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Gait characteristics and falls in Parkinson's Disease: A systematic review and meta-analysis

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Abstract

Introduction

Given the high rate of falls during walking in people with idiopathic Parkinson's disease (PD), identifying at risk individuals and developing targeted interventions to reduce falls incidence is paramount. Numerous studies have investigated gait-related risk factors for falls in PD, however findings are inconsistent across studies, and thus a synthesis of the current evidence is needed to guide clinical practice and the development of interventions to reduce falls risk. The objective of this study was to systematically review the literature regarding the association between walking biomechanics and falls in people with PD, and where possible, perform meta-analyses.

Methods

The study was performed in accordance with the PRISMA guidelines. Databases were searched until January 2018 to identify articles that reported on the association between walking biomechanics and prospective or retrospective falls in people with PD.

Results

Twenty-six articles were included (15 prospective studies, 11 retrospective studies). Articles reported on spatiotemporal and kinematic characteristics, and muscle activation patterns. Meta-analyses revealed slower walking speed, lower cadence, shorter strides and more mediolateral head and pelvis motion in those at higher risk of future falls. Findings from prospective and retrospective articles were largely consistent.

Conclusion

Our findings identify spatiotemporal and kinematic characteristics of gait that are risk factors for falls in PD. Modification of these characteristics may have the potential to mediate falls risk, and future research to investigate this possibility is merited. The influence

of body and ground reaction forces, and muscle activation patterns on falls risk in PD is currently under-researched.

1. Background

Falls represent a significant problem for people with idiopathic Parkinson's Disease (PD), with ~60% of people with PD falling per year [1]. The likelihood of falls is higher than in both healthy elderly [2], and other populations prone to falling [3]. The consequences of falls are significant, including reduced quality of life [4], hospitalization [5], fractures, and subsequent to this, increased mortality [6]. While a wide range of factors are known to influence the risk of falls in people with PD [7], falls are more likely to occur during walking gait than in any other activity [8, 9]. Thus, an understanding of the role that gait mechanics plays in mediating falls risk may aid in identifying those at a higher risk of falling and with developing interventions to reduce the risk of future falls.

Gait is achieved through coordinated muscle activation that results in the development of forces across joints and upon the ground, and ultimately produces movement. These muscle activation patterns (which can be measured with electromyography), joint and ground reaction forces (kinetics), and the resulting movement (kinematics), all have the potential to influence walking stability, and thus influence falls risk. Numerous approaches have been taken to quantify gait and its relation to falls in PD, and they can be broadly separated into two approaches: (i) clinical rating scales, and (ii) quantitative biomechanical measures. Clinical rating scales, such as the BESTest [10], Tinetti gait assessment [11], and Dynamic Gait Index [12], typically incorporate the assessment of multiple tasks (e.g. subjective assessment of balance during rising from a chair, standing, and walking). A summative score is then calculated based on performance across all of these components, in all tasks. As such, they are a useful clinical tool in evaluating an individual's limitations and their risk of

falling [13], but do not identify the specific mechanics that are associated with falls. Alternatively, quantitative biomechanical measures, such as step width or cadence, represent components of walking performance that may not only provide an indication of an individual's risk of falling, but also highlight specific modifiable gait characteristics that can be targeted with interventions to reduce the risk of future falls. With the advent of small, wireless, measurement devices such as inertial measurement units (IMUs), clinical assessment of quantitative biomechanics has now become more feasible in the clinical setting [14].

Recent consensus-based clinical practice guidelines for the management of falls risk in PD recommend basic evaluation of gait, with an emphasis on walking speed and shuffling or small-scaled gait as risk factors for falls in PD [7]. Similarly, clinical falls prediction models for PD also include the evaluation of walking speed [15]. While some prospective studies have identified slower walking speed as a risk factor for falls in PD [16-18], others found walking speed not to be a risk factor for falls in PD [19-22]. Furthermore, with the proliferation of new quantitative measures of gait in PD, with particular reference to falls, and the ability to measure these in the clinical and research environment, there is a need to synthesize these data in order to provide a clearer picture of the gait-related risk factors for falls in this population. Such an undertaking has the potential to improve the identification of "at risk" individuals, as well as inform the development of new interventions to reduce the risk of future falls in PD.

Therefore, the primary aim of this study was to systematically review the biomechanical characteristics of walking gait associated with future falls in people with PD. To ensure all possible associations between gait biomechanics and falls in PD were captured in this review, our secondary aim was to systematically review the biomechanical characteristics of walking gait associated with falls history in people with PD.

2. Methods

A systematic review and meta-analyses were conducted according to the PRISMA guidelines. The study protocol was pre-registered (PROSPERO 2016: CRD42016048097).

2.1 Literature search and article selection

2.1.1 Search strategy

A search in the following databases was conducted in November 2016 and updated in January 2018: MEDLINE (PubMed), EMBASE (OVID), Scopus, CINAHL, SportsDiscus and PsychInfo. The search string was defined as follows:

> ((((Parkinson*) OR parkinson disease[MeSH Terms])) AND ((((((((((biomechanic*) OR kinematic*) OR kinetic*) OR electromyogra*) OR emg) OR motion analys*) OR acceler*) OR walk*) OR gait) OR locomot*) OR mobility) OR Biomechanical Phenomena[MeSH Terms])) AND ((((((((((Fall) OR Falls) OR Falling) OR Falle*) OR Trip) OR Trips) OR Tripp*) OR Slip*) OR Accident*) OR accidental falls[MeSH Terms])

In Scopus the search was performed without MeSH terms. In addition, the reference lists of all included articles were searched for additional articles that may have met the inclusion criteria. No language or publication date restrictions were imposed.

2.1.2 Eligibility criteria

All original research articles investigating the biomechanical characteristics of gait associated with falls in people with idiopathic PD were considered for inclusion. Inclusion criteria were articles: (1) assessing straight-line walking, (2) measuring biomechanics (kinematics, kinetics or electromyography), (3) involving men and/or women with idiopathic PD, and (4) assessing the incidence and/or prevalence of accidental falls. Exclusion criteria were: (1) case studies, review articles, books, book chapters, conference abstracts, editorials and letters, (2) articles where idiopathic PD was not the primary disorder, (3) articles where the association between gait biomechanics and falls was not assessed.

2.1.3 Data extraction and synthesis

Two reviewers (MWC and MHC) independently screened the titles, abstracts and full text of articles against the inclusion/exclusion criteria. Any disagreements were resolved by a consensus discussion between the reviewers. In cases where data from the same cohort were reported in multiple articles, data from only one retrospective and one prospective analyses per factor were included (this may have been across multiple articles). Under these circumstances, inclusion was based on the largest sample size, followed by number of factors in the analysis. Where two or more articles reported the same outcome measures, a meta-analysis was performed for 1) articles that compared biomechanics between groups of prospective fallers (or repeat fallers) and non-fallers, and 2) articles that compared biomechanics between groups of retrospective fallers (or repeat fallers) and non-fallers. Furthermore, if there were three or more correlational studies examining the association between frequency of falls and the same biomechanical outcomes, these studies were also included in the meta-analysis. If we could not retrieve sufficient data from a published article, the authors were contacted and additional data were requested.

Review Manager (Version 5.3, The Nordic Cochrane Centre, Copenhagen, Denmark) was used for meta-analyses. For articles reporting between-group comparisons, effect sizes were calculated based on the standardized mean difference (SMD) in biomechanical factors. The following thresholds were used in the interpretation of the SMDs: ≤0.2 = small, >0.2 to 0.5 = moderate, >0.5 to 0.7 = large, and >0.7 very large [23]. If an article included data on a biomechanical factor that was reported in different units across different articles, e.g., walking time across a fixed distance instead of walking speed, the measure represented in most articles in that specific analysis was included. Furthermore, where possible, data reported in alternative units, e.g. walking speed in km/h rather than m/s, were converted and study authors were contacted if additional data were required. Where articles reported on sub-groups (i.e. single fallers and repeat fallers), data were pooled for the purposes of meta-analysis. A random effects model was used due to the expected heterogeneity between articles stemming from different definitions of "fallers", task conditions (e.g. footwear, walking distance etc.) and follow-up period. Between-article effect size heterogeneity was calculated with the Q-test and expressed as the I^2 statistic, with threshold values of 25%, 50% and 75% considered to indicate low, moderate, and high heterogeneity, respectively [24]. Further, given the expected heterogeneity in study design, in order to evaluate the robustness of our meta-analyses, several sensitivity analyses were run independently with the exclusion of articles that adopted atypical methodological approaches in the following areas: (i) inclusion criteria (i.e. all participants were falls naïve and/or participants were not evaluated in an "on" medication state), (ii) definition of fallers (i.e. repeat fallers only), (iii) observation period (i.e. was not equal to 12 months), and (iv) data collection methods (i.e. manual observation or narrowing walkway).

