Efficacy of Vestibular Rehabilitation in Patients With Neurologic Disorders: A Systematic Review

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Abstract:	Objective The aim of this systematic review is to critically assess the effectiveness of Vestibular Rehabilitation (VR) administered either alone or in combination with other neurorehabilitation strategies in patients with neurological disorders. Data Sources An electronic search was conducted by two independent reviewers in the following databases: MEDLINE (Pubmed), the Physiotherapy Evidence Database (PEDro) and the Cochrane Database of Systematic Reviews (CDSR). Study selection All clinical studies carried out on adult patients with a diagnosis of neurological disorders who performed VR provided alone or in combination with other therapies were included. Data Extraction Screening of titles, abstracts, and full texts and data extraction were undertaken independently by pairs of reviewers. Included studies were quality appraised using a modified version of the Newcastle-Ottawa Scale. Data synthesis The summary of results was reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Twelve studies were included in the review. All the included studies, with one exception, report that improvements provided by customized VR in subject affected by a central nervous system diseases are greater than traditional rehabilitation programs alone. Conclusion Due to the lack of high quality studies and heterogeneity of treatments protocols, clinical practice recommendations on the efficacy of VR cannot be made. Results show that VR programs is safe and could easily implement standard neurorehabilitation protocols in patients affected by neurological disorders. Hence, more high-quality randomized controlled trials of vestibular rehabilitation in patients with neurological disorders are needed.

Title page with author details

Vestibular rehabilitation in neurological rehabilitation

The efficacy of vestibular rehabilitation in patients with neurological disorders: a systematic review

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Abstract

Objective

The aim of this systematic review is to critically assess the effectiveness of Vestibular Rehabilitation (VR) administered either alone or in combination with other neurorehabilitation strategies in patients with neurological disorders.

Data Sources

An electronic search was conducted by two independent reviewers in the following databases: MEDLINE (Pubmed), the Physiotherapy Evidence Database (PEDro) and the Cochrane Database of Systematic Reviews (CDSR).

Study selection All clinical studies carried out on adult patients with a diagnosis of neurological disorders who performed VR provided alone or in combination with other therapies were included.

Data Extraction

Screening of titles, abstracts, and full texts and data extraction were undertaken independently by pairs of reviewers. Included studies were quality appraised using a modified version of the Newcastle-Ottawa Scale.

Data synthesis

The summary of results was reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Twelve studies were included in the review. All the included studies, with one exception, report that improvements provided by customized VR in subject affected by a central nervous system diseases are greater than traditional rehabilitation programs alone.

Conclusion

Due to the lack of high quality studies and heterogeneity of treatments protocols, clinical practice recommendations on the efficacy of VR cannot be made. Results show that VR programs is safe and could easily implement standard neurorehabilitation protocols in patients affected by neurological disorders. Hence, more high-quality randomized controlled trials of vestibular rehabilitation in patients with neurological disorders are needed.

Key Words: Vestibular Rehabilitation, Stroke, TBI, Multiple Sclerosis, Parkinson, Balance, Oculo-motor reflex, VOR adaptation, Sensory-motor Learning

Introduction

Vestibular rehabilitation (VR) is a patient-centred physical therapy that includes a combination of different strategies with the aim to promote gaze stability, improve postural stability, and facilitate somatosensory integration [1]. Through a “brain orchestration of neurological melodies” [2] VR is able to improve symptoms of imbalance, falls, fear of falling, oscillopsia, dizziness, vertigo, motion sensitivity and secondary symptoms such as nausea and anxiety [3,4]. VR has been found to be effective in patients with peripheral vestibular hypofunction [5] and for improving static and dynamic balance in patients with diseases characterized by central vestibular dysfunction [6]. Recent reviews report evidence to support the use of VR in people with unilateral peripheral vestibular disorders [5] and with bilateral vestibular loss, for supporting balance and gaze stability training [7]. In addition, some efficacy of VR in reducing the risk of fall in patients with vestibular hypofunction and in older adults has been reported [8].

Vestibular compensation is a process that allows to get rid of imbalance in tone, and readjusting gain and it is based on several concepts called Restoration, Habituation and Adaptation [9,10]. Restoration means that the lost function is entirely recovered as before the vestibular damage [11,12]. Habituation is aimed at reducing progressively the vestibular lesion-induced asymmetry by the repetition of the triggering signals. On the other hand, adaptation is a powerful recovery mechanism and it used in the literature as two separate entities, called sensory substitution and behavioral substitution [13]. In the last years, several studies, using these concepts, have experienced VR also in patients with neurological diseases [14, 15, 16, 17] reporting promising results for improving postural control, gait and activities of daily living. Furthermore, two RCTs [18, 19], based on vestibulo-spinal stimulation supported the use of VR strategies to improve the double stance phase of the gait in patients with Parkinson Diseases.

Finally, in order to improve the gaze and the postural stability in people with multiple sclerosis, Loyd and co-workers [20] are now developing a new clinical trial based on the principles of VR.

Although VR has proven to be very effective in rehabilitating the balance and postural functions of neurological patients, cases of its use in standards balance protocols are very rare.

