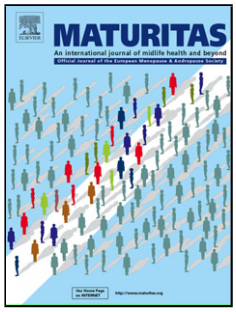

Title: Vitamin D and walking speed in older adults: Systematic review and meta-analysis

Authors: Cedric Annweiler, Samir Henni, Stéphane Walrand, Manuel Montero-Odasso, Gustavo Duque, Guillaume T Duval

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Vitamin D and walking speed in older adults:

Systematic review and meta-analysis

Running title: Vitamin D and gait

Cedric Annweiler, MD, PhD [1,2]

Samir Henni, MD, MSc [3]

Stéphane Walrand, PhD [4]

Manuel Montero-Odasso, MD, PhD [5]

Gustavo Duque, MD, PhD [6,7]

Guillaume T Duval, MD, MSc [1]

1: Department of Neuroscience and Aging, Division of Geriatric Medicine and Memory Clinic; Research Centre on Autonomy and Longevity; Angers University Hospital; UPRES EA 4638, University of Angers, UNAM, Angers, France; 2: Robarts Research Institute, Department of Medical Biophysics, Schulich School of Medicine and Dentistry, the University of Western Ontario, London, Ontario, Canada; 3: Department of Sports Medicine and Vascular Investigations, University Hospital, Angers, France; 4: Université Clermont Auvergne, INRA, UNH, Unité de Nutrition Humaine, CRNH Auvergne, F-63000 Clermont-Ferrand, France; 5: Department of Medicine, Division of Geriatric Medicine, Parkwood Institute; Gait and Brain Lab, Lawson Health Research Institute, University of Western Ontario, London, ON, Canada; 6: Australian Institute for Musculoskeletal Science (AIMSS), The University of Melbourne and Western Health, St. Albans, Victoria, Australia; 7: Department of Medicine – Western Health, Melbourne Medical School, The University of Melbourne, St. Albans, Victoria, Australia.

Corresponding author: Cédric Annweiler, MD, PhD, Department of Geriatric Medicine, Angers University Hospital, 49933 Angers Cedex 9, France; E-mail: CeAnnweiler@chu-angers.fr; Phone: ++33 2 41 35 47 25; Fax: ++33 2 41 35 48 94

Highlights

- Vitamin D is involved in musculoskeletal health.
- Lower circulating levels of 25-hydroxyvitamin D are associated with slower walking speed.
- We found clinically relevant differences in walking speed between people of insufficient vitamin D status and those of adequate status.
- Future analyses should examine the effects of vitamin D supplementation on walking speed.

ABSTRACT

Vitamin D is involved in musculoskeletal health. There is no consensus on a possible association between circulating 25-hydroxyvitamin D (25OHD) concentrations and walking speed, a 'vital sign' in older adults. Our objective was to systematically review and quantitatively assess the association of 25OHD concentration with walking speed. A Medline search was conducted on June 2017, with no limit of date, using the MeSH terms "Vitamin D" OR "Vitamin D Deficiency" combined with "Gait" OR "Gait disorders, Neurologic" OR "Walking speed" OR "Gait velocity". Fixed-effect meta-analyses were performed to compute: i) mean differences in usual and fast walking speeds and Timed Up and Go test (TUG) between participants with severe vitamin D deficiency (≤25nmol/L) (SVDD), vitamin D deficiency (≤50nmol/L) (VDD), vitamin D insufficiency (≤75nmol/L) (VDI) and normal vitamin D (>75nmol/L) (NVD); ii) risk of slow walking speed according to vitamin D status. Of the 243 retrieved studies, 22 observational studies (17 cross-sectional, 5 longitudinal) met the selection criteria. The number of participants ranged between 54 and 4,100 (0-100% female). Usual walking speed was slower among participants with hypovitaminosis D, with a clinically relevant difference compared with NVD of -0.18m/s for SVDD, -0.08m/s for VDD and -0.12m/s for VDI. We found similar results regarding the fast walking speed (mean differences -0.04m/s for VDD and VDI compared with NVD) and TUG (mean difference 0.48s for SVDD compared with NVD). A slow usual walking speed was positively associated with SVDD (summary OR= 2.17[95%CI:1.52–3.10]), VDD (OR=1.38[95%CI:1.01–1.89])

and VDI (OR=1.38[95%CI:1.04–1.83]), using NVD as the reference. In conclusion, this meta-analysis provides robust evidence that 25OHD concentrations are positively associated with walking speed among adults.

KEYWORDS

walking speed; gait disorders; muscles; neurology; vitamin D; vitamin D deficiency; older adults

1. INTRODUCTION

Besides its classical function of bone metabolism regulation, vitamin D exhibits various biological targets mediated by the Vitamin D Receptor (VDR) [1], including the musculoskeletal system and the brain [2]. This explains why hypovitaminosis D, a condition frequently met in older adults [1], is accompanied by various poor health outcomes [3]. For instance, a number of observational studies have reported associations between chronic lower circulating 25-hydroxyvitamin D (25OHD) concentrations and poorer lower-extremity function [4], lower muscle strength [5], lower contraction speed [6] and lower appendicular muscle mass [7]. Several lines of evidence also support an association of hypovitaminosis D with slower nerve conduction [8] and poorer executive functions [9]. Consistently, meta-analyses of observational studies reported lower 25OHD concentrations among older fallers compared to controls without any history of falls [10]. However, despite such evidence for an involvement of vitamin D in motor control, both in its peripheral muscular and central neurological components, the effect of hypovitaminosis D on physical performance remains uncertain.

Walking speed is a simple, objective, and global measure of lower-limb neuromuscular function and physical performance [11]. This measure is particularly important in that it also

relates to functional abilities, morbidity and mortality, making it a potent ‘vital sign’ in older adults [12]. The role of vitamin D on walking speed remains controversial since previous studies have shown conflicting results. Vitamin D status has not received yet a structured critical evaluation as a possible biological determinant of walking speed. The purpose of this systematic review and meta-analysis was to systematically review and quantitatively assess the observational evidence connecting circulating vitamin D concentrations to walking speed in adults.

2. METHODS

2.1 Data sources and searches

A systematic Medline literature search was conducted in June 2017, without limit of date or language restriction, using the Medical Subject Heading (MeSH) terms "Vitamin D" OR "Vitamin D Deficiency" combined with "Gait" OR "Gait disorders, Neurologic" OR "Walking speed" OR the keywords "Gait velocity"[TIAB] OR "Walking speed"[TIAB]. An iterative process was used to ensure all relevant articles had been obtained. A further hand search of bibliographic references of extracted papers and existing reviews was also conducted to identify potential studies not captured in the electronic database searches.

2.2 Study selection and analysis

One member of the team (CA) screened abstracts from the initial search and obtained articles deemed potentially relevant. Initial screening criteria for the abstracts were: 1) epidemiological studies, 2) data collection of physical performance and circulating vitamin D concentration as outcomes, and 3) involvement of adult human participants. If a study met the initial selection criteria or its eligibility could not be determined from the title and abstract, the full text was retrieved. Two reviewers (CA and GTD) then independently assessed the full text for inclusion status. Disagreements were resolved by a third reviewer (SH). The full

articles were screened using the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist which describes items that should be included in reports of cohort studies [13]. Final selection criteria were applied in observational studies (i.e., case-control, case series, cross-sectional and cohort studies) when both circulating vitamin D concentration and walking speed were provided, or alternatively when the correlation and/or association between circulating vitamin D status and walking speed were examined. The study selection is shown on a flow diagram (Figure 1).

Of the 107 originally identified abstracts, 45 met the initial inclusion criteria (See Appendix 1). Following thorough examination, we excluded 23 of those 45 studies because circulating vitamin D was not an outcome (n=2), because walking speed was not an outcome (n=7), or because the paper was an intervention (n=14). The remaining 22 studies were included in this review [14-35]. Important details regarding the methods and results were extracted from selected articles and summarized (Table 1).

2.3 Definition of outcomes

We examined the circulating concentration of 25OHD since this assay is generally accepted as a better indicator of vitamin D status than 1,25-dihydroxycholecalciferol ($1,25(OH)_2D$) [1]. Walking speed was calculated either by measuring the time duration needed to walk a predetermined distance, or by measuring the distance walked during a fixed period of time (in m/s or cm/s). Walking speed was measured either at usual pace, or at fast pace without running. The walking path was in a straight line or with half-turns as in the Timed Up & Go test (TUG).

2.4 Meta-analysis

All studies addressing circulating 25OHD concentrations in relation to walking speed were meta-analysed. Five consecutive analyses were performed.

