index; FMA, Fugl–Meyer motor function score; FRT, Functional reach test; GHQ, General health questionnaire; GHQ-D, General health questionnaire - depression; GQOLI-74: Generic quality of life inventory-74; HAMA, Hamilton anxiety scale; HAMD, Hamilton depression scale; HADD, Hospital anxiety and depression Scale - depression; MD, mean difference; no., number; N/S, non-specified; PSQI, the Pittsburgh sleep quality index; PT, physical therapy; QoL, quality of life; rehab., rehabilitation; SF-36, the Short Form Health Survey 36; SMD, standardized mean difference; SPPB, Short physical performance battery; TC, Tai-Chi; TIS, Trunk impairment scale; TUG, Timed-up and go test; wks., weeks; WMD, weighted mean difference; yrs., years; 6MWT, 6-minute walk test



motor impairmen balance

Fig. 2. Network visualization.

4. Discussion

The present umbrella review provides an overview on the effects of qigong, tai chi, and yoga on motor and nonmotor symptoms in patients with PD or stroke. We analysed 19 systematic reviews that retrieved 74 original studies including 80 meta-analyses. There were no reviews in diseases other than stroke or PD that fulfilled our eligibility criteria, which suggests the need for future research in other neurological conditions of interest. This overview offers relevant information to conduct further high-quality clinical research. In general, qigong, tai chi, and yoga were more effective than controls to improve balance and functional mobility in PD, with no substantial evidence for the rest of outcomes. In stroke, conclusive positive evidence was only found on motor function and independency in daily life after regular tai chi practice.

4.1. Parkinson's disease

Qigong, tai chi, and yoga are suggested as safe, effective, and well

accepted approaches for patients with mild to moderate PD ^{45,46}. Balance problems and resulting increased fall risk are major concerns among persons with PD, as they often lead to dependency, social isolation, higher disability, and increased costs ^{47,48}. Our results suggest that gigong and yoga can be beneficial adjuvant treatments to increase balance in patients with PD 45 , although evidence is still insufficient to strongly support this claim⁴⁹. Tai chi was by far the most investigated mind-body exercise. Our findings support those of a recent overview that concluded a positive effect of tai chi on balance ⁵⁰. Yet, caution is warranted due to the low level of evidence and limited quality of reviews ^{50,51}. Functional mobility, assessed with the TUG, can predict risk of falling in this population ^{52,53}. In all included reviews, tai chi (up to 24 weeks) was superior to controls to improve performance in the TUG, which has been also confirmed following a one-year tai chi program ⁵ The possible underlying mechanisms to explain the impact of regular tai chi practice in adults with PD include enhanced brain network function, reduced inflammation, improved metabolism, and decreased vulnerability to dopaminergic degeneration ⁵⁴. Surprisingly, the positive results

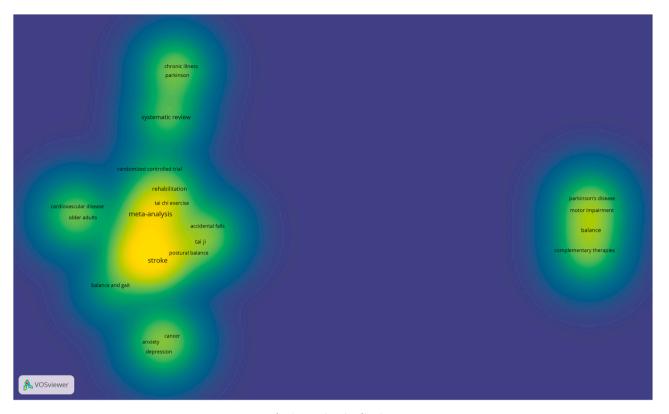


Fig. 3. Density visualization.

on functional mobility did not lead to improvements on motor symptoms and walking ability, contrary to findings from previous research 5^{4-56} . Balance and walking ability may be controlled by different neural circuits 57 and, therefore, depend on distinct underlying mechanisms in adults with PD 58 . Additionally, differences among primary studies in terms of tai chi styles, training routine, controls, and measurement tools could explain these conflicting results. The effect of tai chi on the quality of life across 8 dimensions (including social relations, cognition, communication, and emotional well-being) was similar to that of usual care or other exercise regimes. Previous reviews have demonstrated that the impact of exercise on health-related quality of life depends on the type of exercise (aerobic vs. anaerobic) and treatment duration (more or less than 12 weeks) 59 , which was highly variable among reviews.

