The effectiveness of allied health therapy in the symptomatic management of progressive supranuclear palsy: a systematic review

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Abstract

Background

Progressive supranuclear palsy is an adult onset neurodegenerative condition. Progressive supranuclear palsy is an aggressive condition associated with a continual loss of function and commonly, death due to aspiration pneumonia. Currently there is no cure, and dopaminergic medications have limited symptomatic benefit for patients. Physiotherapy, occupational therapy, and speech therapy strategies to optimize independence and function are important and show promising effectiveness in practice. Mobility, speech and swallowing problems are some of the most commonly experienced symptoms and are experienced across all stages of the disease.

Objectives

This systematic review aimed to identify and examine the effectiveness of physical, occupational, and speech therapy interventions in the symptomatic management of progressive supranuclear palsy.

Inclusion criteria

This review included participants with progressive supranuclear palsy as per the National Institute for Neurological Disorders and Stroke and the Society of Progressive Supranuclear Palsy criteria, aged over 40 years of age from all community and clinical settings. This review included studies evaluating any physical, occupational or speech therapy interventions that addressed mobility, vision, swallowing, communication or cognitive/neuropsychiatric difficulties experienced by patients with progressive supranuclear palsy compared with usual care and/or baseline measurements. Outcomes of interest included the degree of change, or no change in common symptoms including mobility, vision, swallowing, communication and cognition. All types of quantitative study designs were eligible for inclusion.

Methods

A three-step search strategy was utilized to identify published and unpublished English language studies from between 1996 and 2014 from 11 databases. Methodological appraisal was conducted by two independent reviewers using standardized instruments and relevant data was extracted from included papers using standardized data extraction tools and presented in narrative form due to heterogeneity of interventions.

Results

Six studies of varying methodological quality and small sample sizes were included.

No occupational therapy or speech therapy interventions were identified. Five studies examined physiotherapy rehabilitation programs and one study examined non-invasive brain stimulation. There is preliminary evidence to support the use of various physiotherapy rehabilitation programs. Physiotherapy rehabilitation programs that combine a dynamic antigravity postural system and a vibration sound system or combine balance and posture exercises with audiobiofeedback appear to improve balance. Combined balance and eye movement training appear to improve stance time and gait speed. Balance training appears to improve step length. Balance and eye movement training may improve vertical gaze fixation and gaze error scores. Balance and posture exercises with audiobiofeedback may improve cognition and communication aspects of quality of life.

Conclusion

Research into the effectiveness of allied health therapeutic interventions for progressive supranuclear palsy symptoms is in its infancy with what can be understood as preliminary evidence for the effectiveness of a number of physiotherapy interventions. High quality studies with large sample sizes are needed. Further research is urgently required to both add further evidence to these results and to identify and investigate effective interventions including occupational therapy and speech therapy interventions to manage mobility, vision, swallowing, communication and cognitive/neuropsychiatric symptoms associated with this devastating condition.

Keywords

Physiotherapy; physical therapy; occupational therapy; speech therapy; speech pathology; Steele-Richardson-Olszewski syndrome; Richardson's syndrome; PSP; systematic review.

Declaration

I, Erica Tilley, certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Chapter 1: Introduction and Background

1.1. Introduction

Progressive supranuclear palsy (PSP) is an adult onset neurodegenerative condition. In the classic or PSP-Richardson's phenotype, feelings of postural imbalance, subtle personality changes, non-specific blurred vision,[1] dysarthria (slurred speech) and dysphagia (difficulty swallowing)[2] are the first symptoms to emerge. Other complications include recurrent falls (often backwards),[1] fractures of the skull, trunk and spine,[3] incontinence, apathy, depression, anxiety, dry and reddened eyes due to reduced spontaneous blink rate, slowing of vertical saccadic eye movements leading to vertical gaze palsy and aspiration pneumonia.[1] Towards the end stages of the condition, patients with PSP will typically be anarthric (unable to speak), immobile, and require percutaneous endoscopic gastrostomy feeding secondary to severe dysphagia.[1]

Progressive supranuclear palsy is an aggressive condition associated with a continual loss of function. Currently there is no cure for PSP, and dopaminergic medications have limited symptomatic benefit in these patients.[4] Physiotherapy, occupational therapy and speech therapy strategies to optimize independence and function are important. Mobility, speech and swallowing problems are some of the most commonly experienced symptoms by patients with PSP and are experienced across all stages of the disease.[5] Aspiration pneumonia is the leading cause of death in PSP.[6]

A preliminary search of the literature indicated that beyond small case series, there is very little evidence to guide specific therapies in PSP.[4] The systematic review undertaken as part of this thesis will have the potential to shed further light on what is known or not known about the effectiveness of allied health therapy in the symptomatic management of PSP.

The Joanna Briggs Institute methodology for systematic reviews has its origins in evidence-based healthcare. Systematic reviews play an important role in summarizing primary research findings into a form that provides a reliable overview of current knowledge.[7] They are a way of informing policy and practice, and thereby improve health outcomes. The systematic review contained within this thesis achieves three purposes; 1) to expand the knowledge base within this field, 2) to inform allied health management of patients with PSP and 3) to meet the requirements for a Masters of Clinical Science degree.

1.2 Structure of dissertation

This dissertation is organized into four chapters. This dissertation consists of:

Chapter 1: Introduction: The first chapter describes the context of the review including the review objective and question, classification and diagnosis of PSP,

symptoms of PSP, and allied health management of PSP. The need for a systematic review is introduced and the purpose of the systematic review is defined.

Chapter 2: Methods: The second chapter describes the methodological process for the systematic review contained within this thesis. This chapter outlines the inclusion criteria (types of participants, interventions/comparator, outcomes and studies), search strategy, and method of critical appraisal, data collection and data synthesis.

Chapter 3: Results: The third chapter presents the search results, the methodological quality and study characteristics of included studies. The findings of the review are outlined in narrative form.

Chapter 4: Discussion: The fourth and final chapter discusses the main findings from the data extracted in the context of existing literature and identifies limitations within the systematic review. It concludes with implications for practice, implications for research and conclusion.

Following the references, there are ten appendices referred to throughout the dissertation.

As mentioned, the review objective and question, classification and diagnosis of PSP, symptoms of PSP, allied health management of PSP in practice will be outlined. The first chapter will conclude with an overview of evidence synthesis and the need for a systematic review.

1. 3. Review objective/question

The objective of this systematic review was to identify, critically appraise, synthesize and present the best available evidence for the effectiveness of allied health therapy in the symptomatic management of progressive supranuclear palsy. More specifically, the review question addressed was:

- What are effective physiotherapy, occupational therapy and speech therapy techniques used in the symptomatic management of PSP?

1.4. Background

1.4.1. Classifying and diagnosing progressive supranuclear palsy

As described in the introduction, PSP is an adult onset neurodegenerative condition. Some neurodegenerative conditions can be classified by their underlying pathology and whether they are a dementia (associated with cognitive changes and cortical pathology) or parkinsonian condition (associated with parkinsonism symptoms including rigidity, tremor and bradykinesia and basal ganglia pathology).[8] It is useful to understand how PSP is classified as this can provide some indication as to similarities with other conditions that are more common and well known. The prevalence of PSP is 6.5 per 100,000[9] and is considered to be as common as motor

neuron disease.[10] A summary of different dementias and parkinsonian conditions has been provided in Table 1.

Along with Alzheimer's disease, types of frontotemporal dementia and corticobasal degeneration, PSP is considered to be a tauopathy. The hallmark of PSP pathology is collections of the protein tau, that accumulate and form neurofibrillary tangles[11] in the basal ganglia, brainstem, and cortex.[4] In contrast, other conditions such as Parkinson's disease, multiple system atrophy, dementia with lewy bodies and Parkinson's disease with dementia are associated with aggregates of the protein alpha-synuclein.[12] As mentioned, PSP pathology can accumulate in the basal ganglia, brainstem and cortex. Patients with the classic phenotype of PSP can experience symptoms of both parkinsonism, and cognitive changes associated with frontotemporal dementia including disinhibition, impulsivity and personality changes.[8]

Parkinsonian conditions can be divided into Parkinson's disease and atypical parkinsonian conditions; 1) PSP, 2) dementia with lewy bodies, 3) multiple system atrophy and 4) corticobasal degeneration.[2] Compared to Parkinson's disease, atypical parkinsonian conditions are associated with rapid progression of disease, absent, poor or waning response to dopaminergic medications, and an earlier presentation of instability, falls, dysphagia and/or dysarthria.[2] All parkinsonian conditions are associated with the three cardinal signs of parkinsonism, 1) rigidity, 2) rest tremor, and 3) bradykinesia (slowness of movement and reduced decrement of movement).[1] However, in the early stages of the condition, slowed movements may be the only sign of basal ganglia dysfunction in PSP.[1]

To be diagnosed with PSP, a patient must meet a set of inclusion criteria, without the presence of symptoms characteristic of neurological conditions listed in the exclusion criteria.[13] Inclusion criteria for 'probable PSP' are 1) a gradually progressive condition, 2) age of onset at 40 or later, 3) vertical supranuclear gaze palsy, and 4) prominent postural instability with falls in the first year of disease onset.[13] 'Possible PSP' is defined by 1) a gradually progressive condition, 2) age of onset at 40 or later and 3) either vertical supranuclear gaze palsy *or* prominent postural instability with falls in the first year of disease onset. As per the NINDS-SPSP diagnostic criteria, 'Definite PSP' can only be confirmed post-mortem with the pathological hallmarks of abnormal 'tau' protein in the basal ganglia, brainstem, and cortex.[4] Exclusion criteria for PSP are listed below as per NINDS-SPSP:[13]

1. **Corticobasal degeneration:** alien limb syndrome, severe limb apraxia cortical sensory deficits, markedly asymmetric onset of bradykinesia, focal frontal or temporoparietal atrophy.
2. **Parkinson's disease:** asymmetric onset of bradykinesia symptoms, tremor-dominant disease, marked and prolonged levodopa benefit.
3. **Dementia with lewy bodies:** hallucinations or delusions unrelated to dopamine, cortical dementia (especially aphasia).

4. **Alzheimer's disease:** cortical dementia (severe amnesia or aphasia or agnosia NINCDS-ADRDA criteria).
5. **Multiple system atrophy:** prominent cerebellar symptomatology or unexplained early and prominent incontinence, impotence or marked postural hypotension.
6. **Multi-infarct parkinsonism** (vascular parkinsonism): multiple strokes, one of which involves the brainstem and basal ganglia.
7. **Whipple's disease:** ocular-masticatory myorhythmia, laboratory confirmation if indicated.
8. **Postencephalitic parkinsonism:** history of encephalitis, oculogyric crisis.

A clinical diagnosis of PSP may be supported by imaging on magnetic resonance imaging. Atrophy of the midbrain may be observable in the shape of a humming bird. However, the humming bird sign may not always be present in those with PSP. The hummingbird sign has a sensitivity of 68.4% and a 100% specificity in clinicopathologically confirmed PSP.[14]

Table 1: Dementia and parkinsonian conditions:

Condition	Sign/symptoms:
ALZHEIMERS' DISEASE	Earliest symptoms include memory/word-finding.[15]
VASCULAR DEMENTIA	Cognitive decline and history of stroke or transient ischemic attack or neurological deficits consistent with sequelae of previous strokes.[16]
PARKINSON'S DISEASE	Unilateral onset of parkinsonism, dyskinesia and excellent response to levodopa and dyskinesia.[4] Dysphagia later.[4]
VASCULAR PARKINSONISM	Parkinsonism, evidence of cerebrovascular disease (lacunar infarction +/- small vessel disease), two disorders must be related.[17]
PARKINSON'S DISEASE WITH DEMENTIA	Parkinsonism precedes cognitive impairment by more than 1 year (otherwise is dementia with lewy bodies).[18]
DEMENTIA WITH LEWY BODIES	Visual hallucinations and cognitive impairment precedes parkinsonism or begins within a year.[18] Early dysphagia and dysarthria.
PARKINSON'S DISEASE WITH DEMENTIA	Parkinsonism precedes cognitive impairment by more than a year (otherwise diagnosed with dementia with lewy bodies).[18]
MULTIPLE SYSTEM ATROPHY	Parkinsonism (multiple system atrophy-parkinsonism subtype) or cerebellar dysfunction (multiple system atrophy-cerebellar subtype) with severe autonomic dysfunction; urinary urgency, constipation, postural hypotension and erectile dysfunction,[4] early dysarthria (hypokinetic, ataxic, spastic or mixed)[19], dysphonia[20], early dysphagia.[2]
BEHAVIOURAL VARIANT FRONTOTEMPORAL DEMENTIA	Disinhibition, loss of empathy, impulsive eating, ritualized or stereotypical behaviour and apathy.[21] No dysarthria, apraxia of speech or aphasia.[22]
SEMANTIC VARIANT PRIMARY PROGRESSIVE APHASIA	Confrontation naming/single word comprehension.[21] Nil apraxia of speech or dysarthria.[22]
LOGOPENIC VARIANT PRIMARY PROGRESSIVE APHASIA	Impaired single word retrieval and impaired repetition.[21] Apraxia of speech or dysarthria uncommon.[22]
NON-FLUENT VARIANT PRIMARY PROGRESSIVE APHASIA	Aggramatism, apraxia of speech[21], spastic, hypokinetic or mixed spastic-hypokinetic dysarthria.[22]
PRIMARY PROGRESSIVE APRAXIA OF SPEECH	Apraxia of speech and dysarthria (spastic hypokinetic or mixed). No aphasia.[22]

Continued…

Condition	Sign/symptoms:
PROGRESSIVE SUPRANUCLEAR PALSY- Richardson's syndrome	Postural instability with falls, executive dysfunction, slowing of vertical saccades/gaze palsy, dysarthria, dysphagia,[4] impulsive eating/mouth-stuffing, prominent and early hypokinetic, spastic or ataxic dysarthria.[22]
PROGRESSIVE SUPRANUCLEAR PALSY – corticobasal syndrome	Corticobasal degeneration-like.[4] At present almost undistinguishable from those with other underlying pathologies.[1] Unilateral ideomotor apraxia, non-levodopa responsive parkinsonism, myoclonus, dystonia, aphasia, cortical sensory and/or visuospatial deficits.[1]
PROGRESSIVE SUPRANUCLEAR PALSY - parkinsonism	Parkinson disease-like.[4] Progressive parkinsonism (unilateral or bilateral bradykinesia and extrapyramidal rigidity with axial predominance +/- tremor) and at best a modest or good response to levodopa with diminishing effect over time.[1]
PROGRESSIVE SUPRANUCLEAR PALSY - frontotemporal dementia	Frontotemporal dementia-like. Motor symptoms of PSP can appear more than five years later than symptoms of frontotemporal dementia including behavioural variant frontotemporal dementia and primary progressive aphasia.[1]
PROGRESSIVE SUPRANUCLEAR PALSY -pure akinesia with gait freezing	Progressive onset of gait disturbance with start hesitation and subsequent freezing of gait in the absence of limb rigidity, rest tremor, cognitive dysfunction or supranuclear gaze palsy in the first five years of disease.[1]
CORTICOBASAL DEGENERATION- corticobasal syndrome	Markedly asymmetric parkinsonism with limb rigidity, dystonia, myoclonus and apraxia, and cortical sensory loss.[4] Aphasia, apraxia of speech, and dysarthria is common.[22]
CORTICOBASAL DEGENERATION- progressive supranuclear palsy	Progresssive supranuclear palsy-like, more executive and behavioural abnormalities.[4]
CORTICOBASAL DEGENERATION- progressive nonfluent aggramatic aphasia	Most common aphasia subtype in corticobasal degneeration.[4]
CORTICOBASAL DEGENERATION- frontotemporal Dementia	Frontotemporal dementia- like (behavioral, visuospatial and language disturbances).[4]
CORTICOBASAL DEGENERATION- Posterior Cortical Atrophy	Similarities in presentation to Alzheimer's disease. Visuospatial disturbances, apraxia and myoclonus.[4]
CORTICOBASAL DEGENERATION- corticobasal syndrome	Markedly asymmetric parkinsonism with limb rigidity, dystonia, myoclonus and apraxia, and cortical sensory loss.[4] Aphasia, apraxia of speech, and dysarthria is common.[22]