2.1.4 Quality assessment and publication bias

A modified version of the checklist used by Munn et al [25] from the original checklist by Downs and Black [26] was used for assessment of methodological quality of the included articles. In our version, modifications were made to ensure criteria were relevant to retrospective and prospective articles evaluating correlations and/or between-group comparisons. We also included a modified version of item 27 from Downs and Black: "If the study had adequate power to detect any differences". Furthermore, for item 20; "If the main outcomes were valid and reliable", we gave two points if the answer was yes and one point if "accuracy not reported but method clearly described" (Electronic Supplementary Material S1). Articles meeting the inclusion criteria were independently assessed for methodological quality by the two reviewers (MWC and MHC). Any disagreements were resolved by a consensus discussion between the reviewers. Articles scoring 50% or more on the quality index check list were included. Visual inspection of funnel plots was used to identify publication bias.

3. Results

3.1 Article selection

A total of 1,753 abstracts were screened against the inclusion/exclusion criteria, with 155 articles proceeding to full-text screening. Twenty-seven articles proceeded to quality assessment, with one article not reaching the predefined limit of a 50% score on the quality assessment checklist (Electronic Supplementary Material S2), leaving 26 articles in this review (Figure 1; Electronic Supplementary Material S3 and S4). The primary reasons for exclusion from the review were: not assessing walking biomechanics, not assessing falls, or

not evaluating the relationship between walking biomechanics and falls. Authors of 10 articles were contacted for additional data to enable inclusion within the meta-analyses. We were unable to retrieve sufficient data for 3 articles, precluding some of their data from the meta-analyses [20, 27, 28].

3.2 Study characteristics

Of the included 26 articles, 15 were prospective studies, with the remaining 11 retrospective in design (Electronic Supplementary Material S3 and S4). Both retrospective and prospective findings were reported for two participant cohorts, with their data included in the relevant, separate, analyses [21, 29-31]. Three of the articles reporting on a retrospective study design evaluated correlations between gait biomechanics and number of falls [32] or presence/absence of falls [33, 34]. Given these differing definitions of falls between the articles these data could not be pooled for meta-analyses. All of the remaining articles evaluated between-group differences in walking characteristics. Twenty articles reported on walking characteristics at a “preferred” walking speed (also referred to as “comfortable” or “self-selected” pace), five articles reported on “fast” or “as fast as possible” walking speed, and five articles did not report the walking speed adopted in their study. Spatiotemporal characteristics were the most commonly reported biomechanical measures across articles, with walking speed reported in almost all articles. Measures of steps or strides (length, time and time variability) were pooled for meta-analyses as they measure the same construct. Joint and segment kinematics were reported in 5 articles and electromyography in 1 article. Kinetic measures, such as joint moments and reaction forces, were not reported in any articles. In prospective studies the occurrence of falls was monitored for between 2 and 36

months after baseline assessment, while retrospective studies assessed falls over the previous 2 to 12 months.

3.3 Synthesis of results

3.3.1 Spatiotemporal characteristics

Meta-analysis indicated that slower walking speed was associated with increased falls risk, prospectively (Figure 2A); effect sizes were consistent across studies at preferred speed, fast speed, and in articles where walking speed was not reported. This is consistent with retrospective articles where walking speed was slower in previous fallers (SMD: -1.18; 95% CIs: -1.98 to -0.39; Electronic Supplementary Material S5). Of the studies conducted at preferred walking speed, prospective fallers had a mean (±SD) walking speed of 1.03±0.24 m/s (n=486), while prospective non-fallers had a preferred walking speed of 1.14±0.21 m/s (n=626). Slower cadence (Figure 2B), and a shorter step and stride length (Figure 2C), were also observed in prospective fallers, but step width (Figure 2D) did not differ between these groups. Step and stride length were also shorter in retrospective fallers compared with non-fallers (SMD: -0.83; 95% CIs: -1.39 to -0.28; Electronic Supplementary Material S5). Step and stride time, when pooled, were marginally slower in prospective fallers (Figure 2E). Step and stride time variability did not differ between prospective fallers and non-fallers (Figure 2F).

**** INSERT FIGURE 2 HERE ****

In addition to the measures of gait variability reported above, one prospective article evaluated several other measures of the spatiotemporal variability of walking gait. Lord and colleagues [16] found that fallers had greater variability in stance time than non-fallers, despite there being no between-group differences in the variability of step length, step width or swing time. One retrospective article reported greater step time variability in fallers [41], while others reported no differences in stride and swing time variability [42] or walking speed variability [27].

Left-to-right symmetry of gait was reported in one prospective article [16], which showed that fallers had greater swing time asymmetry, but no differences in step time, stance time or step length asymmetry [16]. Similarly, retrospective falls research has highlighted no significant differences in left-to-right swing time symmetry between fallers and non-fallers [42].

3.3.2 Kinematics

Meta-analyses of two prospective articles [22, 36], identified greater mediolateral head and pelvis motion (normalized to walking speed) in fallers versus non-fallers with large and moderate effect sizes, respectively (Figure 3). In meta-analyses of the same two articles, no differences were found in vertical head and pelvis motion normalized to walking speed or in arm swing (Figure 3) [22, 36].

**** INSERT FIGURE 3 HERE ****

In addition to head and pelvis motion, a range of other joint and body segment angles and displacements between prospective fallers and non-fallers have been reported by one research group [22, 36, 43]. Each specific variable, however, was only reported once between datasets (one dataset is reported across two articles [36, 43]), and thus these factors could not be incorporated into meta-analyses. Only knee flexion/extension range of motion was found to significantly differ between groups, with a lower range reported in fallers [36].

Additional kinematic factors only reported in retrospective articles included measures of left-to-right symmetry, head and trunk accelerations and harmonic ratios. No differences in left-to-right symmetry of gait were evident between retrospective fallers and non-fallers with respect to step-to-step trunk accelerations [17], and knee flexion range of motion [27]. The magnitude of head and trunk accelerations were less in those with a history of falls [41]. Similarly, harmonic ratios of the head and trunk were lower in retrospective fallers [41], and were negatively correlated with number of falls [32], indicating less rhythmic movement of the head and trunk in fallers.

3.3.3 Electromyography and Kinetics

Electromyography of three trunk muscles (thoracic erector spinae, lumbar multifidus, external oblique), measured bilaterally, were reported in one prospective article; no differences in muscle activation were reported between PD fallers and non-fallers [22]. Kinetic measures (e.g. forces) were not reported in any of the included articles.

3.3.4 Sensitivity Analyses

Our sensitivity analyses illustrated no change in our findings following the exclusion of studies on the basis of methodological considerations (Electronic Supplementary Material S6). In some cases (step and stride length, and step and stride time, in prospective studies), only one study remained following exclusions, and thus sensitivity analyses were not possible.

3.4 Heterogeneity

Low heterogeneity was observed across all analyses of prospective articles ($I^2 < 25\%$), with the exception of step and stride time variability ($I^2 = 43\%$, moderate heterogeneity), and the sub-groupings of walking speed at fast pace and where pace was not reported ($I^2 = 43\%$ and 45%, respectively, moderate heterogeneity). Analysis of walking speed from retrospective articles was associated with large heterogeneity ($I^2 = 92\%$), primarily resulting from the larger effect size in one article [41]. Similarly, large heterogeneity was observed in the analyses of step and stride length from retrospective articles ($I^2 = 53\text{-}67\%$).

3.5 Quality assessment and publication bias

Of the included 26 articles, the median quality score was 68% (IQR: 63%-77%), with the highest article score of 79%. Items 11 and 12 (external validity), 15 (internal validity, "was an attempt made to blind those measuring the main outcomes to group membership?") and 27 (power) were those that were most frequently not reported. Visual inspection of funnel plots for each of our meta-analyses did not reveal evidence of publication bias (Figure 4).

**** INSERT FIGURE 4 HERE ****

4. Discussion

The findings of this systematic review and meta-analysis demonstrate that slower walking speed (preferred and fast pace), lower cadence, and shorter and slower steps and strides are all associated with future falls in idiopathic PD. In addition, greater mediolateral head and pelvis motion was associated with future falls in this population. Step width did not differ between prospective PD fallers and non-fallers. A number of additional spatiotemporal and kinematic variables relating to gait variability and symmetry were either found not to differ between PD fallers and non-fallers, or were reported in only one article.

Consistent with a recent review [44] and clinical guidelines [7] for the management of falls in PD, our meta-analysis highlights the increased risk of future falls with slower walking speed (at both preferred and fast pace). Similar findings were also reported in a meta-analysis of healthy elderly [45], suggesting that an assessment of walking speed may be a valuable screening tool to identify falls risk in older adults, irrespective of the presence of PD. Of note, walking speed was the most frequently reported factor across articles, and our conclusions are based on a large sample (n=1,945) with low heterogeneity between articles

(I^2=18%). Our meta-analyses of walking gait with retrospective falls also support an association between slower walking speed and falls in PD. These findings remained unchanged in our sensitivity analyses. Of course, it is important to recognize that numerous factors other than gait mechanics will influence the risk of future falls. That said, accurate prediction of future falls risk in the clinical setting can be achieved based on the assessment of falls history, freezing of gait and walking speed [15], underscoring the importance of walking speed in falls risk.