In fact, what is observed is a use of VR in a few patients with predominantly peripheral pathologies and not routinely in neurorehabilitation balance protocols.

In addition, even though considerable attention is paid for balance rehabilitation during neurorehabilitation, VR appears as the neglected issue in balance and postural recovery following central nervous system damage. This is even more surprising considering the central role of vestibular rebalancing of sensory inputs and thus in modulating brain plasticity related to balance network in healthy subjects [18, 21, 22] and athletes as well as in neurological condition. The effectiveness of VR on motor abilities in adult patients with neurological disorders has only been partially proven and, to date, no systematic evaluation of the VR effectiveness was performed in patients with neurological disorders. Thus, the aim of this systematic review is to critically assess the effectiveness of VR administered either alone or in combination with other neurorehabilitation strategies.

Methods

The present systematic review included only controlled clinical trials (i.e., randomized, quasi-randomized or non-randomized trials), non-controlled clinical trials and observational studies.

Inclusion/exclusion criteria

Patients included in the studies were male and female subjects, clinically diagnosed with stroke, multiple sclerosis, traumatic brain injury and Parkinson's disease, with presence of balance impairment and/or dizziness symptoms.

The intervention was based on the specific vestibular exercise rehabilitation as defined by Whitney et al. [3], compared with other standard exercise programmes or no intervention. The primary outcome measures were balance and dizziness. Other outcome measures were walking competencies and fatigue.

Randomised controlled trials regarding the effect of vestibular rehabilitation on improving balance and/or dizziness in patients with multiple sclerosis were included. Full texts in English were included. Retrospective study designs, case reports, case series, commentaries, letters to the editor and expert opinions were excluded. Only studies written in English were included and no year of publication restriction was adopted.

Data sources and searches

Electronic databases searched in August 2019 were MEDLINE (PubMed), PEDro (Physiotherapy Evidence Database) and the Cochrane Database of Systematic Reviews (CDSR).

Search terms used were ("vestibular rehabilitation" OR "vestibular stimulation" OR "vestibular exercis*" OR "balance rehabilitation") AND ("neurological disorde*" OR "stroke" OR "parkinson" OR "multiple sclerosis" OR "traumatic brain injury"). Search terms were modified for each database and appropriate subheadings were used for each database searched (for details see appendix 1).

Study selection and data collection process

Duplicate records were identified and removed using the software EndNOTE. A first selection of studies gathered through bibliographic searches was carried out by 2 reviewers (VR and MT) based on the pertinence and relevance of each study to the topic of the review. Discrepancies were resolved by consensus with a reviewer (GM) as an arbiter.

Data synthesis and methodological quality assessment

The summary of results was reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [23]. The high clinical and methodological heterogeneity of the included studies did not allow for a quantitative summary of results, though a meta-analysis was initially planned, along with subgroup analyses according to the type of neurological condition, clinical outcome and treatment. Thus, we classified studies according to the condition considered; We reported a narrative summary of results and presented the following data in a tabular format: (principal diagnosis, number of participants, gender, intervention and comparison groups' sizes), type of intervention (experimental group and comparison separately), outcomes measures, results, intervention duration, follow up, quality assessment and VR duration (Table 1). The methodological quality of evidence was assessed with a modified version of the Newcastle-Ottawa Scale (NOS) (for details see appendix 2) [24, 25], in which the maximum score that can be achieved is 7, i.e., two points on the selection subscale, two on the treatment subscale and three on the outcome subscale.

Results

Electronic searches identified 277 studies. Titles and abstracts were examined according to inclusion and exclusion criteria. Whenever necessary the full text of the article was read to determine its eligibility. Furthermore, reference lists of identified articles were screened for additional relevant literature. Comparison of the retrieved titles identified 22 studies that were duplicates. The result consisted of 24 articles eligible for inclusion. After a full text analysis 12 articles were excluded due to the following reasons: (a) full text not available, (b) patients with a primary diagnosis of vestibular disorders, c) instrumental vestibular stimulation (i.e. galvanic or caloric stimulation), d) other balance rehabilitation programs. Each study was included just once in the systematic review, totaling 12 studies that met the inclusion criteria (Fig. 1).

[Insert Fig.1 here]

A total of 421 participants were included, 257 of which were women. Patients' main diagnosis was traumatic brain injury [26, 27, 28], stroke [16, 29, 30], multiple sclerosis [15, 31, 32, 33] and Parkinson disease [14, 34].

All the included studies used vestibular rehabilitation as the main intervention either alone or associated with standard physiotherapy program [16, 30, 33]. Vestibular rehabilitation exercises were compared with usual medical care or standard rehabilitation program in the majority of the included studies [14, 16, 29, 30, 32, 33], while 2 studies compared it with a no-intervention group [15, 27, 31] or no intervention condition [26]; lastly 2 studies did not use any control group [28, 34].

