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# Effectiveness of various exercise types in reducing fall risk among older adults with diabetic peripheral neuropathy: A systematic review and meta-analysis

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#### ABSTRACT

*Background:* Diabetic peripheral neuropathy (DPN) increases fall risk in diabetics. Due to varying variables used to assess fall risk, the impact of exercise on fall prevention remains inconsistent. This study reviews and compares the effects of different exercises on fall risk among older adults with DPN.

Methods: A comprehensive literature search was conducted in PubMed, EBSCO, Web of Science, and Cochrane Library up to February 17th, 2025. Inclusion criteria were: older adults with DPN; exercise intervention only, an inactive or non-exercising control group, and randomized controlled trials with outcome variables: timed up and go (TUG) time, gait speed, Berg Balance Scale (BBS) score, one-legged standing (OLS) time with eye open (EO) and closed (EC). The mean difference (MD) and 95 % confidence interval (CI) were calculated.

Results: A total of 21 articles included five exercise types: balance exercise (BE), multi-component exercise (ME), strength exercise (SE), whole-body vibration (WBV) and foot-ankle functional training (FT). BE reduced TUG time (MD = -1.47, 95 % CI = -1.79 to -1.15) and increased gait speed (0.11, 0.04–0.18), BBS score (0.93, 0.49–1.37), and OLS time (EO: 2.72, 1.86–3.58; EC:1.58, 1.0–2.17). ME reduced TUG time (-1.71, -2.26 to -1.17) and increased BBS score (2.0, 1.28–2.72) and OLS time (EO: 7.07, 4.35–9.79; EC: 2.61, 1.28–3.94); SE reduced TUG time (-1.45, -2.75 to -0.15) and increased gait speed (0.09, 0.06–0.12); WBV increased OLS time (EO: 1.94, 1.32–2.56; EC: 1.86, 0.16–3.56) but did not affect TUG time or gait speed. FT did not affect TUG time or gait speed.

Conclusions: Exercise reduced fall risks among older adults with DPN. BE and ME were effective in reducing fall risks, followed by SE. WBV improved static balance but failed in dynamic balance. FT showed limited effects on fall prevention and was not recommended.

#### 1. Introduction

As the most prevalent neuromuscular disorder of diabetes, <sup>1</sup> diabetic peripheral neuropathy (DPN) affects up to 50 % of patients with diabetes, <sup>1,2</sup> with symptoms like numbness, tingling, and pain in a stocking-glove pattern that starts at the feet and spreads proximally. <sup>1,3,4</sup> DPN predisposes to muscle weakness, postural instability, and dysesthesia (unpleasant sensations of burning or tingling), and the risk of falls among older adults with DPN is 43.3 % higher than those without DPN<sup>5</sup> and 2.3 times higher than those with diabetes but no other

neuropathies.<sup>4,6</sup> Falls lead to serious consequences like fractures, cerebral haemorrhages, and even deaths,<sup>4,6</sup> as well as long-term clinical symptoms such as psychological distress, fear of falling, or reduced physical activities due to unsteadiness.<sup>3</sup>

Increasing evidence demonstrates that various exercises have the potential to reduce fall risks among older adults with DPN, however, there is a lack of consensus on the effectiveness of a certain type of exercise across studies. For instance, a study demonstrated that foot-ankle functional training (FT) potentially reduced fall risks by increasing gait speed, while Sartor et al. reported that FT did not reduce fall risks by

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assessing the Activities-specific Balance Confidence Scale among older adults with DPN $^8$ ; Similarly, a few studies illustrated that strength exercise (SE) reduced fall risk by enhancing lower extremity muscle strength among older adults with DPN, $^{9-11}$  whereas another study showed that SE could not increase muscle strength and reduce fall risks. $^{12}$  To the best of our knowledge, few studies have identified which exercise is more effective than others in reducing fall risks among older adults with DPN. Addressing this issue could provide clinical recommendations on fall prevention among older adults with DPN.

The controversy in the literature may arise from the selection of variables used to predict falls in patients with neuromuscular disorders (e.g., DPN). The predictable variables based on functional performance could be categorized into dynamic balance measures (e.g., Time Up and Go (TUG) test, gait speed, and Berg Balance Scale (BBS)) and static balance measures (e.g., One-Leg Stand (OLS) test). <sup>13</sup> The TUG time, with high reliability (0.99), sensitivity (87 %), and specificity (87 %), uses a 15-s threshold to predict falls. 14,15 Gait speed, which is a reliable indicator as demonstrated by the average speed in both the 6-min walk test  $(0.98 \text{ m/s})^{16}$  and the 10-m walk test  $(0.98 \text{ m/s})^{17}$  exhibits high to moderate sensitivity (80 %) and specificity (72 %) with a cut-off point of 0.98 m/s in distinguishing between fallers and non-fallers. 18 The BBS score, which is reliable (0.866), <sup>19</sup> has high to moderate sensitivity (78 %) and specificity (70 %) with a threshold score of 45 for predicting falls.<sup>20</sup> OLS time is considered reliable (0.960)<sup>21</sup> and has moderate to low accuracy in predicting falls, with a sensitivity of 46.6 % and specificity of 68.2 %. 13,22 Other variables, such as center of pressure, 23 dynamic gait index, <sup>24</sup> and modified gait abnormality rating scale, <sup>25</sup> have been used to represent fall risk, but their predicting validity has not been confirmed.

This study aims to review and compare the effectiveness of various exercises on fall risks among older adults with DPN by pooling data from literature and selecting representative variables for fall risks.

#### 2. Methods

## 2.1. Protocol and registration

This study was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 statement. Its protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) with an ID of CRD42023436799.

# 2.2. Eligibility criteria

The PICOS (populations, interventions, comparator interventions, outcomes and study types) framework was used to determine eligibility criteria.  $^{26}\,$ 

## 2.2.1. Types of studies

This study included randomized controlled trials (RCTs), in which exercises were considered as an exposure or intervention among older adults with DPN in all settings (community, hospital, and institutional).