1.4.2. Types of progressive supranuclear palsy

Using the existing NINDS-SPSP criteria,[13] there is a set of specific criteria that exclude the presence of other neurological conditions (listed previously). However, it has been suggested that PSP, along with corticobasal syndrome and motor neuron disease, can overlap clinically and pathologically with types of frontotemporal dementia including primary progressive aphasia and primary progressive apraxia of speech.[22] Regardless, PSP is now considered more heterogeneous than previously thought and several subtypes of PSP have been described.[1] The five subtypes of PSP and a brief description are provided below and have been summarized in Table 1.[1]

1. **PSP -Richardson's syndrome (PSP-RS)** is the 'classic subtype' and is characterized by the development of two of the following symptoms within two years of presentation; progressive gait disturbance and spontaneous falls, loss of ocular vergence and hypometric vertical saccades and subcortical cognitive decline including reduced verbal fluency.[1]
2. **PSP –parkinsonism (PSP-parkinsonism)** is defined by progressive parkinsonism (unilateral or bilateral bradykinesia and extrapyramidal rigidity with axial predominance +/- tremor) and at best a modest or good response to levodopa with diminishing effect over time.[1]
3. **PSP-pure akinesia with gait freezing (PSP-PAGF)** is characterized by progressive onset of gait disturbance with start hesitation and subsequent freezing of gait in the absence of limb rigidity, rest tremor, cognitive dysfunction or supranuclear gaze palsy in the first five years of disease.[1]
4. **PSP -corticobasal syndrome (PSP-CBS)** are at present almost undistinguishable from those with other underlying pathologies. Corticobasal syndrome is characterized by unilateral ideomotor apraxia, non-levodopa responsive parkinsonism, myoclonus, dystonia, aphasia, cortical sensory and/or visuospatial deficits. These symptoms are typically associated with corticobasal degeneration pathology, however has been increasingly recognized with a number of different underlying pathologies including PSP.[1]
5. **PSP-frontotemporal dementia (PSP-FTD)** is characterized by the development of the typical motor symptoms of PSP which may take more than five years to present. Initial symptoms are characteristic of those considered amongst the frontotemporal dementia syndromes. Symptoms of behavioural variant of frontotemporal dementia include disinhibition, loss of empathy, impulsive eating, ritualized or stereotypical behaviour and apathy. Non-fluent variant primary progressive aphasia is characterized by aggrammatism, apraxia of speech and spastic, hypokinetic or mixed spastic-hypokinetic

dysarthria.[1] Primary progressive apraxia of speech is defined by apraxia of speech without aphasia.[22]

For the purposes of this thesis, the existing NINDS-SPSP criteria[13] have been utilized as they are the preferred diagnostic criteria for use in clinical research trials[23], and are most commonly used within the literature. The existing NINDS-SPSP criteria[13] are thought to best correlate with the classic subtype of PSP, which is PSP-Richardson's syndrome.[1] As such, it is anticipated that this systematic review will have clinical application to those with the PSP-Richardson's phenotype rather than PSP-parkinsonism, PSP-pure akinesia with gait freezing, PSP-corticobasal syndrome and PSP-frontotemporal dementia.

1.4.3. Symptoms of progressive supranuclear palsy

There are similarities and differences in the symptoms of PSP compared to Parkinson's disease. This will now be explored across each of the domains pertinent to allied health therapy; mobility, vision, communication, swallowing and cognition/neuropsychiatric difficulties.

Mobility: The temporal-spatial gait characteristics of PSP are largely similar to Parkinson's disease.[24] However, shorter stride length and gait changes associated with postural instability (increased step width and double support percentage) are more pronounced in patients with PSP compared to those with Parkinson's disease, despite similar disease duration. Recurrent spontaneous falls, often backwards, from postural instability are more of a feature of PSP than Parkinson's disease.[1]

Vision: Reduced spontaneous blink rate may be apparent in both PSP and Parkinson's disease. However, vertical supranuclear gaze palsy, fixation instability, high square-wave jerk to blink ratio, blepharospasm and apraxia of eyelids opening and closing is more common in PSP than Parkinson's disease:[25]

Abnormal eye movements: In PSP-Richardson's phenotype, slowing of vertical saccadic eye movements (ability to direct visual axes of the eyes either up or down) will progress to a frank vertical gaze palsy or inability to look up or down.[25]

Fixation instability: Normally, the eyes will turn inwards when fixating near a target, however patients with PSP may have fixation instability associated with square-wave jerks (side-to-side movements of the head). Fixation abnormalities also include heterophoria, which is the inability for the eyes to line up properly when one eye is covered. Heterorphoria can be characterized by one eye moving out (esophoria) or in (exophoria) and can cause diplopia or double vision.[25]

Eyelid changes: In PSP, reduced spontaneous blink rate can cause blephorospasm or involuntary twitching or blinking of the eyelids, and dry

eyes. Patients with PSP may also have difficulty opening or closing their eyes associated with apraxia of eyelid opening and closing.[25]

Vestibulo-ocular reflex: Vestibulo-ocular reflex is eye movement that stabilizes images on the retina during movements of the head. Normally when the head is moved rapidly to the side, the eyes will remain looking in the same direction, however in PSP no compensatory eye movements are made.[25]

Swallowing: It is hypothesized that PSP and Parkinson's disease have overlapping pathophysiology of swallow dysfunction. [26] Salient characteristics of dysphagia minimally differ between the two conditions.[26] However, some differences in swallowing dysfunction do exist. Firstly, dysphagia presents earlier in PSP (median latency of 3 years and 6 months) compared to Parkinson's disease (median latency of 10 years and 10 months).[27] In addition, oral phase difficulty (slow mastication and inadequate mastication or chewing) is significantly more common in PSP.[28] This may be related to increased neck hyperextension and rigidity,[28] and impulsive mouth-stuffing eating behaviors observed frequently in PSP.[29] Patients with PSP also have difficulty seeing their meals and self-feeding secondary to vertical gaze palsy.[28]

Communication: 'Pure' hypokinetic dysarthria nearly always found in Parkinson's disease is characterized by monopitch, inappropriate silences, imprecise vowels, and occasionally harsh voice, disfluency/stuttering and short rushes of speech.[30] In contrast, patients with PSP have been described to have harsh vocal quality and a 'growling' dysarthria often in the presence of disfluency or stuttering.[30] Dysarthria characteristics of PSP are considered to share some overlapping features with the hypokinetic dysarthria of Parkinson's disease, however spastic dysarthria (slow rate and strain-strangled voice) and ataxic dysarthria (excess pitch and volume fluctuations, prolonged phonemes and vocal tremor) may be present. Dysarthria dominates communication difficulties in PSP as aphasia (language difficulties) and apraxia of speech are uncommon.[22] Dysarthria occurs earlier in PSP (median latency of 2;years) compared to Parkinson's disease (median latency of 7 years).[27]

Cognition/neuropsychiatric: Reduced processing speed in PSP may be an early symptom, and can progressively deteriorate into severe cognitive slowing in advance stages of the condition.[1] On cognitive assessment, using the Addenbrooke's Cognitive Examination (ACE),[31] patients with PSP present with a similar profile to patients with multiple system atrophy but to a more severe degree.[32] Patients with PSP have impairments across all domains including orientation, attention, memory, verbal fluency, language, and visuospatial skills.[32] Impairments in memory and orientation associated with PSP are less severe than those found in Alzheimer's disease.[32] Of note, verbal fluency is particularly impaired (letter task>category task) more so than in Alzheimer's disease.[32] Poor performance on the ACE verbal fluency task is also able to discriminate patients with PSP, from patients with Parkinson's

disease.[33] Depression and anxiety is a feature of both Parkinson's disease and PSP.[34] Other neuropsychiatric symptoms of PSP include apathy (lack of subjective distress and unresponsiveness to negative as well as positive events), sleeping problems, agitation, irritability and disinhibition.[35]

1.4.4. Allied health management of progressive supranuclear palsy and current literature within the field

Importance of allied health therapy in managing PSP:

People with PSP experience a range of symptoms[5] that reduce quality of life across mobility, self-care, usual activities, pain/discomfort and anxiety/depression domains.[36] Currently there is no cure for PSP, and dopaminergic medications have limited symptomatic benefit in these patients.[4] As such, therapeutic strategies to optimize independence and function are important. A multidisciplinary team should include the primary care-giver, neurologist, primary-care physician and an allied healthcare team that includes a physiotherapist, occupational therapist and speech therapist.[4] Mobility, speech and swallowing problems are some of the most commonly experienced symptoms by patients with PSP and are experienced across all stages of the disease.[5] Aspiration pneumonia is the leading cause of death in PSP.[6]

Current literature within the field:

A preliminary search of the literature indicated that beyond small case series, there was very little evidence to guide specific therapies in PSP.[4] A number of strategies are used in practice by allied health practitioners and have been summarized in Table 2. Therapeutic interventions include falls prevention, aerobic, strength and balance training, care-giver training in assistive techniques, eye-movement exercises, regular swallowing evaluation, communication strategies, home modifications and equipment for mobilizing, activities of daily living and self-feeding.[37, 38]

In addition, many of the strategies for optimizing independence and function for PSP predominately rely on data extrapolated from the study of rehabilitation in Parkinson's disease.[4] Similarities between PSP and Parkinson's disease across mobility, vision, swallowing, communication and cognitive/neuropsychiatric domains include short step length,[24] reduced rate of blinking,[25] hypokinetic speech features,[30] dysphagia across all phases of swallowing,[28] anxiety and depression. [34] However, postural instability (associated with wide step width,[24] recurrent falls and backward falls),[1] slowing of vertical saccades,[25] impulsive self-feeding, [29] ataxic and spastic speech features,[30] and reduced verbal fluency[33] are much more of a feature of PSP than Parkinson's disease. As such, strategies designed for patients with Parkinson's disease may not always be suitable for patients with PSP.

A conference abstract of a systematic review examining the effectiveness of rehabilitation in adults with Parkinson's plus syndromes (including multiple system atrophy, corticobasal degeneration and PSP) up to June 2010 was identified.[39] However, at the time of writing, this study has not yet been published in full-text form. Furthermore, there is an absence of systematic reviews on this topic as shown by a preliminary search of the literature.

Table 2: Discipline-specific strategies used in practice in the management of PSP summarized from CurePSP (2012)[37] with additions from PSP Association UK (2008):[38]

Category of symptoms	Physiotherapy	Occupational therapy	Speech therapy
Mobility difficulties	• Aerobic, strength and balance exercises • Gait training focusing on large steps with adequate foot clearance • Teach safe turning • Fall prevention training • Avoid bending low and standing up quickly to prevent posterior loss of balance • Caregiver training in assistive techniques • Education to caregiver regarding likelihood of increased movement impulsivity and decreased safety judgment with disease progression • Appropriate assistive device (swivel-wheeled rollators with brakes, wheelchair, scooter). • Heel wedge in or on shoe to shift weight anteriorly • Home modifications	• Fall prevention training • Use safe turns and wide staggered stance during Activity of Daily Living (ADL) tasks • Use shower bench with a back and grab bars to eliminate loss of balance • Use hand held shower to reduce turning • Use long handled sponge to reduce bending over • Dress in a seated position • Caregiver training in assistive techniques • Assistive devices such as wheeled rollators • Install a non-skid surface in tub/shower	
Vision difficulties	• Eye movement exercises • Scanning environment before walking • Tilting head down to assist looking down	• Prism glasses for double vision • Tilting head down to assist looking down during ADL's	

Continued….

Category of symptoms	Physiotherapy	Occupational therapy	Speech therapy
Swallowing difficulties	• Breathing exercises/ manual techniques in the prevention/management of chest infections[38]	• Raise height of plate to face level • Use rocker knives, deep spoons and food guards to assist with self-feeding	• Early and frequent swallowing evaluation • Early and frequent discussions regarding feeding tube placement • Optimize oral hygiene • Moist, soft and tender food • Thickened fluids[38] • Use chin-tuck position • Supervision with meals to manage impulsivity • Restrict liquid and food bolus volumes • Mealtime adaptive devices • Medications with puree consistency • Ask Neurologist about medications to assist with excess salivary secretions •
Communication difficulties			• Lee Silverman Voice Technique emphasizing increased loudness (but may be difficult to habituate) • Consider assistive communication devices including a personal portable amplifier • Establish the context of conversation • Speak loudly and slowly • Keep sentences short • Use repetition • Use gestures Caregiver training: • Reduce background noise • Use yes/no questions • One topic at a time • Keep comments/questions brief
Cognition/ neuropsychiatric difficulties		• Reduce background distractions • Break down tasks to one step at a time	

1.5. Overview of the science of evidence synthesis and the need for a systematic review

1.5.1. Evidence-based practice and evidence-based healthcare:

Evidence-based practice involves the judicious weighing together of the experience of the clinician, the needs of the patient, the demands of the healthcare system and the most up-to-date, best available evidence so that the best care is given.[40] The concept of evidence-based practice was first coined in the field of medicine by Sackett et al. in 1996.[41] Evidence-based medicine was defined as a means of 'integrating individual clinical expertise with the best available external clinical evidence from systematic research' (Sackett et al., 1996, p.76).[41] The philosophical origins of evidence-based medicine are attributed to mid-nineteenth-century Paris,[41] where Pierre Charles Alexander Louise utilized statistical analysis to demonstrate that blood-letting had no value as a clinical intervention.[40] Since this time, evidence-based practice has grown to include many other healthcare fields including nursing and allied health.[42]

According to the *Joanna Briggs Institute (JBI) Model of Evidence-based Healthcare,* evidence can be defined 'as the basis of belief; the substantiation or confirmation that is needed in order to believe something is true' (Pearson et al., 2005, p.210).[43] Within evidence generation, there are four types of evidence.[43] Evidence of feasibility is about whether or not an activity or intervention is physically, culturally or financially possible. Evidence of meaningfulness is the extent to which an activity is positively experienced by the patient. Evidence of appropriateness is how an activity or intervention relates to the context in which care is given, whilst evidence of effectiveness is the extent to which an intervention is able to achieve the intended clinical outcome.[43] The Joanna Briggs Institute regards the results of well-designed research studies grounded in any methodological position, qualitative or quantitative, as providing more credible evidence than anecdotes or personal opinion. However, in the absence of such research, expert opinion can be considered as the best available evidence.[43]

Quantitative research generates numerical data by using traditional scientific methods that seek to establish relationships between two or more variables.[44] Quantitative study designs include randomized control trials (RCTs), non-randomized control trials, cohort studies, cross sectional studies, case series and case reports.[44] Qualitative research examines human experiences and cultural and social phenomena.[44] There are a range of qualitative research methods including ethnography, phenomenology, qualitative inquiry, action research, discourse analysis and grounded theory.[44]

A major criticism of evidence-based practice, is that it will become prescriptive and will lead to cost cutting and 'cook-book' practice,[41] where there is one recognized cheap intervention for a specific problem regardless of which patient is being treated.[40] However, according to Sackett's definition of evidence-based practice, a bottom up approach is required that integrates the best external evidence with individual clinical expertise and the patient's choice.[41] Thereby, 'external clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patient at all, and if so, how it should be integrated into a clinical decision.' (Sackett et al., 1996, p.72).[41] Evidence-based practice has also drawn criticism for the emphasis on evidence of effectiveness, and the meta-analysis of RCTs.[42]

The Cochrane Collaboration (established in 1993) focuses primarily 'on the systematic review of RCTs for specific medical conditions, client groups of specific health professional interventions.' (Pearson, 2014, p.456).[42] With an emphasis on RCTs, there is a risk that qualitative research can be overlooked despite being equally valid forms of research.[42] In the *JBI Model of Evidence-based Healthcare, '*any indication that a practice may be effective, appropriate, meaningful, or feasible - whether derived from experience or expertise or inference or deduction or the results of rigorous inquiry- can be regarded as a form of evidence.' (Pearson, 2014, p.458).[42]