The first analysis aimed to compare the usual-pace walking speed according to the vitamin D status (i.e., severe vitamin D deficiency [SVDD] ≤25nmol/L, vitamin D deficiency [VDD] ≤50nmol/L, or vitamin D insufficiency [VDI] ≤75nmol/L versus normal vitamin D status [NVD] >75nmol/L) (to convert to ng/mL, divide by 2.496) [1]. The between-group mean difference in walking speed was expressed in m/s. Individual study data were then pooled using an inverse-variance method, and a fixed-effects meta-analysis was performed on the estimates with Review Manager (RevMan) version 5.1 (The Nordic Cochrane Centre, Copenhagen, Denmark) to generate the summary value. Results were presented as forest plots (Figure 2). The second and third analyses were similar, but focused respectively on fast-pace walking speed (Figure 3) and on the time to perform the TUG (Figure 4).

In the fourth analysis, aimed at determining the proportion of participants with slow usual-pace walking speed according to the vitamin D status (i.e., SVDD, VDD or VDI), we pooled individual study data with a fixed-effects (inverse-variance estimates) meta-analysis (Open Meta-Analyst for Windows 8). Results were presented as forest plots (Figure 5).

Finally, the fifth meta-analysis aimed to summarize the risk of slow usual-pace walking speed according to the vitamin D status (i.e., SVDD or VDD or VDI versus NVD). When applicable, odds ratio (OR) [95% confidence interval (CI)] were extracted from selected papers, or calculated with contingency tables and Dag-stat [36]. Statistical analyses were then performed using Review Manager (RevMan) version 5.1 (The Nordic Cochrane Centre, Copenhagen, Denmark). Results were presented as forest plots for the prediction of slow walking speed according to NVD versus SVDD (Figure 6A), or VDD (Figure 6B), or VDI (Figure 6C).

Lastly, heterogeneity between studies was assessed using Cochran's Chi-squared test for homogeneity (Chi^2), and amount of variation due to heterogeneity was estimated by calculating the I^2 [37].

3. RESULTS

3.1 Study characteristics

Table 1 summarizes the 22 studies included in this review [14-35]. All studies were published since 2002. They were conducted both in the Northern [14-22,25,27,28,30-35] and Southern hemispheres [23,24,26,29]. Data collection was based either on cross-sectional or prospective longitudinal design. The research process did not identify any previous systematic review and meta-analysis on this specific issue.

The number of participants ranged from 54 [21,23] to 4,100 [15]. Both middle-aged and elderly participants were recruited. Participants were mostly female, from 0% [26] to 100% [14,16,17,22,23,33]. Walking speed was measured over a predetermined distance [14-35] or a limited period of time [19,25]. Six studies used a standardized TUG test [18,28,30-32,35]. Finally, while most studies examined usual-pace walking speed, 6 studies also focused on fast-pace walking speed without running [16,18,21,22,30,31]. Four studies used the circulating 25OHD concentration as a continuous variable [19,21,29,34], while the other 18 studies used a categorized variable (i.e., quartiles [17,18,20,26,30] or quintiles [15,25] or cut-offs defined *a priori* for SVDD [14,22,24,27,28,32,35], VDD [14,16,20,22,23,24,27,28,31,35] and VDI [16,22,27,28,32,33,35]). Three studies also examined the circulating concentration of the active form of vitamin D, ie $1,25(OH)_2D$ [17,21,26]. As reported in Table 1, different methods were used to measure 25OHD concentrations, the most frequent one being radioimmunoassay [14,15,17,20,22,23,25-27,29,31,32].

Finally, 15 of 22 studies could contribute to meta-analyses of the evidence connecting circulating 25OHD concentrations to walking speed in adults [15-17,20,22,24-28,30-33,35].

3.2 Results of the meta-analyses

The first meta-analysis computed the differences in usual-pace walking speed between 943 participants with SVDD and 888 participants with NVD (Figure 2A) [18,22,24,25,30], between 3313 participants with VDD and 4310 participants with NVD (Figure 2B) [15,20,22,24,25,30,31], and between 2167 participants with VDI and 2097 participants with NVD (Figure 2C) [15,22,25,30,33]. The summary mean difference of -0.18m/s [95% CI: -0.20;-0.17] indicated a slower walking speed among people with SVDD compared to NVD. Similarly, those with VDD exhibited a slower walking speed compared to those with NVD with a mean difference of -0.08m/s [95% CI: -0.09;-0.07], and those with VDI exhibited a slower walking speed compared to those with NVD with a mean difference of -0.12m/s [95% CI: -0.13;-0.10] (Figure 2).

Second, we performed a similar same meta-analysis for fast-pace walking speed. Results showed a mean difference of -0.04m/s [95% CI: -0.05;-0.03] between participants with VDD and those with NVD [16,17,22,30], and a mean difference of -0.04m/s [95% CI: -0.06;-0.03] between those with VDI and those with NVD [16,17,22,30] (Figure 3).

The third meta-analysis showed that the TUG was performed faster among participants with NVD compared to those with SVDD, with a summary mean difference of 0.48s [95% CI: 0.09;0.87] (Figure 4) [30-32].

The fourth meta-analysis examined the proportion of participants with a low walking speed according to the vitamin D status. Results showed that 26% of participants with SVDD had a low walking speed [27,28,35]; a greater proportion compared to the groups with VDD (19%) [27,28,35] and VDI (13%) [27,28,33,35] (Figure 5).

Finally, a meta-analysis of low walking speed according to the vitamin D status was conducted. While comparing the participants with SVDD to those with NVD, the summary random OR for low walking speed was 2.17 [95%CI: 1.52–3.10] (Q=4.93, df=3, P=0.177; I^2=39.2%) (Figure 6A) [22,26,27,35]. While comparing the participants with VDD to those

with NVD, the summary random OR for low walking speed was 1.38 [95%CI: 1.01–1.89] (Q=5.28, df=3, P=0.153; I^2=43.1%) (Figure 6B) [22,26,27,35]. Finally, while comparing the participants with VDI to those with NVD, the summary random OR for low walking speed was 1.38 [95%CI: 1.04–1.83] (Q=8.48, df=4, P=0.075; I^2=52.9%) (Figure 6C) [22,26,27,33;35].

4. DISCUSSION

This systematic review and meta-analysis provides evidence that circulating 25OHD concentrations are positively associated to walking speed among adults, and that all definitions of hypovitaminosis D (i.e., SVDD, VDD, and VDI) are associated with slower walking speed.

4.1 Vitamin D and walking speed

Slower walking speed is a major turning point in the life course of older adults since it illustrates different aspects of the aging process that may be involved in the onset of adverse outcomes including falls [12], hospitalization within one year [38], cognitive disorders [39], brain changes [40], functional decline [41], frailty [38], institutionalization [38], and death [38]. Progression of walking speed has also been linked to clinical meaningful changes in quality of life [42] and in home and community walking behaviour [43]. Thus, prevention strategies based on the eviction of triggers or aggravating factors of slower walking speed may be of interest in this population. The findings of the present meta-analysis strengthen the idea that there might be a link between hypovitaminosis D and walking speed, regardless of the cut-off used to define hypovitaminosis D (i.e., SVDD, VDD, VDI), with a tendency to target VDI and SVDD as the mean difference in walking speed compared to NVD was of 0.18m/s and 0.12m/s respectively; a difference greater than the clinically relevant change in walking speed established at 0.1m/s [11]. It may therefore be possible that correction of VDI

could improve the prognosis of people with slower walking speed. This assumption is consistent with the results of the longitudinal studies showing that low baseline 25OHD concentrations were associated to greater decline in walking speed [14,34,35]. Although the observational design of these studies did not allow formal causal inferences, it suggested a protective effect of vitamin D against walking decline.

Various theories can explain a possible association between lower circulating vitamin D concentration and slowing down of the walking speed. It has been argued that low vitamin D levels could be rather a consequence, than a cause of slower walking speed. In this scenario, the primary abnormality would be the impaired physical performance illustrated by slower walking speed, followed by related loss of functional autonomy, possible reduction in dietary intakes and sunlight exposure, which can ultimately cause hypovitaminosis D. This hypothesis, although not invalidated by one longitudinal study reported here [17], was yet not supported by the fact that most odds ratios used here were adjusted for covariates including body mass index and/or season/sunlight exposure time/recreational physical activity/autonomy. Consequently, a scenario of reverse causation appears likely, with hypovitaminosis D preceding the slowing down of the walking speed. Walking requires correct neuromuscular function to maintain posture and balance during motor activities. Several lines of evidence suggest the existence of a link between vitamin D and muscles. Cases of myopathy have been described in hypovitaminosis D, associated with proximal lower-limb muscle weakness [44]. Muscle biopsies showed predominantly type II muscle fibre atrophy [44], i.e. specifically the fast-twitch fibres recruited for fast-pace walking speed (Figure 3). The relationship between vitamin D and muscular strength remains yet controversial as a higher number of clinical trials documenting a lack of effect of vitamin D supplementation on muscle strength have been published compared to studies showing beneficial effects [45]. A recent meta-analysis found no improvement of muscle strength after

vitamin D supplementation [46]. It thus appears that vitamin D might affect neuromuscular function and walking speed in a way that does not involve only the muscle but also the nervous system [2]. Growing evidence supports that vitamin D is involved in brain health and function [8,9,47]. It regulates the gene expression of several neurotrophins and neurotransmitters, the intra-neuronal calcium homeostasis, and various oxidative and inflammatory changes in the brain [8,47], thus promoting neuron viability and function. Specifically, VDRs are present in almost all brain areas including structures involved in motor control and balance such as the substantia nigra, the hypothalamus and the cerebellum [1,8]. The influence of vitamin D on the high levels of motor control was recently confirmed with magnetic resonance spectroscopy, as a reduced neuronal function was reported in the caudal primary motor cortex of older adults with hypovitaminosis D [48]. Moreover, this neurocognitive mechanism was strengthened by the present finding of a positive association between serum 25OHD concentration and fast-pace walking speed (Figure 3), as fast-pace walking is considered a more attention-demanding task than usual-pace walking [22].