## 2.2.2. Types of participants

Inclusion criteria: 1) with type 1 or 2 diabetes, and have been diagnosed with DPN<sup>27</sup>; 2) aged over 45 years<sup>28,29</sup>; 3) ability to walk independently, without the use of assistive devices. Exclusion criteria: 1) lower limb deformities, injuries, or prior surgeries; 2) other diabetes-related complications, e.g., diabetic retinopathy, nephropathy, foot ulcers; 3) other neurological disorders, e.g., stroke, Parkinson's disease; 4) regular exercise in the previous 6 months; 5) receiving any structured supervised physical therapy interventions.

## 2.2.3. Types of interventions

Exercise interventions included single or combined modalities, such as BE, SE, FT, whole-body vibration (WBV), and multi-component

exercise (ME). However, participants who received two or more types of interventions were excluded, except for those who engaged in exercise while also taking part in regular DPN medications. The control intervention consisted solely of maintaining a habitual lifestyle without engaging in physical activity.

#### 2.2.4. Types of outcomes

This review selected five variables to represent fall risks. Timed up and go (TUG) time: time taken by participants to stand up from a standard armchair, walk a distance of 3 m, turn, and walk back to the chair  $^{15,30}$ ; Gait speed: self-selection gait speed or average speed during a 6-min walk test (6MinWT) or a 10-m walk test (10MeterWT)  $^{16,17}$ ; Berg Balance Scale (BBS) score: the total score of 14 tasks, determined by the quality of the performance or the time taken to complete the tasks  $^{13,31}$ ; One-legged standing (OLS) time: maximum unilateral standing time under two conditions, EO and EC.  $^{22}$ 

## 2.3. Databases and search strategy

A three-step search strategy was conducted according to the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions. <sup>26</sup> First, four databases (PubMed, Web of Science, EBSCO, Cochrane Library) were searched for records published up to February 17th, 2025, and only peer-reviewed studies published in English were included. Medical Subject Headings (MeSH) terms and keywords were selected based on the study design ("Randomized Controlled Trials"), exposure ("Exercise" OR "Training" OR "Physical activity"), outcomes ("Postural Control" OR "Gait Performance" OR "Fall risks") and participants ("Diabetic Peripheral Neuropathy").

#### 2.4. Study selection

All articles were screened for inclusion by two reviewers (DW, XP) based on the title and abstract. The two reviewers obtained and screened the full texts of the remaining articles according to the eligibility criteria. Discrepancies were resolved through discussion with a third reviewer.

## 2.5. Data collection process and data items

Data extracted from included articles comprised authors, year of publication, sample size, participants information (age, gender, body mass index (BMI), duration of diabetes), detailed descriptions of the exercise and control interventions (type, duration, frequency), and outcomes. Means and standard deviations (SDs) were recorded at baseline and post-intervention. The Meta-Analysis Accelerator tool was used to calculate the mean and SDs of pre- and post-intervention difference.<sup>33</sup> In cases where necessary data were unavailable or could not be imputed, corresponding authors were contacted for further information.

## 2.6. Study risk of bias assessment

Two authors (DW and XP) independently assessed the risk of bias using the Cochrane Risk of Bias tool (RoB 2).<sup>34</sup> RoB 2 is structured into five bias domains: the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome and selection of the reported result. The potential risk of bias under each domain was evaluated as "low risk of bias", "some concerns", or "high risk of bias". Disagreements were resolved through consensus with a third reviewer. No articles were excluded based on quality assessment.

## 2.7. Statistical analysis

Means, SDs and sample size were entered into the Review Manager software (RevMan 5.3, Cochrane Collaboration, Oxford, UK) to calculate

the mean difference (MD) and a 95 % confidence interval (CI). Forest plots were employed to illustrate the effect size and 95 % CI across articles. Effect sizes of 0.2, 0.5 and 0.8 were considered small, moderate and large, respectively. The Heterogeneity was assessed using Higgins I<sup>2</sup> and chi-square tests (p). If I<sup>2</sup> value < 50 % with p > 0.010, indicating low heterogeneity, a fixed-effects model was used to calculate the effect size; Otherwise, a random-effects model was used. Subgroup analyses were performed to examine the impact of different exercise types on fall risks, with no overlap in 95 % CIs as the criterion for distinguishing differences among types.

#### 3. Results

#### 3.1. Study selection

A total of 628 records were retrieved in this study, of which 144 duplicates were excluded. Moreover, 308 records were excluded after reviewing the titles and abstracts. After a full-text assessment, 155 records were excluded, including non-RCT (n = 24), control groups with exercise (n = 22), participants without DPN (n = 17), non-exercise intervention (n = 30), lacking or fall risk representative variables (n = 61) and missing data (n = 1). Lastly, 21 articles were included in the systematic review and meta-analyses. A flow diagram of the selection process is presented in Fig. 1.

#### 3.2. Characteristics of included studies

A summary of participant baselines, exercise and control details, and outcomes is presented in Table 1. A total of 21 articles involving 1023

participants with DPN were included. These articles encompassed six types of exercise interventions: nine focused on BE, three on WBV, three on ME, three on FT, and three on SE. The duration of interventions ranged from 3 to 24 weeks, and the frequency ranged from 1 to 5 times/week. Most articles select a frequency of 2–3 times per week for 8 or 12 weeks.

#### 3.3. Risk of bias

The RoB 2 tool was used to assess the risk of bias for each study in Table 2. Ten articles were determined as low risk of bias,  $^{7,9,37-45}$  nine as some concerns,  $^{23,46-53}$  and two as high risk of bias.  $^{10,54}$  Eight studies did not report blinding for participants or therapists,  $^{10,39,46,48-52}$  leading to some concerns about bias due to deviations from the intended interventions. Two studies did not report baseline differences between the exercise and control groups,  $^{10,54}$  resulting in a high risk of bias in outcome measurement. Five studies did not report blinding for assessors,  $^{43,46,49,52,53}$  leading to some concerns about bias in outcome measurement.