1.5.2. Evidence-based practice in allied health:

As mentioned, evidence-based practice first arose in the field of medicine, and since this time it has grown to include other fields including nursing and allied health.[42] There is no universally accepted definition of allied health. However within Australia, allied health disciplines include physiotherapists, occupational therapists, speech therapists, dieticians, social workers, psychology and podiatry.[45] In the year preceding Sackett et al.'s (1996)[41] publication, Enderby and Emerson (1995) authored *Does Speech and Language Therapy Work?*[46] The primary aim of this book was to 'establish the state of knowledge regarding the efficacy of speech language therapy' (Enderby and Emerson, 1995, p.1).[46] In 1998, Bury and Mead published *Evidence-based Healthcare: a practical guide for therapists,*[47] a basic text to help therapists across a range of disciplines understand what evidence-based practice was and what it meant in relation to their clinical practice.[48] There are now a range of texts, publications and resources to provide a basis for the understanding of evidence-based practice that are specific to the fields of physiotherapy,[48, 49] occupational therapy[40, 50] and speech therapy.[51]

Overall, allied health clinicians have positive attitudes towards evidence-based practice and agree that evidence-based practice is necessary, helpful to practice and improves the quality of patient care.[45] Despite this, many allied health clinicians do not often participate in evidence-based practice activities.[45] A qualitative study of 60

allied health professionals, including physiotherapists, occupational therapists and speech therapists, examined the attitudes and barriers to evidence-based practice in a large metropolitan health services in Victoria, Australia.[45] The primary theme from focus groups was that clinicians felt they did not have time for evidence-based practice. Many felt that actively seeing patients in direct clinical care was seen as the priority. This led to feelings of guilt when engaging in evidence-based practice activities.[45] A perception also emerged that some clinicians lacked the understanding about what evidence-based practice means, found searching the literature overwhelming, and did not have the skills to efficiently access information.[45] Some clinicians reported a perception that quality evidence was lacking in their clinical field leading to a feeling of futility when searching literature. This perception was stronger in the fields of social work and speech therapy compared to other disciplines such as dietetics.[45]

Nearly ten years ago, it was identified that there were few RCTs in the field of speech therapy. Randomized controlled trials are the gold standard for measuring efficacy of an intervention.[52] It was proposed by Reilly,[52] that rather than this being a reason not to engage with evidence-based practice, it was simply a challenge to researchers to produce the highest quality of evidence possible, for clinicians to access the highest quality evidence and for professional bodies to educate and create clinical guidelines.

Perhaps one of the greatest contributions to evidence-based practice in the field of speech pathology has been the establishment of a freely available online database speechBITE in 2008. SpeechBITE consists of articles relevant to speech pathology practice, obtained from eight databases, and reports on the methodological quality, thereby benefitting speech pathology clinicians and researchers alike.[53] It has received over a million hits and has been accessed by individuals from 120 countries, with the top five being Australia, USA, UK, Germany and Canada.[53]

The speechBITE database includes systematic reviews, RCTs, non-randomized controlled trials, case series and case studies.[53] All RCTs and non-randomized controlled trials are critically appraised for methodological quality by a team of trained raters using the Physiotherapy Evidence-Database - Evidence Database – (PEDro-P) scale.[54] There are a range of index categories that allow speech therapy clinicians to perform individual customized searches relevant to their clinical practice. Studies can be arranged by target area of speech therapy practice (speech, language, voice, fluency, swallowing and literacy), intervention type, service delivery method, research method or design, client subgroup or etiology, and age group.[53]

There has been a significant growth in the number of publications pertinent to the field of speech pathology in recent years. In 2012 it was reported that, 595 (16%) articles were published between 1951 and the year 2000, 378 (10%) articles for 2000-2003, 980 (26%) for 2004-2007, and 1619 (44%) for 2008-2011.[53] The majority

of these articles were case series studies (42%) and case studies (22%). In total, 18% were RCTs and 11% were non-randomized controlled trials whilst systematic reviews (7%) were the least represented.[53] It appears researchers are rising to the challenge to produce high quality evidence. From 2006, RCTs have increased in frequency, so much so they surpassed the number of single case studies for the year 2011.[53]

As of 2012, the most common etiology represented in speech therapy articles was stroke/cerebrovascular accident (17%).[53] Only 3% of articles pertained to Alzheimer's disease and other dementias.[53] This is of concern given that in the context of an ageing population, an epidemic of Alzheimer's disease is looming. Worldwide prevalence is expected to quadruple to 106.2 million by 2050 with 1 in 85 persons living with the condition.[55] Progressive supranuclear palsy (PSP) is thought to be under-recognized and underdiagnosed.[56] An autopsy cohort study identified 3.5% of adults aged 75 years at the time of recruitment had PSP pathology on autopsy.[57] A search of the speechBITE database for interventions for PSP identified only one single case study for delayed auditory feedback for the treatment of dysarthria.[58] The study was published in 1980, 16 years before the clinical diagnostic criteria for PSP[59] were established.

The national organization for speech therapy in Australia, Speech Pathology Australia, have published ten clinical guidelines thus far.[60] With the limited availability of systematic reviews, these guidelines rely heavily on a variety of levels of evidence including Good Practice Points. As per the National Health and Medical Research Council levels of evidence,[61] good practice points are recommendations provided according to consensus opinion amongst expert working committee members, in the absence of an evidence base.

Physiotherapy and occupational therapy also have freely available online databases consisting of studies pertinent to their field. The Physiotherapy Evidence Database (PEDro) consists of over 31,000 RCTs, systematic reviews and clinical practice guidelines.[49] All RCTs are rated using the PEDro-P scale.[54] OTseeker is a database that consists of over 12,000 RCTs and systematic reviews relevant to occupational therapy interventions.[50] The OTseeker team also utilise the PEDro-P[54] scale to rate RCTs.

All three databases, speechBITE, PEDro and OTseeker, provide a significant contribution to allied health evidence-based practice. However, they are reliant on funding for ongoing development and maintenance. The OTseeker team have identified a rapid increase in the number of RCTs being published, so much so that in future it will not be possible for them to continue to rate all new trials that are entered into the database.[50] A search of 'progressive supranuclear palsy' inPEDro and

OTseeker identified one quasi-randomized controlled study examining a physiotherapy intervention,[62] and no results from the latter database.

1.5.3. Need for a systematic review:

In the *Joanna Briggs Institute (JBI) Model of Evidence-based Healthcare*, the cyclical process begins with the derivation of questions, concerns or interests from the identification of global healthcare needs by clinicians or consumers.[43] This systematic review, examining the effectiveness of allied health therapy in the management of PSP, stems from a professional development session conducted in 2013 for allied health professionals in the Adelaide region (Australia).

Due to a noticeable rise in the number of patients with Parkinson's disease, multiple system atrophy and PSP referred to Domiciliary Care (a community organization for adults living in their own home aged 65 years and over), a professional development session was arranged. It consisted of six presentations delivered by expert clinicians in the field, and staff from several Adelaide based and South Australian country services were invited to attend. The professional development session was attended by 240 health professionals, mainly physiotherapists, occupational therapists and speech therapists, from nine metropolitan hospitals (across acute, rehabilitation, private and public settings) and a variety of community services (across Domiciliary Care, Disability SA, community health centers, and nursing home based day rehabilitation centers).

Following feedback from the professional development session, a need for a quantitative systematic review evaluating the effectiveness of physiotherapy, occupational therapy and speech therapy interventions for the management of PSP was identified. As discussed, mobility, speech and swallowing problems are some of the most commonly experienced symptoms by patients with PSP and are experienced across all stages of the disease.[5] Aspiration pneumonia is the leading cause of death in PSP.[6] Currently there is no cure for PSP, and dopaminergic medications have limited symptomatic benefit in these patients.[4]

A systematic review will have the potential to shed further light on what is known or not known about the effectiveness of allied health therapy in the symptomatic management of PSP. Clinical guidelines are often generated from systematic reviews, and therefore this process of evidence synthesis is considered central to improving health outcomes through getting the best available evidence into action in policy and practice.[42] In cases where there is little good quality information in the literature, the main conclusion of systematic reviews may be that further research is required.[7] This can also be useful in that it highlights areas in need of further primary research.[7]

1.5.4. Evidence synthesis:

Evidence synthesis refers to the systematic review of evidence, and plays a central role in evidence-based practice.[42] Clinicians need to make informed and rapid decisions in everyday practice. They rely on their training, clinical expertise and high quality scientific evidence to guide this process.[7] However, new literature emerges all the time, and it is challenging for both clinicians and researchers to keep their knowledge up to date.[7]

Two main approaches to reviewing literature include 1) narrative reviews and 2) systematic reviews.[7] Narrative reviews are considered to be the more traditional approach to summarizing literature.[7] However, they are at increased risk of bias compared with systematic reviews.[7]

Systematic reviews play an important role in summarizing primary research findings into a form that provides a reliable overview of current knowledge.[7] The systematic review is a more rigorous approach to reviewing the literature and consists of several steps:[42]

1) The development of *a priori* protocol which stipulates a predetermined plan to ensure rigor and minimize potential bias.[44] All stages of the intended systematic review methodology are described in detail and the protocol is typically subjected to peer review prior to publication.[44]
2) The question or hypothesis to be pursued is stated clearly. The objective of the systematic review provides a basis for the development of inclusion and exclusion criteria.[44]
3) Appropriate inclusion and exclusion criteria are developed. The types of participants, study settings, types of interventions, types of outcome measures and types of studies to be included in the systematic review should be stipulated. This provides a transparent process for including or excluding studies for the systematic review.[44]
4) An appropriate strategy to identify all relevant literature is established. The credibility of a systematic review relies on access to an extensive range of electronic databases for literature searching, and documentation of the databases searched.[44] The number of databases searched should be as wide as considered appropriate for the focus of the review. Grey literature, such as papers, reports, technical notes or other documents produced and published by governmental agencies, academic institutions and other groups that are not distributed or indexed by commercial publishes, should be considered. Grey literature may have the potential to complement and communicate findings to a wider audience.[44]

5) The process for critical appraisal of methodological quality of the studies, and any exclusion criteria based on quality considerations is identified. Critical appraisal is important as it involves determining the extent to which a study has excluded the possibility of bias in its design, conduct and analysis.[44] If bias has not been excluded, then the results of a study may be questionable and potentially invalid. A standardized tool should be utilized for critical appraisal,[44] such as the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix II).

6) Details of how data will be extracted from primary studies are identified. A standardized data extraction instrument is recommended to reduce errors in data extraction. In addition to data extracted related to the research question and outcomes of interest, any information that may impact upon the generalizability of the review findings (study method, setting and population characteristics) should also be extracted and reported.[44]

7) A plan of how data extracted will be synthesized is established. This should be a transparent process as the method of data synthesis will influence the findings of the systematic review.[44] If the data was heterogeneous, it should be presented in narrative form with an explanation of the potential sources of heterogeneity (clinical, methodological, statistical) as well as on what basis was it deemed inappropriate to combine the data statistically.[44] Where meta-analysis was used, the statistical methods and software used should be described.[44]

1.6. Methodological Approach

This systematic review examining the effectiveness of allied health therapy in the symptomatic management of PSP was based on the Joanna Briggs Institute (JBI) methodology assessing quantitative evidence for the effectiveness of an intervention, utilising the JBI-SUMARI software package incorporating the JBI Comprehensive Review Management System (CReMS) and specifically the Meta-Analysis of Statistics Assessment and Review (MAStARI) to critically appraise and extract data from the included studies. Assessment of methodological quality in JBI systematic reviews is determined by critical appraisal undertaken by two independent reviewers using standardized instruments.

For questions of effectiveness for which there are no RCTs, using alternative approaches that take the best available evidence limits the likelihood of arriving at an empty review (whereby virtually no conclusions or clinical recommendations can be made).[63] Therefore studies using quasi-randomized control,[64] case series[65-68] and case study[69] designs have been included in this systematic review. These types of study designs are considered to be less robust as they lack random allocation to an intervention. Chapter 2 outlines the systematic review methods including eligibility

criteria, search strategy, study selection including critical appraisal, data extraction and data synthesis methods. The *a priori* systematic review protocol[70] has been published previously.

Chapter 2: Methods

2.1. Inclusion criteria

2.1.1. Types of participants

This systematic review included participants with a diagnosis of probable or possible PSP as per the established diagnostic criteria for PSP (NINDS-SPSP).[13] Participants were required to be over the age of 40 years, as age of onset under the age of 40 years is not supportive of a diagnosis of PSP.[13] All participants were included regardless of length of time from diagnosis. Participants from all settings including community, hospital or residential care were considered. Exclusion criteria included additional conditions not usually associated with PSP likely to affect mobility, vision, swallowing, communication or cognition i.e. congenital conditions, structural abnormalities, or cancer in particular regions of the body (oral, laryngeal, pharyngeal or esophageal cancer affecting swallowing).

2.1.2. Types of interventions/comparator

This systematic review considered studies that evaluated any allied health therapy that addressed mobility, vision, swallowing, communication or cognitive difficulties experienced by patients with PSP. Interventions currently within the scope of practice for speech pathology, occupational therapy, and physiotherapy included a range of techniques including: carer and patient education, caregiver training, assistive equipment, exercises, compensatory strategies, monitoring of difficulties, modified diet and fluids, and discussion regarding need for percutaneous endoscopic gastrostomy feeding options. This review also considered non-invasive brain stimulation therapy. Non-invasive brain stimulation therapy is an emerging intervention used by allied health researchers, however is not yet considered to be within the current scope of practice. All studies addressing current and emerging allied health interventions were eligible for inclusion, regardless of mode, frequency of delivery or length of intervention duration.

The effectiveness of interventions of interest was compared to usual care and/or baseline measurements as described by studies. It was acknowledged that in the case of descriptive studies, there might not always be a comparator. Before and after intervention outcome measures were compared.

2.1.3. Outcomes

Outcomes of interest included the degree of change, or no change, in the symptoms experienced by patients with PSP under the domains of mobility, vision, swallowing, communication and cognitive difficulties. Examples of outcome measures include

those for general functioning (Unified Parkinson's Disease Rating Scale),[71] mobility (the Berg Balance Scale[72] and the Timed Up and Go Test),[73] vision (The Vertical Gaze Fixation Score),[74] and swallowing (Endoscopic Swallowing Parameters using Fibreoptic Endoscopic Evaluation of Swallowing.[75] It was anticipated that a broad range of outcome measures would be identified. In addition, the consequences of symptoms experienced by patients with PSP were of interest. Potential outcome measures included, but were not limited to, falls rates, number of fractures (from falls), episodes of aspiration pneumonia (from swallowing difficulties), extent or presence of weight loss (from swallowing difficulties), reduced quality of life (Parkinson's Disease Questionnaire-39),[76] and reduced survival time.

2.1.4. Types of studies

Any quantitative study (experimental, quasi-experimental, analytical observational, descriptive observational) that examined the effectiveness of management strategies of PSP, more specifically physiotherapy, occupational therapy or speech therapy interventions was considered for inclusion.

2.2. Search strategy

The search strategy aimed to find both published and unpublished studies. A three-step search strategy was utilized in this review. An initial limited search via MEDLINE (PubMed), CINAHL, Health Informit, PsycINFO, PEDRO, OTSeeker, and SpeechBite was undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms (Appendix I) was then undertaken across all included databases. Thirdly, hand-searching was conducted in the New England Journal of Medicine and the reference list of all identified reports and articles were searched for additional studies. Only studies published in English language were considered due to the unavailability of resources for translation services. As the NINDS-SPSP criteria[13] were first published in July 1996,only studies published between July 1996 and April 2014 were considered for inclusion in this review.