4.2 Critical analysis of literature

Differences in populations and methodology may partly explain some inconsistencies in previous studies. Firstly, studies did not include power calculations. As a consequence, equivocal or negative results could be the result of small sample sizes with a lack of statistical power.

Secondly, mixed results could also be linked to the definition of the 'slow walking speed' outcome, which varied between studies. Although most studies used walking speed as a continuous variable, others chose a dichotomization based either on the clinically relevant threshold value of 0.8m/s [27,33] or on quartiles [28] or quintiles [22,26,35]. In contrast, the cut-offs used for 25OHD concentrations were more consensual and mostly based on previously admitted definitions for SVDD, VDD and VDI (Table 1). Historically, desirable

vitamin D concentrations have been defined based on the prevention of adverse health consequences. For instance, the cut-off at 25nmol/L, which defines SVDD, is the minimum concentration required to prevent rickets and osteomalacia [1]. Similarly, the cut-off at 50nmol/L, which defines VDD according to the World Health Organization [49] and the US Institute of Medicine [50], is the minimum concentration to prevent secondary hyperparathyroidism [1]. Finally, it has been reported that the most advantageous concentrations for avoiding non-skeletal effects range between 50 and 100nmol/L, with a clear tendency toward a target of 75nmol/L [51], as recommended by the US Endocrine Society [52]. Of note, the results of one study confirmed that the nonskeletal implications of vitamin D (i.e., the magnitude of the association between 25OHD concentration and walking speed) increased from values around 75nmol/L (i.e., 67.8nmol/L for fast-pace walking, and 96.5nmol/L for usual-pace walking) [22].

Thirdly, another explanation for inconclusive results may be related to the VDR gene polymorphisms since recent biomedical literature suggests that the VDRs may confer genetic physical aptitudes. Some human variants appear less sensitive to vitamin D and more likely to develop muscle weakness or to experience cognitive decline. For instance, higher quadriceps isometric and concentric strength was found in f/f homozygotes compared to F allele carriers [53]. Similarly, a significant association has been shown between the VDR gene *APA1* polymorphism and Alzheimer onset [54], the *Aa* genotype multiplying by 2.3 the risk of Alzheimer disease compared to the *AA* genotype. Taken together, these findings suggest that the polymorphism in the ligand-binding site of the VDR gene affects vitamin D neuromuscular effects and walking speed. Unfortunately, none of the selected studies took the polymorphism of the VDR gene into account, although it could obviously shed new light on inconclusive and negative results.

Finally, only few of the selected studies have indicated the duration and methods of serum/plasma collection and preservation before 25OHD assay. The effects of temperature, light and nature of the vial as well as the effects of long-term serum storage on measurements are yet not certain, especially regarding 25OHD stability.

4.3 Implications for practice and research

The existing body of evidence provides evidence that i) adults with hypovitaminosis D (i.e., SVDD, VDD or VDI) exhibit a meaningful slower walking speed than those with NVD, and ii) hypovitaminosis D is associated with more frequent slow walking speed at usual and fast pace. The implications for practice and research are manifold. First, our results support the idea that age-related hypovitaminosis D is a risk factor for slowing down the walking speed, and may explain part of the physical decline of seniors and their propensity to fall [10]. Second, they reinforce the conceptualization of hypovitaminosis D as a biological characteristic of disabled seniors, which supports older adults with slower walking speed and functional decline should receive vitamin D supplementation in clinical routine to prevent and/or correct both skeletal and neuromuscular adverse events. Third, they provide a rationale for guiding the conduct of clinical trials designed to test the efficacy of vitamin D supplements to prevent the onset and progression of gait disorders among older adults. In particular, future clinical trials should recruit older adults with an initial concentration of 25OHD below 75nmol/L, and preferentially below 25nmol/L since the mean difference of walking speed was greatest below the latter cut-off (Figure 2). Also, it appears that the most judicious choice for the outcome in clinical trials should be the usual-pace walking speed rather than the fast-pace walking speed or the TUG since the between-group differences found with the two latter tests (i.e., 4cm/s and 0.5s respectively) were not clinically relevant. This finding is consistent with the observation that the TUG test is a mobility measure that may provide valuable information for individual patients, but that is also susceptible to floor

effects and may not be useful as a screening tool at a primary care level [55]. Alternatively, the usual-pace walking speed is a simple, inexpensive, validated and clinically meaningful measure in older adults [55].

4.4 Limitations

The findings of our systematic review and meta-analysis should be tempered by a number of limitations. First, we chose to include only observational studies in this systematic review and meta-analysis. Therefore, our conclusions need to be confirmed by interventional studies. Of note, a recent meta-analysis found scarce data reporting an improvement of the TUG after vitamin D supplementation compared to controls [46]. Second, it is possible that the heterogeneity and relatively small size of some studied samples may have exposed the analysis to a lack of statistical power with the risk of missing significant associations between 25OHD concentration and walking speed. Third, the duration of hypovitaminosis D was not reported in selected studies, although the length of exposure appears to be an important factor to take into account. It is tempting to speculate that shorter durations of hypovitaminosis D might be less commonly associated with neuromuscular decline and slower walking speed. Fourth, the 22 studies selected in our literature review did not assess walking speed in the same way (i.e., with or without acceleration, with or without turn, at usual or fast pace). Harmonization of outcome measures seems thus desirable. Finally, some potential limitations of the meta-analysis should be considered. In particular, the summary values we found should be interpreted with caution as some quantitative analyses indicated substantial heterogeneity.

5. CONCLUSIONS

In conclusion, this systematic review and meta-analysis provides robust evidence that circulating 25OHD concentrations are positively associated to usual- and fast-pace walking speed in adults; those with hypovitaminosis D (i.e., SVDD, VDD or VDI) walking

significantly slower than those with NVD. Of note lower 25OHD concentrations and slower walking speed are two frequently reported findings in older adults [1,11]. We and others hypothesize that lower 25OHD concentrations may contribute to neuromuscular disorders and slower walking speed; however further well-designed interventional studies remain needed for a better understanding of the involvement and direct effect of vitamin D on walking speed. Benefits of supplementation on walking speed would offer a powerful mechanism to act on physical activity in older adults and maintain function late in life.

Contributors

CA was responsible for the study concept and design, acquisition and interpretation of data, and drafting of the manuscript.

SH was responsible for acquisition of data, and critical revision of the manuscript for important intellectual content

SW was responsible for interpretation of data, and critical revision of the manuscript for important intellectual content

MM-O was responsable for critical revision of the manuscript for important intellectual content

GD was responsable for critical revision of the manuscript for important intellectual content

GTD was responsible for theacquisition and interpretation of data, and drafting of the manuscript.

All of the authors reviewed the manuscript prior to submission.