4.2. Stroke

In line with previous studies ^{60,61}, yoga was proven useful to improve balance in stroke survivors. Yoga postures (asanas) are challenging to keep an optimal balance ⁶², which requires proper muscle activation ⁶³. In patients with stroke, especially those at the chronic stage, a yoga training program needs to last at least 12 weeks to be successful ⁶⁰. The present promising results should be interpreted carefully. Most primary trials show low methodological quality ⁶⁰ and are highly heterogeneous, including different therapy doses, duration, and yoga styles⁶⁴. It is important to individually tailor the yoga routine ⁶⁵ and avoid physical barriers that may impair practice ⁶⁶, thus a 'one size fits all' approach is not always desirable for patients, regardless of their condition. Our findings agree with the lack of conclusive evidence on the impact of tai chi on balance ^{50,67}. Although most research suggests a positive effect of tai chi on walking ability ^{68,69}, the current findings do not support this idea. The practice of diverse tai chi styles, e.g., sitting vs. standing ^{70,71}, in patients in different stages after stroke, e.g., subacute vs. chronic ^{70,71}, may lead to different results for sitting or standing balance and walking ability, which could partially explain the controversial findings among studies. Tai chi has shown to increase motor control and coordination⁷

which supports the results on motor function. The benefits of tai chi to decrease the self-reported level of dependency ^{67,69,73} and promote well-being ⁷⁴ could lead to improve quality-of-life-related measures, e. g., depression and quality of sleep. However, current literature is not enough to recommend tai chi over other forms of physical exercise. As occurs in PD, the type of exercise and the duration of the training protocol may influence the results ⁷⁵.

4.3. Clinical implications

Movement-based mindful exercises should be considered unique forms of physical activity as they involve a psychological and spiritual component ⁷⁶. These are increasingly common practices in western culture, with purported benefits for people with chronic conditions, e.g., cancer ⁷⁷, or musculoskeletal pain ⁷⁸. However, how to incorporate these therapies into the clinical setting needs to be elucidated ⁷⁹. Qigong, tai chi, and yoga share common grounds, but they differ in the nature of their physical practice, especially yoga ⁷⁶. This may explain that qigong and tai chi are wrongfully considered as the same intervention modality ⁸⁰. For patients with neurological diseases, mind-body exercises can be challenging, but they also represent a feasible strategy to enhance awareness and cognitive function, even in those with cognitive impairments ⁸¹. Exercise adaptations are always possible if needed, with individually-tailored rehabilitation programs being strongly recommended in neurological care.

To understand the clinical impact of movement-based mindful exercises in neurological diseases, future research should avoid multicomponent therapies or the use of mindful approaches as a control intervention. This was a reason to exclude several systematic reviews. The lack of high-quality research in other neurological conditions, e.g., multiple sclerosis, and the scarce evidence on the effect of yoga and qigong open future lines of research.

Table 3

Methodological quality of the included reviews: AMSTAR 2 Tool.