## 3.4. Meta-analysis

#### 3.4.1. TUG time

As shown in Fig. 2, 11 studies with 551 participants presented TUG time and included five types of exercise: BE, ME, SE, WBV and FT. The heterogeneity was low in TUG time (I $^2$  = 48 %, p = 0.030). Pooled data demonstrated that exercise was more effective than non-exercise in reducing TUG time (MD = -1.39, 95 % CI = -1.77 to -1.01). In subgroup analysis, BE (MD = -1.47, 95 % CI = -1.79 to -1.15), ME (MD =

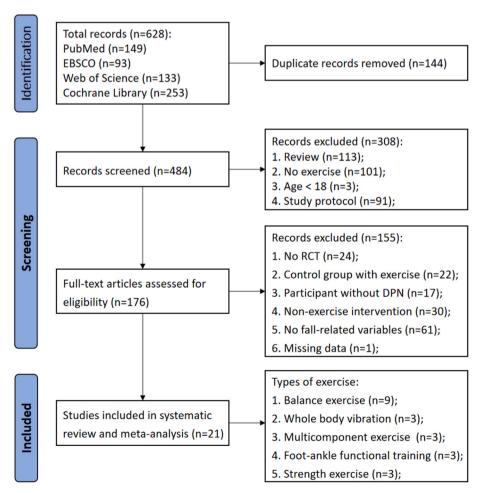


Fig. 1. Prisma flow diagram.