CA has full access to all of the data in the study, takes responsibility for the data, the analyses and interpretation, and the conduct of the research, and has the right to publish any and all data, separate and apart from the attitudes of the sponsor.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1. Summary of included studies (n=22)

Reference	Design	Settings / Population	Vitamin D		Walking speed		Association between vitamin D status and walking speed?
			Methods	Measure	Methods	Measure	
Verreault et al. 2002 [14] *WHAS*	Longitudinal study	– n=628 – Age ≥65y – 100% females – Follow-up, 3y Disabled community-dwellers≥65y in Baltimore, MD (39.2°N), USA	– Radioimmunoassay method	– 25OHD – Mean, 52.9nmol/L – SVDD <25nmol/L (n=80) – VDD <53nmol/L	– 4-meter walking speed – At baseline, and change during follow-up	– Mean decrease in walking speed=-0.08m/s per year (12.9% of baseline)	– No association between 25OHD and walking speed at baseline (P>0.05) – Adjusted β=-0.09(SE:0.02), P=0.98 for the association between baseline SVDD and average change per year in walking speed compared to NVD (ref) Adjusted β=-0.09(SE:0.02), P=0.81 for the association between baseline VDD and average change per year in walking speed compared to NVD (ref)
Bischoff-Ferrari et al. 2004 [15] *NHANES III*	Cross-sectional study	– n=4100 – Mean age: 71.4±7.9y – 49% females – Older community-dwellers ≥60y in USA	– Radioimmunoassay method	– 25OHD – Mean, 65.7±26.2nmol/L – Quintiles: ≤43.4; 43.7-56.7; 56.9-69.4; 69.6-85.9; ≥86.1 nmol/L	– 2.4-meter walking speed – Continuous variable	– Mean time to walk 2.4m=3.7±1.6s	– Mean time to walk 2.4m=4.1±2.2s in Q1 vs 3.8±1.4s in Q2 vs 3.7±1.4s in Q3 vs 3.6±1.6s in Q4 vs 3.5±1.1s in Q5, P<0.0001 – Mean walking speed=0.59±0.32m/s in Q1 (n=821) vs 0.65±0.25m/s in Q3 (n=815) vs 0.69±0.22m/s in Q5 (n=820), P<0.0001 – Adjusted β=-0.17 [95CI: -0.36;-0.02] for the association between Q2 and time to walk 2.4m compared to Q1 (ref) – Adjusted β=-0.22 [95CI: -0.39;-0.05] for the association between Q3 and time to walk 2.4m compared to Q1 (ref) – Adjusted β=-0.20 [95CI: -0.36;-0.05] for the association between Q4 and time to walk 2.4m compared to Q1 (ref) Adjusted β=-0.27 [95CI: -0.44;-0.09] for the association between Q5 and time to walk 2.4m compared to Q1 (ref)
Gerdhem et al. 2005 [16] *OPRA*	Longitudinal study	– n=986 – Mean age: 75.2y (range, 75-76) – 100% females – Follow-up, 3y (range 2.9-3.4) Older community-dwellers in Malmö (55.6°N), Sweden	– Chemiluminescence detection	– 25OHD – Mean, 95±30nmol/L – VDD <50nmol/L (n=43) – VDI <75nmol/L (n=256)	– 30-meter fast-pace walking speed (with one turn) – Continuous variable	– Mean time to walk 30m at fast pace=24.2s	– Mean time to walk 30m at fast pace=29±10s in VDD vs 24±9s in NVD, P<0.001 – Mean time to walk 30m at fast pace=27±12s in VDI vs 24±7s in NVD, P<0.001 – Correlation between 25OHD concentration and baseline walking speed (r=0.17, P<0.001)
Faulkner et al. 2006 [17] *SOF*	Longitudinal study	– n=389 – Median age: 70y (IQR:67–75) – 100% females – Mean follow-up, 3.7y – Community-dwellers ≥65y in Baltimore, MD (39.2°N), Portland, OR (45.5°N),	– Radioimmunoassay method	– 25OHD – Quartiles: <50; 50-62.4; 62.5-77.4; ≥77.5 nmol/L – $1,25(OH)_2D$ – Quartiles: <27; 27-32; 33-39; ≥40 pg/mL	– 6-meter walking speed at usual pace and fast pace – At baseline, and change during follow-up	– Mean baseline usual-pace walking speed=1.01±0.22m/ – Mean decrease in usual-pace walking speed=0.8±0.19m/s	– Mean fast-pace walking speed=1.27±0.03m/s in Q1-25OHD vs 1.27±0.04m/s in Q2-25OHD vs 1.26±0.04m/s in Q3-25OHD vs 1.31±0.04m/s in Q4-25OHD, P=0.384 – Mean fast-pace walking speed=1.27±0.03m/s in Q1-$1,(25(OH)_2D$ vs 1.26±0.04m/s in Q2-$1,(25(OH)_2D$ vs 1.34±0.04m/s in Q3-$1,(25(OH)_2D$ vs 1.27±0.04m/s in Q4-$1,(25(OH)_2D$, P=0.504 – Baseline 25OHD not associated with changes of usual-pace and fast-pace walking speeds during follow-up (P>0.05)

		Minneapolis, MN (44.6°N), and Pittsburgh, PA (40.4°N), USA					– Baseline $1,25(OH)_2D$ not associated with changes of usual-pace and fast-pace walking speeds during follow-up (P>0.05)
Kwon et al. 2007 [18]	Cross-sectional study	– n=1,094 – Mean age: 77.7±84.0y in males and 77.8±8 4.2y in females – 58.3% females Community-dwellers≥70y in in the province of Tokyo, Japan (35.7°N)	– Radioimmunoassay method	– 25OHD – Mean, 71.7±13.2nmol/L in males and 65.8±12.5nmol/L in females – Lowest quartile versus other quartiles combined: ≤62.5nmol/L for males and ≤57.5nmol/L for females	– Usual-pace TUG test – Fast-pace TUG test – Continuous variables	– Mean TUG=6.3±1.7s in males and 7.1±2.8s in females – Mean fast-pace TUG= 6.0±1.6s in males and 6.7±2.7s in females	– Adjusted β=0.02(SE:0. 20), P=0.698 for the association between Q1 and usual-pace TUG time compared to other quartiles combined (ref) in males – Adjusted β=-0.02(SE:0. 26), P=0.590 for the association between Q1 and usual-pace TUG time compared to other quartiles combined (ref) in females – Adjusted β=0.02(SE:0. 21), P=0.750 for the association between Q1 and fast-pace TUG time compared to other quartiles combined (ref) in males – Adjusted β=-0.02(SE:0. 26), P=0.629 for the association between Q1 and fast-pace TUG time compared to other quartiles combined (ref) in females
Boxer et al. 2008 [19]	Cross-sectional study	– n=60 – Mean age: 77±10y – 28% females Older patients with an ejection fraction of ≤40% in Cleveland, OH (41.5°N), USA	– Enzyme immunoassay	– 25OHD – Mean, 66.6±31.2nmol/L – Continuous variable	– 2.4-meter walking speed – 6-minute walk test – Continuous variables	– Mean time to walk 2.4m: 3.1±1.5s – Mean distance after 6 minutes=309±121m	– Correlation between 25OHD concentration and time to walk 2.4m among patients with heart failure (r=-0.39, P<0.05) – Correlation between 25OHD concentration and distance walked in 6 minutes among patients with heart failure (r=0.42, P<0.05) – Adjusted β=3.04 (SE:0.93), P=0.002 for the association between 25OHD (continuous variable) and distance after 6-minute walking
Suzuki et al. 2008 [20]	Cross-sectional study	– n=2957 – Mean age: 75.1y (range, 65-92) – 67.9% females Older community-dwellers ≥65y in Itabashi ward in Tokyo, Japan (35.7°N)	– Radioimmunoassay method	– 25OHD – Mean, 71.1±12.5nmol/Lin males and 60.4±12.2nmol/L in females – Lowest quartile versus other quartiles combined: ≤62.5nmol/L for males (n=249) and ≤52.5nmol/L for females (n=576) – VDD < 50nmol/L (n=46 in males and n=355 in females)	– 5-meter walking speed – Continuous variable	– Mean walking speed= 1.23± 0.26m/s in males and 1.18±0.29 in females	– Mean walking speed=1.19±0.26m/s in Q1 vs 1.25±0.26m/s in other quartiles combined among males, P=0.061 – Mean walking speed=1.12±0.28m/s in Q1 vs 1.21±0.27m/s in other quartiles combined among females, P<0.001 – Mean walking speed=1.16±0.79m/s in VDD vs 1.24±0.26m/s in NVD among males, P=0.138 – Mean walking speed=1.11±0.29m/s in VDD vs 1.20±0.27m/s in NVD among females, P<0.001 – Adjusted β=0.111 (SE:0.002), P=0.012 for the association between 25OHD (continuous variable) and walking speed among males – Adjusted β=0.143 (SE:0.001), P<0.001 for the association between 25OHD (continuous variable) and walking speed among females
Shahar et al 2009 [21]	Cross-sectional study	– n=54 – Mean age, 78.4 y – 73% females Healthy institution-dwellers ≥65y in the Beer-Sheva region, Israel (31.3°N)	– Enzyme-immunoassay method	– 25OHD – Mean, 86.9nmol/L – $1,25(OH)_2D$ – Mean, 30.5pg/mL	– TUG test – Continuous variable	– Mean TUG=8.4s –	– Correlation between 25OHD concentration and TUG (r=-0.37, P<0.001 Correlation between $1,25(OH)_2D$ concentration and TUG (r=-0.43, P<0.001)