The databases and resources searched included: MEDLINE (PubMed), CINAHL, Cochrane Library (CENTRAL), Embase, Biosis, Health Informit, Best Practice (formally Clinical Evidence BMJ), PsycINFO, PEDRO, OTseeker, and SpeechBite.

The search for unpublished studies included: MedNar (including publications from PSP Associations), US National Institute of Health (including National Institute of Neurological Disorders and Stroke and Clinical Trials), US Department of Health and Human Services (National Institute of Ageing), American College of Physicians and Natural Standard and dissertations and theses in ProQuest. In addition, searches through the Google search engine were completed.

2.3. Assessment of methodological quality

Quantitative papers selected for retrieval were assessed by two independent reviewers (ET and AM) for methodological validity prior to inclusion in the review using the standardized critical appraisal instrument, the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix II). Any disagreements that arose between the reviewers were resolved through consultation with a third and fourth reviewer (SW and MP). Given the number of publications in the field of PSP is relatively limited, a low threshold for methodological quality was instated in order to capture the greatest number of studies for inclusion. Studies to be considered for inclusion only had to score one yes using the JBI-MAStARI instrument, as studies that scored zero were not considered to be of sufficient quality to include in the systematic review.

2.4. Data collection

Quantitative data was extracted from papers included in the review using the standardized data extraction tool from JBI-MAStARI (Appendix III). The data extracted included specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

2.5. Data synthesis

As the quantitative papers all examined different interventions, pooling of data in statistical meta-analysis using the JBI-MAStARI software was not appropriate. Instead, the findings were presented in narrative summary and tabular form.

Chapter 3 outlines the search results, reasons for excluded studies, critical appraisal of methodological quality, and an overview of the six studies included in the systematic review. A PRISMA flow diagram for the identification of studies for inclusion and exclusion has been provided (Figure 1).

Chapter 3: Results

3.1. Search results

Searching the 11 databases and sources of unpublished literature and hand-searching yielded 10,333 titles for review, of which 8,145 remained following the removal of duplicate articles (Appendix I). Title and abstract content was screened for relevance to the review, and 76 articles were retrieved in full text for detailed examination. A further 69 articles were excluded following full text examination full text examination (Table 3).

Six articles were published in a language other than English,[77-82] 22 articles were not quantitative studies,[29, 83-103] three articles did not contain an intervention[104-106], two articles did not pertain to patients with PSP[107, 108], 19 articles were non full text items[109-127] and three articles discussed studies that were currently underway.[104-106] It was identified that a PhD thesis[64] reported on findings that overlapped with two published studies using identical interventions.[62, 128] The PhD thesis was chosen for inclusion in this review as it contained a crossover component for the intervention that was not reported on in the published studies.

Following the exclusion of 69 full text articles, seven studies remained.[64-69, 129] As part of the third stage of the searching process, the reference lists of all seven studies was examined to identify possible additional studies. No further studies were identified and subsequently the studies underwent critical appraisal.

In discussion with experts in the field (JM and SD), eight studies were excluded as they did not examine the efficacy of an allied health intervention.[26, 130-136] The study by Warnecke, Oelenberg and Teismann (2010),[26] reported speech therapy strategies of chin-tuck maneuver, hard swallow and modification of food consistency were the most effective interventions for dysphagia in PSP. However, outcome data specific to these interventions was not provided.[26] The main focus of the study was to examine the endoscopic characteristics and responsiveness to levodopa in swallowing function in patients with PSP. The study was not included as the administration of levodopa medication is not considered within the scope of allied health practice.

The study Hohler by et al.[137] was excluded on the basis that it was not possible to extract population characteristics and outcome data specific to PSP. The study examined the effectiveness of an inpatient movement disorders program on 91 patients with different types of parkinsonism including four patients with PSP. The study reported on the population as a whole, regardless of the type of parkinsonism. The author of the study was contacted to request data specific to their population with PSP, but no response has been received at the time of writing.

For inclusion for the systematic review, study participants had to be diagnosed with PSP using NINDS-SPSP diagnostic criteria.[13] The participants in the two studies by Steffan et al.[138, 139] had mixed corticobasal degeneration and PSP. Therefore, these studies were excluded as corticobasal degeneration is an exclusion criteria for the diagnosis of probably or possible PSP. It was unclear whether NINDS-SPSP diagnostic criteria[13] were used in four studies.[67, 69, 129, 140] The authors of each study were contacted to clarify this information. Sandyk[129] and Sale et al.[67] responded in the affirmative, however no response was received from Spagnolo et al.[140] or Suteerawattananon, MacNeill and Protas.[69] After consideration, the study by Spagnolo et al.[140] was excluded as it was unlikely the participant had PSP as per NINDS-SPSP diagnostic criteria[13] or the PSP-Richardson's subtype. The participant presented with a Mini Mental Examination Score of 13 indicating severe cognitive impairment,[141] and had apraxia of speech. Cortical dementia is an exclusion criteria in NINDS-SPSP[13] and apraxia of speech is uncommon in PSP-Richardson's phenotype.[22] The study by Suteerawattananon, MacNeill and Protas[69] was included on the basis that there were no reasons to presume that the participant did not have PSP as per NINDS-SPSP criteria.[13]

Table 3: Studies excluded following retrieval of full text articles, and their reasons for exclusion.

Reason for exclusion following retrieval: (n=69)	Number of studies:	Citations:
Published in languages other than English	6	77-82
Non-quantitative study design	22	29, 84-103, 142
No intervention	3	104-106
Non allied health intervention	8	26, 130-136
Population do not have PSP	2	107, 108
Data for subjects with PSP can not be extracted from population	1	137
Population did not meet the clinical NINDS-SPSP* criteria[13]	3	138-140
Non full text articles**	19	109-127
Published studies with overlapping findings within a PhD thesis[64]	2	62, 128
Details of studies currently underway (i.e. postural instability, use of Lokomat to improve efficiency of treadmill training, and foot mechanical stimulation to improve gait).	3	143-145

*NINDS-SPSP: National Institute for Neurological Disorders and Stroke (NINDS) and the Society of Progressive Supranuclear Palsy (PSP).[13]

**non-full text articles were searched for their full text counterparts online and in Scopus. Of these, two full text articles had already been identified in the initial search, and the remaining articles were not available in full text form.

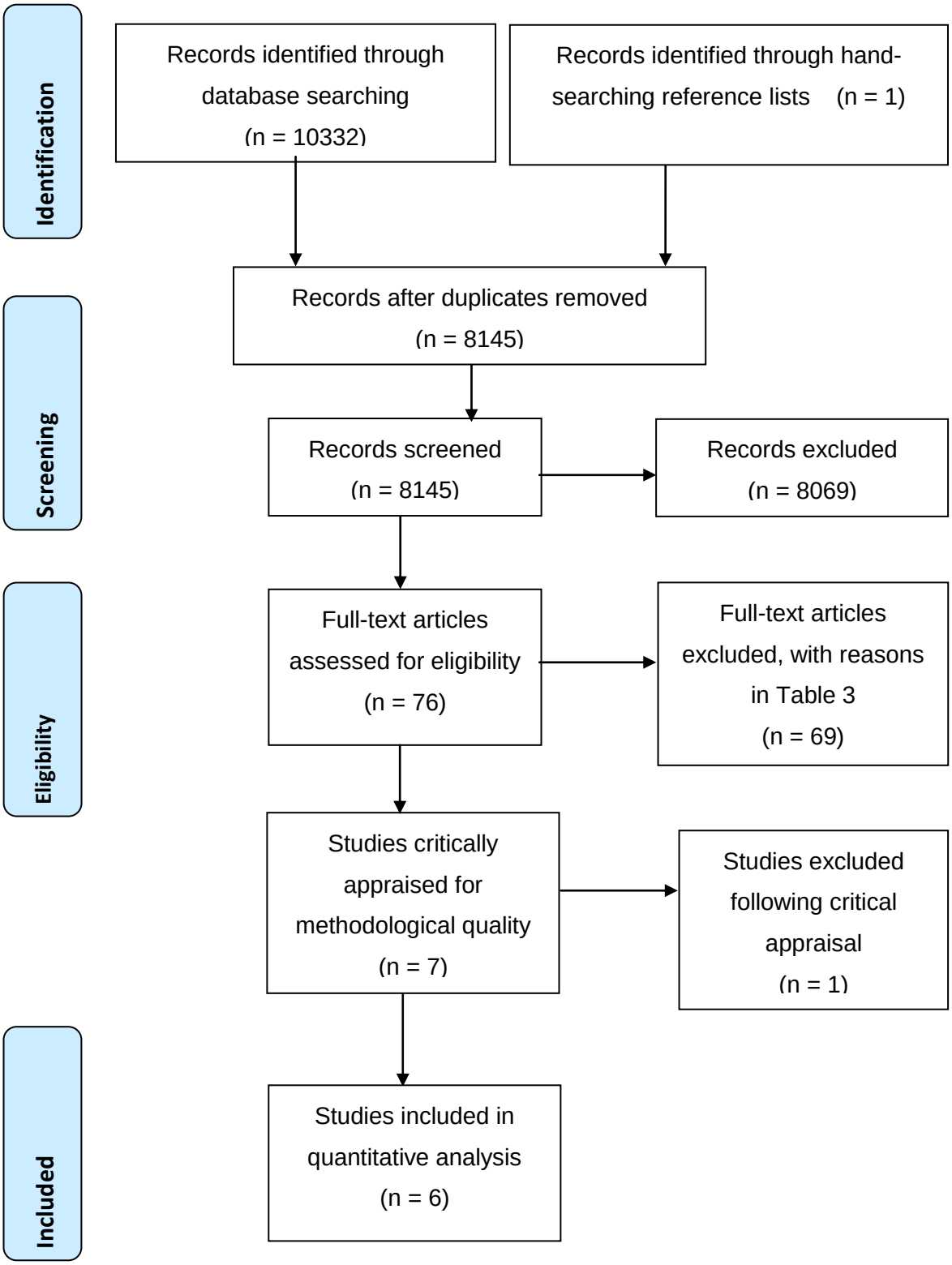

Figure 1: **Study identification flow diagram: PRISMA 2009 Flow Diagram**[146]

3.2. Assessment of methodological quality

Table 4 and Table 5 outline the critical appraisal scores for each of the seven appraised studies. The PhD thesis by Zampieri[64] utilized a quasi-randomized controlled study design. Therefore, it was appraised using the JBI Critical Appraisal Checklist for Randomized Control/Pseudo-randomized trial (Appendix II), which consists of ten items. The six descriptive/case studies were appraised using nine items contained in the JBI Critical Appraisal Checklist for Descriptive/Case Series (Appendix II). They were scored from a possible seven points, as two questions (five and seven) were not considered applicable as none of the studies had participants who withdrew, or had groups to compare. Of the six descriptive/case studies, statistical analysis was not undertaken in three studies.[68, 69, 129]

Four studies used interventions within the current scope of practice for physiotherapy, and scored highly on critical appraisal. The study by Di Pancrazio et al.[65] scored poorly on using appropriate statistical analysis. However, it was the only case study included in the review that used a random sample and was therefore not open to possible selection bias. In the thesis by Zampieri,[64] methodological quality was reduced, as participants were only quasi-randomized to the treatment and control group. Possible geographical bias is possible as participants who resided in distant locations to the testing center were allocated to the treatment group. The study by Sandyk[129] examined the effectiveness of transcranial AC pulsed applications of weak electromagnetic fields in reducing freezing and falling in a single patient with PSP. The electromagnetic fields were applied using the Sandyk Electromagnetic Stimulator[SM,TM]. The study was excluded on the basis of poor methodological quality reflected in a critical appraisal score of zero. Data for each outcome measure was not taken at uniform time-points in the study, and the intervention was introduced simultaneously with a change to the participant's medication regime.[129] The case series by Santens et al.[68] lacked sham stimulation however provided an indication of the future potential of repetitive transcranial magnetic stimulation (rTMS) in improving gait and midline symptoms in PSP.

Table 4: Critical appraisal scores for case studies meeting eligibility for inclusion for the review.

Study:	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total
Di Pancrazio (2013)[65]	Y	Y	Y	Y	NA	Y	NA	Y	N	6/7
Nicolai (2010)[66]	Y	Y	Y	Y	NA	Y	NA	Y	Y	6/7
Sale (2014)[67]	N	Y	Y	Y	NA	N	NA	Y	Y	5/7
Sandyk (1998)[129]	N	N	N	N	NA	N	NA	N	NA	0/6
Santens (2009)[68]	N	N	UC	1	NA	N	NA	Y	NA	2/6
Suteerawattananon (2002)[69]	N	N	UC	Y	NA	Y	NA	Y	NA	3/6
	Y= yes, N= no, UC= unclear, NA=not applicable.									

JBI Critical Appraisal Checklist for Comparable Cohort/Case Control

Q1. Is sample representative of patients in the population as a whole?
Q2. Are the patients at a similar point in the course of their condition/illness?
Q3. Has bias been minimized in relation to selection of cases and of controls?
Q4. Are confounding factors identified and strategies to deal with them stated?
Q5. Are outcomes assessed using objective criteria?
Q6. Was follow up carried over a sufficient time period?
Q7. Were the outcomes of people who withdrew described and included in the analysis?
Q8. Were outcomes measured in a reliable way?
Q9. Was appropriate statistical analysis used?

Table 5: Critical appraisal scores for the quasi-randomized study meeting eligibility for inclusion for the review.

Study:	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Total
Zampieri (2006)[64]	N	UC	N	Y	Y	Y	Y	Y	Y	Y	7/10
	Y= yes, N= no, UC= unclear, NA=not applicable.										

JBI Critical Appraisal Checklist for Randomized Control/Pseudo-randomised Trial

Q1. Was the assignment to treatment groups truly random?
Q2. Were participants blinded to treatment allocation?
Q3. Was allocation to treatment groups concealed from the allocator?
Q4. Were the outcomes of people who withdrew described and included in the analyses?
Q5. Were those assessing outcomes blind to the treatment allocation?
Q6. Were the control and treatment groups comparable at entry?
Q7. Were groups treated identically other than for the named interventions?
Q8. Were outcomes measured in the same way for all groups?
Q9. Were outcomes measured in a reliable way?
Q.10 Was appropriate statistical analyses used?

3.3. Description of included studies

3.3.1. Overview of studies

Six studies were included in the review. An overview has been provided in Table 6, with a description of the participants from each study in Table 7. Date of publication ranged from 2002 and 2014 and all studies were published in English as a requirement for inclusion. One study utilized a quasi-randomized controlled study design,[64] four studies were case series[65-68] and one study was a single participant case study.[69] Of the six studies, five studies used interventions currently considered within the scope of practice for physiotherapy.[69] One study examined a non-invasive brain stimulation therapy using rTMS.[68] No studies were identified that included interventions within the current scope of practice for occupational therapy or speech therapy.

3.3.2. Study settings

Two studies were conducted in the USA,[64, 69] two studies were conducted in Italy,[65, 67] and one study each in Belgium[68] and Germany.[66] Two studies were conducted in universities (motion analysis laboratory at the University of Minnesota,[64] and the university center for motor sciences of the University G.d'Annunzio of Chieti-Pescara[65]), one study was conducted in a geriatric rehabilitation center,[66] and three studies did not specify the study setting.