Given that PD patients are known to walk at a slower speed than their healthy elderly counterparts [36, 46, 47], and as we have demonstrated slower walking speed in PD is associated with increased falls risk, one may consider interventions aimed at increasing walking speed. This assumes that slower walking speed plays a causative role in increasing the risk of falls in PD, however evidence of a prospective association between predictor and outcome is not sufficient to infer causation [48]. There is evidence from healthy elderly populations that faster walking speed also increases the risk of falls [49], and that gait is more stable when walking at slower speeds [50], suggesting that one may be less likely to fall when walking more slowly. Similarly, in people with PD, imposed faster walking speeds lead to a decrease in gait stability [51]. Furthermore, if ambulating at a slower walking speed, one will have a longer period of time to react to trip hazards, also potentially contributing to decreased likelihood of falls at a slower walking speed. Thus, it is possible that people with PD, particularly those with poor balance, attempt to minimize falls risk by walking slower [47], rather than slower walking speed being a risk factor for falls. A clearer understanding of the potential causative role of slower walking speed in falls may be gleaned from intervention studies aimed at increasing walking speed: if falls incidence

decreases when we increase walking speed, in combination with the prospective association between walking speed and falls, this would provide strong evidence of a causative relationship. While a number of studies have now examined the effect of treadmill training to increase walking speed [52], and there is some evidence of a short-term (2 week post-intervention) effect on falls incidence [53], as yet no studies have reported on the longer term influence on falls incidence [52]. Thus, there is not yet sufficient evidence available to recommend the use of interventions to increase walking speed in order to decrease the risk of falls. Further investigation of the longer-term effects of such interventions on falls incidence is recommended.

Walking speed is a product of the number of strides taken per unit of time (cadence) and the average length of each stride (stride length). Clinical guidelines for falls risk factors in PD do not currently specify whether it is a short stride length, lower cadence, or a combination of both that are associated with increased falls risk [7]. While the slowing of gait that occurs with the onset of PD is thought to occur due to a downscaling of stride length and not a decrease in cadence [54], our findings indicate that both shorter strides and a lower cadence are associated with increased risk of future falls in PD. Thus, future research trialing interventions to mediate falls risk may wish to consider the manipulation of both stride length and cadence, as both of these are compromised in PD patients at risk of future falls.

By synthesizing data from two different cohorts, albeit from the same lead researcher [22, 36], we have found evidence of greater mediolateral movement of the head and pelvis (when normalized to walking speed) in prospective PD fallers versus non-fallers. This may be indicative of movement of the center of mass of the body toward the outer limits of the

base of support, which would have the potential to compromise balance. Alternatively, it may be indicative of an impaired capacity for people with PD to stabilize the head during gait, thereby affecting the important role the visual and vestibular systems play in providing feedback regarding balance [55, 56]. Notably, these prospective studies found no differences in vertical head and pelvis kinematics, and did not report on anterior-posterior kinematics of the head and pelvis [22, 36]. In reviewing the retrospective literature, we identified two studies that report – in all three planes – an association between the accelerations [41] and regularity of movement [32, 41] of the head, trunk and/or pelvis and prior falls. Thus, future research regarding whether movement patterns of the upper body, particularly in the mediolateral plane, are sensitive predictors of falls risk and/or can be modified to reduce the risk of falls in PD is recommended. Furthermore, in light of the retrospective evidence [32, 41], prospective investigation of the possible role of accelerations and movement regularity in falls risk, including motion in the anterior-posterior plane, would seem prudent. Given the advent of portable measurement technologies, such as inertial measurement units, it is conceivable that the use of these metrics to screen for falls risk and "retrain" movement patterns could be employed in the clinical setting in the near future.

Only one article included in our review reported on differences in muscle activation patterns during walking between PD fallers and non-fallers [22]; no articles reported on the forces or moments acting on the body. While the kinematic factors (i.e. movement) reported in the included articles are typically easier to measure in a clinical setting (with the use of video or pressure mats), they do not necessarily provide a clear indication of the underlying motor patterns of the patient that drive the resulting movements. Given the differences in

movement patterns that we have identified, future research to elucidate differences in joint forces, moments and muscle activation patterns between PD fallers and non-fallers could identify specific targets for intervention to modify gait and reduce the risk of future falls. For example, the ankle plantarflexors play a significant role in driving the body forward and therefore modulating walking speed [57], their function is known to be compromised in people with PD [58] and, hence, ankle plantarflexor activation patterns and kinetics may play a role in the slower walking speeds we have identified as a risk factor for falls in this population.

4.1 Limitations

Our work should be considered in light of the following limitations. First, the meta-analyses relate to the bivariate associations between biomechanical factors and falls. It is possible that these relationships are influenced by a range of other factors, and thus the bivariate relationships presented in our results may not hold equally for all patients with PD. Thus, the clinician and researcher should always be cognizant of the broader range of physiological, psychological and environmental factors that are likely to influence the associations with falls that we have identified [7]. Moreover, investigation of multivariate models of falls risk (based on the characteristics associated with falls in our analyses), and subsequent evaluation of the model's discriminative ability, would aid the clinician in delineating patients at high and low risk of falls. Second, while the data from prospective analyses provide an indication of whether biomechanical factors are risk factors for future falls, they do not provide an indication of the sensitivity and specificity of these factors in predicting future falls. Such an understanding is necessary in the utilization of these data for clinical prediction of future falls. This evidence is already available elsewhere for some

factors, such as walking speed [15, 19, 59], but is yet to be established for others, such as mediolateral head and pelvis motion. Third, other than our prospective analysis of walking speed, each of our meta-analyses were limited to between two and six studies. Thus, our power to detect publication bias was limited in these cases [60]. However, considering that the findings of our sensitivity analyses were consistent with our primary findings and that there was no visual evidence of publication bias in our funnel plots, we consider the likelihood of publication bias to be minimal. Fourth, the current study was limited to straight line walking biomechanics, yet falls frequently occur during an array of other tasks such as turning and upright standing [9]. Some studies have attempted to identify falls risk factors in some of these tasks [20, 61, 62], and this may represent an important area for future research. However, given that straight line walking is the most common task in which falls occur in people with PD [8, 9], and the ease with which this measurement can be taken in a clinical setting, it would seem prudent to focus our attention on falls-related risk factors in walking as a priority.

5. Conclusions

We have identified differences in some spatiotemporal and kinematic characteristics of walking gait between people with PD who fall and those who do not. From the prospective evidence, two sets of risk factors were identified: (i) spatiotemporal characteristics of slower walking speed, lower cadence, shorter step and stride length, and (ii) kinematic characteristics of greater mediolateral head and pelvis motion. This evidence may aid in identifying individuals at a higher risk of future falls, and the kinematic characteristics may represent suitable targets for intervention to reduce the risk of future falls.

Authors' roles

Mark W. Creaby, PhD: Research Project (Conception, Organization, Execution); Statistical Analysis (Design, Execution); Manuscript Preparation (Writing of the first and final draft).

Michael H. Cole, PhD: Research Project (Conception, Organization, Execution); Statistical Analysis (Design, Review and Critique); Manuscript Preparation (Review and Critique).

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Figures

Figure 1. Flow chart of the article inclusion process.

Figure 2. Differences in spatiotemporal characteristics of gait between prospective fallers and non-fallers. A: walking speed (n=1,945); B: cadence (n=241); C: step and stride length (n=681); D: step width (m; n=205); E: step and stride time (n=339); F: step and stride time variability (n=388). SD = standard deviation; Std. Mean Difference = Standardized mean difference; CI = Confidence interval.

Figure 3. Differences in kinematic characteristics of gait between prospective fallers and non-fallers. A: normalized mediolateral head motion (n=128); B: normalized mediolateral pelvis motion (n=128); C: normalized vertical head motion (n=128); D: normalized vertical pelvis motion (n=128); E: arm swing (n=128). SD = standard deviation; Std. Mean Difference = Standardized mean difference; CI = Confidence interval.

Figure 4. Funnel plot of walking speed in prospective fallers versus non-fallers. Each point on the funnel plot represents the standardized mean difference (SMD) for an individual study (x-axis), plotted against the standard error (SE) of the standardized mean difference (y-axis).

Electronic Supplementary Material

ESM S1. Table. Modified Downs and Black study quality assessment tool.

ESM S2. Table. Itemized scoring of risk of bias with the modified Down and Black assessment tool.