Annweiler et al. 2010 [22] *EPIDOS*	Cross-sectional study	– n=739 – Mean age: 80.2±3.5 y – 100% females – Community-dwellers ≥75y from Amiens (49.9°N), Lyon (45.7°N), Montpellier (43.6°N), Paris (48.9°N) and Toulouse (43.6°N), France	– Radioimmunoassay method	– 25OHD – Mean, 43.4±26.2nmol/L – SVDD <25nmol/L (n=126) – VDD <50nmol/L (n=406) – VDI <75nmol/L (n=133)	– 6-meter walking speed at usual pace and fast pace – Cut-off: lowest quintiles of usual-pace walking speed and fast-pace walking speed	– Mean usual-pace walking speed= 86.8±21.9cm/s – Mean fast-pace walking speed=109.7±26.5cm/s	– Mean usual-pace walking speed=83.9±22.6cm/s in SVDD vs 87.2±21.9cm/s in VDD vs 85.7±22.0cm/s in VDI vs 91.5±20.4cm/s in NVD, P=0.145 – Mean fast-pace walking speed=105.2±28.5cm/s in SVDD vs 110.1±26.2cm/s in VDD vs 108.7±26.5cm/s in VDI vs 116.9±25.6cm/s in NVD, P=0.021 – Adjusted β=0.10 [95CI: -0.03;0.24], P=0.130 for the association between 25OHD (continuous variable) and usual-pace walking speed – Adjusted β=0.18 [95CI: 0.01;0.34], P=0.033 for the association between 25OHD (continuous variable) and fast-pace walking speed – Adjusted OR=5.44 [95CI: 1.75;16.92], P=0.003 for slow usual-pace walking speed among SVDD vs NVD – Adjusted OR=3.76 [95CI: 1.28;11.00], P=0.016 for slow usual-pace walking speed among VDD vs NVD – Adjusted OR=3.79 [95CI: 1.21;11.83], P=0.022 for slow usual-pace walking speed among VDI vs NVD – Adjusted OR=6.95 [95CI: 2.14;22.60], P=0.001 for slow fast-pace walking speed among SVDD vs NVD – Adjusted OR=4.10 [95CI: 1.33;12.58], P=0.014 for slow fast-pace walking speed among VDD vs NVD – Adjusted OR=6.01 [95CI: 1.86;19.46], P=0.003 for slow fast-pace walking speed among VDI vs NVD
Mastaglia et al. 2011 [23]	Cross-sectional study	– n=54 – Mean age: 71±4y – 100% females Postmenopausal women ≥65y from Buenos Aires (34.6°S), Argentina	– Radioimmunoassay method	– 25OHD – Mean, 21±9nmol/L – VDD <50nmol/L (n=29)	– 2.4-meter walking speed –	– NA	– Walking speed test 0.4s longer when VDD compared to NVD
Boersma et al. 2012 [24]	Cross-sectional study	– n=145 – Mean age: 79.2 y – 60.7% females Community-dwellers ≥65y in Falls and Fractures Clinic with history of fall in preceding 6months, in Penrith (33.75°S), Australia	– Chemiluminescence immunoassay	– 25OHD3 – Mean, 52.9nmol/L – SVDD <30nmol/L (n=38) – VDD <50nmol/L (n=28)	– Walking speed on a 810cm long electronic walkway with integrated pressure sensors – Continuous variable	– Visual estimation: mean walking speed=70cm/s	– Visual estimation: mean walking speed=55±7cm/s in SVDD vs 76±8cm/s in VDD vs 75±7cm/s in NVD, P<0.01 – Adjusted β=0.26, P=0.045 for the association between 25OHD (continuous variable) and walking speed – Correlation between 25OHD concentration and walking speed test (r=0.316, P<0.05)
Toffanello et al. 2012 [25]	Cross-sectional study	– n=2694 – Mean age: 75.6±7.5 in females, 76.2±7.8 in males – 59.3% females	– Radioimmunoassay method	– 25OHD – Mean, 65.0±41.3nmol/L in females, 101.9±62.4nmol/L in	– 4-meter walking speed – 6-minute walking test – Continous variables	– Mean walking speed=0.63m/s in females – Mean 6-min walking test=290.1m in females	– Female: mean 4-m walking speed=0.55±0.2m/s in Q1 vs 0.61±0.21m/s in Q2 vs 0.64±0.18m/s in Q3 vs 0.67±0.18m/s in Q4 vs 0.70±0.18m/s in Q5, P<0.0001 – Male: mean 4-m walking speed=0.63±0.21m/s in Q1 vs

Pro.V.A		Caucasian community-dwellers ≥65y in 2 areas, Camposampiero (45.6°N) and Rovigo (45.1°N), Italy		males – Quintiles: ≤32; 32.1-49; 49.1-68; 68.1-93; >93 nmol/L in females – Quintiles: ≤53; 53.1-79; 79.1-103; 103.1-143; >143 nmol/L in males		– Mean walking speed=0.73m/s in males – Mean 6-min walking test=350.6m in males	0.72±0.20m/s in Q2 vs 0.76±0.19m/s in Q3 vs 0.77±0.17m/s in Q4 vs 0.80±0.17m/s in Q5, P<0.0001 – Female: mean 6-min walking test=221.5±117.8m in Q1 vs 283.5±109.9m in Q2 vs 297.3±109.1m in Q3 vs 321.4±96.8m in Q4 vs 332.8±86.4m in Q5, P<0.0001 – Male: mean 6-min walking test=281.6±133.8m in Q1 vs 345.6±119.0m in Q2 vs 349.7±119.4m in Q3 vs 384.1±96.3m in Q4 vs 395.8±92.5m in Q5, P<0.0001 – Adjusted β=0.15(SE:0.05), P=0.007 for the association between 25OHD (continuous variable) and 6-min walking test in females; adjusted β=0.14(SE:0.05), P=0.004 in males
Hirani et al. 2013 [26] *CHAMP*	Cross-sectional study	– n=1659 – Mean age: 77 y (range, 70-97) – 0% females – Community-dwellers ≥65y in Sydney, Australia (33.9°S)	– Radioimmunoassay method	– 25OHD – Mean, 55.9nmol/L – Quartiles: <39.9; 40-52.9; 53-68.9; ≥69 nmol/L – $1,25(OH)_2D$ – Mean, 110.7pmol/L – Quartiles: <62; 62-96.9; 97-145.9; ≥146 pmol/L	– 6-meter walking speed – Cut-off: the lowest CHS study quintile for walking speed	– n=231 (14.1%) with slow walking speed	– Mean 25OHD=52.7±22.9nmol/L if slow walking speed vs 56.5±22.1nmol/L if normal walking speed – Mean $1,25(OH)_2D$=106.1±72.9pmol/L if slow walking speed vs 111.6±65.2pmol/L if normal walking speed – Adjusted OR=1.62 [95CI: 1.03;2.56], P=0.04 for slow walking speed among participants with Q1-25OHD vs Q4 – Adjusted OR=1.02 [95CI: 0.64;1.62], P=0.95 for slow walking speed among participants with Q2-25OHD vs Q4 – Adjusted OR=1.07 [95CI: 0.68;1.69], P=0.77 for slow walking speed among participants with Q3-25OHD vs Q4 – Adjusted OR=1.65 [95CI: 1.05;2.63], P=0.03 for slow walking speed among participants with Q1-$1,25(OH)_2D$ vs Q4 – Adjusted OR=0.84 [95CI: 0.51;1.39], P=0.51 for slow walking speed among participants with Q2-$1,25(OH)_2D$ vs Q4 Adjusted OR=1.16 [95CI: 0.72;1.87], P=0.55 for slow walking speed among participants with Q3-$1,25(OH)_2D$ vs Q4
Kositsawat et al. 2013 [27] *NHANES*	Cross-sectional study	– n=1826 – Age: ≥ 50 y – 49.6% females – Noninstitutionalized civilian population in the USA (25-49°N)	– Radioimmunoassay method	– 25OHD – SVDD <25nmol/L (n=106) – VDD <50nmol/L (n=637) – VDI <75nmol/L (n=785)	– 6.1-meter walking speed – Cut-off <0.8m/s	– NA	– 30.8(SE:4.9)% with slow walking speed in SVDD vs 19.7(1.5)% in VDD vs 13.5(0.9)% in VDI vs 10.1(2.0)% in NVD, Ptrend<0.001 – Adjusted OR=2.77 [95CI: 1.08-7.10], P=0.03 for slow walking speed in SVDD vs NVD – Adjusted OR=1.60 [95CI: 0.95-2.70], P=0.08 for slow walking speed in VDD vs NVD – Adjusted OR=1.13 [95CI: 0.71-1.79], P=0.65 for slow walking speed in VDI vs NVD – Positive linear association between 25OHD and walking speed as continuous variables (P=0.04)
Matheï et al. 2013 [28] *BELFRAIL*	Cross-sectional study	– n=367 participants – Mean age: 84.7±3.6 y – 63% females – Caucasian community-dwellers ≥80y in Wallonia, Brussels and Flanders,	– Chemiluminescent immunoassay method	– 25OHD – SVDD <25nmol/L (n=129) – VDD <50nmol/L (n=119) – VDI <75nmol/L (n=75)	– TUG test – Cut-off : lowest gender-adjusted quartile	– n=86 (24.6%) with slow walking speed	– 19.1% with slow walking speed in SVDD vs 28.4% in VDD vs 28.9% in VDI vs 21.4% in NVD, P=0.286 – Adjusted OR=1.02 [95CI: 0.99–1.05] for slow walking speed according to 25OHD concentration