**Table 1** Characteristics of the included studies.

| Authors (years)  | Participants (Exercise)  | Participants (Control)  | Type and Duration (Exercise)                     | Type and Duration (Control)            | Outcomes   |  |
|--|--|---|--|--|--|--|
| Allet et al. (2010) <sup>37</sup>                          | $n=35,$ age $=63.0\pm8.0$ years, BMI $=30.5$ $\pm~6.0~kg/m^2$  | $\begin{aligned} n &= 36; \text{ age} = 64.0 \pm 8.9 \text{ years; BMI} = 31.5 \\ &\pm 5.3 \text{ kg/m}^2 \end{aligned}$            | ME (Gait + BE); 12<br>weeks, 2 times/<br>week    | None                                   | Gait<br>speed                                      |  |
| Song et al. (2011) <sup>39</sup>                           | $n$ = 19, female = 12, age = 72.9 $\pm$ 5.6 years, duration = 11.8 $\pm$ 9.2 years   | $n=19,$ female $=11,$ age $=73.2\pm5.4$ years, duration $=13.2\pm10.2$ years  | BE; 8 weeks, 2 times/week                        | Health education; 8 weeks, 1 time/week | OLS time<br>BBS score<br>TUG time<br>Gait<br>speed |  |
| Lee et al. (2013) <sup>40</sup>                            | ME: n = 19, female = 10, age = 76.3 $\pm$ 4.8 years, duration = 13.2 $\pm$ 4.3 years   | $n=18, female=10, age=75.8\pm5.7~years,   duration=11.3 \pm5.8~years$   | ME (WBV + BE); 6<br>weeks, 3 times/<br>week;     | None                                   | OLS time   |  |
| 10   | BE: n = 18, female = 11, age = 74.1 $\pm$ 5.4 years, duration = 12.3 $\pm$ 5.0 years   |   | BE; 6 weeks, 2 or 3 times/week                   |  | BBS score  |  |
| Melai et al. (2014) <sup>10</sup>                          | n = 48, female = 8, age = $68.2 \pm 7.3$ years,<br>BMI = $30.2 \pm 6.3$ kg/m <sup>2</sup>  | $n = 46, F = 10, age = 65.5 \pm 7.4 \text{ years, BMI} = 30.9 \pm 4.9 \text{ kg/m}^2$   | SE; 24 weeks, 2<br>times/week                    | None                                   | Gait<br>speed                                      |  |
| Yoosefinejad et al.<br>(2015) <sup>46</sup>                | $n = 10$ , female = 6, age = 57.0 $\pm$ 1.8 years,<br>BMI = 28.5 $\pm$ 1.0 kg/m <sup>2</sup> , duration = 11.0 $\pm$ 6.5 years   | $n = 10$ , female = 6, age = 57.0 $\pm$ 1.8 years,<br>BMI = 28.9 $\pm$ 1.0 kg/m <sup>2</sup> , duration = 12.0 $\pm$ 2.0 years      | WBV; 6 weeks, 2<br>times/week                    | None                                   | TUG time<br>OLS time                               |  |
| Rojhani-Shirazi et al.<br>(2016) <sup>41</sup>             | n = 40, female = 27, age = $54.8 \pm 5.3$ years,<br>BMI = $27.8 \pm 1.4$ kg/m <sup>2</sup> , duration = $11.6$<br>$\pm 2.6$ years  | n = 20, female = 12, age = $53.8 \pm 5.6$ years, BMI = $27.1 \pm 1.4$ kg/m $^2$ , duration = $10.7 \pm 2.6$ years                   | BE; 3 weeks, 5 times/week                        | None                                   | OLS time<br>BBS score                              |  |
| Ahmad et al.<br>(2019) <sup>32</sup> (2021) <sup>47</sup>  | n = 20, female = 6, age = $61.2 \pm 8.2$ years,<br>BMI = $24.6 \pm 3.3$ kg/m <sup>2</sup> , duration = $13.9$<br>$\pm 6.3$ years   | n = 17, female = 7, age = $58.6 \pm 5.7$ years, BMI = $26.3 \pm 3.7$ kg/m², duration = $14.1 \pm 6.0$ years                         | BE; 8 weeks, 3 times/week                        | Care education; 1 time/2 weeks         | TUG time<br>OLS time<br>Gait<br>speed              |  |
| Jamal et al. (2019) <sup>42</sup>                          | $n = 13$ , female = 4, age = $60.69 \pm 5.08$<br>years, BMI: $26.48 \pm 2.4$ kg/m <sup>2</sup>   | $n = 13$ , female = 6, age = $59.54 \pm 4.25$<br>years, BMI = $26.53 \pm 2.31 \text{ kg/m}^2$                                       | WBV; 6 weeks, 3 times/week                       | None                                   | TUG time   |  |
| Hung et al. (2019) <sup>48</sup>                           | n = 12, female = 10, age = 71.0 $\pm$ 1.22 years, BMI = 24.76 $\pm$ 1.26 kg/m <sup>2</sup>   | n = 12, female = 6, age = $66.5 \pm 2.1$ years, BMI = $25.83 \pm 0.72$ kg/m <sup>2</sup>  | BE; 6 weeks, 3 times/week                        | None                                   | TUG time<br>BBS score<br>OLS time                  |  |
| Win et al. (2019) <sup>49</sup>                            | $n = 32$ , female = 24, age = $55.38 \pm 9.54$<br>years, BMI = $24.56 \pm 4.49$ kg/m², duration<br>= $6.09 \pm 6.25$ years   | $n = 43$ , female = 33, age = $55.72 \pm 10.55$<br>years, BMI = $24.96 \pm 3.62$ kg/m², duration = $6.74 \pm 8.70$ years            | FT; 8 weeks, 2–3 times/week                      | Usual care and care education          | TUG time   |  |
| Venkataraman et al.<br>(2019) <sup>54</sup>                | n = 70, female = 34, age = 61.9 $\pm$ 6.5 years, BMI = 28.4 $\pm$ 5.6 kg/m², duration = 13.8 $\pm$ 10.3 years  | n = 73, female = 46, age = 62.3 $\pm$ 7.4 years, BMI = 28.4 $\pm$ 5.9 kg/m <sup>2</sup> , duration = 16.8 $\pm$ 11.1 years          | ME (SE + BE); 8 weeks, 1 time/week               | Routine clinical care                  | TUG time   |  |
| Abdelbasset et al. (2020) <sup>50</sup>                    | n = 14, female = 6, age = $53.4 \pm 5.3$ years, BMI = $26.4 \pm 2.8$ kg/m², duration = $7.5 \pm 3.4$ years   | n = 14, female = 7, age = 52.8 $\pm$ 5.7 years, BMI = 27.2 $\pm$ 2.7 kg/m², duration = 8.1 $\pm$ 3.5 years                          | BE; 8 weeks, 3 times/week                        | None                                   | BBS scor<br>Gait<br>speed                          |  |
| Monteiro et al.<br>(2020) <sup>51</sup><br>Monteiro et al. | $\begin{aligned} &n = 15, \text{ female} = 9, \text{ age} = 62.5 \pm 6.8 \text{ years,} \\ &BMI = 28.9 \pm 5.3 \text{ kg/m}^2 \\ &n = 39, \text{ age} = 61.5 \pm 11.7 \text{ years} \end{aligned}$ | $n=15,  female=5,  age=64.6\pm6.9  years, \\ BMI=28.1\pm7.0  kg/m^2 \\ n=39,  age=60.1\pm8.9  years$                                | FT; 12 weeks, 4<br>times/week<br>FT; 12 weeks, 4 | Usual Care Usual care                  | Gait<br>speed<br>Gait                              |  |
| (2022) <sup>7</sup><br>Khan et al. (2022) <sup>9</sup>     | $n=15$ , female $=10$ , age $=63\pm8$ years,<br>BMI $=34\pm5$ kg/m², duration $=10\pm8$  | $n=15$ , female $=10$ , age $=63\pm8$ years,<br>BMI $=34\pm5$ kg/m <sup>2</sup> ,   | times/week<br>SE; 12 weeks, 2–3<br>times/week    | None                                   | speed<br>Gait<br>speed                             |  |
| Rodríguez-Reyes<br>et al. (2022) <sup>43</sup>             | years $n=20,\text{female}=14,\text{age}=60.0\pm6.1\text{years},\\ \text{duration}=2.85\pm1.6\text{years}$  | $n=21$ , female $=17$ , age $=58.1\pm8.1$ years, duration $=2.95\pm1.7$ years   | WBV; 12 weeks, 3 times/week                      | Usual care                             | Gait<br>speed                                      |  |
| Arani et al. (2023) <sup>44</sup>                          | $n=22$ , female = 22, age = $52.4 \pm 11.5$<br>years, duration = $6.2 \pm 0.3$ years   | $n=22$ , female = 22, age = 49.3 $\pm$ 9.3 years, duration = 6.3 $\pm$ 0.3 years  | BE; 8 weeks, 3<br>times/week                     | Health education                       | BBS scor   |  |
| Saleh et al. (2024) <sup>45</sup>                          | $n = 20$ , female = 12, age = $57.7 \pm 4.9$ years,<br>BMI = $27.13 \pm 1.69$ kg/m <sup>2</sup> , duration = $9.6 \pm 2.0$ years   | $n = 20$ , female = 11, age = $58.8 \pm 4.5$ years,<br>BMI = $26.72 \pm 1.41$ kg/m <sup>2</sup> , duration = $10.1$ $\pm 2.1$ years | BE; 6 weeks, 3 times/week                        | Usual care                             | Gait<br>speed                                      |  |
| Hosseini et al. (2024) <sup>52</sup>                       | SE: n = 15, female = 15, age = $54.8 \pm 3.3$<br>years, BMI = $30.41 \pm 0.12$ kg/m², duration = $11.2 \pm 3.2$ years  | n = 15, female = 15, age = 55.5 $\pm$ 2.5 years, BMI = 28.44 $\pm$ 14.11 kg/m², duration = 11.3 $\pm$ 2.3 years                     | SE; 12 weeks, 3 times/week.                      | None                                   | TUG tim  |  |
|  | FE: n = 15, female = 15, age = $56.1 \pm 3.4$ years, duration = $11.2 \pm 1.9$ years   |   | FE; 12 weeks, 3 times/week                       |  | Gait<br>speed                                      |  |
| Jimenez-Mazuelas<br>et al. (2024) <sup>53</sup>            | n = 21, female = 10, age = 70 $\pm$ 8.15 years, BMI = 28.2 $\pm$ 4.81 kg/m <sup>2</sup> , duration = 21 $\pm$ 15.56 years  | n = 23, female = 8, age = $70 \pm 9.63$ years,<br>BMI = $27.4 \pm 5.78$ kg/m <sup>2</sup> , duration = $19 \pm 12.59$ years         | BE; 8 weeks, 2 times/week                        | Usual care                             | TUG tim  |  |

BE: balance exercise, SE: strength exercise, ME: multi-component exercise, FT: foot-ankle functional training, WBV: whole-body vibration; TUG: Timed up and go, BBS: Berg Balance Scale, OLS: One-legged stance.

 $-1.71,\,95~\%$  CI =-2.26 to -1.17), and SE (MD  $=-1.45,\,95~\%$  CI =-2.75 to -0.15) could reduce TUG time, while both WBV (MD  $=-3.85,\,95~\%$  CI =-9.18-1.48) and FT (MD  $=-0.57,\,95~\%$  CI =-2.03-0.89) did not reduce TUG time. The 95~% CIs for the four interventions overlapped, suggesting no significant difference among them.