The longest main intervention extent were 14 weeks [31] and 12 weeks [28], while the shortest was 3 weeks [16]. Overall, vestibular rehabilitation was administered in a time period ranging between 4 and 8 weeks [14, 15, 26, 27, 29, 30, 32, 33, 34]. Lastly, follow-up was conducted by 9 studies [15, 16, 26, 27, 28, 30, 31, 33, 34], while only 3 studies did not perform any follow-up [14, 29, 32]. Among these 9 studies, only two [30, 33] performed a one-year follow-up; however, only the study by Tramontano and colleagues [30] included all the original subjects, carrying out two follow-ups to evaluate the fall events after six months and one year.

Studies included in the present review used a wide range of primary and secondary outcomes, as it is shown in Table 1, in which are reported main findings and the characteristics of each study. The most used balance measures were Dizziness Handicap Inventory (DHI) for self-reported disability due to dizziness or disequilibrium, Timed up and Go test (TUG) to measure the time taken to stand up from a chair (46 cm chair height), walk a distance of 3 meters, turn, walk back to the chair, and sit down, and Berg Balance Scale (BBS) to assess the patient's ability to sit, stand, lean, turn, and maintain an upright position on one leg. Another frequently used measure was the Dynamic Gait Index (DGI), assessing gait performance. Psychological factors, such as anxiety and depression, were evaluated using Beck Depression Inventory (BDI) or Hospital Anxiety and Depression Scale in 3 studies [15, 27, 32].

The overall methodological quality was high, ranging from a minimum of 5 [16, 26, 28 - 30, 34] to a maximum of 6 [14, 15, 27, 31 - 33]. None of the included studies reached the maximum of 7 stars mostly because of participants' selection.

Discussion

A systematic review was performed in order to investigate the effectiveness of vestibular rehabilitation for individuals with neurological diseases characterized by balance and gait disorders.

Results of the present systematic review suggest that vestibular rehabilitation programs are safe and represent a beneficial intervention for neurological patients, producing significant results especially in reducing balance impairments and fatigue perception. VR showed positive effects on balance in particular when administered in addiction to other neurorehabilitation programs during 3-12 weeks. All the included studies report that improvements provided by customized vestibular rehabilitation (for the details of the intervention see Table 2) could be greater than traditional rehabilitation programs, with one exception: Balci and colleagues [29] did not find any significant difference between the group performing vestibular rehabilitation and the control group performing home exercises in terms of post-treatment values. Nonetheless, the small sample size is probably accountable for this result. Kleffelgaard and colleagues [27] found that the between-group differences emerged after the 8-weeks intervention showing that vestibular rehabilitation fastened the recovery in the intervention group, were no longer statistically significant two months after the end of the intervention. In fact, control group improvement continues to increase until it reached the same level of the intervention group. Nevertheless, an opposite and encouraging trend was found in most of the studies included in the present systematic review, showing that reported improvements tend to persist over time. For instance, Tramontano and colleagues [30] found that 12 months after dismissals the number of falls observed in the intervention group decreased compared to the initial trend, supporting the hypothesis that vestibular rehabilitation could be effective in improving patients' balance confidence. Supporting evidences regarding wider time ranges were found by Rossi-Izquierdo and colleagues [33], who performed a long-term follow-up in 8 out of 10 patients. Results highlighted that vestibular rehabilitation could be useful in order to improve outcomes such as balance and gait velocity, reducing the risk of falls as well, with long lasting benefits.

The duration of each vestibular rehabilitation session was specified by almost every study, the only exception being the studies by Kleffelgaard and colleagues [27] and Hebert and colleagues [31]. From the collected data emerges that each session of vestibular rehabilitation lasts approximately 40 minutes, with a minimum of 20 minutes and a maximum of 60 minutes. This result proves that vestibular rehabilitation can be easily implemented with standard rehabilitation practice due to its short duration. Three studies analyzed the effects of vestibular rehabilitation on mood disorders such as anxiety and depression. Two of them [15, 27] reported no statistically significant differences among groups, instead, Ozgen and colleagues [32] underlined the potential effectiveness of vestibular rehabilitation on somatic symptoms of depression in patients with multiple sclerosis.

Actually a number of balance training with technological devices, multimodal sensory augmentation technologies with video-feedback and with biofeedback have been shown an interesting potentiality in improving balance [44]. This might induce two considerations: first balance network is more plastic than previously believed; secondly balance training benefit when is integrated with real-time visual feedback and or other augmented feedback such as vibrotactile - proprioceptive, auditory and vestibular. However, the mechanism by which sensory augmentation information is processed by the CNS is not fully understood [2, 45].

More in general the brain neurophysiology oriented to vestibular understanding has been known an interesting growth and a renowned fascination. In add emerging evidence suggests that the vestibular network contributes to modulate space, body and self-awareness expanding into dimensions of emotion processing, mental health, and social cognition [47].

This scenario should induce the rehabilitation staff to pay more attention to vestibular deficits and vestibular training before to expose a subject with neurological deficit to functional and motivating balance training with or without new technology strategies.