3.3.3. Age/participant numbers/gender

Ages of participants ranged from 57 years[64, 66] to 83 years old[64]. In Zampieri's quasi-randomized controlled study,[64] the treatment group (71.2 ± 5.28) was older than the comparison group (67.55± 7.28). In other studies, the mean age of participants was 69±7[65] and 67.8±11.7.[67] The number of participants ranged from 19 in the quasi-randomized controlled study[64] to a single case study.[69] The number of participants in the case series studies ranged from five to ten participants.[65-68] The single case study was of male gender.[69] The four case series and one quasi-randomized controlled study all had a mix of both male and female gender, although the gender balance was more equal in some studies[64, 67] than others.[65, 66, 68]

3.3.4. Medications/co-morbidities

Four studies specified no changes to participant medication during the intervention,[64-67] and two studies did not specify changes to medications or otherwise.[68, 69] The Mini-Mental Score Examination (MMSE) is an assessment of cognitive impairment. It has a maximum score of 30 and a score below 27 is indicative of mild cognitive impairment.[147] A score of less than 18 indicates severe cognitive impairment.[141] An MMSE score of <23 was an exclusion criteria in Nicolai,[39] and an MMSE score of <24

was an exclusion criteria in Zampieri.[44] MMSE scores were normal in other studies recording baseline MMSE.[65, 69]

3.3.5. Baseline activity and onset of disease duration

Four studies outlined minimal mobility requirements including ability to walk short distances,[64] ability to walk at least 25ft,[67] ability to stand alone[65] and ability to stand with technical support.[66] Three studies used the PSP-Rating scale to measure disease severity.[64-66] The participants in Di Pancrazio et al.'s study[65] (39±4) were on average less severe than the participants in Nicolai et al.'s study[66] (46.5, range 22-58). In Zampieri's study,[64] the control group (28.44± 8.38) was less severe than the treatment group (30.10± 10.34). Duration of disease was shorter in the comparison group (40.6± 31.8 months) than the treatment group (53.0±34.66 months).[64]

Table 6: Overview of the six included studies.

Study:	Setting:	Intervention/comparator:	Intensity/duration:	Study design:
Di Pancrazio (2013)[65]	Italy: University center for motor sciences University G.d'Annunzio of Chieti-Pescara.	Effectiveness of a rehabilitation program combining a dynamic antigravity postural system (SPAD) and a vibration sound system (ViSS). Comparator: baseline measurements	20 minutes, three times a week for two months.	Case series.
Nicolai (2010)[66]	Germany: geriatric rehabilitation centre, 1:1.	Effectiveness of balance and posture exercises with audio-biofeedback in improving balance. Comparator: baseline measurements	45 minutes, three times a week for six weeks, 1:1.	Case series.
Sale (2014)[67]	Italy: setting not specified.	Rehabilitative program of robot-assisted walking on spatiotemporal parameters. Comparator: baseline measurements	45 minutes, five times a week for four weeks.	Case series.
Santens (2009)[68]	Belgium; setting not specified.	Effectiveness of repetitive transcranial magnetic stimulation (rTMS) in improving gait/midline symptoms. Comparator: baseline measurements	1000 pulses per session, each day for five days (n=5). 1000 pulses per session, each day, for five days repeated three times with 4-week intervals (n=1).	Case series.
Suteerawattan-anon (2002)[69]	USA; setting not specified.	Use of a modified body weight support treadmill training program to reduce falls and improve the balance and gait. Comparator: baseline measurements	Three times a week for 90 minutes for eight weeks.	Case study.
Zampieri (2006)[64]	USA; motion analysis laboratory at the University of Minnesota.	Effects of balance and eye movement training compared to balance training alone on gait and gaze control. Comparator: balance and eye movement vs balance training alone.	One hour, three times a week for four weeks.	Quasi-randomized control.

Table 7: Characteristics of participants from each study.

Characteristics	Di Pancrazio (2013)[65]	Nicolai (2010)[66]	Sale (2014)[67]	Santens (2009)[68]	Suteera-wattan-anon (2002)[69]	Zampieri (2006)[64]
N=	10	8	5	6	1	Treatment: 10 Control: 9
Gender	7M,3F	2M,6F	3M,2F	5M,1F	1M	Treatment 5M,5F Control: 5M,4F
Age (years)	69±7	66, 57-74	67.8±11.7	60-77	62	Treatment: 71.2±5.28, 64-83 Control: 67.55± 7.28, 57-78
Symptom onset or duration of disease (yrs)[66-68]/(months)[64]	Not specified.	4.8, 1.5-13.4	3.6± 1.85	2-7	Not specified.	Treatment: 40.6±31.8 Control: 53.0±34.66
Minimal Mobility Requirements	Can stand alone	Can stand with technical support	Able to walk at least 25ft	Not specified.	Not specified.	Treatment/ Control: Able to walk short distances
Mini-Mental State Examination[147]	29±1	26, 25-29	Not specified.	Not specified.	27	Treatment: 25.7±1.05 24-28 Control: 27.44±2.0 24-30
PSP-Rating Scale (Total)[148]	39±4	46.5, 22-58	Not specified.	Not specified.	Not specified.	Treatment: 30.10± 10.34 Control: 28.44±8.38
PSP-Rating Scale sub-scores[148]	History (6±2), mentation (2±1), bulbar (3±1), ocular (11±2) and limb (11±2).	Not specified.	Not specified.	Not specified.	Not specified.	Treatment/ control: Not specified.
Unified Parkinson's Disease Rating Scale (Total)[71]	Not specified.	Not specified.	Not specified.	Not specified.	47	Treatment/ control: Not specified.

Continued…

Characteristics	Di Pancrazio (2013)[65]	Nicolai (2010)[66]	Sale (2014)[67]	Santens (2009)[68]	Suteera-wattan-anon (2002)[69]	Zampieri (2006)[64]
Unified Parkinson's Disease Rating Scale (motor sub-scare)[71]	Not specified.	Not specified.	Not specified.	Not specified.	24	Treatment: 19.9± 6.74 Control: 22.11±7.33
Unified Parkinson's Disease Rating Scale (other sub-scores)[71]	Not specified.	Not specified.	Hoehn and Yahr disability scale (2.4± 0.5)	Not specified.	Hoehn and Yahr (3), Schwab and England ADL (30%), mentation , behaviour and mood (4), ADL (19), drug therapy (1).	Treatment/ control: Not specified.

3.3.6. Interventions/comparators

All six studies utilized different interventions and thus combining data in meta-analysis was deemed not appropriate. Physiotherapy interventions included a dynamic antigravity postural system and a vibration sound system rehabilitation program,[65] balance and posture exercises with audio-biofeedback,[66] robot-assisted walking,[67] body-weight supported treadmill training,[69] and balance and eye movement training.[64] The case series by Santens, Sieben and Letter,[68] examined the effectiveness of rTMS targeting gait/midline symptoms. The comparator in studies was often baseline measurements with the exception of the quasi-randomized control study,[64] which examined the effectiveness of combined balance and eye movement training compared with balance training alone. These interventions will now be explored beginning with interventions considered within the scope of practice for allied health therapy.

Physiotherapy interventions:

The study by Di Pancrazio et al.[65] explored the effectiveness of a rehabilitation program combining a dynamic antigravity postural system (SPAD) and a vibration sound system (ViSS) on postural instability of 10 patients affected by PSP. The rehabilitation program containing SPAD and ViSS treatments was conducted three times a week for two months. The comparison was made with baseline measurements. The dynamic antigravity postural system encourages the patient to walk in a straight line on a treadmill by suspending the patient through a mechanical anti-gravity vertical traction system that follows their center of gravity and stabilizes

the patient. Each SPAD treatment lasted 20 minutes. The patient's weight was alleviated by 20-30% whilst they were instructed to walk on a treadmill composed and aligned, straight pull, looking in the mirror positioned in front, to walk with correct and long strides, and to properly roll their foot on the floor (heel-plant-toes). The vibration sound system consists of focalized mechanic-sound vibrations to muscle tissue. The study did not state the mechanism of application of the ViSS therapy.

In the case series study by Nicolai et al.[66], the effectiveness of balance and posture exercises with audiobiofeedback in improving balance in eight patients with PSP was explored, in comparison with baseline measurements. The audiobiofeedback system consists of a sensing unit (worn near the center of mass), which measures trunk acceleration along the anterior-posterior and medio-lateral anatomical axes. The sensing unit provides real-time signal processing to modulate a stereo sound (via headphones) to deliver an augmented sensory experience about trunk sway. The balance and posture exercises consisted of six items of increasing difficulty and complexity: 1) posture control in sitting 2) standing positions (range of motion, endurance of maintaining predefined positions), 3) transfers (sit-to-stand, stand-to-sit), 4) sway (differences in base of support, weight shifting, additional upper body movements), 5) reaching and/or stepping in one direction and 6) stepping in different directions with the option of additional upper body movements, walking and stopping and turning. The progression within the exercises was decided on an individual basis based on physical progression during training. The intervention was conducted 1:1, for 45 minutes, three times a week for six weeks.

In the case series study by Sale et al.[67] five participants with PSP underwent a rehabilitative program of robot-assisted walking sessions for 45 minutes, five times a week for four weeks, in comparison with baseline measurements. The end effector system machine used was the G-EO system device (Reha Technology AG; Olten, Switzerland). During each session, the participants practiced 5-30 minutes of simulated floor walking followed by 5-10 minutes of repetitive simulated stair climbing up and down. Participants practiced a minimum of 300 steps on the simulated floor and climbed a minimum of 50 steps on the simulated stair during each session. Rest breaks were optional, but uninterrupted training intervals of at least five minutes for simulated floor walking and three minutes for simulated stair climbing were required.

In the case study by Suteerawattananon, MacNeill and Protas,[69] they examined the use of a modified body weight support treadmill training program to reduce falls and improve the balance and gait of a male patient with PSP. Baseline measures were recorded prior to the start of the study. The participant underwent walk training, balance perturbation and step training using body weight support with a treadmill. The intensity of therapy was 90 minute sessions, three times a week for eight weeks. A Pacer Treadmill was used for the training. An unloading system (SOMA Incremental Weightbearing System) was used to support 15% body weight during

training. Each training session consisted of walking forward at 3mph for 5-7 minutes, walking backward at 1.5mph for 5-7 minutes, and walking sideways with the left and right side leading at 1.5mph for 2 minutes each. During the balance perturbation and step training, the participant was given 0% unloading but was placed in the harness system for safety and prevention of falls. He was asked to stand on the treadmill belt and hold the handrails. The therapist than disturbed the participant's balance by suddenly turning the treadmill on (speed=1.5mph) and letting him walk until he was able to regain his balance in an erect posture. The treadmill was then turned off. Most training sessions consisted of about 15-20 perturbations in the forward and backward directions and 10-15 perturbations for both left and right sideways positions.

In the quasi-randomized controlled study with partial crossover by Zampieri,[64] the effects of balance and eye movement training compared to balance training alone on gait and gaze control were examined. During Phase I, patients from both groups were tested before and after four weeks of intervention. In Phase II, patients assigned to the comparison group (balance training only) crossed over to receive the balance and eye intervention and were tested again before and after the intervention. The frequency and intensity of treatment was 60 minutes, three times a week for four weeks.

Participants of both the treatment and comparison group received the same set of balance exercises for 60 minutes per week. These exercises included tandem stance with eyes open and closed, turning while standing, and rising from a chair. Gentle perturbations were introduced during selected trials to encourage each subject to maintain balance. For the remaining two 60 minute sessions per week, the treatment group received exercises that emphasized visual awareness (scanning the environment to identify hidden objects), computer assisted saccade training (responding with key press to visual stimuli presented in random locations on the computer screen using Vision Builder software developed by Optometric Extension Program Foundation, Inc), sensory feedback (where a change in the direction of eye movement produced different sounds), and attention training with balance perturbations to enhance eye-foot coordination using a stimulus-response compatibility paradigm. The comparison group received additional balance exercises for two 60 minute sessions per week. The subjects practiced self-initiated stepping, heel-to-toe walking, toe and heel-lifts while standing, rising from a chair, single leg stance, and platform stepping up and down.

Occupational therapy and speech therapy interventions:

No studies identified examined interventions currently within the scope of practice or emerging in the field of occupational therapy or speech therapy.

Emerging/experimental interventions:

In the case series study by Santens, Sieben and Letter,[68] the effectiveness of rTMS in improving gait and midline symptoms in six patients with PSP was explored. The stimulation site was defined by identifying a maximal motor evoked potential in the anterior tibial muscle. The motor threshold was defined as that minimal stimulator output current resulting in a motor evoked potential of at least 50μV in at least 5 of 10 trials. The rTMS procedure consisted of 10Hz stimulation at stimulator output current of 80% of the motor threshold for 5 seconds, with 55 seconds rest following. The cycle was repeated 20 times per session resulting in 100 pulses per session. All six participants underwent daily sessions of rTMS for five consecutive days. One patient underwent the entire procedure three times with 4-week intervals. The comparator was baseline measurements.

3.3.7. Outcome measures

The vast majority of outcome measures pertained to mobility. Physical capacity, balance and gait parameters were measured using 21 different outcome measures. The experimental intervention using rTMS[68] utilized the PSP Rating Scale only.[148] Communication and swallowing outcome measures were typically contained within rating scales that assessed a broad range of domains such as the Unified Parkinson's Disease Rating Scale,[71] and the PSP-Rating Scale.[148] Less commonly used outcome measures included Digital Biometry Images Scanning (objective postural instability measures),[65] gaze control measures (Vertical Gaze Fixation Score and Gaze Error Index),[74] Activities-specific Balance Confidence scale,[149] and the Geriatric Depression Scale.[150] A detailed description of each outcome measure has been provided in Appendix V, including whether they are an objective measure, a subjective measure or contain both objective and subjective components.

3.3.8. Statistical analysis used

Four studies utilized statistical analysis on outcome measure data (see Appendix VI).[65,66,67,64] As per Table 4, in the critical appraisal assessment, three studies[66,67,64] were allocated a score for appropriate use of statistical analysis whilst one study was not.[65] The study by Nicolai (2010)[66] and Sale (2014)[67] both used the exact Wilcoxon signed rank test to compare baseline,[66, 67] post-intervention[66, 67] and follow-up[66] for their single group population. This was considered appropriate as the Wilcoxon signed-rank test is a nonparametric test and is used on ordinal data or when continuous data does not conform to a normal distribution. It can be used to determine if the dependent variable has changed across repeated measurements in a single group.[151]

In the study by Zampieri,[64] gait outcomes differences between groups were analyzed with a 2-sample *t* test. When data did not conform to a normal distribution, a Mann-Whitney *U test* for the difference in means was used and a *z* score was

approximated with correction for continuity. Within-group comparisons of gait outcomes were analyzed using matched pairs *t* test to compare pretest and posttest scores. When data did not conform to a normal distribution, a Wilcoxon signed rank test for the difference in medians was used, and a *z* score was approximated with correction for continuity. This was considered appropriate as all outcomes utilized in the study by Zampieri[64] measured continuous data. The unpaired t-test compares the means or medians of two sample groups (unpaired data) with normally distributed continuous data and the paired t-test compares means or medians of two sample groups (paired data) with normally distributed continuous data.[152] The Mann-Whitney *U* test is a nonparametric test and is used on ordinal data, or when continuous data does not conform to a normal distribution. It is used to measure the location of two populations using independent samples i.e. the difference in two treatments (two populations).[152]

The gaze control outcomes in the study by Zampieri[64] analyzed differences between the group with two ways ANOVA for Vertical Gaze Fixation Score and Gaze Error Index.[74] All hypotheses were non-directional (Ho: no difference between means) and the alpha level was set at 0.05. Within group comparison was analyzed with matched pairs t-test for each dependent variable. When data did not conform to a normal distribution, a Wilcoxon signed-ranks test for the difference in medians was used and a z-value was approximated with correction for continuity (alpha level set at 0.05). There are two ways ANOVA can be used on normally distributed data to compare means or medians on two or more sample groups (paired data).[152] This would be typically used for within group analysis only, where as single way ANOVA might be suggested for between group analysis where there are two independent groups (unpaired data).[152] Given the majority of statistical analysis methods used in Zampieri[64] were considered standard, a score was allocated for appropriate use of statistical analysis.