## 3.4.2. Gait speed

As shown in Fig. 3, 11 studies with 456 participants presented the

gait speed and included four types of exercise: BE, SE, WBV and FT. The heterogeneity was moderate in gait speed (I $^2=42\,\%,p=0.060$ ). Pooled data demonstrated that exercise was more effective than non-exercise in increasing gait speed (MD = 0.07, 95 % CI = 0.04–0.11). In subgroup analysis, both BE (MD = 0.11, 95 % CI = 0.04–0.18) and SE (MD = 0.09, 95 % CI = 0.06–0.12) could increase gait speed, while WBV (MD = 0.03, 95 % CI = -0.13–0.20) and FT (MD = -0.02, 95 % CI = -0.09–0.05) did not increase gait speed. In addition, the effect size for SE was larger

Table 2
Risk of bias summary.

| Studies                           | Randomization process | Deviations from the intended | Missing outcome data | Measurement of the outcome | Selection of the reported result | Overall<br>Bias |
|-----------------------------------|-----------------------|------------------------------|----------------------|----------------------------|----------------------------------|-----------------|
| Allet et al. (2010)               | L                     | L                            | L                    | L                          | L                                | L               |
| Song et al. (2011)                | L                     | S                            | L                    | L                          | L                                | L               |
| Lee et al. (2013)                 | L                     | L                            | L                    | L                          | L                                | L               |
| Melai et al. (2014)               | L                     | S                            | L                    | Н                          | L                                | H               |
| Yoosefinejad et al. (2015)        | L                     | S                            | L                    | S                          | L                                | S               |
| Rojhani-Shirazi et al.<br>(2016)  | L                     | L                            | L                    | L                          | L                                | L               |
| Ahmad et al. (2019) (2021)        | L                     | L                            | L                    | L                          | L                                | S               |
| Jamal et al. (2019)               | L                     | L                            | L                    | L                          | L                                | L               |
| Hung et al. (2019)                | L                     | S                            | L                    | L                          | L                                | S               |
| Win et al. (2019)                 | L                     | S                            | L                    | S                          | L                                | S               |
| Venkataraman et al. (2019)        | L                     | L                            | L                    | Н                          | L                                | H               |
| Abdelbasset et al. (2020)         | L                     | S                            | L                    | L                          | L                                | S               |
| Monteiro et al. (2020)            | L                     | S                            | L                    | L                          | L                                | S               |
| Monteiro et al. (2022)            | L                     | L                            | L                    | L                          | L                                | L               |
| Khan et al. (2022)                | L                     | L                            | L                    | L                          | L                                | L               |
| Rodríguez-Reyes et al. (2022)     | L                     | L                            | L                    | S                          | L                                | L               |
| Arani et al. (2023)               | L                     | L                            | L                    | L                          | L                                | L               |
| Saleh et al. (2024)               | L                     | L                            | L                    | L                          | L                                | L               |
| Hosseini et al. (2024)            | L                     | S                            | L                    | S                          | L                                | S               |
| Jimenez-Mazuelas et al.<br>(2024) | L                     | L                            | L                    | S                          | L                                | S               |

L: low risk, H: high risk, S: some concern.

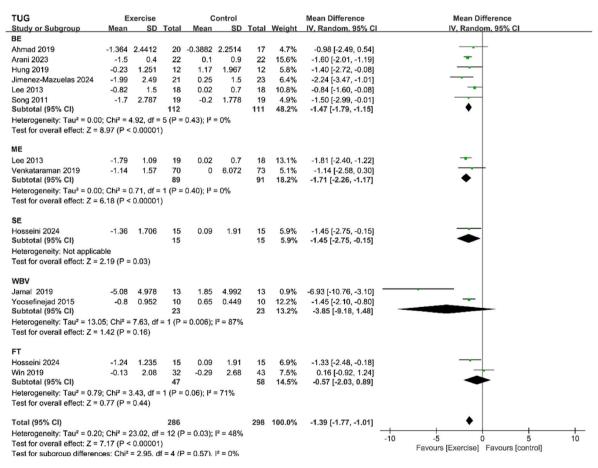


Fig. 2. Forest plot of exercise effects on TUG time.

SD: standard deviation, 95 % CI: 95 % confidence interval, df: degree of freedom, BE: balance exercise, ME: multi-component exercise, SE: strength exercise, WBV: whole-body vibration, FT: foot-ankle functional training; TUG: Timed up and go.

than FT, with no overlap in 95 % CIs, indicating that SE was superior in increasing gait speed.

#### 3.4.3. BBS score

As shown in Fig. 4, six studies with 249 participants presented BBS scores and included two types of exercise: BE and ME. The heterogeneity

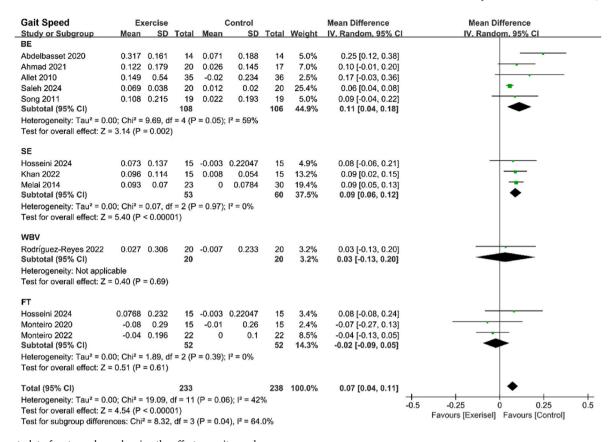


Fig. 3. Forest plot of meta-analyses showing the effect on gait speed.