ESM S3. Table. Methodological design of the included articles.

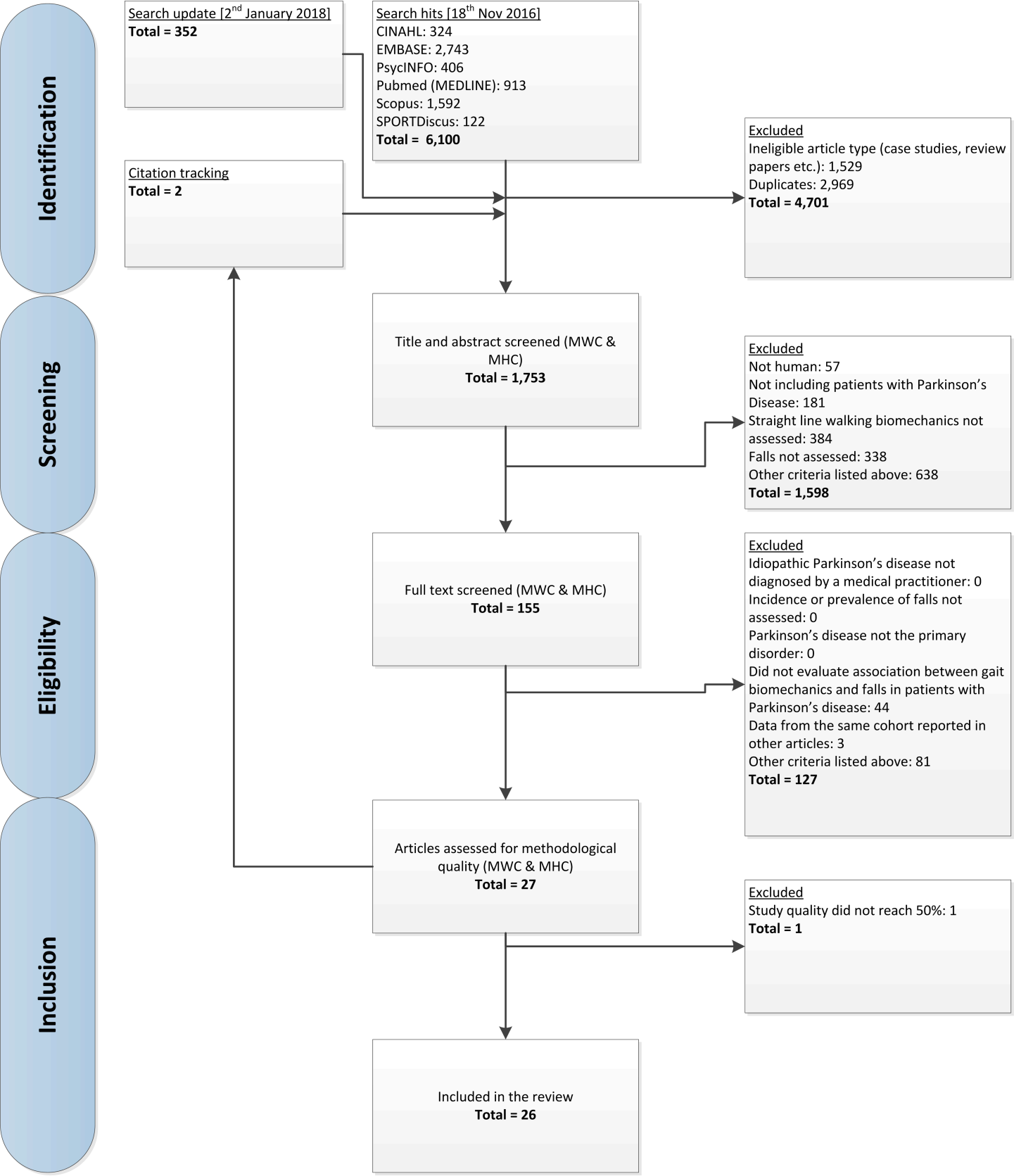
ESM S4. Table. Characteristics of participants in the included articles.

ESM S5. Figure. Differences in spatiotemporal characteristics of gait between retrospective fallers and non-fallers. A: preferred walking speed (m/s; n=401); B: step and stride length (n=126). SD = standard deviation; Std. Mean Difference = Standardized mean difference; CI = Confidence interval.

ESM S6. Table. Sensitivity analysis of meta-analytic findings.

Highlights

- Spatiotemporal characteristics of gait are indicative of falls risk in Parkinson's disease.
- Slower walking speed, lower cadence and shorter strides increase the risk of future falls.
- Emerging evidence indicates greater head and trunk movement increases falls risk.


Identification
Screening
Eligibility
Inclusion
Search update [2nd January 2018]
Total = 352
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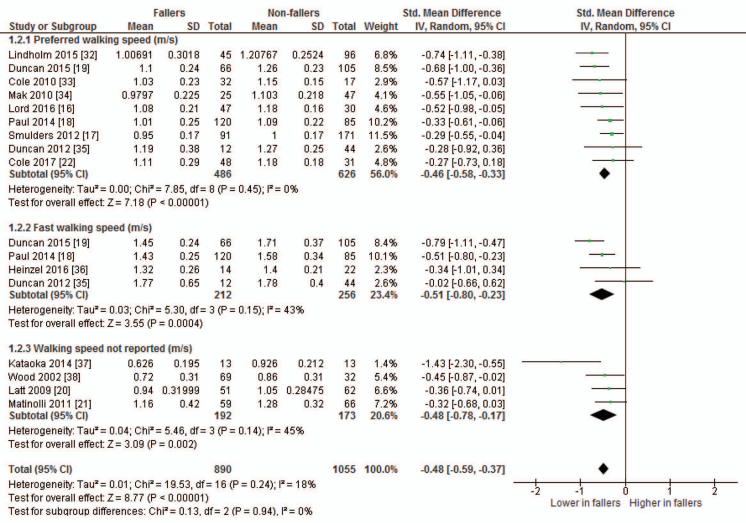
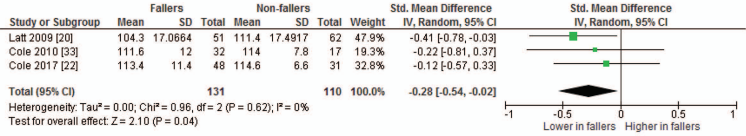
CINAHL: 324
EMBASE: 2,743
PsycINFO: 406
Pubmed (MEDLINE): 913
Scopus: 1,592
SPORTDiscus: 122
Total = 6,100
Citation tracking
Total = 2
Excluded
Ineligible article type (case studies, review papers etc.): 1,529
Duplicates: 2,969
Total = 4,701
Title and abstract screened (MWC & MHC)
Total = 1,753
Excluded
Not human: 57
Not including patients with Parkinson's Disease: 181
Straight line walking biomechanics not assessed: 384
Falls not assessed: 338
Other criteria listed above: 638
Total = 1,598
Full text screened (MWC & MHC)
Total = 155
Excluded
Idiopathic Parkinson's disease not diagnosed by a medical practitioner: 0
Incidence or prevalence of falls not assessed: 0
Parkinson's disease not the primary disorder: 0
Did not evaluate association between gait biomechanics and falls in patients with Parkinson's disease: 44
Data from the same cohort reported in other articles: 3
Other criteria listed above: 81
Total = 127
Articles assessed for methodological quality (MWC & MHC)
Total = 27
Excluded
Study quality did not reach 50%: 1
Total = 1
Included in the review
Total = 26