In Di Pancrazio (2013),[65] single way ANOVA was applied to each evaluation tests with evaluation session as a factor (pre, T1, T2, T3, POST, 15 day follow-up, 30-day follow-up). For the total load % and total area cm^2 two-ways ANOVA were performed with evaluation session and side (left and right foot) as factors. One-way ANOVA can be used on normally distributed data to compare means or medians of two or more sample groups (unpaired data).[152] There were two main issues with the choice of statistical analysis in the study by Di Pancrazio.[65] The first pertains to data type. ANOVA tests are typically used on continuous normally distributed data.[152] Whilst the baropodometry static,[65] baropodometry dynamic,[65] stabilometry[65] and myometry[65] measures in the study produced continuous data, other outcome measures (Berg Balance Scale,[72] Progressive Supranuclear Palsy Rating Scale,[148] and the Parkinson's Disease Questionnaire-39)[76] produced ordinal data. In addition, there was only one sample group in the study by Di Pancrazio[65] therefore tests for one

sample group might be suggested such as one sample *t*-test for normally distributed continuous data, and Wilcoxon Rank Sum test for ordinal data.[152]

3.4. Findings of the review

Given each study utilized a different intervention, findings were presented in narrative synthesis. The primary outcomes of the included studies were related to physical capacity, gait, balance, quality of life, and disease progression (Appendix VII-Appendix IX). Physical capability is defined as an individual 's capacity to undertake physical tasks needed for daily living including the ability to sit-to-stand and stand-to-sit on a chair, and to step up and back down from a step.[153] The following results are organized by the primary outcome/s targeted, commencing with interventions that are within the current scope of practice for physiotherapy. Finally, the findings of an experimental intervention are explored. No studies included in the review primarily targeted cognition, swallowing and communication outcomes.

Physiotherapy intervention(s) for balance only:

In the case series by Di Pancrazio (2013),[65] the effectiveness of a 2-month rehabilitation program combining a dynamic antigravity postural system and a vibration sound system was examined in 10 participants with PSP. Balance, indicated by a change in Berg Balance Scores,[72] improved from a baseline mean of 37.7 with a standard deviation (SD) of 12.2 to a mean of 47.6 with SD of 9.2, p=0.02 post-intervention. However, as mentioned, the study utilized statistical analysis typically used for two or more independent sample groups (one way ANOVA), despite there being only one sample group. Therefore statistical significance of these outcome measures should be interpreted with caution. The study also measured Myometry[65] (assesses the mechanical properties of muscle), Digital Biometry Images Scanning (assesses balance),[65] Parkinson's Disease Questionnaire-39[76] and the Progressive Supranuclear Palsy-Rating Scale,[148] but only data for the Berg Balance Scale[72] was provided.

Balance was also a primary outcome in the study by Nicolai et al.[66] The effectiveness of balance and posture exercises with audiobiofeedback in improving balance in eight patients with PSP was examined. There was a significant improvement in balance indicated by a 25.7% increase in Berg Balance Scores[72] from a mean of 35 (range: 6-50) to a mean of 44 (range: 9-50) post-intervention, p=0.016. The benefits of the intervention appeared to reduce, indicated by a 6.8% decrease in Berg Balance Scores[72], by the time of follow-up four weeks post intervention (mean: 41, range:10-52) but remained higher than baseline levels, p=0.008. Quality of life as per the Parkinson's Disease Questionnaire-39[76] improved from a baseline mean of 36.2 (range: 28.6-55.4) to a mean of 26.7 (range: 22.3-44.0) post-intervention but did not reach statistical significance, p=0.25. However, there were significant improvements from baseline to follow-up four weeks post intervention, p=0.039. Although the

primary target of the intervention was mobility, the greatest gains in quality of life were observed in cognition and communication subtests of the Parkinson's Disease Questionnaire-39[76] rather than mobility. Cognition significantly improved from a baseline mean of 37.5 (range: 0.0-50) to a follow-up mean of 18.8 (range: 0.0-31.3), p=0.031. Communication significantly improved from a baseline mean of 66.7 (range 50.0-75.0) to a post-intervention mean of 41.7 (range: 16.7-66.7), p=0.047 but remained stable from post-intervention to follow-up four weeks post intervention. Balance confidence measured using the Activities-specific Balance Confidence scale[149] reduced 50% from a baseline mean of 13.8 (range: 1.3-28.1) to a post-intervention mean of 6.9 (range: 0.0-21.3), p=0.047. There was no significant differences in levels of depression measured using the Geriatric Depression Scale[150] from a baseline mean of 4 (range:1-11), to a post-intervention mean of 6 (range:3-10).

Physiotherapy intervention(s) for gait only:

In the case series by Sale et al.,[67] the effectiveness of robot-assisted walking on spatiotemporal parameters of gait was examined in five participants with PSP. There were improvements from baseline to post-intervention in all outcome measures, namely gait velocity, cadence, step length, and step width. Gait velocity improved 15% from baseline mean of 0.54 with SD of 0.173m/s to a mean of 0.69 with SD of 0.150m/s post intervention, and cadence improved 23.8% from a baseline mean of 83.00 with SD of 9.618 steps per min to a mean of 93.60 with SD of 15.437 steps per min. Step width reduced 9% from a mean of 166.60mm with SD of 24.460mm to a mean of 153.60mm with SD of 43.678mm.

Physiotherapy intervention(s) for gait and balance:

The case report by Suteerawattananon, MacNeill and Protas,[69] examined the use of a modified body weight support treadmill training program to reduce falls and improve the balance and gait of a male patient with PSP. Patient outcomes were followed for 12 weeks (2 weeks prior to training, 8 weeks of training, and 2 weeks after training). However, outcome data provided by the study was taken at baseline, 4-weeks mid training and on the completion of the intervention. Statistical analysis determining the significance of results was not performed on outcome measure data from this case study. The 5-step test and Get up-and-Go Test are both measures of physical capacity. Improvements were more apparent on the 5-step test (baseline mean time of 16.23s with SD of 3.35s to a mean time of 14.51s with SD of 0.75s post-intervention) than the Get Up-and-Go Test (baseline mean time of 12.80s with SD of 1.74s to a mean time of 13.50s with SD of 2.47s post-intervention). Improvements of balance were observed on the Foam Standing (80% increase from a baseline of mean time of 9.60s and SD of 1.45s to post-intervention mean time of 17.28s with SD of 0.38s) and the Functional Reach Test (14.97% increase from a baseline of

mean length of 23.93cm and SD of 3.35cm to post-intervention mean length of 27.51cm and SD of 6.53cm), but less so on the Berg Balance Scale[72] (4.4% increase from a baseline of mean score of 45 to post-intervention mean score of 47). Spatiotemporal gait characteristics improved including step length, stride length, heel-to-heel base support, step time, gait speed and cadence. Gait speed improved 25.79% on the 15.2m (50ft) walk from a baseline of mean time of 17.02s with SD of 1.45s to a post-intervention mean time of 12.63s with SD of 0.64 seconds, and 26% on gait analysis from a baseline mean speed of 73.40cm/s with SD of 10.47cm/s to a mean speed of 100.05cm/s with SD of 0.78cm/s post-intervention.

Physiotherapy intervention(s) for gait and gaze control:

In the quasi-randomized control group design with partial crossover by Zampieri,[64] the effects of balance and eye movement training compared to balance training alone on gait and gaze control were investigated. During Phase I, patients from both groups were tested before and after four weeks of intervention. In Phase II, patients assigned to the comparison group (balance training only) crossed over to receive the balance and eye intervention and were tested again before and after the intervention.

Gait: Both the thesis[64] and associated publication[101] reported a range of statistical findings pertaining to gait improvements, however actual outcome measure data was not provided. In Phase I of the study, there was a significant decrease in stance time and gait speed in the 8ft walk in the treatment group, but not in the comparison group. Step length increased significantly in the comparison group but not in the treatment group. In Phase II, the only significant finding was an improvement in swing time. No statistically significant differences in gait function were observed in the final retention phase of the study.

Gaze control: At baseline, the pretest values for vertical gaze fixation score were higher for the treatment group than the comparison group. A between group one-way ANCOVA found that pretest vertical gaze fixation score was not a significant covariate ($F_{1,1}$ 2.76, p=0.10). The treatment group in phase I of the study, had a significant difference between baseline (mean of 0.48 with SD of 0.31) and post-intervention (mean of 0.30 with SD of 0.23) vertical gaze fixation score, p=0.004. No difference was found for the comparison group. Two ways ANOVA showed a significant main effect of test ($F_{1,\ 17}$=6.98, p=0.01) and a significant interaction ($F_{1,17}$2.57, p=0.001). There was a significant difference between baseline (mean of 64.11 with SD of 8.87) and post-intervention (mean of 56.95 with SD of 8.61) gaze error, p<0.001, for the treatment group. No difference in the gaze error scores was found in the comparison group. Between group comparison using a two ways ANOVA, showed a significant main effect of test $F_{1,17}$=9.76, p=0.006, and significant interaction $F_{1,17}$=9.56, p=0.006. There were no significant improvements in vertical gaze fixation score or gaze error in the cross-over component of the study in Phase II

or in the final retention phase of the study.

Emerging/experimental interventions:

In the case series study by Santens, Sieben and Letter,[68] the effectiveness of rTMS in improving gait and midline symptoms in six patients with PSP was explored. The only outcome measure was the PSP-Rating Scale.[148] In five of the six patients, the total score of the PSP-Rating Scale[148] subsections improved post-intervention, with most prominent improvements found on the gait/midline symptoms. Repetition of the intervention in one patient resulted in similar improvements on all three occasions.

Chapter 4 provides an overview of the findings and limitations of the systematic review. This chapter also outlines implications for practice, implications for research and finishes with the conclusion.

Chapter 4: Discussion

4.1. Overview of findings

This systematic review is the first of its kind, having identified, critically appraised, syntehsised and presented the best available evidence for the effectiveness of allied health therapy in the symptomatic management of progressive supranuclear palsy. This systematic review has highlighted major gaps in current practice and existing literature. At this time, many strategies for optimizing independence and function for PSP predominately rely on data extrapolated from the study of rehabilitation in Parkinson's disease.[4] However, given there are differences in the symptoms of PSP compared to Parkinson's disease, these interventions may not always be appropriate.

An evidence base to inform allied health care delivered to patients with PSP is critical. Progressive supranuclear palsy is a debilitating condition. By the end stages of the condition, patients with PSP may be unable to walk, speak, eat or drink.[1] Aspiration pneumonia is the leading cause of death.[6] Currently, there is no cure for PSP and dopaminergic medications are minimally effective in alleviating symptoms. It is essential that healthcare teams incorporate physiotherapy, occupational therapy and speech therapy when managing patients with PSP.[4]

The systematic review searched for physiotherapy, occupational therapy and speech therapy interventions for PSP across 11 databases and several sources of grey literature. Since the development of clinical diagnostic criteria for PSP nearly a decade ago,[13] only six studies met the appropriate inclusion criteria and were of adequate methodological quality. This systematic review has identified that the existing literature fails to inform the management of speech therapy and occupational therapy needs of patients with PSP. All six studies were confined to current and emerging practice within the scope of physiotherapy.

The six studies included for the review all utilized different physiotherapy interventions and as such pooling of results was not appropriate. Interventions were typically applied to older community dwelling participants with PSP in the outpatient or university clinic setting. They included 1) robot-assisted walking,[67] 2) modified body weight support treadmill training,[69] 3) rTMS targeting gait and midline symptoms,[68] 4) a rehabilitation program combining a dynamic antigravity postural system and a vibration sound system,[65] 5) balance and posture exercises with audio-biofeedback,[66] and 6) balance and eye movement compared to balance training alone.[64]

One study targeted gait outcomes only, using robot-assisted walking.[67] There were

improvements from baseline to post-intervention in all outcome measures, namely gait velocity, cadence, step length, and step width. However, these improvements did not reach significance and the authors suggested that this was due to the use of a small sample size.[67] The case study examining the effectiveness of a modified body weight support treadmill training program in a participant with PSP reported improvements across a range of physical capacity, balance and gait outcome measures.[69] Following rTMS in the pilot study by Santens, Sieben and Letter,[68] five of six patients, had improved Progressive Supranuclear Palsy Rating Scale scores, with the most prominent improvements found on the gait/midline symptoms. Repetition of the intervention in one patient resulted in similar improvements on all three occasions. A limitation of the study acknowledged by the authors was absence of sham stimulation control. It was difficult to draw findings from the study by Di Pancrazio (2013),[65] which utilized a dynamic antigravity postural system and vibration sound system. Data for most outcomes was not provided and it was unclear if appropriate statistical analysis was conducted.

In the study by Nicolai et al.,[66] the balance and posture exercises with audibiofeedback were effective in improving balance. There was a significant improvement in Berg Balance Scores[72] from baseline to post-intervention. The benefits sustained until four weeks after the completion of the training, which does support the possible prolonged benefit of training. Balance confidence measured using the Activities-specific Balance Confidence scale[149] reduced 50% from baseline to post-intervention which possibly indicated increased insight into balance deficits by the study participants.[66] Although the primary target of the intervention was balance, the greatest gains in quality of life were observed in cognition and communication subtests of the Parkinson's Disease Questionnaire-39[76] rather than mobility. Increased social inclusion and the development of a therapeutic relationship between participants and their physiotherapists, as a by-product of the balance rehabilitation program, was a suggested and plausible explanation for their findings.

The quasi-randomized control group design with partial crossover by Zampieri,[64] examined the effects of balance and eye movement training compared to balance training alone on gait and gaze control. There were significant improvements in stance time and walking speed on the 8-foot walk test for the treatment group. There were statistically significant improvements in the step length of the comparison but not the treatment group. The suggested reason for this was that those receiving balance training alone practiced more standing and stepping activities and therefore had more chance to improve stepping than participants receiving balance and eye training who were seated during the eye training component. Further study is required to determine whether or not eye movement exercises as a complementary therapy for balance training, compared to balance training alone, is more effective in improving gait in PSP. In regards to gaze control outcomes, the vertical gaze fixation

score and gaze error scores in the treatment group (eye movement and balance training) significantly improved whereas no significant improvement was observed in the comparison group (balance training alone).[64]

Without further primary research, the broader implications of these findings are difficult to draw. The association between different mobility outcome measures, incidence of falls, morbidity, mortality, quality of life, carer-burden and entry to residential care has not been examined adequately in PSP. However, in older community-dwelling adults, there is some evidence to suggest that physical capability assessments may predict subsequent health[153] and that specific changes to spatio-temporal characteristics of gait[154] and balance[155] are associated with falls. The Parkinson's Disease Questionaire-39 is a useful measure of quality of life in PSP, however it is acknowledged that it lacks reference to additional issues pertinent to PSP including visual disturbances, dysphagia, dysarthria, and apathy.[156]

4.2. Limitations to the systematic review

Progressive supranuclear palsy is relatively rare, and currently the field of allied health research to manage symptoms associated with this condition is limited. The small number of studies was further compounded by only including studies published in English, and participants who had PSP as per the NINDS-SPSP diagnostic criteria.[13] Progressive supranuclear palsy is now considered to be more heterogeneous than previously thought,[1] and it is possible that participants in three case studies[138-140] who did not meet the NINDS-SPSP diagnostic criteria[13] may meet future revisions to the diagnostic criteria for PSP.

The systematic review was unable to report on the efficacy of occupational therapy or speech therapy interventions for the symptomatic management of PSP as there was an absence of primary research studies. The six included studies each examined a different physiotherapy intervention.[64-69] Heterogeneity of the studies precluded the possibility of conducting a meta-analysis and therefore the findings were presented in narrative form.

Given the rarity of the condition, there are tangible challenges associated with primary research methodology in this field including adequate sample size, random sampling and choice of study design. For example, RCTs would depend on the availability of a large number of participants diagnosed with PSP. Of the six studies, one was a quasi-randomized control study on 19 participants,[64] and other study designs were either case series[65-68] or single-case study.[69] However, methodological quality in some studies could have been improved by performing appropriate statistical analysis for the type of data collated[64, 65] and measuring outcomes after a follow-up period.[67, 68] In addition, many studies did not provide full data sets[64, 65, 69] or results of statistical analysis for all outcomes assessed[64, 66] which placed further limitations on this systematic review.