SD: standard deviation, 95 % CI: 95 % confidence interval, df: degree of freedom, BE: balance exercise, SE: strength exercise, WBV: whole-body vibration, FT: footankle functional training.

| BBS                        | Exercise   |                        | Control               |         | Mean Difference       |        | Mean Difference |                    |  |
|----------------------------|------------|------------------------|-----------------------|---------|-----------------------|--------|-----------------|--------------------|--|
| Study or Subgroup          | Mean       | SD                     | Total                 | Mean    | SD                    | Total  | Weight          | IV. Fixed, 95% C   | IV. Fixed, 95% CI                                  |
| BE                         |            |                        |                       |         |                       |        |                 |                    |  |
| Abdelbasset 2020           | 3.8        | 3.907                  | 14                    | 0.5     | 4.69                  | 14     | 1.4%            | 3.30 [0.10, 6.50]  | -  |
| Arani 2023                 | 0.9        | 1.7                    | 22                    | 0.2     | 0.9                   | 22     | 21.6%           | 0.70 [-0.10, 1.50] | <del>  -</del>                                     |
| Hung 2019                  | 3.41       | 1.471                  | 12                    | 2.09    | 3.519                 | 12     | 3.0%            | 1.32 [-0.84, 3.48] | <del> </del>                                       |
| Lee 2013                   | 0.61       | 1.2                    | 18                    | -0.11   | 0.47                  | 18     | 39.4%           | 0.72 [0.12, 1.32]  | <del></del>  |
| Rojhani-Shirazi 2016       | 2.275      | 4.8656                 | 40                    | -0.2    | 4.997                 | 20     | 2.0%            | 2.48 [-0.18, 5.13] | <del></del>  |
| Song 2011                  | 2.1        | 2.343                  | 19                    | 0.1     | 2.674                 | 19     | 5.5%            | 2.00 [0.40, 3.60]  | <del></del>  |
| Subtotal (95% CI)          |            |                        | 125                   |         |                       | 105    | 72.8%           | 0.93 [0.49, 1.37]  | ♦  |
| Heterogeneity: Chi2 = 6    | 6.05, df = | 5 (P = 0               | ).30); l <sup>2</sup> | = 17%   |                       |        |                 |                    |  |
| Test for overall effect: 2 | Z = 4.17   | (P < 0.00              | 001)                  |         |                       |        |                 |                    |  |
|                            |            |                        |                       |         |                       |        |                 |                    |  |
| ME                         |            |                        |                       |         |                       |        |                 |                    |  |
| Lee 2013                   | 1.89       | 1.52                   | 19                    | -0.11   | 0.47                  | 18     | 27.2%           | 2.00 [1.28, 2.72]  | 🛨  |
| Subtotal (95% CI)          |            |                        | 19                    |         |                       | 18     | 27.2%           | 2.00 [1.28, 2.72]  | ◆  |
| Heterogeneity: Not app     | licable    |                        |                       |         |                       |        |                 |                    |  |
| Test for overall effect: 2 | Z = 5.47   | (P < 0.00)             | 0001)                 |         |                       |        |                 |                    |  |
|                            |            |                        |                       |         |                       |        |                 |                    |  |
| Total (95% CI)             |            |                        | 144                   |         |                       | 123    | 100.0%          | 1.22 [0.85, 1.59]  | •  |
| Heterogeneity: Chi2 = 1    | 2.27, df   | = 6 (P =               | 0.06);                | 2 = 51% | 5                     |        |                 |                    | -10 -5 0 5 10                                      |
| Test for overall effect: 2 | Z = 6.40   | (P < 0.00)             | 0001)                 |         |                       |        |                 |                    | -10 -5 0 5 10 Favours [Exercise] Favours [Control] |
| Test for subgroup diffe    | rences:    | Chi <sup>2</sup> = 6.2 | 22, df =              | 1 (P =  | 0.01), l <sup>2</sup> | = 83.9 | %               |                    | Favours [Exercise] Favours [Control]               |

Fig. 4. Forest plot of meta-analyses showing the effect on BBS. SD: standard deviation, 95 % CI: 95 % confidence interval, df: degree of freedom, BE: balance exercise, ME: multi-component exercise, WBV: whole-body vibration; BBS: Berg Balance Scale.

was moderate in the BBS scores (I $^2=51$  %, p=0.060). Pooled data demonstrated exercise was more effective than non-exercise in increasing BBS score (MD = 1.22, 95 % CI = 0.85–1.59). In subgroup analysis, both BE (MD = 0.93, 95 % CI = 0.49–1.37) and ME (MD = 2.0, 95 % CI = 1.28–2.72) were associated with a significant increase in BBS scores. The 95 % CIs for BE and ME overlapped, indicating no significant difference between the two interventions.

## 3.4.4. OLS time

As shown in Fig. 5, seven studies with 260 participants presented the OLS time with EO and included three types of exercise: BE, ME and WBV. The heterogeneity was moderate in the OLS\_EO time ( $I^2 = 56 \%$ , p = 0.030). Pooled data illustrated that exercise was more effective than non-exercise (MD = 2.37, 95 % CI = 1.87–2.86). Subgroup analysis demonstrated that all three types of exercise, BE (MD = 2.72, 95 %CI =

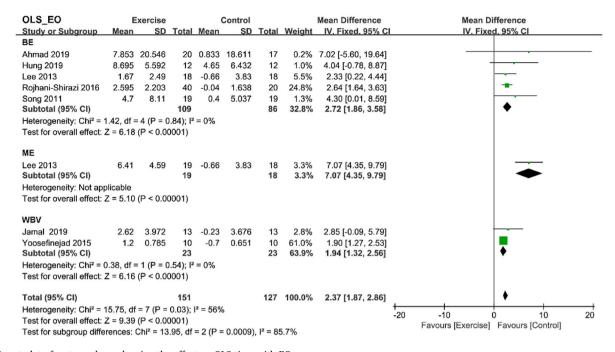


Fig. 5. Forest plot of meta-analyses showing the effect on OLS time with EO.

SD: standard deviation, 95 % CI: 95 % confidence interval, df: degree of freedom, BE: balance exercise, ME: multi-component exercise, WBV: whole-body vibration, OLS: One-legged stance, EO: eyes open.

1.86–3.58), ME (MD = 7.07, 95 %CI = 4.35–9.79), and WBV (MD = 1.94, 95 %CI = 1.32–2.56), significantly increased the time of OLS with EO. Additionally, the effect size for ME was larger than those of BE and WBV, with no overlap in 95 % CI, indicating that ME was superior in increasing OLS time with EO.