This consideration is emphasized during neurorehabilitation in acute and subacute central nervous damage due to the higher neuroplastic potentiality. It is not far that we have understood the importance of the precocity of the verticalization and more in general of the task-oriented and functional training and probably we need more years to translate the understood central role of the vestibular system in balance neuroplasticity into subacute neurehabilitation. In other words, if we would recover balance we have to train all balance components: gaze stability and dynamic postural stability. Patients with neurological disorders could be highly dependent on visual, proprioceptive and vestibular information in order to control their standing posture at rest and they individually differ in their relative sensitivity to each of these sensory stimulations [49, 50]. According to the results of this review we should call into question the rationale of standard balance rehabilitation programs. The reviewed articles showed in add that VR is safe and feasible taking no more than 20 minute during an integrated rehabilitation program.

However, it is difficult to generalize the results founded for the relatively few studies enrolled for each CNS and for the heterogeneity of the interventions.

Despite this finding VR indication surprisingly lack in neurorehabilitation guidelines and appear as a neglected issue. There is the need of the multicenter RCT that include VR in neurorehabilitation program. Lastly, the clinical consensus conference with otorinolaringologist, physiatrist, neurologist, physiotherapist and ophthalmologist should integrate vestibular concerns in routinely neurorehabilitation after central nervous system diseases.

The strengths of this systematic review are: i) the emphasize how vestibular rehabilitation is safe and feasible when integrated into rehabilitation protocols, even if rarely is performed routinely; ii) the systematic review made including subjects affected by different CNS pathologies give us the opportunity to highlight how VR could represent an emerging treatment for managing dizziness, and imbalance regardless of the specific CNS disease (even if adapted for subjects functions and pathological conditions); iii) the consideration of the feasibility of VR in add on to standard therapy could probably help in improving the paradigm of the balance and walking rehabilitation in neurological conditions.

Strengths of the systematic review

The strengths of this systematic review are: i) to have highlighted that vestibular rehabilitation is safe and could easily implement standard rehabilitation program in patients affected by traumatic brain injury, stroke, multiple sclerosis and Parkinson disease both if administered alone and in combination with a neurorehabilitation program; ii) our methods were based on Preferred Reporting Items for Systematic reviews to minimize potential sources of bias; iii) inclusion and exclusion criteria were defined to minimize selection bias; iv) studies included in the review were adhered to best practice guidelines.

Study Limitations

This review presents some limitations: i) the clinical and methodological heterogeneity of the included studies did not allow to perform a quantitative summary of results as the conduction of a meta-analysis;

ii) study literature reports a high heterogeneity regarding vestibular rehabilitation interventions limiting the generalizability of the results; iii) the lack of instrumental assessment of the vestibular system before and after VR.

Conclusion

Clinical practices recommendation on the efficacy of VR cannot be made due to the lack of high quality studies and heterogeneity of treatments protocols. A vestibular rehabilitation protocol are safe and could easily implement standard rehabilitation program. However, initial findings that need to be confirmed in more large and high quality randomized controlled trial provide following indications:

- subjects affected by stroke in subacute phase might probably benefit from VR improving gait performances at least after 3 weeks, in add on to standard physiotherapy.
- subjects affected by Parkinson disease who perform VR in add one to the conventional physiotherapy might improve their balance, gait and might reduce their risk of falls.
- subject affected by multiple sclerosis might have a positive effect on balance and fatigue perception when VR is in add on to a standard physiotherapy program.
- subjects affected by TBI, to perform VR in add on to standard therapy might produce some beneficial effects on the improvement of concussion-related symptoms, particularly in patients with dizziness.

Future studies should define in add the optimal VR protocol, regarding duration, frequency and type of exercises. Finally, more high quality and large-scale randomized controlled trials of vestibular rehabilitation in patients with neurological disorders are needed.

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Figures captions

Fig 1. Flow chart showing study selection for the systematic review.

Table 1: Studies Included in the Systematic Review and their main characteristics.

Table 2: Vestibular Rehabilitation Details.

Key Words: Vestibular Rehabilitation, Stroke, TBI, Multiple Sclerosis, Parkinson, Balance, Oculo-motor reflex, VOR adaptation, Sensory-motor Learning