4.3. Implications for practice

Based on the findings of this systematic review, recommendations for practice have been outlined below using the Joanna Briggs Institute Grades of Recommendations.[157] The Joanna Briggs Institute Grades of Recommendations were developed to assist healthcare professionals when implementing evidence into practice. There are two grades of recommendation.[157] Grade A is a strong recommendation for a specific healthcare intervention, whereas Grade B is a weak recommendation for a specific healthcare intervention (See Appendix X).[157]

- **Balance:**
  - Physiotherapy rehabilitation programs that combine a dynamic antigravity postural system (SPAD) and a vibration sound system (ViSS) may improve balance among people affected by PSP. (Grade B)
  - Physiotherapy programs that combine balance and posture exercises with audiobiofeedback may improve balance among people affected by PSP. (Grade B)
- **Gait:**
  - Combined balance and eye movement training may improve stance time and gait speed among people affected by PSP. (Grade B)
  - Balance training improves step length among people affected by PSP. (Grade B)
- **Gaze control:**
  -Balance and eye movement training may improve vertical gaze fixation and gaze error scores among people affected by PSP. (Grade B)
- **Quality of life:**
  -Balance and posture exercises with audiobiofeedback may improve cognition and communication aspects of quality of life in people affected by PSP. (Grade B)

There is weak preliminary evidence for other physiotherapy interventions however further research is required before practice recommendations can be made *(See implications for research).*

4.4. Implications for research

- Further research into allied health therapeutic interventions may have the potential to inform future policy guidelines and practice for people with PSP.
- There are major gaps in the field of literature for allied health therapy for PSP. Studies examining the effectiveness of interventions for people with PSP within the scope of practice for speech therapy and occupational therapy are urgently required.
- There are promising results for a range of interventions within the scope of physiotherapy however further research should be conducted examining the

effectiveness of the following interventions before recommendations for practice can be made:

  - **Balance:** A modified body weight support treadmill training program may improve balance among people with PSP.
  - **Gait:** Robot-assisted walking may improve gait velocity, cadence, step length and step width among people with PSP.
  - **Physical capability:** A modified body weight support treadmill training program may improve physical capability outcomes in people affected by PSP.

- Additional physiotherapy intervention studies using appropriate statistical analysis, follow-up periods, and broader outcome measures including incidence of falls, quality of life, carer-burden, mortality, and entry to residential care are required. This research would strengthen recommendations for practice provided above.
- A case series study has identified that rTMS improved gait and midline symptoms in participants with PSP.[68] This type of intervention is considered experimental and not yet within the scope of physiotherapy but may inform future research directions.

4.5. Conclusion

Allied health therapeutic interventions are important in the management of PSP. This thesis has identified major gaps in the existing literature. No research pertains to the effectiveness of occupational or speech therapy interventions for PSP. Research into the effectiveness of non-invasive stimulation to improve gait/midline symptoms in PSP is in its infancy. A case series study has identified that rTMS improved gait and midline symptoms in participants with PSP, however the authors have acknowledged the study lacked sham control.[68]

Two rehabilitation programs, 1) combining a dynamic antigravity postural system (SPAD) and a vibration sound system (ViSS)[65] and 2) balance and posture exercises with audiobiofeedback[66] resulted in statistically significant improved balance. Combined balance and eye movement training compared with balance training alone[64] resulted in statistically significant improvements in stance time and gait speed, however the group receiving balance training alone had significantly improved step length compared with the treatment group. The same study[64] also resulted in statistically significant improvements in vertical gaze fixation and gaze error scores in the treatment group. Quality of life was reported on by one study using balance and posture exercises with audiobiofeedback.[66] Statically significant results were obtained in the cognition and communication subtests only of the Parkinson's Disease Questionnaire (PDQ-39)[76] only.

There were other findings that showed promise for various physiotherapy interventions to improve balance, gait and physical capability outcomes among people affected by PSP, however further research is required before recommendations for practice can be made. Balance was improved in a study using a modified body weight support treadmill training program[69] though statistical analysis was not performed. Robot-assisted walking[67] improved gait velocity, cadence, step length and step width in participants with PSP, however these changes did not reach significance. The modified weight support treadmill program[69] resulted in improved step length, stride length, heel-to-heel base support, step time, gait speed and cadence however statistical analysis was not performed. Physical capability outcomes were targeted by two rehabilitation programs, 1) balance and posture exercises with audiobiofeedback[66] and 2) a modified body weight support treadmill training program.[69] There were no significant differences in the first study, but improvements were identified in the latter though statistical analysis was not performed.

Overall, there is preliminary evidence based on statistically significant results which indicates various physiotherapy rehabilitation programs may improve balance, gait, gaze control and some aspects of quality of life in those affected by PSP. However, additional studies using larger sample sizes, appropriate statistical analysis, follow-up periods, and broader outcome measures including incidence of falls, quality of life, carer-burden, mortality, and entry to residential care are required. The evidence for modified body weight support treadmill training,[69] robot-assisted walking[67] and non-invasive stimulation[68] to improve mobility outcomes in people with PSP is weak, however further research may be justified from the positive findings thus far. Finally, there is an urgent need for evidence supporting the use of speech therapy and occupational interventions for people with PSP.

Appendix I: Search Strategy

OVERALL SEARCH TERMS

1. Progressive supranuclear palsy
2. Supranuclear palsy progressive
3. Steele-Richardson-Olszewski
4. Richardson's Syndrome
5. Richardson Syndrome
6. Progressive nuclear palsy
7. supranuclear gaze palsy *(this was identified during the first stage as an additional term)*
8. PSP AND Parkin*
9. PSP AND PD

Using "opthalmoplegia" did not result in additional results.

PubMed:

Progressive Supranuclear Palsy
Supranuclear palsy, progressive[mh] OR progressive supranuclear palsy[tw] OR Steele-Richardson-Olszewski[tw] OR Richardson's Syndrome[tw] OR Richardson Syndrome[tw] OR progressive nuclear palsy[tw] OR supranuclear gaze palsy[tw] OR (PSP[tw] AND (parkin*[tw] OR PD[tw]))

CINAHL:

Progressive Supranuclear Palsy
MH supranuclear palsy, progressive+ OR TI supranuclear palsy, progressive OR AB supranuclear palsy, progressive OR TI progressive supranuclear palsy OR AB progressive supranuclear palsy OR TI steele richardson olszewski OR AB steele richardson olszewski OR TI richardson's syndrome OR AB richardson's syndrome OR TI richardson syndrome OR AB richardson syndrome OR TI progressive nuclear palsy OR AB progressive nuclear palsy OR TI supranuclear gaze palsy OR AB supranuclear gaze palsy

*TI PSP OR AB PSP did not yield any relevant results not covered by existing search terms.

Cochrane library:

Progressive supranuclear palsy
“Progressive supranuclear palsy” OR “Supranuclear palsy progressive” OR “Steele-Richardson-Olszewski” OR “Richardson’s Syndrome” OR “Richardson Syndrome” OR “Progressive nuclear palsy” OR “supranuclear gaze palsy” OR (PSP AND Parkin*) OR (PSP AND PD)

*Using the MeSH term “supranuclear palsy, progressive” did not yield any additional results.

Embase:

Progressive supranuclear palsy
('progressive supranuclear palsy'/syn) OR ('richardsons syndrome') OR ('progressive nuclear palsy') OR ('supranuclear gaze palsy') OR (('psp':ti,ab) AND ((parkin*:ti,ab) OR ('pd':ti,ab))) AND ([embase]/lim NOT [medline]/lim)

* progressive supranuclear palsy and supranuclear palsy progressive was included in ‘/syn, Richardson’s syndrome came up with an error as it used an apostrophe, and Richardson syndrome did not yield any additional results.

Biosis:

Progressive Supranuclear Palsy
(“Progressive supranuclear palsy”) OR (“Supranuclear palsy progressive”) OR (“Steele-Richardson-Olszewski”) OR (“Richardson’s Syndrome”) OR (“Richardson Syndrome”) OR (“Progressive nuclear palsy”) OR (“supranuclear gaze palsy”) OR (“PSP” AND “Parkin*”) OR (“PSP” AND “PD”)

*The search terms searched with TOPIC as searching the same terms under TITLE did not yield any further additional results.

Informit health:

Progressive supranuclear palsy
Progressive supranuclear palsy

The following search terms did not yield any relevant studies; Supranuclear palsy progressive, Steele-Richardson-Olszewski, Richardson’s Syndrome, Richardson Syndrome, Progressive nuclear palsy, supranuclear gaze palsy, PSP AND Parkin, PSP AND PD.

Best Practice (Clinical evidence BMJ):

Best Practice was handsearched with each overall search term listed at the beginning of Appendix I. In the case of PSP and Parkin* the truncation did not work and therefore “PSP” AND “Parkinson’s”, "PSP" AND "Parkinsons" and "PSP" AND "Parkinsonian" was searched. No relevant studies were identified.

PsycINFO:

Progressive Supranuclear Palsy
(Progressive supranuclear palsy/) OR (Progressive supranuclear palsy OR Supranuclear palsy progressive OR Steele-Richardson-Olszewski OR Richardsons Syndrome OR Richardson Syndrome OR Progressive nuclear palsy OR supranuclear gaze palsy OR (PSP AND Parkin*) OR (PSP AND PD)).mp.

PEDro:

Searched the terms 1-9 individually, 1 article identified.

OT Seeker:

Searched the terms 1-9 individually, 0 articles identified.

Speech Bite:

Searched the terms 1-9 individually, 0 articles identified.

Mednar:

Searched the terms 1-9 individually:

1. Progressive supranuclear palsy (841)
2. Supranuclear palsy progressive (472)
3. Steele-Richardson-Olszewski (277)
4. Richardson's Syndrome (343)
5. Richardson Syndrome (277)
6. Progressive nuclear palsy (227)
7. supranuclear gaze palsy (378)

8. PSP AND Parkin* (492)
9. PSP AND PD (728)

4081 results (removed 1848 duplicates) = 2233 results.

ProQuest:

Progressive Supranuclear Palsy
"Progressive supranuclear palsy" OR "Supranuclear palsy progressive" OR "Steele-Richardson-Olszewski" OR "Richardson's Syndrome" OR "Richardson Syndrome" OR "Progressive nuclear palsy" OR "supranuclear gaze palsy"

(PSP AND Parkin*) OR (PSP AND PD) did not yield any relevant results not covered by existing search terms.

Appendix II: Critical Appraisal Instruments

JBI Critical Appraisal Checklist for Descriptive / Case Series

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Was study based on a random or pseudo-random sample?	☐	☐	☐	☐
2. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
3. Were confounding factors identified and strategies to deal with them stated?	☐	☐	☐	☐
4. Were outcomes assessed using objective criteria?	☐	☐	☐	☐
5. If comparisons are being made, was there sufficient descriptions of the groups?	☐	☐	☐	☐
6. Was follow up carried out over a sufficient time period?	☐	☐	☐	☐
7. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
8. Were outcomes measured in a reliable way?	☐	☐	☐	☐
9. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

_____

_____

_____

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

Appendix III: Data Extraction Instruments

JBI Data Extraction Form for Experimental / Observational Studies

Reviewer _____ Date _____

Author _____ Year _____

Journal _____ Record Number _____

Study Method

RCT	☐	Quasi-RCT	☐	Longitudinal	☐
Retrospective	☐	Observational	☐	Other	☐

Participants

Setting

Population

Sample size

Group A _____ Group B _____

Interventions

Intervention A

Intervention B

Authors Conclusions:

Reviewers Conclusions:

Study results

Dichotomous data

Outcome	Intervention ( ) number / total number	Intervention ( ) number / total number

Continuous data

Outcome	Intervention ( ) number / total number	Intervention ( ) number / total number

Appendix IV: Authors Contacted

Contact:	Outline of message:	Response:
F. Spagnolo via email.	To determine if the participant in the study *Deep magnetic stimulation in a progressive supranuclear palsy patient with speech involvement*[140] was diagnosed with PSP utilizing the NINDS-SPSP diagnostic criteria.[13]	Nil response.
E. Protas via email.	To determine if the participant in the study *Supported treadmill training for gait and balance in a patient with progressive supranuclear palsy*[69] was diagnosed with PSP utilizing the NINDS-SPSP diagnostic criteria.[13]	Nil response.
P. Sale via email.	To determine if the participants in the study *Effects of robot assisted gait training in progressive supranuclear palsy (PSP): a preliminary report*[67] were diagnosed with PSP utilizing the NINDS-SPSP criteria.[13]	Yes all patients were: "Definite PSP requires a history of probable or possible PSP and histopathologic evidence of typical PSP"
R. Sandyk via post.	To determine if the participant in the study *Transcranial AC pulsed applications of weak electromagnetic fields reduces freezing and falling in progressive supranuclear palsy: a case report*[129] was diagnosed with PSP utilizing the NINDS-SPSP criteria.[13]	The patient reported in this case met the NINDS-SPSP diagnostic criteria of PSP. In terms of diagnostic certainty she meets the degree of probable PSP.
A. Hohler via email.	To determine if it was possible to obtain the baseline characteristics and outcome measure data for just the participants with PSP in the study *Effectiveness of an inpatient movement disorders program for patients with atypical parkinsonism.*[137]	Nil response.

Appendix V: Description of outcome measures/baseline characteristics used in the six intervention studies meeting the methodological quality requirements:

MOBILITY ASSESSMENTS: Physical Capability		Type of Data	Study used:
Five Chair Rise (5CR)[158]	Assesses the ability to perform sit-to-stand and stand-to-sit transfers. It is the time taken to stand up and sit down five times as fast as possible.	Objective continuous data	**Nicolai (2010)[66]**
5 step test[159]	Assesses the time taken to step up and back down a 10.2cm (4 inches) step continuously five times.	Objective continuous data	**Suteera-wattananon (2002)[69]**
Timed Up-and-Go (TUG)/[73] Get up and Go Test[160]	This assesses functional mobility and balance, and is the time taken to stand up from a chair, walk for a distance of 3m at comfortable speed, turn, walk back and sit down on the chair again.[73] TUG is the timed version of the Get up and Go test.[160]	Objective continuous data	**Nicolai (2010)[66] Suteera-wattananon (2002)[69] Zampieri (2006)[64]**
MOBILITY ASSESSMENTS: Other		**Type of Data**	**Study used:**
Myometry[65]	A non-invasive method of measuring mechanical properties of muscles including tone, elasticity and strength.	Objective continuous data.	**Di Pancrazio (2013)[65]**
MOBILITY ASSESSMENTS: Balance		**Type of Data**	**Study used:**
360 turning[161]	Time taken to turn 360 degrees as fast as possible. 360 degree turns are a measure of dynamic balance.[162]	Objective continuous data	**Suteera-wattananon (2002)[69]**
Berg Balance Scale (BBS)[72]	The BBS assesses static and dynamic balance in 14 items including standing, reaching, bending and transferring abilities. Items a scored from 0-4 determined by ability to perform the assessed activity. The BBS ranges from 0-56 points in total where 56 is the best performance possible.[72]	Subjective ordinal data	**Di Pancrazio (2013)[65] Nicolai (2010)[66] Suteera-watta-nanon (2002)[69]**
Digital Biometry Images Scanning (DBIS)[65]	Baropodometry static; total area in cm^2 covered by the left and right foot during standing for five seconds as a measure of posture. Baropodometry dynamic; measure of steps of body support with visualization of the center of pressure of each foot during walking. Stabilometry; measure of the body's center of pressure.	Objective continuous data	**Di Pancrazio (2013)[65]**
Foam standing[69]	Assesses the time until loss of balance or opening of eyes when standing on a 12.7cm width medium density foam pad without shoes, with arms folded across the chest and with closed eyes. Increased time on the foam standing assessment indicates improved balance.[69]	Objective continuous data	**Suteera-wattananon (2002)[69]**
Functional Reach Test (FRT)[163]	Assesses the distance of forward reach when standing measured in centimeters. It is a measure of antero-posterior stability while standing with a stable base of support.[163]	Objective continuous data	**Suteera-wattananon (2002)[69]**