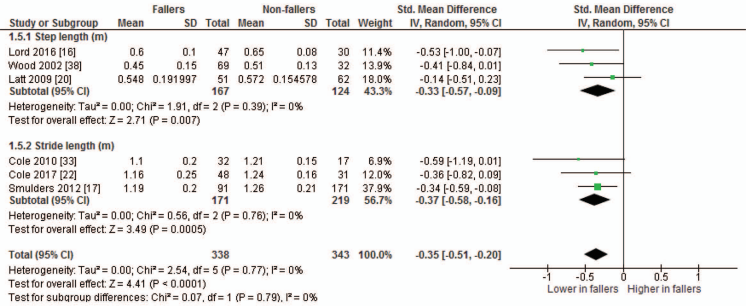
A: Walking Speed



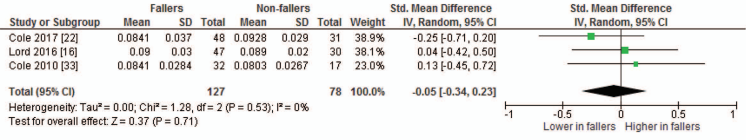
B: Cadence



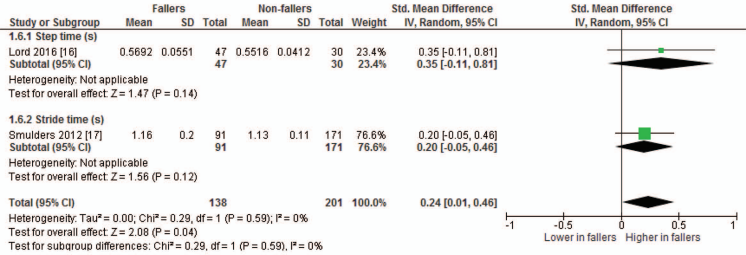
C: Step and stride length



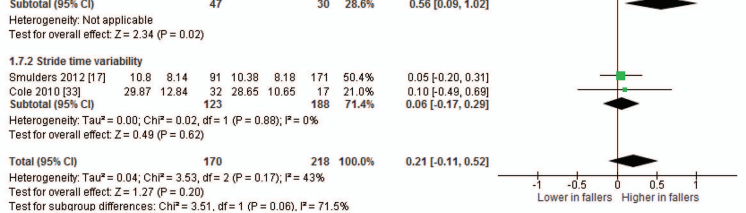
D: Step width



E: Step and stride time



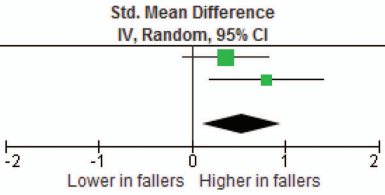
F: Step and stride time variability



A: Normalized mediolateral head motion

Study or Subgroup	Fallers Mean	Fallers SD	Fallers Total	Non-fallers Mean	Non-fallers SD	Non-fallers Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cole 2017 [22]	0.0887	0.0675	48	0.0686	0.0229	31	61.3%	0.36 [-0.09, 0.82]
Cole 2010 [33]	0.0543	0.02	32	0.0401	0.0109	17	38.7%	0.80 [0.19, 1.41]
Total (95% CI)			80			48	100.0%	**0.53 [0.12, 0.95]**

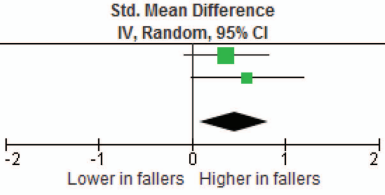
Heterogeneity: Tau² = 0.02; Chi² = 1.26, df = 1 (P = 0.26); I² = 21%
Test for overall effect: Z = 2.51 (P = 0.01)



B: Normalized mediolateral pelvis motion

Study or Subgroup	Fallers Mean	Fallers SD	Fallers Total	Non-fallers Mean	Non-fallers SD	Non-fallers Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cole 2017 [22]	0.0693	0.0315	48	0.0589	0.021	31	63.5%	0.37 [-0.09, 0.82]
Cole 2010 [33]	0.0444	0.0148	32	0.0365	0.0089	17	36.5%	0.59 [-0.01, 1.19]
Total (95% CI)			80			48	100.0%	**0.45 [0.09, 0.81]**

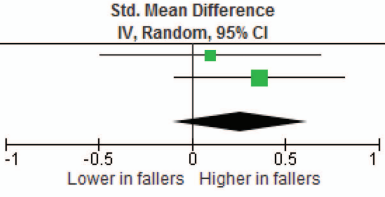
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.44 (P = 0.01)



C: Normalized vertical head motion

Study or Subgroup	Fallers Mean	Fallers SD	Fallers Total	Non-fallers Mean	Non-fallers SD	Non-fallers Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cole 2010 [33]	0.0286	0.0066	32	0.028	0.0045	17	37.4%	0.10 [-0.49, 0.69]
Cole 2017 [22]	0.036	0.0105	48	0.0328	0.0051	31	62.6%	0.36 [-0.10, 0.82]
Total (95% CI)			80			48	100.0%	**0.26 [-0.10, 0.62]**

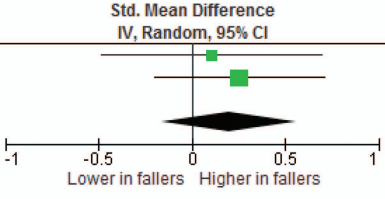
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.43 (P = 0.15)



D: Normalized vertical pelvis motion

Study or Subgroup	Fallers Mean	Fallers SD	Fallers Total	Non-fallers Mean	Non-fallers SD	Non-fallers Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cole 2010 [33]	0.0287	0.0061	32	0.0281	0.0041	17	37.2%	0.11 [-0.48, 0.70]
Cole 2017 [22]	0.0343	0.0071	48	0.0327	0.0046	31	62.8%	0.25 [-0.20, 0.71]
Total (95% CI)			80			48	100.0%	**0.20 [-0.16, 0.56]**

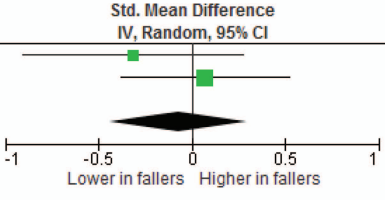
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.09 (P = 0.28)

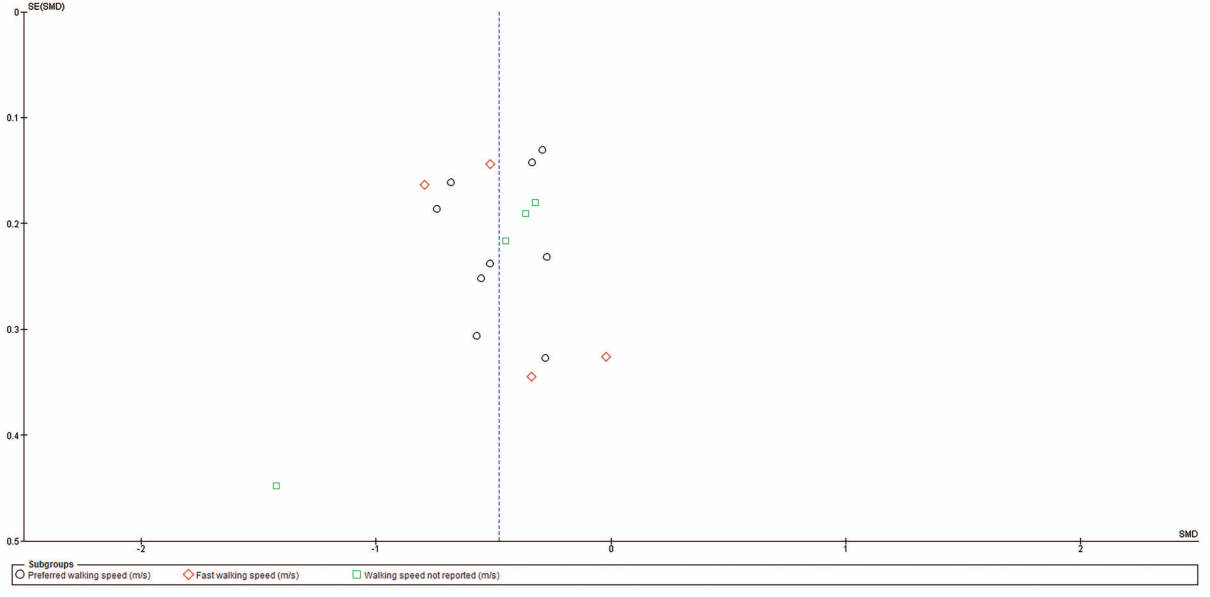


E: Arm swing

Study or Subgroup	Fallers Mean	Fallers SD	Fallers Total	Non-fallers Mean	Non-fallers SD	Non-fallers Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cole 2010 [33]	0.2155	0.1318	32	0.2539	0.0892	17	37.4%	-0.32 [-0.91, 0.27]
Cole 2017 [22]	0.3281	0.1658	48	0.3156	0.182	31	62.6%	0.07 [-0.38, 0.52]
Total (95% CI)			80			48	100.0%	**-0.07 [-0.44, 0.30]**

Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 1 (P = 0.31); I² = 5%
Test for overall effect: Z = 0.39 (P = 0.69)




SE(SMD)
0
0.1
0.2
0.3
0.4
0.5
-2
-1
0
1
2
SMD
Subgroups
Preferred walking speed (m/s)
Fast walking speed (m/s)
Walking speed not reported (m/s)

Electronic Supplementary Material S1. Table. Modified Downs and Black study quality assessment tool.