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Appendix
Appendix 1.docx

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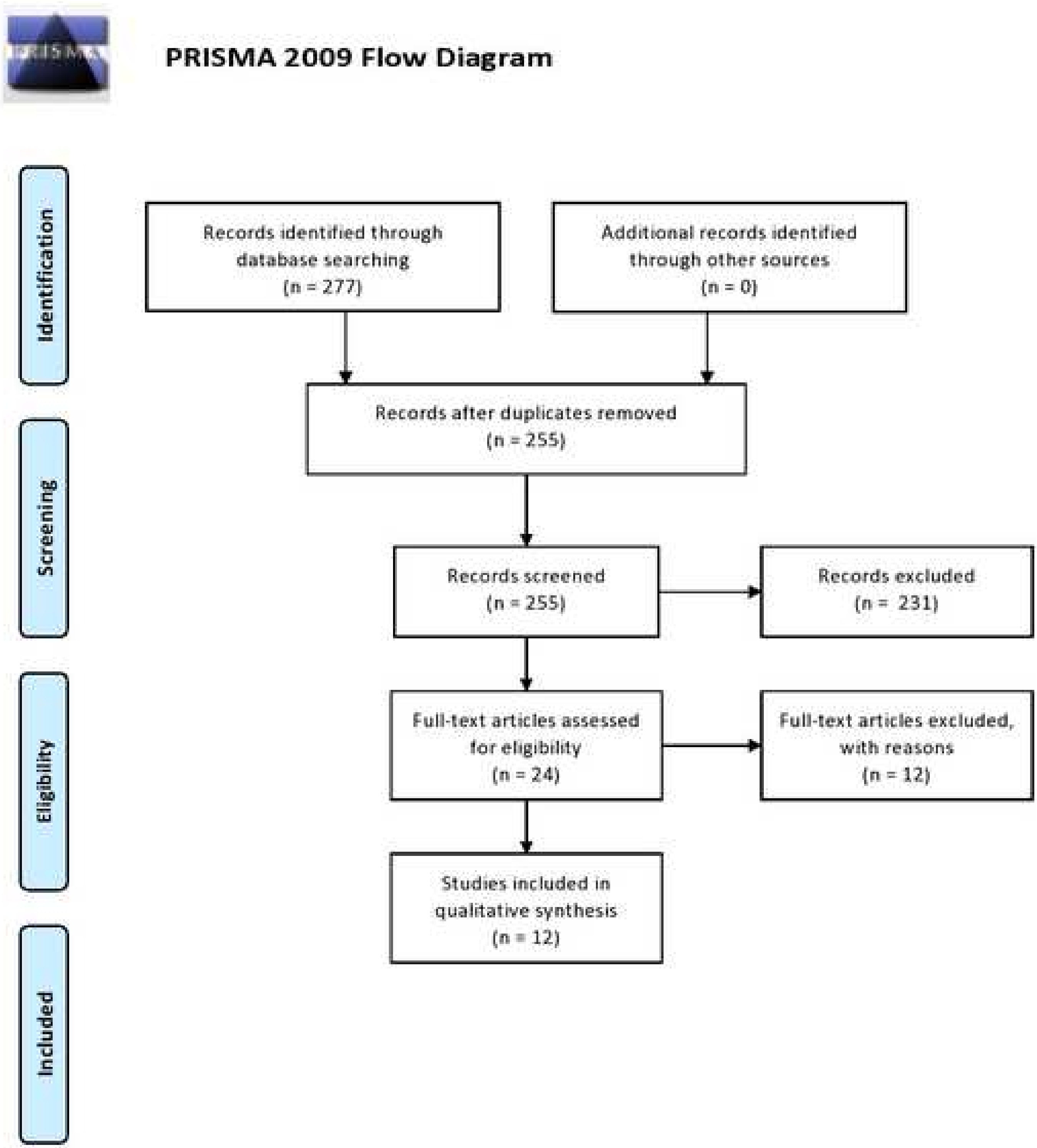
PRISMA 2009 Flow Diagram
Identification
Screening
Eligibility
Included
Records identified through database searching (n = 277)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n = 255)
Records screened (n = 255)
Records excluded (n = 231)
Full-text articles assessed for eligibility (n = 24)
Full-text articles excluded, with reasons (n = 12)
Studies included in qualitative synthesis (n = 12)

Table

Table 1 Characteristics of included studies

First Author, Year of Publication	Diagnosis	Participants	Intervention	Comparison	Outcomes	Results	Intervention duration (weeks)	Follow-up (weeks)	NOS score	Intervention Session duration
Kleffelgaard, 2019	mild to moderate TBI	TOT = 65 patients (45 women) VG = 33 CG = 32 Mean age (SD) = 39.4 (13)	16 sessions of group based VR intervention twice weekly for 8 weeks.	The control group did not receive any rehabilitation intervention in place of the group based vestibular rehabilitation intervention.	**Primary outcome:** 1) Dizziness Handicap Inventory (DHI). **Secondary outcome:** 1)High-Level Mobility Assessment Tool. **Other outcomes:** 1) Vertigo Symptom Scale 2) Rivermead Post-concussion Symptoms Questionnaire 3) Hospital Anxiety and Depression Scale 4) Balance Error Scoring System.	The 8-weeks intervention appeared to speed up recovery for patients with dizziness and balance problems after traumatic brain injury. However, the benefits had dissipated two months after the end of the intervention.	8	8	6	not specified.
Hebert, 2018	Multiple Sclerosis	TOT = 88 patients (75 women) VG = 44 (37 women) Mean age(SD) = 46.5 (8.8) CG= 44 (38 women) Mean age(SD) = 43.0 (10.8)	The Balance and Eye-Movement Exercises for Persons with MS (BEEMS) protocol consisted of 2 phases: in the first phase it was administered twice weekly with supervision and daily home exercise and in the second phase it was administered in one supervised session weekly with daily home exercise.	The control group did not receive any rehabilitation intervention (wait-listed control).	**Primary Outcomes:** 1) Computerized Dynamic Posturography-Sensory Organization Test (CDP-SOT) **Secondary Outcomes:** 1) Timed 25-Foot Walk (T25FW) 2) Gaze Stabilization Test (GST) 3) Dynamic Visual Acuity Test (DVAT) 4) Perceived Deficits Questionnaire (PDQ) 5) Short Form-36 Health Status Questionnaire (SF-36) 6) Dizziness Handicap Inventory (DHI) 7) Modified Fatigue Impact Scale (MFIS)	BEEMS improved multiple outcomes regardless of whether brainstem/cerebellar lesions were present, supporting the generalizability of BEEMS for ambulatory people with MS who have at least minimally impaired balance and fatigue.	14	8	6	not specified.
Tramontano, 2018a	Subacute Stroke	TOT = 25 patients (13 women) VG = 13 Mean age (SD) = 63.1 (8.5) CG = 12 Mean age(SD) = 65.1 (15.5)	Standard physiotherapy program (2 times/week for 4 weeks) + 3 times/week for 4 weeks VR with Gaze Stability Exercises and Upright Postural Control.	standard physiotherapy program (2 times/week for 4 weeks) + 3 times/week for 4 weeks Balance Exercises.	**Primary Outcomes:** 1) 10-Meter Walk Test (10MWT) 2) Functional Ambulation Classification (FAC) 3) Tinetti Balance and Gait (TBG) 4) Berg Balance Scale (BBS) 5) Barthel Index (BI)	Higher values of walking speed and stride length were observed in the VR group. Conversely, no significant difference was found in terms of trunk stability.	4	First follow up after 12 weeks Second follow up after 48 weeks	5	Gaze stability exercises = 10 min Upright postural control = 10 min TOT = 20 min