As shown in Fig. 6, five studies with 215 participants showed the OLS time with EC and included three types of exercise: BE, ME and WBV. The heterogeneity was low in the OLS\_EC time ( $I^2=0\,\%, p=0.850$ ). Pooled data demonstrated that exercise interventions were more effective than non-exercise in increasing OLS time (MD = 1.76, 95 % CI = 1.25–2.27). Subgroup analysis showed that BE (MD = 1.58, 95 % CI = 1.0–2.17), ME

(MD = 2.61, 95 % CI = 1.28–3.94), and WBV (MD = 1.86, 95 % CI = 0.16–3.56) had significant effects on increasing OLS\_EC time. The 95 % CIs for the three interventions overlapped, suggesting no significant difference among them.

#### 4. Discussion

Falls are one of the major concerns for older adults, and those with DPN especially have a high risk of falls. <sup>4,5</sup> This study included 21 studies that evaluated the effectiveness of five types of exercise in reducing fall risks among older adults with DPN, represented by TUG, gait speed, BBS,

| OLS_EC                              | E          | xercise    |                       | (        | Control                |       | Mean Difference |   | Mean Difference                      |
|-------------------------------------|------------|------------|-----------------------|----------|------------------------|-------|-----------------|---|--------------------------------------|
| Study or Subgroup                   | Mean       | SD         | Total                 | Mean     | SD                     | Total | Weight          | IV, Fixed, 95% CI                       | IV. Fixed, 95% CI                    |
| BE                                  |            |            |                       |          |                        |       |                 |   |                                      |
| Ahmad 2019                          | 2.207      | 4.2898     | 20                    | 0.2429   | 4.2705                 | 17    | 3.4%            | 1.96 [-0.80, 4.73]                      | -                                    |
| Lee 2013                            | 1.01       | 1.86       | 18                    | -0.52    | 2.58                   | 18    | 12.1%           | 1.53 [0.06, 3.00]                       | -                                    |
| Rojhani-Shirazi 2016                | 1.28       | 1.5459     | 40                    | -0.28    | 1.2002                 | 20    | 51.5%           | 1.56 [0.85, 2.27]                       | -                                    |
| Song 2011                           | 2.05       | 2.7851     | 19                    | 0.4      | 2.4761                 | 19    | 9.3%            | 1.65 [-0.03, 3.33]                      | -                                    |
| Subtotal (95% CI)                   |            |            | 97                    |          |                        | 74    | 76.3%           | 1.58 [1.00, 2.17]                       | •                                    |
| Heterogeneity: Chi2 = 0             | 0.09, df = | 3 (P = 0   | ).99); I <sup>2</sup> | = 0%     |                        |       |                 |   |                                      |
| Test for overall effect: 2          | Z = 5.31   | (P < 0.0   | 0001)                 |          |                        |       |                 |   |                                      |
| ME                                  |            |            |                       |          |                        |       |                 |   |                                      |
| Lee 2013                            | 2.09       | 1.3        | 18                    | -0.52    | 2.58                   | 18    | 14.6%           | 2.61 [1.28, 3.94]                       | -                                    |
| Subtotal (95% CI)                   |            |            | 18                    |          |                        | 18    | 14.6%           | 2.61 [1.28, 3.94]                       |                                      |
| Heterogeneity: Not app              | licable    |            |                       |          |                        |       |                 |   |                                      |
| Test for overall effect:            | Z = 3.83   | (P = 0.00) | 001)                  |          |                        |       |                 |   |                                      |
| WBV                                 |            |            |                       |          |                        |       |                 |   |                                      |
| Jamal 2019                          | 1.39       | 2.281      | 13                    | -0.47    | 2.141                  | 13    | 9.0%            | 1.86 [0.16, 3.56]                       |                                      |
| Subtotal (95% CI)                   |            |            | 13                    |          |                        | 13    | 9.0%            | 1.86 [0.16, 3.56]                       |                                      |
| Heterogeneity: Not app              | licable    |            |                       |          |                        |       |                 | • |                                      |
| Test for overall effect: 2          |            | (P = 0.0   | 3)                    |          |                        |       |                 |   |                                      |
| Total (95% CI)                      |            |            | 128                   |          |                        | 105   | 100.0%          | 1.76 [1.25, 2.27]                       | •                                    |
| Heterogeneity: Chi <sup>2</sup> = 2 | 2.01. df = | 5 (P = 0   | ).85); l²             | = 0%     |                        |       |                 |   | <del></del>                          |
| Test for overall effect: 2          |            |            |                       | - , •    |                        |       |                 |   | -4 -2 0 2 4                          |
| Test for subgroup diffe             |            |            | ,                     | 2 (P = 0 | .38), J <sup>2</sup> = | 0%    |                 |   | Favours [Exercise] Favours [Control] |
|                                     |            |            | _,                    | - 1.     | ,,                     |       |                 |   |                                      |

 $\textbf{Fig. 6.} \ \ \textbf{Forest plot of meta-analyses showing the effect on OLS time with EC.}$ 

SD: standard deviation, 95 % CI: 95 % confidence interval, df: degree of freedom, BE: balance exercise, ME: multi-component exercise, OLS: One-legged stance, EC: eyes closed.

and OLS with EO or EC, and further analyzed the different effects of the five types of exercise on each variable.

This study confirmed the positive effects of exercise on fall risks among older adults with DPN, represented by the five variables that predict falls. Previous reviews support this finding.  $^{55-57}$  Thukral et al. pointed out that exercises improved postural control by using TUG, BBS and OLS,  $^{57}$  and Streckmann et al. reported that exercises reduced the risk of falls by using TUG, BBS and OLS among older adults with DPN.  $^{56}$ 