ITEM		Yes	Unable to determine	No	N/A	Comment
1.	Is the hypothesis/aim/objective of the study clearly described?	☐		☐		
2.	Are the main outcomes to be measured clearly described in the Introduction or Methods sections?	☐		☐		
3.	Are the characteristics of the subjects included in the study clearly described?	☐		☐		
5.	Are the distributions of principle confounders in each group of subjects to be compared clearly described?	☐	☐ partially	☐		
6.	Are the main findings of the study clearly described?	☐		☐		
7.	Does the study provide estimates of the random variability in the data for the main outcome?	☐		☐		
10.	Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.01?	☐		☐		
External validity						
11.	Were the subjects <u>asked to participate</u> in the study representative to the entire population from which they were recruited?	☐	☐	☐		
12.	Where those subjects who were <u>prepared to participate</u> representative of the entire population from which they were recruited?	☐	☐	☐		
Internal validity – Bias						
15.	Was an attempt made to blind those measuring the main outcome?	☐	☐	☐		
16.	If any of the results was based on "data dredging", was this made clear?	☐	☐	☐		
18.	Were the statistical tests used to assess the main outcomes appropriate?	☐	☐	☐		
20.	Were the main outcome measures used accurate (valid and reliable)?	☐	☐ Accuracy not reported but method clearly described	☐		
Internal validity – confounding (selection bias)						
21.	Were the subjects (e.g. the two groups to be compared) recruited from the same population?	☐	☐	☐		
22.	Were the study subjects (the two groups to be compared) recruited over the same period of time?	☐	☐	☐		
25.	Were there adequate adjustments for confounding in the analyses from which the main findings were drawn?	☐	☐	☐		
Bias						
27.	Did the study have sufficient power to detect a clinically important effect?	☐	☐	☐		

Every question was given 1 point for “yes” and zero points for “unable to determine” and “no” except for item 5 and 20, where 2 points were given for “yes” and 1 point for “partially” and “Accuracy not reported but method clearly described”, respectively. To be able to receive 2 points for item 20, the studies have to report accuracy for all gait-related outcomes.

For studies that did not compare groups i.e. correlation studies, items 21 and 22 were excluded. For retrospective studies, items 9, 17 and 26 were excluded.

Electronic Supplementary Material S2. Table. Itemised scoring of risk of bias with the modified Downs and Black assessment tool.

Author, year	Quality score																				Total	
	Reporting								External validity		Internal validity - Confounding									Power	n	%
Item	1	2	3	5	6	7	9†	10	11	12	15	16	17†	18	20	21‡	22‡	25	26†	27		
Maximum score	/1	/1	/1	/2	/1	/1	/1	/1	/1	/1	/1	/1	/1	/1	/2	/1	/1	/1	/1	/1		
Retrospective, correlational studies (/17)																						
(Christofoletti et al. 2016)	1	1	1	2	1	1	N/A	1	0	0	0	1	N/A	1	1	N/A	N/A	1	N/A	0	12	71
(Hubble et al. 2016)	1	1	1	0	1	0	N/A	1	0	0	0	1	N/A	1	1	N/A	N/A	0	N/A	1	9	53
(Paker et al. 2015)	1	1	1	1	1	1	N/A	1	0	0	0	1	N/A	1	2	N/A	N/A	0	N/A	0	11	65
Retrospective, between-group comparison (/19)																						
(Kataoka et al. 2011)	1	1	1	2	1	1	N/A	1	0	0	0	1	N/A	1	1	1	1	1	N/A	0	14	74
(Landers et al. 2008)	1	1	1	1	1	1	N/A	1	0	0	0	1	N/A	1	2	0	1	0	N/A	0	12	63
(Latt et al. 2009a)	1	1	1	2	1	1	N/A	0	0	0	0	1	N/A	1	2	1	0	0	N/A	0	12	63
(Matinolli et al. 2009)	1	0	1	2	1	1	N/A	1	1	0	0	1	N/A	1	1	1	1	1	N/A	0	14	74
(Plotnik et al. 2011)	1	1	1	2	1	1	N/A	1	0	0	0	1	N/A	1	2	1	1	1	N/A	0	15	79
(Soyuer et al. 2017)	0	0	1	2	1	1	N/A	1	0	0	0	0	N/A	1	0	1	1	1	N/A	0	10	53
(Toosizadeh et al. 2015)	1	1	1	2	1	1	N/A	1	0	0	0	1	N/A	1	1	1	1	0	N/A	0	13	68
(Weiss et al. 2014)	1	1	1	2	1	1	N/A	1	0	0	0	1	N/A	1	1	1	1	0	N/A	0	13	68
(Weller et al. 1992)	0	1	1	0	1	1	N/A	1	0	0	0	0	N/A	1	0	0	1	0	N/A	0	7	37*

†=criteria only rated in prospective studies; ‡=criteria only rated in between-group comparison studies; *=study excluded from further analysis due to total score <50%.

Electronic Supplementary Material S2. Table continued. Itemised scoring of risk of bias with the modified Downs and Black assessment tool.

Author, year	Quality score																				Total	
	Reporting								External validity		Internal validity - Confounding									Power	n	%
Item	1	2	3	5	6	7	9†	10	11	12	15	16	17†	18	20	21‡	22‡	25	26†	27		
Maximum score	/1	/1	/1	/2	/1	/1	/1	/1	/1	/1	/1	/1	/1	/1	/2	/1	/1	/1	/1	/1		
Prospective, between-group comparison (/22)																						
(Cole et al. 2010)	1	1	1	2	1	1	0	0	0	0	0	0	1	1	1	1	1	1	0	0	13	59
(Cole et al. 2011)	1	1	1	2	1	1	0	0	0	0	0	1	1	1	2	1	1	1	0	0	15	68
(Cole et al. 2017)	1	1	1	2	1	1	1	0	0	0	0	1	1	1	1	1	1	0	1	1	16	73
(Duncan et al. 2012)	1	1	1	2	0	0	0	1	0	0	1	1	1	1	1	1	1	0	0	0	13	59
(Duncan et al. 2015)	1	1	1	1	1	1	0	1	0	0	0	1	1	1	1	1	1	0	0	0	13	59
(Heinzel et al. 2016)	1	1	0	2	1	1	0	1	0	0	0	1	1	1	0	1	1	1	0	0	13	59
(Kataoka et al. 2014)	1	1	1	2	1	1	1	1	0	0	0	1	1	1	0	1	1	1	0	0	15	68
(Latt et al. 2009b)	0	1	1	1	1	1	1	0	0	0	0	1	1	1	1	1	1	0	1	0	13	59
(Lindholm et al. 2015)	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	0	17	77
(Lord et al. 2016)	1	1	1	2	1	1	0	1	0	0	0	1	1	1	2	1	1	1	1	0	17	77
(Mak et al. 2010)	1	1	1	2	1	1	1	1	0	0	0	1	1	1	2	1	1	0	1	0	17	77
(Matinolli et al. 2011)	1	0	1	2	1	1	0	1	1	1	0	1	1	1	1	1	1	1	0	0	16	73
(Paul et al. 2014)	1	1	1	2	1	1	1	1	0	0	0	1	1	1	2	1	1	0	1	0	17	77
(Smulders et al. 2012)	1	1	1	2	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	0	17	77
(Wood et al. 2002)	1	1	1	2	1	0	1	1	1	0	0	1	1	1	1	1	1	1	1	0	17	77

†=criteria only rated in prospective studies; ‡=criteria only rated in between-group comparison studies; *=study excluded from further analysis due to total score <50%.

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Electronic Supplementary Material S3. Table. Methodological design of the included articles.