Tramontano, 2018b	Multiple Sclerosis	TOT = 30 patients (17 women) VG = 15 (9 women) Mean age (SD) = 50.64 (11.73) CG= 15 (8 women) Mean age(SD) = 45.77 (10.91)	2 daily 40-minute sessions 5x/wk for 4 weeks of conventional neurorehabilitation therapy for MS and 4 weeks of VR.	2 daily 40-minute sessions 5x/wk for 4 weeks of conventional neurorehabilitation therapy for MS.	**Primary Outcomes:** 1) Berg Balance Scale (BBS) 2) Barthel Index (BI) 3) Fatigue Severity Scale (FSS) 4) Two-Minute Walking Test (2MWT) 5) Expanded Disability Status Scale (EDSS) 6) Tinetti Balance and Gait Scale (TBG) 7) Timed 25-Foot 154 Walk test (T25FW)	Significant improvement was found in the experimental group with respect to the control group ($p < 0,05$) in balance, fatigue perception, activities of daily living and short distance gait. No significant improvements were found for gait endurance as measured by Two Minute Walking Test.	4	first follow up after 4 weeks Second follow up after 8 weeks	6	Gaze stability exercises = 10 min Postural control exercises = 10 min TOT = 20 min
Mitsutake, 2017	Stroke	TOT = 28 patients (6 women) VG = 14 (3 women) Mean age (SD) = 67.6 (9.0) CG= 14 (3 women) Mean age (SD) = 68.1 (13.5)	Conventional physical therapy for 40 min and VR for 20 min, as a 60 min session, during the first 3 weeks and then completed only the conventional intervention for 60 min for the following 3 weeks.	60 min conventional physical therapy for 6 weeks.	**Primary Outcomes:** 1) Gaze stabilization test (to assess vestibulo–ocular reflex) 2) 10-Meter Walk test (10MWT) 3) Timed up and go test (TUG) 4) Dynamic Gait Index (DGI) (to assess gait performance)	The experimental group showed an improvement in gaze stabilization test scoring, which increased significantly after 3 weeks compared with the baseline. The dynamic gait index was also significantly increased after 3 and 6 weeks compared with the baseline.	3	6 (conventional intervention)	5	20 min
Ozgen, 2016	Multiple Sclerosis	TOT = 40 patients (28 women) VG = 20 (16 women) Mean age = 42.5 CG= 20 (12 women) MEAN AGE = 39.5	8-weeks of customized VR.	Usual medical care.	**Primary Outcomes:** 1) Dizziness Handicap Inventory (DHI) 2) Activities-Specific Balance Confidence (ABC) Scale 3) VAS for balance or/and dizziness 4) Tandem Romberg Test 5) Foam Romberg Test 6) Static posturography 7) Five Times Sit-to-Stand Test (FTSTS) 8) Timed Up and Go Test (TUG) 9) Six-Meter Walk Test (6WT) 10) Dynamic Gait Index (DGI) 11) Functional Gait Assessment (FGA) 12) Berg Balance Scale (BBS) **Secondary Outcomes:** 1) Six-Minute Walking Test (6MWT) 2) Beck Depression Inventory (BDI) 3) Expanded Disability Status Scale (EDSS) 4) Multiple Sclerosis Quality of Life Scale–54 (MSQoL-54)	Customized VR is an effective method for treating balance disorders in patients with MS.	8	absent	6	30-45 min
Moore, 2016	TBI	TOT = 14 patients (8 women)	Supervised home exercise program consisting of VR combined with aerobic training.	NO CONTROL GROUP	**Primary Outcomes:** 1) Rivermead Post-Concussion Questionnaire symptom (RPQ-3) and function (RPQ-13) subcategories 2) Dizziness Handicap Inventory (DHI) 3) Activities-specific Balance Confidence Scale (ABC) 4) functional gait assessment (FGA) 5) return to work/study (RTW) 6) return to activity (RTA).	Following 6 months of participation in a supervised home exercise VR program with aerobic training, significant home exercise VR program with aerobic training, significant improvements were observed in participants’ report of concussion-related symptoms, function, and return to meaningful activities.	12	24	5	40-45 min