		Belgium (49.3-51.3°N)					
Carrasco et al. 2014 [29]	Cross-sectional study	– n=90 participants – Age: 60-98 y – 52.6% females – Healthy community-dwellers in Santiago, Chile (33.4°S)	– Radioimmunoassay method	– 25OHD – Mean: 43.2±15.2nmol/L – Continuous variable	– 8-meter walking speed – Continuous variable –	– Mean 1.27±0.22m/s	Correlation between 25OHD concentration and walking speed (r=0.322, P=0.001)
Gschwind et al. 2014 [30]	Cross-sectional study	– n=404 – Mean age: 77.6±5.8y – 53.5% females Older aduts ≥65y from the Memory Clinic of Basel, Switzerland (47.6°N)	– Enzyme-immunoassay method	– 25OHD – Mean, 63.2±33.9 nmol/L – Quartiles: <39; 39-54; 55-81; >81 nmol/L	– Usual-pace walking speed and fast-pace walking speed on a 972cm long electronic walkway with integrated pressure sensors – TUG test	– Mean usual-pace walking speed=110.0±22.7cm/s – Mean fast-pace walking speed=150.3±31.6cm/s – Mean TUG=12.1±3.3s	– Mean usual-pace walking speed=102.3±21.6cm/s in Q1 vs 110.8±23.4cm/s in Q2 vs 113.5±22.0cm/s in Q3 vs 113.3±22.2cm/s in Q4, P<0.001 – Mean fast-pace walking speed=137.3±27.8cm/s in Q1 vs 151.9±32.9cm/s in Q2 vs 155.3±31.5cm/s in Q3 vs 156.6±30.6cm/s in Q4, P<0.001 – Mean TUG=12.9±3.2s in Q1 vs 12.0±3.3s in Q2 vs 11.8±3.2s in Q3 vs 11.8±3.2s in Q4, P<0.001
Yumrutepe et al. 2014 [31]	Cross-sectional study	– n=147 – Mean age: 59.7 y (range, 40-75) – 6.8% females – n=90 with COPD and n=57 healthy controls in Malatya, Turkey (38.4°N)	– Radioimmunoassay method	– 25OHD – Mean, 60.6nmol/L – VDD <37.5nmol/L (n=44 among COPD)	– 15.2-meter walking speed – TUG test – Continuous variables	– Mean 15.2-m walking speed=1.8m/s – Mean TUG=7.2s	– Mean 15.2-m walking speed=1.78±0.18m/s in VDD vs 1.76±0.16m/s in NVD, P=0.07 – Mean TUG=7.6±1s in VDD vs 7.3±1s in NVD, P=0.45 – Correlation between 25OHD concentration and time to walk 15.2m among COPD patients (r=0.011, P=0.915) – Correlation between 25OHD concentration and TUG among COPD patients (r=-0.158, P=0.138)
Beauchet et al. 2015 [32] *GAIT*	Cross-sectional study	– n=359 participants – Mean age: 70.4±4.8 y – 40.7% females – Nondemented patients with memory complaint in Angers, France (47.5°N)	– Radioimmunoassay method	– 25OHD – SVDD <25nmol/L (n=10) – VDI <75nmol/L (n=256)	– TUG test – Continuous variable	– Mean TUG=10s	– Mean TUG=11.2±3.5s in SVDD vs 10.0±2.6s in VDI vs 10.0±2.8s in NVD, P=0.01
Iolascon et al. 2015 [33]	Case-control study	– n=80 (46 cases with insufficiency; 34 controls) – Mean age: 65.9±7.7 y – 100% females – Post-menopausal women referring to outpatient rehabilitation unit for prevention and management of osteoporosis in Naples, Italy (40.9°N)	– NA	25OHD – Mean: 31.42 ± 17.30 nmol/L – VDI <75nmol/L (n=46)	– 4-meter walking speed, with cut-off ≤0.8m/s SPPB walking speed test	– n=38 (47.5%) with slow 4-meter walking speed – Mean SPPB walking test=4.83±1.54s	– 63% with slow walking speed in cases with VDI vs 26.5% in controls, P=0.002 – Mean SPPB walking test=5.48±1.61s in cases with VDI vs 3.93±0.85 in controls with NVD, P=0.001 – Correlation between 25OHD concentration and SPPB walking speed test (r=-0.457, P<0.05) – OR calculation=3.03 [95CI: 1.16-7.89] for slow walking speed in VDI vs NVD
Shardell et al.	Longitudinal	– n=860	– Enzyme-	– 25OHD	– SPPB walking speed	– NA	Adjusted β=0.17 (95CI: 0.09;0.25), P<0.001 for the association

2015 [34] *InCHIANTI*	study	– Mean age: 75.3 y – 55.6% females Community-dwellers ≥55y from Greve in Chianti (43.6°N) and Bagno a Ripoli (43.7°N), Italy	immunoassay method	– Mean 74.2nmol/L – Continuous variable	test Measured longitudinally at 3-y, 6-y and 9-y visits		between ln[25OHD] (continuous variable in ng/mL) and SPPB walking speed test
Vogt et al. 2015 [35] *KORA-Age*	Longitudinal study	– n=727 – Mean age: 75.5±6.5 y – 49.1% females – Mean follow-up, 2.9±0.1y – Non-frail participants ≥65y from Augsburg, Bavaria, Germany (48.4°N)	– Enhanced chemiluminescence immunoassay	– 25OHD – Mean, 46.7±4.5nmol/L – SVDD <37.5nmol/L (n=297) – VDD <50nmol/L (n=193) – VDI <75nmol/L (n=260)	– TUG test after follow-up – Cut-off: highest quintile	– n=168 (22.2%) with prospective low walking speed	– 39.4% with prospective low walking speed among SVDD vs 16.8% among VDD vs 20.0% among VDI vs 8.3% among NVD, P<0.0001 – Adjusted OR=3.1 [95CI: 1.23;7.82] for prospective low walking speed among participants with baseline SVDD vs NVD – Adjusted OR=1.34 [95CI: 0.47;3.85] for prospective low walking speed among participants with baseline VDD vs NVD – Adjusted OR=2.18 [95CI: 0.88;5.44] for prospective low walking speed among participants with baseline VDI vs NVD

1,25(OH)$_2$D: 1,25-dihydroxyvitamin D; 25OHD: 25-hydroxyvitamin D; BFC80+: BelFrail study; CHAMP: Concord Health and Ageing in Men Project; CHS: Cardiovascular Health Study; CI : confidence interval; EPIDOS: EPIDémiologie de l'Ostéoporose ; GAIT: Gait & Alzheimer Interactions Tracking; InCHIANTI: Invecchiare in Chianti; KORA-Age: [Cooperative Health Research in the Region of Augsburg]-Age; NHANES: National Health and Nutrition Examination Survey; NVD: normal vitamin D status; OPRA: Osteoporosis Prospective Risk Assessment; OR: odds ratio; Pro.V.A: Progetto Veneto Anziani; SE: standard error; SOF: Study of Osteoporotic Fractures; SVDD: severe vitamin D deficiency; TUG: Timed Up & Go; USA: United States of America; VDD: vitamin D deficiency; VDI: vitamin D insufficiency; WHAS: Osteoporosis Prospective Risk Assessment; y: years