Article	Faller Definition	Observation period	Walking speed	Biomechanical outcomes Variables	Measurement tool
Retrospective, correlational studies					
(Christofoletti et al. 2016)	Two or more falls	6 months	Preferred; Fast	Walking speed	Pressure sensitive walkway
(Hubble et al. 2016)	One or more falls	12 months	Preferred	Walking speed Axial kinematics (accelerations)	Timing gates Accelerometers
(Paker et al. 2015)	NR	12 months	Preferred	Walking speed	NR
Retrospective, between-group comparison studies					
(Kataoka et al. 2011)	One or more falls	6 months	Preferred	Walking speed Spatiotemporal characteristics	Video camera (two-dimensional)
(Landers et al. 2008)	One or more falls	12 months	Preferred	Walking speed	NR
(Latt et al. 2009a)	One or more falls	12 months	Preferred	Walking speed Spatiotemporal characteristics Axial kinematics (accelerations)	Accelerometers
(Matinolli et al. 2009)	One or more falls	3 months	Preferred	Walking speed	NR
(Plotnik et al. 2011)	NR	12 months	Preferred	Walking speed Spatiotemporal characteristics	Stopwatch Pressure sensitive insoles
(Soyuer et al. 2017)	NR	6 months	NR	Walking speed	Stopwatch
(Toosizadeh et al. 2015)	One or more falls	12 months	Preferred	Walking speed Spatiotemporal characteristics Appendicular kinematics	Integrated accelerometers & gyroscopes
(Weiss et al. 2014)	One or more falls	12 months	Preferred	Walking speed	NR
Prospective, between-group comparison studies					
(Cole et al. 2010)	One or more falls	12 months	Preferred	Walking speed Spatiotemporal characteristics Axial & appendicular kinematics	Opto-electronic motion analysis (three-dimensional)
(Cole et al. 2011)	One or more falls	12 months	Preferred	Walking speed Spatiotemporal characteristics Axial & appendicular kinematics	Opto-electronic motion analysis (three-dimensional)
(Cole et al. 2017)	One or more falls	12 months	Preferred	Walking speed Spatiotemporal characteristics Axial & appendicular kinematics Axial muscle activation patterns	Opto-electronic motion analysis (three-dimensional) Electromyography
(Duncan et al. 2012)	Two or more falls	6 months	Preferred; fast	Walking speed	Pressure sensitive walkway
(Duncan et al. 2015)	One or more falls	6 months	Preferred; fast	Walking speed	Stopwatch
(Heinzel et al. 2016)	One or more falls	2.8 ± 1 years; varied between participants	Fast	Walking speed	NR
(Kataoka et al. 2014)	One or more falls	24 months	NR	Walking speed Spatiotemporal characteristics	Video camera (two-dimensional)
(Latt et al. 2009b)	One or more falls	12 months	NR	Walking speed Spatiotemporal characteristics	Accelerometers
(Lindholm et al. 2015)	One or more falls	6 months	Preferred	Walking speed	NR
(Lord et al. 2016)	One or more falls; no previous history of falls	36 months	Preferred	Walking speed Spatiotemporal characteristics	Pressure sensitive walkway
(Mak et al. 2010)	One or more falls	12 months	Preferred	Walking speed	Pressure sensitive walkway
(Matinolli et al. 2011)	Two or more falls	24 months	NR	Walking speed	NR
(Paul et al. 2014)	One or more falls	6 months	Preferred; fast	Walking speed	Stopwatch
(Smulders et al. 2012)	Two or more falls	12 months	Preferred	Walking speed Spatiotemporal characteristics	Accelerometers
(Wood et al. 2002)	One or more falls	12 months	NR	Walking speed Spatiotemporal characteristics	NR

NR = Not reported.

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Electronic Supplementary Material S4. Table. Characteristics of participants in the included articles.

Article	Fallers					Non-fallers				
	n (% female)	Age (mean ± SD)	Disease severity UPDRS	H&Y	LEDD (mg/d)	n (% female)	Age (mean ± SD)	Disease severity UPDRS	H&Y	LEDD (mg/d)
Retrospective, correlational studies										
(Christofoletti et al. 2016)	NR Data for total sample: 114 (NR)	NR 66.6 ± 9.4	NR UPDRS-MDS III: 34.8 ± 10.4	NR 2.4 ± 0.4	NR 810.6 ± 640.3	NR	NR	NR	NR	NR
(Hubble et al. 2016)	23 (NR) Data for total sample: 29 (28%)	NR 64.7 ± 6.4	NR UPDRS III: 14.4 ± 11.5	NR 1.7 ± 0.7	NR 618.3 ± 432.1	6 (NR)	NR	NR	NR	NR
(Paker et al. 2015)	24 (NR) Data for total sample: 50 (44%)	NR 66.7 ± 8.6	NR NR	NR 1.96 ± 1.2	NR NR	26 (NR)	NR	NR	NR	NR
Retrospective, between-group comparison studies										
(Kataoka et al. 2011)	15 (NR) Data for total sample: 30 (53%)	69.1 ± 7.5 68.3 ± 7	UPDRS III: 21.2 ± 10.7 UPDRS III: 19.3 ± 8.7	3.0 ± 0.0 3.0 ± 0.0	397.8 ± 291.2 390.3 ± 245.0	15 (NR)	67.4 ± 6.5	UPDRS III: 17.4 ± 5.9	3.0 ± 0.0	382.7 ± 198.6
(Landers et al. 2008)	25 (44%)	71.8 ± 7.4	UPDRS III: 16.3 ± 5.3	3.0 ± 0.55	NR	24 (63%)	70.1 ± 6.9	UPDRS III: 11.8 ± 5.1	2.1 ± 0.61	NR
(Latt et al. 2009a)	33 (55%)	67 ± 2	UPDRS Total: 42 ± 5	3, 3-4‡	958 ± 241	33 (55%)	63 ± 4	UPDRS Total: 25 ± 4	1, 1-1‡	666 ± 133
(Matinolli et al. 2009)	42 (38%)	69.4 ± 9.3	UPDRS Total: 53.1 ± 19.7	2.4 ± 0.6	533.3 ± 425.9	77 (31%)	66.6 ± 10.7	UPDRS Total: 39.1 ± 15.4	2.1 ± 0.6	337.7 ± 266.6
(Plotnik et al. 2011)	16 (31%)	68.6 ± 6.7	UPDRS Total: 36.2 ± 10.8	2.1 ± 0.6	NR	14 (29%)	62.8 ± 6.8	UPDRS Total: 32.7 ± 9.7	2.1 ± 0.6	NR
(Soyuer et al. 2017)	22 (50%)	62.09 ± 12.5	UPDRS Total: 21.27 ± 13.7	2.1 ± 0.8	NR	65 (40%)	60.77 ± 12.1	UPDRS Total: 15.54 ± 13.7	1.9 ± 0.7	NR
(Toosizadeh et al. 2015)	NR Data for total sample: 15 (47%)	NR 71.2 ± 6.3	NR UPDRS III: 34.8 ± 13.9	NR 2.9 ± 0.9	NR 517 ± 380	NR	NR	NR	NR	NR
(Weiss et al. 2014)	40 (35%)	66.5 ± 8.21	UPDRS-MDS III: 40.78 ± 13.1	2.9 ± 0.8	400.1 ± 353.6	67 (19%)	64 ± 9.76	UPDRS-MDS III: 40.15 ± 13.35	2.4 ± 0.5	454.6 ± 341.8

UPDRS = Unified Parkinson's Disease Rating Scale; UPDRS III = Motor sub-score of the UPDRS; UPDRS-MDS III = Motor sub-score of the Movement Disorders Society revision of the UPDRS; H&Y = Hoehn & Yahr stage; LEDD = Levodopa equivalent daily dosage; NR = Not reported; †=median; ‡=inter-quartile range; ¥ = absolute range.

Electronic Supplementary Material S4. Table continued. Characteristics of participants in the included articles.

Article	Fallers					Non-fallers				
	n (% female)	Age (mean ± SD)	Disease severity UPDRS	H&Y	LEDD (mg/d)	n (% female)	Age (mean ± SD)	Disease severity UPDRS	H&Y	LEDD (mg/d)
Prospective, between-group comparison studies										
(Cole et al. 2010)	32 (38%)	66.9 ± 11.9	UPDRS Total: 34.5 ± 15.3	1.8 ± 0.6	688.8 ± 617.6	17 (24%)	66.2 ± 5.77	UPDRS Total: 26.6 ± 15.3	1.6 ± 0.6	598.8 ± 312.6
(Cole et al. 2011)	32 (38%)	66.9 ± 11.9	UPDRS Total: 34.5 ± 15.3	1.8 ± 0.6	688.8 ± 617.6	17 (24%)	66.2 ± 5.77	UPDRS Total: 26.6 ± 15.3	1.6 ± 0.6	598.8 ± 312.6
(Cole et al. 2017)	48 (40%)	69.1 ± 8.31	UPDRS Total: 38.2 ± 14.5	2.1 ± 0.7	763.0 ± 493.5	31 (29%)	66.5 ± 7.79	UPDRS Total: 29.4 ± 10	1.4 ± 0.4	489.7 ± 337.9
(Duncan et al. 2012)	12 (42%)	68.7 ± 10.7	NR	2.7 ± 0.5	NR	44 (41%)	69.6 ± 7.96	NR	2.3 ± 0.4	NR
(Duncan et al. 2015)	66 (45%)	68.5 ± 9.53	UPDRS-MDS III: 35 ± 15.4	NR	NR	105 (42%)	65.51 ± 9.13	UPDRS-MDS III: 29.96 ± 10.79	NR	NR
(Heinzel et al. 2016)	14 (36%)	64.6 ± 7.9	UPDRS-MDS III: 36.8 ± 16	2.6 ± 0.7	NR	22 (41%)	64.2 ± 6.7	UPDRS-MDS III: 28.4 ± 12.7	2.3 ± 0.7	NR
(Kataoka et al. 2014)	13 (NR)	63.8 ± 7.3	UPDRS III: 22.7 ± 10.3	3.0 ± 0.0	405.6 ± 225.8	13 (NR)	66.8 ± 6.1	UPDRS III: 14.6 ± 4.6	3.0 ± 0.0	352.1 ± 246.0
(Latt et al. 2009b)	51 (43%)	68.3 ± 7.47	NR	2.5 ± 0.7	NR	62 (44%)	64.4 ± 10.6	NR	1.6 ± 0.7	NR
(Lindholm et al. 2015)	45 (NR) Data for total sample: 141 (46%)	NR 68 ± 9.7	NR UPDRS III: 13†, 8-18‡	NR 2†, 2-3‡	NR 400†, 286-600‡	96 (NR)	NR	NR	NR	NR
(Lord et al. 2016)	47 (32%)	68.8 ± 10.7	UPDRS-MDS III: 24.6 ± 9	2.0 ± 0.7	164.3 ± 151.2	30 (17%)	68 ± 8.2	UPDRS-MDS III: 23.6 ± 11.7	1.8 ± 0.6	164.1 ± 129.5
(Mak et al. 2010)	25 (48%)	62.99 ± 7.8	UPDRS III: 25.93 ± 9.77	2.8 ± 0.6	590.5 ± 415.9	47 (47%)	63.7 ± 8.4	UPDRS III: 21.3 ± 9.4	2.6 ± 0.4	379.9 ± 310.9
(Matinolli et al. 2011)	59 (36%)	68.9 ± 10.4	UPDRS Total: 51.6 ± 21	2.4 ± 0.7	526.3 ± 406.5	66 (32%)	67.1 ± 10.1	UPDRS Total: 39.4 ± 14.7	2.1 ± 0.6	309.9 ± 235.9
(Paul et al. 2014)	120 (48%)	68.7 ± 9.6	UPDRS III: 25.9 ± 11.7	2.6 ± 0.6	NR	85 (35%)	66.8 ± 8.8	UPDRS III: 23.4 ± 10.9	2.4 ± 0.6	NR
(Smulders et al. 2012)	91 (37%)	66.3 ± 7.5	UPDRS III: 36.7 ± 9.4	2.0 ± 0.3	NR	171 (35%)	64.6 ± 8.1	UPDRS III: 32.7 ± 9.1	2.0 ± 0.2	NR
(Wood et al. 2002)	69 (46%)	75†, 54-92¥	UPDRS Total: 37†, 8-64¥	2.0†, 1-4¥	400†, 0-1250¥	32 (59%)	75†, 60-92¥	UPDRS Total: 28†, 9-44¥	1.5†, 1-3¥	375†, 0-800¥