Acare, 2015	Parkinson Disease	TOT = 40 patients (15 women) VG = 29 (12 women) Mean age = 67 (51–81) CG = 11 (3 women) Mean age = 60 (40–71)	Customized VR 1 session per week for 8 weeks + instructions and diagrams of exercises to perform as a home exercise program.	Usual medical care.	<u>**Primary outcomes:**</u> 1) Unified Parkinson's Disease Rating Scale (motor score) 2) Parkinson's Disease Questionnaire-39 (quality of life) 3) Activities-Specific Balance Confidence Scale (ABC; balance) 4) Timed Up and Go Test (balance) 5) Dynamic Gait Index (DGI; balance) 6) Berg Balance Scale (BBS; balance) 7) Modified Clinical Test for Sensory Interaction on Balance (postural stability)	VR was found to be effective for improving balance in patients with Parkinson's disease (both subjectively and objectively). No improvement was seen in motor functions, quality of life.	8	absent	6	VR session in the rehab unit = 30 - 45 min Home exercise programs = 30 - 40 min
Balci, 2013	Stroke	TOT = 25 patients (18 women) VG = 12, 6 of which received VR, the other 6 patients performed visual feedback posturography training (VFPT) Mean age (SD) = 61.0 (10.1) CG= 13 Mean age (SD) = 65.6 (9.3)	6 weeks VR program.	6 weeks Home exercise composed of basic balance and mobility exercises.	<u>**Primary Outcomes:**</u> 1) Berg Balance Scale (BBS) 2) Timed up and go test (TUG) 3) Dynamic Gait Index (DGI) 4) Dizziness Handicap Inventory (DHI)	The improvements of balance and gait function in rehabilitation groups did not differ from the home exercise group. Rehabilitation programs were equally effective to improve the recovery in acute central vestibulopathy.	6	absent	5	20–30 minutes
Hebert, 2011	Multiple Sclerosis	TOT = 38 patients (20 women) VG = 12 (9 women) Mean age (SD) = 46.8 (10.5) Exercise Control Group (ECG) = 13 (11 women) Mean age (SD) = 42.6 (10.4) CG = 13 (11 women) Mean age(SD) = 50.2 (9.2)	60-min sessions, twice weekly, of VR and fatigue management.	ECG = 60-min sessions, twice weekly, of bicycle ergometry, stretching, fatigue management. CG = no intervention.	<u>**Primary Outcomes:**</u> 1) 21-item Modified Fatigue Impact Scale (MFIS) (for self-reported fatigue) 2) Six-Minute Walk Test (6MWT) (to assess walking capacity) 3) Sensory Organization Test (SOT) (to assess Static upright postural control) <u>**Secondary Outcomes:**</u> 1) 25-item Dizziness Handicap Inventory (DHI) (for self-reported disability due to dizziness or disequilibrium) 2) 21-item Beck Depression Inventory–II (BDI-II) (for self reported depression)	A 6-week vestibular rehabilitation program demonstrated both statistically significant and clinically relevant change in fatigue, impaired balance, and disability due to dizziness or disequilibrium in patients with MS.	6	4	6	55 min
Rossi-Izquierdo, 2009	Parkinson Disease	TOT = 10 patients (5 women) Mean age =69.3 VG = 10	VR was performed in 9 half-hour sessions over a period of a month.	NO CONTROL GROUP	<u>**Primary Outcomes:**</u> 1) Dizziness Handicap Inventory (DHI) 2) Computerised dynamic posturography (CDP) 3) timed up and go test (TUG)	VR in PD has shown to be effective in improving the activities of daily life, gait velocity and balance, as well as in reducing the risk of falls. Moreover, these benefits persist over time.	4	48 (8 out of 10 patient s)	5	30 min

Gurr, 2001	TBI	TOT = 18 patients (within subj.) Vestibular/Control Group = 18 (7 women) Mean age = 46.9	6 weekly 1 hour treatment sessions: Education/re-orientation,VR, Anxiety management and cognitive behavioural strategies to challenge dysfunctional thoughts and beliefs, Coping strategies.	Participants were used as their own controls and had to wait 4 weeks before commencement of vertigo therapy after the initial assessment.	**Primary Outcomes:** 1) sway-monitor assessment 2) five point vertigo rating scale 3) Vertigo Coping Questionnaire (VCQ) 4) Vertigo Symptom Questionnaire (VSS, short version) 5) Vertigo Handicap Questionnaire (VHQ) 6) Hospital Anxiety and Depression Scale (HAD) 7) Standardized set of vertigo exercises.	VR program proved very effective and beneficial for the 18 patients, as their scores on measures of vertigo symptoms, handicap, emotional distress, physical flexibility and postural stability improved significantly post-therapy in comparison to no improvement during a waiting list period.	6	4	5	60 min

Abbreviations: VR, Vestibular Rehabilitation; VG, Vestibular group; Control Group, CG; SD, Standard Deviation;PD, Parkinson Disease; BEEMS, Balance and Eye-Movement Exercises for Persons with Multiple Sclerosis;MS, Multiple Sclerosis; TBI, Traumatic Brain Injury.