Author(s)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Parkinson disease		1		1	1	1				1	1	1	1			1
Chen et al., 2020																
Kwok et al., 2016																
Liu et al., 2019																
Monteiro-Mazzarin et al., 2017			•													
Ni et al., 2014																
Yang et al., 2014			•													
Yu et al., 2021																
Zhou et al., 2015																
Stroke																
Cai et al., 2022																
Lawrence et al., 2017																
Li et al., 2017			•													
Li et al., 2018																
Lyu et al., 2018																
Lyu et al., 2021																
Si et al., 2020																
Taylor-Piliae et al., 2020																
Wu et al., 2018																
Zheng et al., 2021																
Parkinson + stroke																
Winser et al., 2018																

Abbreviations: AMSTAR; A MeaSurement Tool to Assess systematic Reviews. Green colour = yes; Red colour = no; Orange colour = Partial yes.

Items: AMSTAR 1: Did the research questions and inclusion criteria for the review include the components of PICO? AMSTAR 2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? AMSTAR 3: Did the review authors explain their selection of the study designs for inclusion in the review? AMSTAR 4: Did the review authors use a comprehensive literature search strategy? AMSTAR 5: Did the review authors perform study selection in duplicate? AMSTAR 6: Did the review authors perform data extraction in duplicate? AMSTAR 7: Did the review authors provide a list of excluded studies and justify the exclusions? AMSTAR 8: Did the review authors describe the included studies in adequate detail? AMSTAR 9: Did the review authors use a satisfactory technique for assessing the risk of bias in individual studies that were included in the review? AMSTAR 10: Did the review authors report on the sources of funding for the studies included in the review? AMSTAR 11: If meta-analysis was performed did the review authors assess the potential impact of risk of bias in individual studies on the results of the review? AMSTAR 12: If meta-analysis was performed, did the review authors account for risk of bias in individual studies when interpreting/ discussing the review? AMSTAR 14: Did the review authors account for risk of bias in individual studies when interpreting/ discussing the review? AMSTAR 15: If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the review? AMSTAR 16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

4.4. Methodological considerations

The main methodological issues of the reviews were related to the search strategy, exclusion of studies, and the risk of bias of individuals RCTs. A comprehensive literature search strategy is key for any systematic review and allows the reproducibility of results. Thus, concerns in how this item is reported lead to selection bias. Guidelines for conducting systematic reviews, e.g., PRISMA 2020 or PRIO-harms, state the need to include a list of excluded studies. However, this item was just satisfied in 2 out of the 19 systematic reviews. Another concern was the overall lack of assessment of the quality of the evidence using, for example, the GRADE framework. Therefore, the strength of evidence for clinical recommendation of movement-based mindful exercises in neurological diseases remains uncertain. We recommend future systematic reviews to use a GRADE approach to provide information on the quality of the available evidence. Additionally, systematic reviews should include a sensitive analysis to reflect the impact of the individual studies in the calculated effect size.

4.5. Limitations

As opposed to other reviews, we decided not to use the ROBIS tool to evaluate the methodological quality of the studies, as both the AMSTAR 2 and the ROBIS address many similar constructs ⁸². One of the main limitations of the current umbrella review is that only studies written in Spanish or English were considered, so potential records could have been missed, also due to lack of response from corresponding authors when contacted. In addition, the different protocols and study outcomes of the included systematic reviews may influence the clinical relevance of the present results. Findings from tai chi studies should be considered with caution for the high overlap among reviews. This was our main reason not to conduct a meta-meta-analysis or to assess the certainty of evidence, contrary to recent umbrella reviews ⁸³. Finally, we have not investigated the possible adverse events associated with qigong, tai chi and yoga. This remains a matter for further research.

5. Conclusion

The conclusions of this umbrella review are:

- In patients with PD, yoga appears to be more effective than controls to improve balance and motor function.
- Tai chi regular practice can improve motor function and the level of independence in people with stroke.
- Serious methodological concerns of the included reviews must be accounted for when interpreting the present results.

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CRediT authorship contribution statement

All authors have contributed to the design of the study and have drafted and revised the manuscript, giving approval to the final submitted version.

Declaration of interest

None of the authors has any financial or other interests relating to the manuscript.

Data availability statement

The data that support the study findings are available from the corresponding author upon reasonable request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ctim.2022.102912.

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