UPDRS = Unified Parkinson's Disease Rating Scale; UPDRS III = Motor sub-score of the UPDRS; UPDRS-MDS III = Motor sub-score of the Movement Disorders Society revision of the UPDRS; H&Y = Hoehn & Yahr stage; LEDD = Levodopa equivalent daily dosage; NR = Not reported; †=median; ‡=inter-quartile range; ¥ = absolute range.

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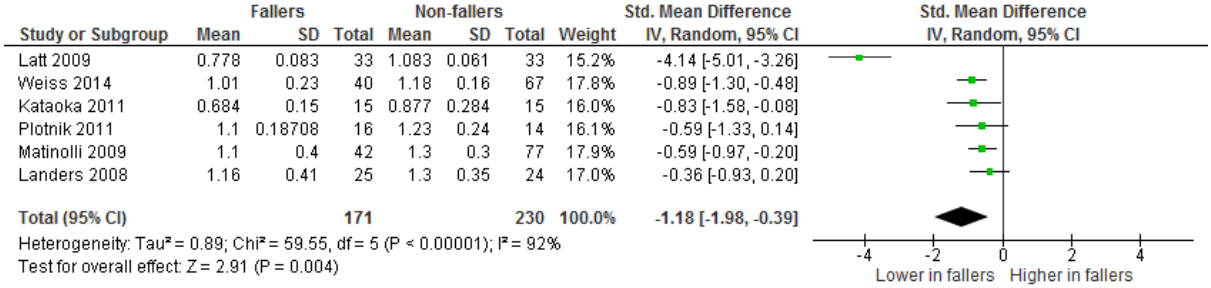
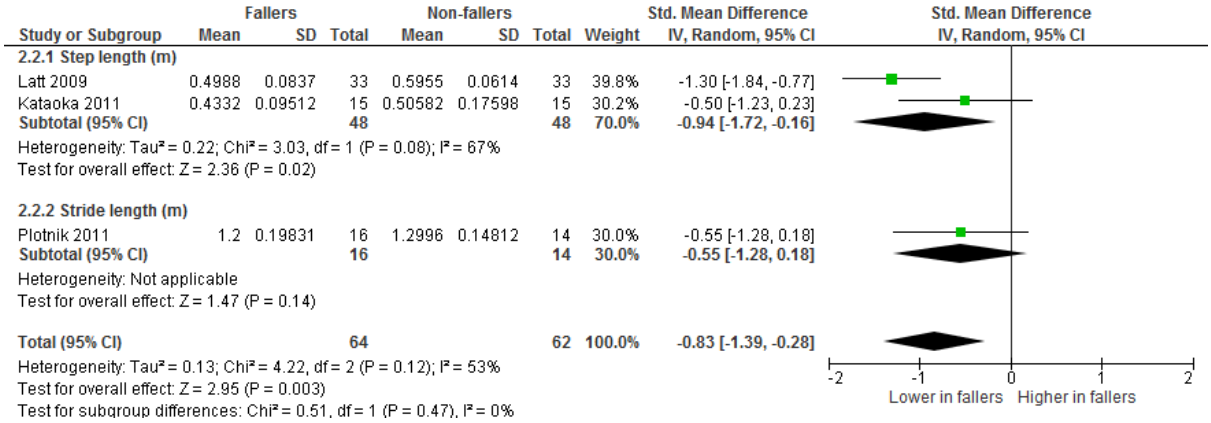
Electronic Supplementary Material S5. Figure. Differences in spatiotemporal characteristics of gait between retrospective fallers and non-fallers. A: preferred walking speed (m/s; n=401); B: step and stride length (n=126). SD = standard deviation; Std. Mean Difference = Standardized mean difference; CI = Confidence interval.

A: Preferred walking speed



B: Step and stride length



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Electronic Supplementary Material S6. Table. Sensitivity analysis of meta-analytic findings.

	All studies			Atypical inclusion criteria			Atypical definition of fallers			Atypical observation period			Atypical data collection methods			Findings with exclusion of studies
Factor	**Studies (n)**	**Participants (n)**	**SMD**	**Studies (n)**	**Participants (n)**	**SMD**	**Studies (n)**	**Participants (n)**	**SMD**	**Studies (n)**	**Participants (n)**	**SMD**	**Studies (n)**	**Participants (n)**	**SMD**	
Prospective studies																
Walking speed	14	1945	-0.48 [-0.59, -0.37]	8	1216	-0.52 [-0.66, -0.37]	11	1446	-0.54 [-0.66, -0.43]	6	676	-0.37 [-0.53, -0.21]	13	1919	-0.46 [-0.56, -0.37]	No changes
Cadence	3	241	-0.28 [-0.54, -0.02]	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No changes
Step width	3	205	0.05 [-0.34, 0.23]	2	128	-0.11 [-0.47, 0.26]	No studies removed	N/A	N/A	2	128	-0.11 [-0.47, 0.26]	No studies removed	N/A	N/A	No changes
Step / stride length	6	681	-0.35 [-0.51, -0.20]	3	205	-0.29 [-0.55, -0.03]	5	419	-0.36 [-0.56, -0.16]	5	604	-0.33 [-0.50, -0.16]	5	580	-0.35 [-0.51, -0.18]	No changes
Step/stride time	2	339	0.24 [0.01, 0.46]	0	N/A	N/A	1	N/A	N/A	1	N/A	N/A	No studies removed	N/A	N/A	No changes; in three analyses insufficient studies retained to perform meta-analyses
Step/stride time variability	3	388	0.21 [-0.11, 0.52]	1	N/A	N/A	2	126	0.36 [-0.08, 0.81]	2	311	0.06 [-0.17, 0.29]	No studies removed	N/A	N/A	No changes; in one analysis insufficient studies retained to perform meta-analyses
Normalized mediolateral head motion	2	128	0.53 [0.12, 0.95]	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No changes
Normalized mediolateral pelvis motion	2	128	0.45 [0.09, 0.81]	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No changes
Normalized vertical head motion	2	128	0.26 [-0.10, 0.62]	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No changes
Normalized vertical pelvis motion	2	128	0.20 [-0.16, 0.56]	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No changes
Arm swing	2	128	-0.07 [-0.44, 0.30]	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No studies removed	N/A	N/A	No changes
Retrospective studies																
Walking speed	6	401	-1.18 [-1.98, -0.39]	4	264	-1.38 [-2.72, -0.04]	5	371	-1.30 [-2.23, -0.37]	4	252	-1.46 [-2.78, -0.14]	5	371	-1.26 [-2.19, -0.33]	No changes
Step / stride length	3	126	-0.83 [-1.39, -0.28]	2	96	-0.97 [-1.70, -0.23]	2	96	-0.94 [-1.72, -0.16]	2	96	-0.97 [-1.70, -0.23]	2	96	-0.97 [-1.70, -0.23]	No changes