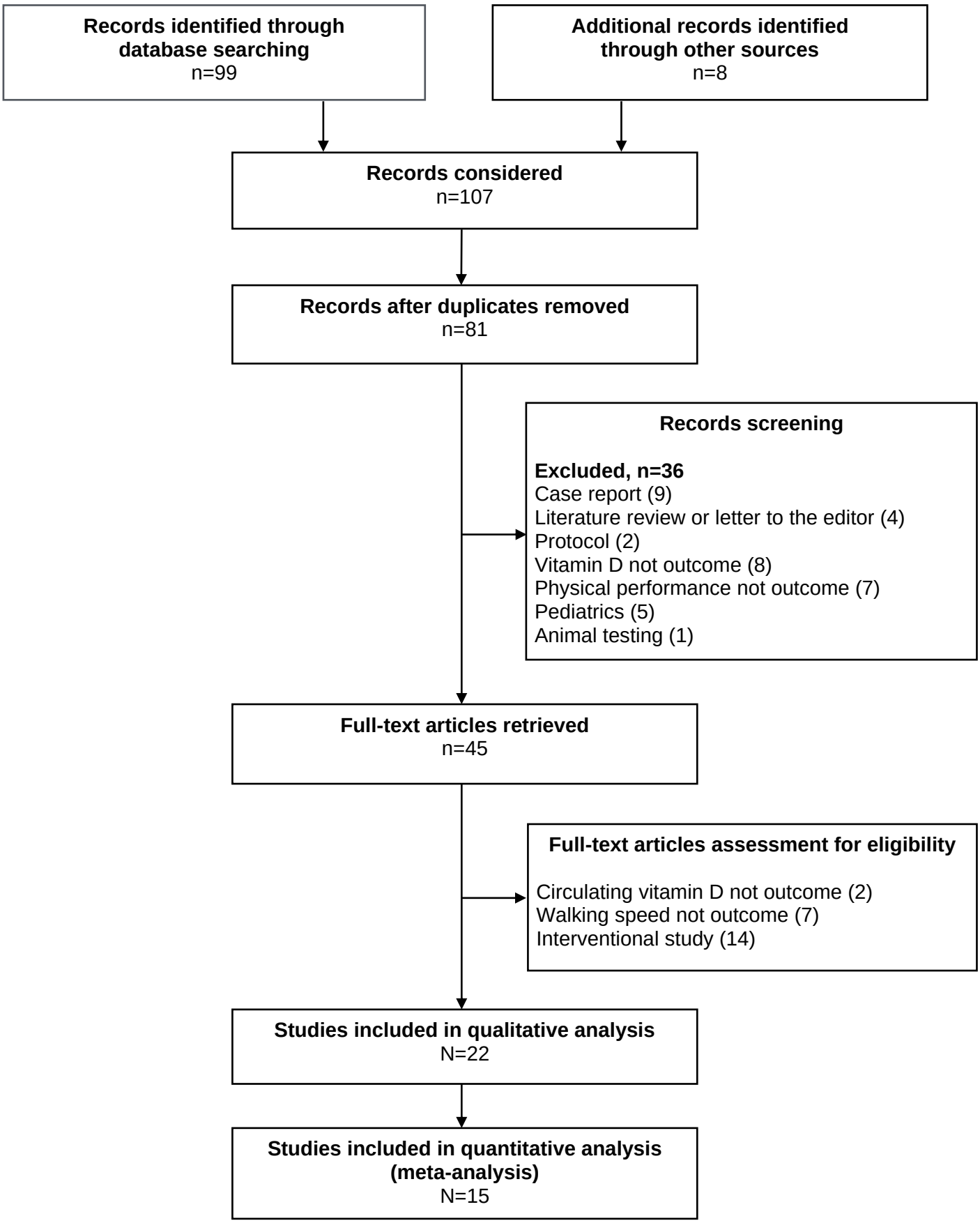

Figure 1. Flow diagram of selection of studies focusing on vitamin D and walking speed

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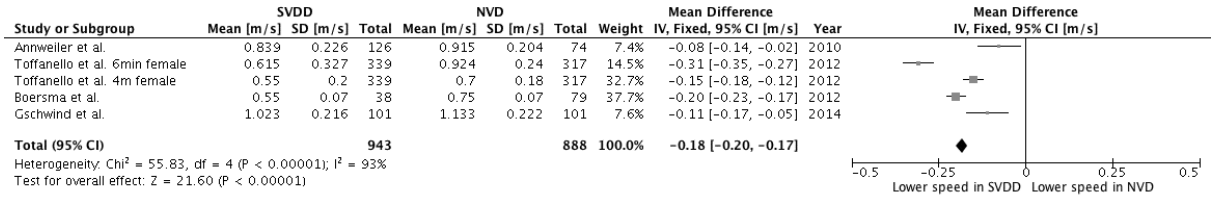

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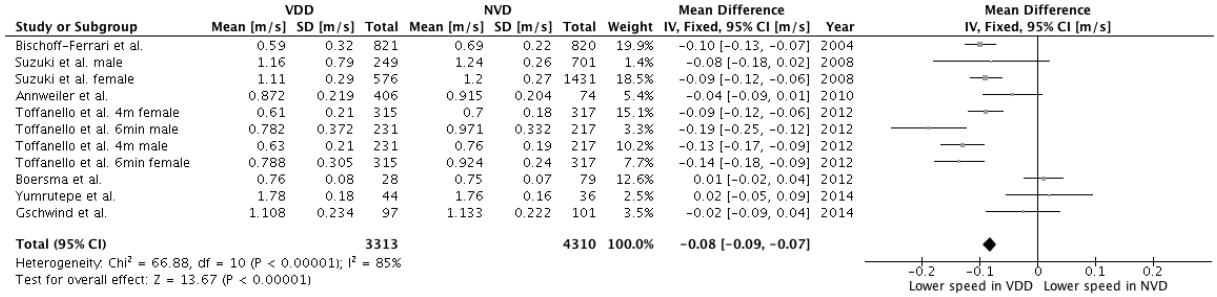

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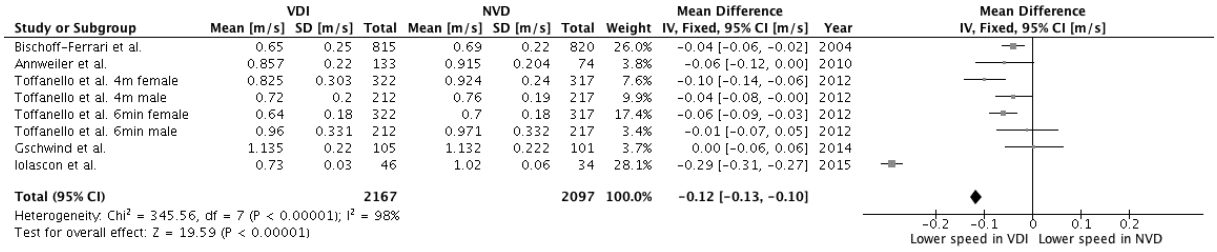
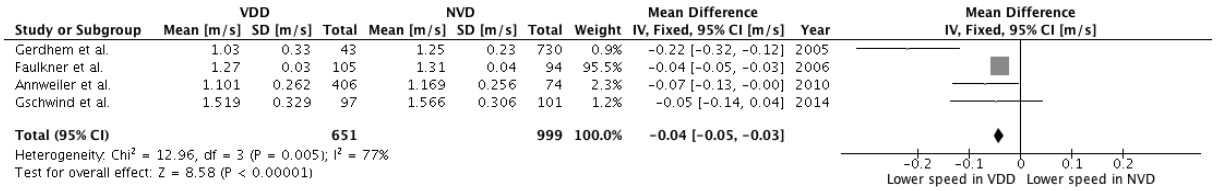


Figure 2. Forest plot comparing the usual-pace walking speed among participants with (A) severe vitamin D deficiency (SVDD) compared to normal vitamin D status (NVD); (B): vitamin D deficiency (VDD) compared to normal vitamin D status (NVD); (C) vitamin D insufficiency (VDI) compared to normal vitamin D status (NVD).

The grey box area is proportional to the weight of each study, and horizontal lines correspond to the 95% confidence interval. Black diamond represents the summary value. The vertical line corresponding to 0.0m/s is equivalent to no difference between groups.

(A)



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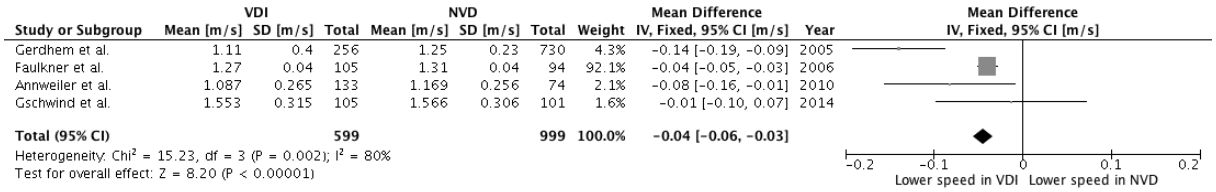


Figure 3. Forest plot comparing the fast-pace walking speed among participants with (A) vitamin D deficiency (VDD) compared to normal vitamin D status (NVD); (B) vitamin D insufficiency (VDI) compared to normal vitamin D status (NVD).

The grey box area is proportional to the weight of each study, and horizontal lines correspond to the 95% confidence interval. Black diamond represents the summary value. The vertical line corresponding to 0.0m/s is equivalent to no difference between groups.