This study demonstrated that both BE and ME could reduce fall risks among older adults with DPN, as assessed by dynamic (e.g., TUG time, gait speed and BBS score) and static balance measures (e.g., OLS time). Previous studies supported our findings regarding  $\mathrm{BE}^{53,58}$  and  $\mathrm{ME}^{59,60}$  in reducing fall risks. Notably, since BE was a component of all ME interventions in included studies, <sup>37,40,54</sup> we refer that the effectiveness of ME lines in the including of BE, with the mechanisms of increasing somatosensory function and improving neuromuscular activation. <sup>61</sup> BE could enhance somatosensory function, which are critical for maintaining postural stability. 3,62 Peripheral sensory deficits caused by DPN reduce motor neuron excitability and delay muscle activation, thereby increasing the risk of falls. 62,63 BE could stimulate mechanoreceptors in the muscles and tendons during unstable surface training, thereby increasing sensory input to the central nervous system. 45,53 Studies have shown that both BE32,44 and ME63 increased ankle proprioception among older adults with DPN. 63 In addition, BE might improve neuromuscular activation to reduce fall risks.<sup>64</sup> Neuromuscular activation deficits in DPN might result from motor axon loss and motor neuron demyelination, leading to reduced lower limb muscle strength and delayed motor responses.<sup>65</sup> BE, which targets postural control during dynamic and static tasks, might enhance motor unit recruitment and increase motor neuron excitability, ultimately improving neuromuscular activation and optimizing postural control strategies. 53,66 Ahmad et al. supported our view by pointing out that BE increased knee and ankle extensor activation during walking and standing among older adults with DPN.63

SE could reduce the risk of falls among older adults with DPN, as evidenced by improving dynamic balance (e.g., TUG time and gait speed). Our observations agree with reports from most previous studies. 12,67,68 The mechanisms by which SE improves dynamic balance may include enhancing muscle strength and power.<sup>69</sup> Muscle strength serves as a crucial determinant of fall risk, <sup>70</sup> especially when it comes to enhancing dynamic balance.<sup>71</sup> Compared to healthy older adults, those with DPN exhibit knee and ankle extensor weakness, reducing gait stability and increasing fall risks.  $^{72}$  This weakness was largely attributed to reduced muscle functions.  $^{65,69}$  Orlando et al. reported that SE could promote muscle fiber hypertrophy, increase fiber recruitment and improve muscle co-activation.<sup>65</sup> Studies showed that SE enhances maximal extensor and flexor strength at the ankle and knee joints in older adults with DPN, improving muscle coordination and gait stability.<sup>3</sup> Moreover, SE could enhance lower limb muscle power among older adults, helping reduce movement reaction time during functional activities. 65,73 Studies indicated that older adults with DPN exhibit reduced muscle power at high angular velocities during isokinetic muscle testing, attributed to the loss of fast-switch muscle fibers. 65 For older adults with DPN, SE could promote motor unit recruitment and enhance post-activation potentiation, consequently increasing muscle contraction velocity and reducing movement reaction time. 73,74 Hosseini et al. further reported that SE could increase the muscle power in the ankle and knee extensors, contributing to improved postural control ability.6

WBV increased the static balance but failed to improve dynamic balance among older adults with DPN, consistent with the results of previous studies. <sup>42,46</sup> The improvement in static balance observed with WBV can be attributed to its inherent static training nature and its effectiveness in enhancing tactile sensation. <sup>42</sup> During WBV training, participants remain stationary, which primarily contributes to enhancing standing balance. <sup>75</sup> This improvement can be assessed solely

through the tests, as it is the primary measure used under static conditions. Additionally, during WBV training, vibrations are transmitted to the human body through the feet. DPN causes distal sensory nerve impairment (e.g., numbness, burning, tingling), resulting in reduced sensory feedback during foot contact and impairing CNS regulation of postural control. It is believed that WBV can improve tactile sensation among older adults with DPN, which primarily contributes to maintaining static balance.  $^{71,75}$ 

This study did not support the effect of FT in reducing fall risk among older adults with DPN, as it showed no improvement in TUG time or gait speed. The finding was supported by Monteiro et al., who reported that FT did not affect gait speed.<sup>7</sup> The ineffectiveness of FT may be attributed to two potential reasons. First, FT is a foot- and ankle-targeted exercise intervention which focuses on increasing the range of motion and reducing plantar pressures. 7,51 A study also indicated that the FT could increase the range of motion in the ankle and reduce forefoot plantar pressures but did not reduce the risk of falls among older adults.<sup>70</sup> However, gait stability depends not only on the local function of the foot-ankle complex but also on the coordination of lower limb joints, somatosensory feedback, and integration capabilities of the central nervous system. 56,77 Second, FT is a low-intensity intervention designed to enhance adherence and incorporate foot exercises into daily routines to mitigate the progression of ulcers. 78 Evidence suggests that FT could require up to one year of training to improve gait characteristics and increase functional activity. 79 However, this study included three articles on FT,7,49,51 with durations of 8-12 weeks, which might not be sufficient to improve TUG time or gait speed.

This study has several limitations. First, the approaches of "control intervention" varied across studies. Second, one study involving BE utilized a 3-week intervention period, which is significantly shorter compared to other studies with durations ranging from 6 to 12 weeks. However, this particular study had a higher frequency of five sessions per week, amounting to a total of 15 exercise sessions, which is comparable to the 12 to 24 sessions reported in other studies. Third, the number of studies including ME, SE, WBV, and FT was relatively smaller (3 articles for each intervention) compared to those involving BE (9), thereby limiting the robustness of the conclusions drawn regarding ME, SE, WBV, and FT.

#### 5. Conclusions

Exercise effectively reduces fall risks among older adults with DPN. Both BE and ME improved dynamic and static balance. SE improved dynamic balance, yet its effect on static balance remains uncertain. WBV improved static balance but did not improve dynamic balance. However, FT had no impact on dynamic balance, and its effect on static balance remains unclear. To reduce fall risks among older adults with DPN, it is recommended to prioritize BE and ME in clinical rehabilitation treatments, followed by SE. WBV is recommended for older adults with DPN who have static balance deficits. Given its ineffectiveness, FT should not be considered for fall prevention.

## Availability of data and material

All data will be made available on request to the corresponding author.

### **Ethics approval**

Not applicable.

# **Author contributions**

Dongmei Wang and Qipeng Song were involved in the conception of the idea. Dongmei Wang and Xiangsheng Pang collaborated on the literature review and produced the figures and tables. All authors performed the meta-analysis and worked together to interpret the results. Dongmei Wang and Qipeng Song wrote the major parts of the manuscript. All authors contributed to the article, approved the submitted version, and read and approved the final.

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#### Declaration of competing interest

Dongmei Wang, Xiangsheng Pang, Peixin Shen, Dewei Mao, and Qipeng Song declare that research was conducted in the absence of any commercial or financial relationships as well as professional interests, personal relationships, or personal beliefs that could be construed as a potential conflict of interest.

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