Table

Table 2 Vestibular Rehabilitation Details

Kleffelgaard et al., 2019	Guidance, individually tailored exercises (Brandt–Daroff exercises, habituation exercises, gaze-stabilization exercises and exercises for reduced balance focusing on improving sensory integration), a home exercise program (two to five individually modified exercises and general physical activity like walking, biking, and skiing), and an exercise diary (used to enhance awareness and motivation and to register the performed exercises, activities, and the patients' responses to them.).
Hebert et al., 2018	BEEMS has 3 main components: standing balance on different surfaces, mobility-based balance in walking with and without head movements, and visual stability, including voluntary saccadic eye, smooth pursuit movements, and dynamic gaze fixation. Visual input alterations included the following: absent, eyes closed; conflicting, head and body movements without gaze fixation; and visual field movement and hand eye coordination, ball tossing and catching, eyes open. Somatosensory input alterations included the following: base of support, progressive narrowing; and progressive complexity of surface (i.e., firm, compliant, rocking, reactive). Vestibular input alterations or stimulation of the peripheral end organ included head movements in the yaw and pitch directions and body movements in elevation and translation.
Tramontano et al., 2018a	Gaze Stability Exercises (VORx1) and Upright Postural Control Exercises on a foam cushion (Each patient, blindfolded, was asked to "hold the standing position for one minute" or "march in place on the cushion for one minute" depending on the patient's ability. At the end of the first minute, remaining blindfolded, the patient made 90◦ clockwise turn and repeated the exercise for another minute. The same procedure was carried out at 180◦ and 270◦ for a total of four minutes).
Tramontano et al., 2018b	Exercises for gaze stability (VORx1) and those for postural stability in a standing position on a foam cushion (Each patient, blindfolded, was asked to "hold the standing position for one minute" or "march in place on the cushion for one minute" depending on the patient's ability. At the end of the first minute, remaining blindfolded, the patient made 90◦ clockwise turn and repeated the exercise for another minute. The same procedure was carried out at 180◦ and 270◦ for a total of four minutes).
Mitsutake et al., 2017	Eye-head coordination exercises (VORx1, VORx2). The exercises progressed under more challenging conditions from sitting to standing with feet apart, feet together, and walking. For the balance exercises, patients were asked to maintain balance while rotating their neck and trunk to the right and left, and weight shifting forward-backward and side to side.
Moore et al., 2016	Gaze stabilization (dynamic - VORx1 and VORx2 - and static), sensory organization (postural control challenges such as standing on varying surfaces, bases of support of varying width and varying complexity of static and dynamic visual input), and gait (ambulation with head motion in all planes and varying complexity of static and dynamic visual input while ambulating).
Ozgen et al., 2016	Adaptation exercises (VORx1, VORx2), Substitution exercises (designed to foster the development of alternative strategies as substitutes for lost vestibular function), Balance exercises (switching between dynamic balance exercises), Sitting balance (sit upright and to reach sideways in a roll plane while focusing on a single target. Sit-to-stand activities were also performed), Standing Balance (stand with eyes open or closed while narrowing the base of support progressively), Standing dynamic balance exercises (stand and move without walking), Habituation exercises (movements and positions sufficient to cause mild-to-moderate symptoms during the patient's daily activities), Ambulation Exercises (walk forward, eyes open or closed, backward, sideways, along a line and around cones).
Acarer et al., 2015	Adaptation exercises (to improve gaze stability), Substitution exercises (for the lost vestibular function), Habituation exercises (movements and positions to cause mild-to-moderate symptoms during daily activities), Balance exercises (while switching between static and dynamic movements by altering visual, somatosensory, and vestibular impulses.).
Balci et al., 2013	Vestibular adaptation and specific balance exercises under the supervision of a physiotherapist: Eye-head coordination exercises (VORx1, VORx2, VOR cancellation, smooth pursuits and saccades), Balance exercises in sitting and standing position.

Hebert et al., 2011	Upright postural control (static body position and dynamic body motion) and eye movement exercises
Rossi-Izquierdo et al., 2009	Visual biofeedback together with sensitive, real-time monitoring of movement.
Gurr and Moffat, 2001	Standardized set of vertigo exercises and graded exposure to movements and activities, and encouragement to explore the nature and cause of symptoms in a safe setting and to gain control over them by doing exercises and using active coping strategies.

Abbreviations: VORx1, Vestibular Ocular Reflex exercises with a fixed point; VORx2 Vestibular Ocular Reflex exercises with a mobile point; BEEMS, Balance and Eye-Movement Exercises for Persons with Multiple Sclerosis

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.