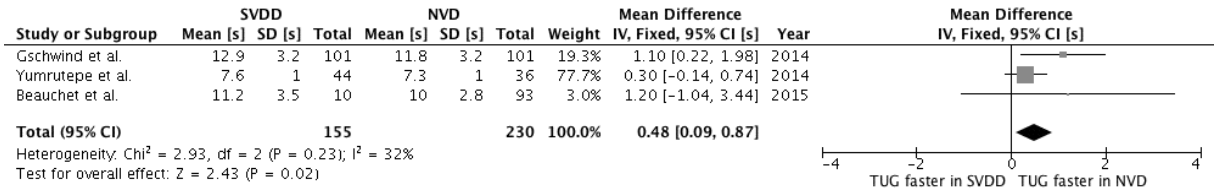
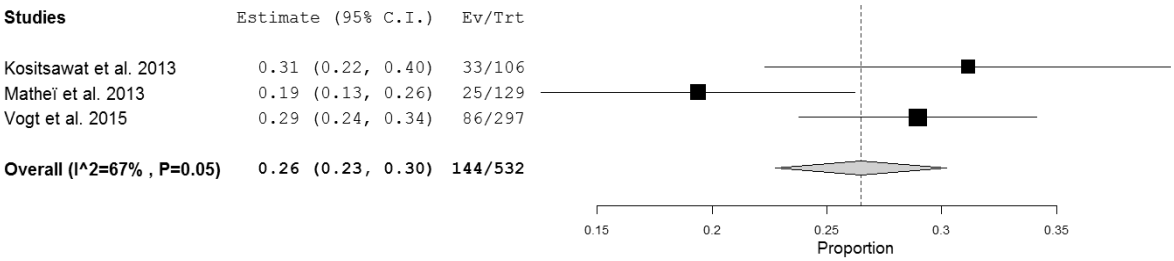


Figure 4. Forest plot comparing the time to perform the Timed Up & Go (TUG) test among participants with vitamin D deficiency (SVDD) compared to normal vitamin D status (NVD).

The grey box area is proportional to the weight of each study, and horizontal lines correspond to the 95% confidence interval. Black diamond represents the summary value. The vertical line corresponding to 0.0m/s is equivalent to no difference between groups.

(A)



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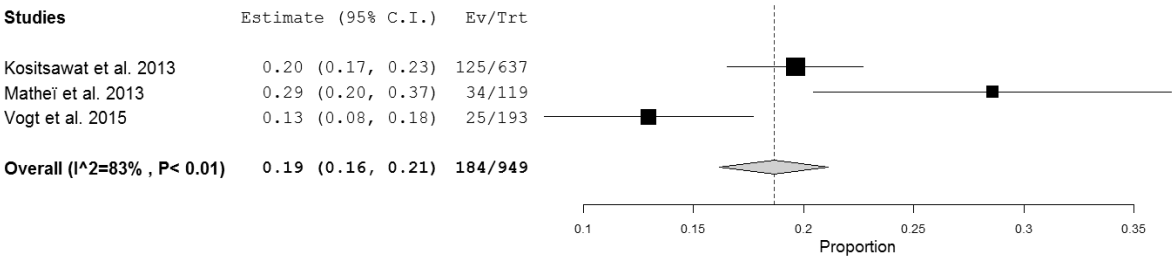

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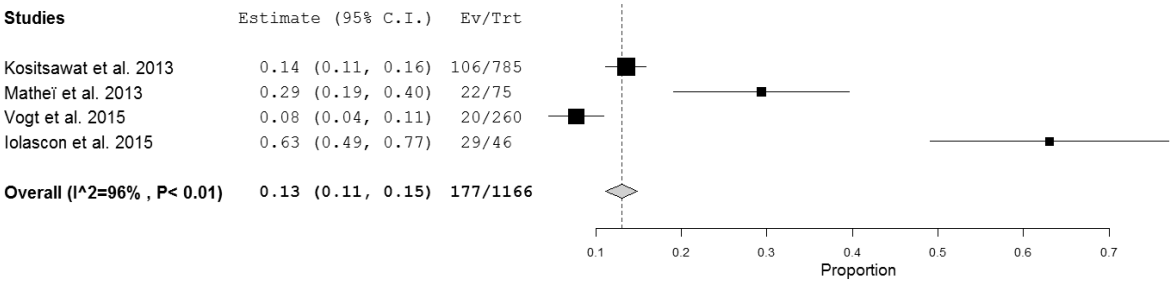
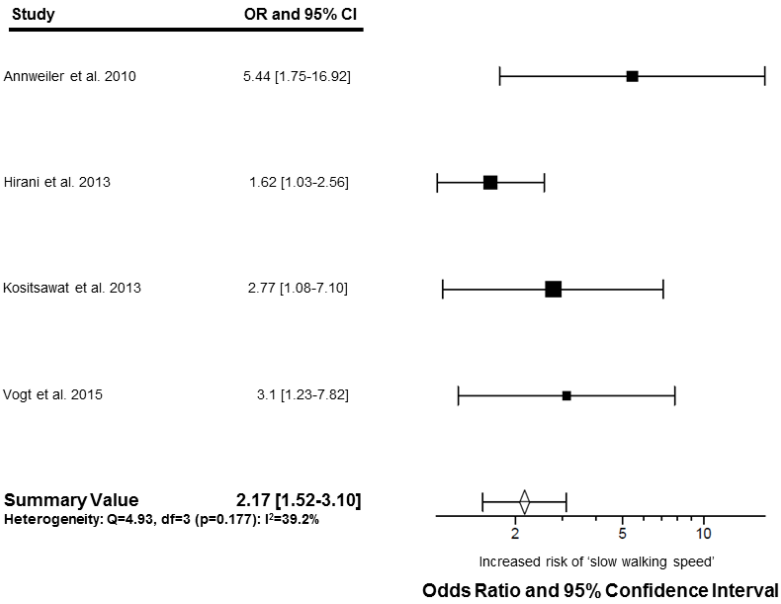


Figure 5. Meta-analysis of observational studies assessing the proportion of participants with slow walking speed in the groups with (A) severe vitamin D deficiency (SVDD); (B): vitamin D deficiency (VDD); (C) vitamin D insufficiency (VDI).

The square area is proportional to the sample size of each study, and horizontal lines correspond to the 95% confidence interval (95% CI). The grey diamond with vertical dashed line represents the summary value.

(A)



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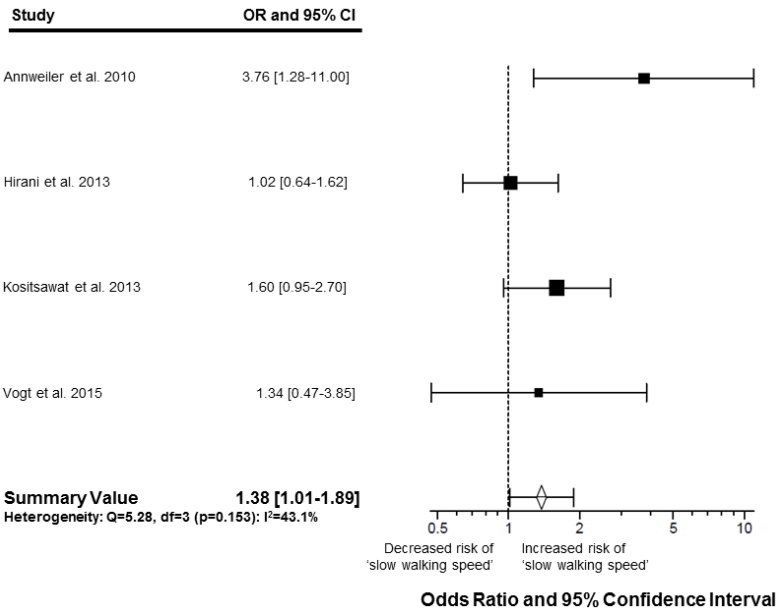

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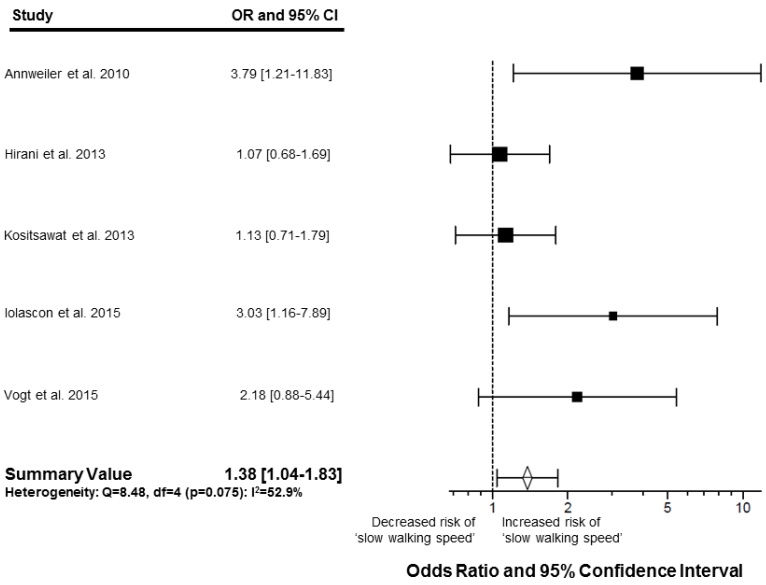

Figure 6. Forest plots for risk of 'slow usual-pace walking speed' according to: (A) severe vitamin D deficiency (SVDD) versus normal vitamin D status (NVD); (B): vitamin D deficiency (VDD) versus normal vitamin D status (NVD); (C) vitamin D insufficiency (VDI) versus normal vitamin D status (NVD).

The black box area is proportional to the weight of each study, and horizontal lines correspond to the 95% confidence interval. White diamonds represent the summary values. The vertical dashed line corresponding to an odds ratio of 1.0 is equivalent to no association.