MOBILITY ASSESSMENTS: Gait Speed and Gait Analysis		Type of Data	Study used:
2.4m (8ft) walk[158]	Assesses the time taken to comfortably walk 2.4m.	Objective continuous data	**Zampieri (2006)**[64]
15.2m (50ft) walk[164]	This is the time taken to walk 25 feet, turn and walk 25 feet.	Objective continuous data	**Suteera-wattananon (2002)**[69]
Gait velocity[165]	Gait velocity; rate of change of position in meters per second.	Objective continuous data.	**Sale (2014)**[67] **Suteera-wattananon (2002)**[69]
Cadence[165]	Cadence; measure of the number of steps taken in a given period of time then converted into the number of steps taken per minute.	Objective discrete data.	**Sale (2014)**[67] **Suteera-wattananon (2002)**[69]
Step length[166]	Step length; measure of the distance from the heel strike of one foot to the heel strike of the opposite foot in the forward direction.[64]	Objective continuous data.	**Sale (2014)**[67] **Suteera-wattananon (2002)**[69] **Zampieri (2006)**[64]
Step width[67]	Step width; the medio-lateral distance between two feet during double support.	Objective continuous data.	**Sale (2014)**[67]
Stride length[166]	Stride length; the length between two successive placements of the same foot.	Objective continuous data.	**Suteera-wattananon (2002)**[69]
Stance time[165]	Stance time; duration of the stance phase (amount of time the foot was in contact with the ground)	Objective continuous data.	**Sale (2014)**[67] **Zampieri (2006)**[64]
Swing time[67]	Swing time; duration of the swing phase (amount of time that the foot was not in contact with the ground).	Objective continuous data.	**Sale (2014)**[67]
Step length over 3 m[69]	The number of steps taken over 3m.	Objective continuous data.	**Suteera-wattananon (2002)**[69]
Heel-to- heel base of support[166]	The vertical distance from heel centre of one footprint to the line of progression formed by two footprints of the opposite foot in centimetres.	Objective continuous data.	**Suteera-wattananon (2002)**[69]
Double support[67]	Double support; duration of double support. Increased duration of double support is associated with postural instability.[24]	Objective continuous data.	**Sale (2014)**[67]
VISION ASSESSMENTS:		**Type of Data**	**Study used:**
Vertical Gaze Fixation Score (vGFS):[74]	Vertical Gaze Fixation Score (vGFS); a measure of eye-head coordination. A decrease in vGFS is an indication of improvement in gaze shift ability.	Objective continuous data.	**Zampieri (2006)**[64]
Gaze Error Index:[74]	Gaze Error Index; measurement of discrepancy between the participants' actual gaze angle and the angle they would need if they were to fixate on the footfall location. A decrease in Gaze Error Index is an improvement in ocular mobility.	Objective continuous data.	**Zampieri (2006)**[64]

SWALLOWING ASSESSMENTS:		Type of Data	Study used:
No measure assessing swallowing only.			
COMMUNICATION ASSESSMENTS		**Type of Data**	**Study used:**
No measure assessing communication only.			
COGNITIVE/ NEUROPSYSCHIATRIC ASSESSMENTS		**Type of Data**	**Study used:**
Geriatric Depression Scale (GDS)[150]	The GDS is a measure of emotional well-being and depressive mood. Ranges from 0-15 where 15=worst.	Subjective ordinal data.	**Nicolai (2010)[66]**
MEASURES ASSESSING MULTIPLE DOMAINS		**Type of Data**	**Study used:**
Progressive Supranuclear Palsy Rating Scale (PSPRS)[148]	This assesses 28 items in six categories: daily activities (by history), behavior, bulbar, ocular motor, limb motor and gait/midline. Ranges from 0-100 where 100=worst.	Subjective and objective ordinal data	**Di Pancrazio (2013)[65] Nicolai (2010)[66]**
Unified Parkinson's Disease Rating Scale (UPDRS)[71]	The UPDRS is a combination of subjective (based on reports) and objective assessment and is used to measure Parkinson-specific features. It is an accurate measure of disease progression in PSP.[167] Ranges from 0-100 where 100=worst.	Subjective and objective ordinal data	**Nicolai (2010)[66]**
MEASURES ASSESSING CONSEQUENCES OF SYMPTOMS:		**Type of Data**	**Study used:**
Parkinson's Disease Questionnaire (PDQ-39)[76]	This questionnaire has a scale score system and covers various domains of quality of life including mobility, activity of daily living, emotional well-being stigma, social support, cognitive impairment, communication and bodily discomfort. Ranges from 0-100 where 100=worst.	Subjective ordinal data	**Di Pancrazio (2013)[65] Nicolai (2010)[66]**
Activities-specific Balance Confidence (ABC)[149]	The scale consists of 16 items which cover a wide spectrum of activities from reaching at eye level to walking on icy sidewalks. Each item is then ranked from 0% (no confidence) to 100% (complete confidence) in performing the task without losing balance or becoming unsteady. The ABC is able to detect loss of balancing confidence for community-dwelling older persons.	Subjective ordinal data	**Nicolai (2010)[66]**

Appendix VI: Description of statistical analysis performed on outcome measures by studies:

Statistical test:	Description:	Studies used in:
ANOVA:	• One way ANOVA: normally distributed data, compares means or medians of two or more sample groups (unpaired data).[152] • Two ways ANOVA: normally distributed data, compares means or medians on two or more sample groups (paired data).[152]	**Di Pancrazio (2013)[65]:** One way ANOVA was applied to each evaluation tests with evaluation session as a factor. For the total load % and total area cm^2 two ways ANOVA were performed with evaluation session and side (left and right foot) as factors. **Zampieri (2006)[64]:** Differences between groups for gaze control outcomes were analyzed with a two ways ANOVA for Vertical Gaze Fixation Score and Gaze Error Index.[74]
Kolmogorov- Smirnov tests:	• Kolmogorov-Smirnov test: able to determine if data is normally distributed.[152]	**Sale (2014)[67]:** Kolmogorov-Smirnov tests were used to determine that parameters were not normally distributed.
Mann-Whitney *U* test	• The Mann-Whitney *U* test is used on ordinal data, or when continuous data does not conform to a normal distribution. It is used to measure the location of two populations using independent samples i.e. the difference in two treatments (two populations).[152]	**Zampieri (2006)[64]:** When data for gait outcomes did not conform to a normal distribution, a Mann-Whitney *U test* for the difference in means used to compare within groups. A *z* score was approximated with correction for continuity.
Wilcoxon signed rank test:	• Wilcoxon signed-rank test: for use with ordinal data or continuous data that does not conform to a normal distribution. It can be used to determine if the dependent variable has changed across repeated measurements in a single group.[151]	**Nicolai (2010)[66]:** Differences from baseline, post-intervention and follow-up were examined using the exact Wilcoxon signed rank test. **Sale (2014)[67]:** Wilcoxon's tests were used to detect significant changes between data at baseline and end-point as parameters were not normally distributed. **Zampieri (2006)[64]:** When data for gaze control outcome measures did not conform to a normal distribution, a Wilcoxon signed-ranks test for the difference in medians was used to compare within groups. A z-value was approximated with correction for continuity (alpha level set at 0.05).
		Continued…

Statistical test:	Description:	Studies used in:
***T*-test**	• Unpaired *t*-test: compares means or medians of two sample groups (unpaired data) with normally distributed continuous data.[152] • Paired *t*-test: compares means or medians of two sample groups (paired data) with normally distributed continuous data.[152]	**Zampieri (2006)[64]:** Differences between groups for gait outcomes were analyzed with a 2-sample *t* test when they were normally distributed. Within-group comparisons for gait outcomes were analyzed using matched pairs *t* test to compare pretest and posttest scores when they were normally distributed.

Appendix VII: Summary of results from the six studies:

MOBILITY- PHYSICAL CAPACITY ASSESSMENTS:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Five Chair Rise (5CR)[158]*(s)*	**Nicolai (2010)**[66]	40.1 (30.5-93.7)	46.2 (28.6-89.5)	51.6 (29.8-122.4)	No significant difference between the three time-points.
5 step test[159]*(s)*	**Suteera-watta-nanon (2002)**[69]	Baseline-16.23±3.35 Mid-14.79±0.18	Post-14.51±0.75	Nil follow-up data provided by study.	% change pre-training to post-training: 10.60% increase
Timed Up-and-Go (TUG)/[73] **Get up and Go Test**[160]*(s)*	**Nicolai (2010)**[66]	24.5 (19.3-50.7)	22.5 (15.3-66.7)	24.95(16.6-95.7)	No significant difference.
	Suteera-watta-nanon (2002)[69]	Baseline-12.80±1.74 Mid-15.74±1.04	Post-13.50±2.47	Nil follow-up data provided by study.	% change pre-training to post-training: 5.47% reduction
	Zampieri (2006)[64] (n=19)	T: 24.32 ±10.57 C: 23.41 ±11.80	T: 20.42 ±10.10 C: 21.84 ±9.73	Nil follow-up	Change scores from T0 to T1: T: -3.90±10.33 vs C: -1.56±3.18, p=0.52
	Zampieri (2006)[64] (n=5, crossover)	28.17 ±14.63	25.47 ±12.25	Nil follow-up	Change scores from before crossover to after crossover; 2.69±3.83 vs 7.62±12.59, p=0.29
	Zampieri (2006)[64] (n=10, retention)	Not used.	Not used.	Nil follow-up	Not used.
MOBILITY-OTHER:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Myometry[65]	**Di Pancrazio (2013)**[65]	Nil data provided by study.	Nil data provided by study.	Nil data provided by study.	Nil data provided.

Continued…

MOBILITY ASSESSMENTS-BALANCE:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
360 turning[161] *(s)*	**Suteera-watta-nanon (2002)**[69]	Baseline-17.02±1.45 Mid-14.24±2.50	Post-12.63±0.64	Nil follow-up data provided by study.	% change pre-training to post-training: 25.79% increase
Berg Balance Scale (BBS)[72]	**Di Pancrazio (2013)**[65]	37.7±12.2	47.6±9.2	Nil follow-up data provided by study.	**T0 vs T1, p=0.02.**
	Nicolai (2010)[66]	35(6-50)	44(9-50)	41(10-52)	**T0:T1 improved 25.7%, p=0.016. T1:T2 reduced 6.8%, p=0.047. T0 higher than T2, p=0.008**
	Suteera-watta-nanon (2002)[69]	Baseline-45 Mid- 49	Post- 47	Nil follow-up data provided by study.	% change pre-training to post-training: 4.44% increase
Digital Biometry Images Scanning (DBIS)[65]	**Di Pancrazio (2013)**[65]	Nil data provided by study.	Nil data provided by study.	Nil data provided by study.	Nil data provided by study.
Foam standing[69] *(s)*	**Suteera-watta-nanon (2002)**[69]	Baseline-9.60±1.45 Mid-16.98±2.49	Post-17.28±0.38	Nil follow-up data provided by study.	% change pre-training to post-training: 80% increase
Functional Reach Test (FRT)[163] *(cm)*	**Suteera-watta-nanon (2002)**[69]	Baseline-23.93±3.35 Mid-24.97±1.93	Post-27.51±6.53	Nil follow-up data provided by study.	% change pre-training to post-training: 14.97% increase

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MOBILITY ASSESSMENTS- GAIT SPEED AND GAIT ANALYSIS MEASURES:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
2.4m (8ft) walk[158] *(s)*	**Zampieri (2006)**[64] (n=19)	Nil data provided by study.	Nil data provided by study.	Nil follow-up.	Change scores from T0-T1: T: 10.85±11.23 vs C: 0±13.73, p=0.07 Within group comparison: **T: T0 vs T1 significant decrease, p=.01,** C: T0 vs T1 nil significant decrease, p=1.00
	Zampieri (2006)[64] n=5 crossover	Nil data provided by study.	Nil data provided by study.	Nil follow-up.	Change scores: T0: 4.45±15.00 vs T1: 1.64±7.76, p=0.46
	Zampieri (2006)[64] n=10 retention	59.57±17.86	68.78±17.77	65.46±23.24	T0 higher than T1, p=0.06, T1 difference to T2, p=0.26
15.2m (50ft) walk[164] *(s)*	**Suteera-watta-nanon (2002)**[69]	Baseline-17.02±1.45 Mid-14.24±2.50	Post-12.63±0.64	Nil follow-up data provided by study.	% change pre-training to post-training: 25.79% increase
MOBILITY ASSESSMENTS- GAIT SPEED AND GAIT ANALYSIS MEASURES:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Gait velocity[165] *(m/s)*[67] *(cm/s)*[69]	**Sale (2014)**[67]	0.54± 0.173	0.69±0.150	Nil follow-up.	T0:T1 improved 15%. No statistical significance.
	Suteera-watta-nanon (2002)[69]	73.40±10.47	100.05±0.78	Nil follow-up data provided by study.	% change pre-training to post-training: 26% increase
Cadence[165] *(steps/min)*	**Sale (2014)**[67]	83.00± 9.618	93.60± 15.437	Nil follow-up.	T0:T1 improved 23.8%. No statistical significance.
	Suteera-watta-nanon (2002)[69]	93.75±3.04	109.85±0.50	Nil follow-up data provided by study.	% change not measured.

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MOBILITY ASSESSMENTS- GAIT SPEED AND GAIT ANALYSIS MEASURES:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Step length[64] *(cm)*[64, 69] *(mm)*[69]	**Sale (2014)**[67]	R: 363.20± 94.767 L: 421.00± 98.831	R: 429.80± 67.570 L: 466.70± 105.749	Nil follow-up.	Right T0:T1 improved 35% Left T0:T1 improved 11% No statistical significance.
	Suteera-watta-nanon (2002)[69]	R: 49.66± 4.32 L: 43.76± 5.52	R: 58.74± 3.80 L: 51.27± 0.44	Nil follow-up data provided by study.	% change not measured.
	Zampieri (2006)[64] (n=19)	Nil data provided by study.	T: 61.86 ±15.15 C: 68.56 ±11.68	Not measured	Change scores: T: 3.60±5.93 vs C: 6.71±6.74, p=0.29 Within group comparison: T: T0 vs T1 nil significant improvement p=0.08 **C: T0 vs T1 significant improvement, p=0.01**
	Zampieri (2006)[64] (n=5, crossover)	Nil data provided by study.	Nil data provided by study.	Not measured	Change scores: T0: 7.05±3.05 vs T1: 2.09±10.19, p=0.33
	Zampieri (2006)[64] (n=10, retention)	Not reported.	Not reported.	Not reported.	Not reported.
Step width[67] *(mm)*	**Sale (2014)**[67]	166.60± 24.460	153.60± 43.678	Nil follow-up.	T0:T1 reduced 9% No statistical significance.
Stride length[67] *(cm)*	**Suteera-watta-nanon (2002)**[69]	R:90.49±8.70 L:94.80±11.57	R:109.16 ±5.76 L:110.92± 0.89	Nil follow-up data provided by study.	% change not reported.
	Zampieri (2006)[64] (n=19)	Nil data provided by study.	T:61.86±15.15 C:68.56± 11.68	Nil follow-up.	Change scores: T:3.60±5.93 vs C:6.71±6.74, p=0.29.
	Zampieri (2006)[64] (n=5, crossover)	Nil data provided by study.	Nil data provided by study	Nil follow-up.	
	Zampieri (2006)[64] (n=10, retention)	Nil data provided by study.	Nil data provided by study.	Nil follow-up.	

MOBILITY ASSESSMENTS- GAIT SPEED AND GAIT ANALYSIS MEASURES (cont):					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Stance time[165] *(% stride)*[67] *(s)*[64]	**Sale (2014)**[67]	R:62%±0.017 L:64%±0.057	R:62%±0.024 L:60%±0.028	Nil follow-up.	% change not reported.
	Zampieri (2006)[64] (n=19)	Nil data provided by study.	T: 0.79±0.11 C: 1.07±0.65	Not measured.	Change scores: T: -0.14±0.22 vs C: -0.04±0.11, p=0.13 Within group comparison: **T: T0 vs T1 significant decrease, p=.01** C: T0 vs T1 nil significant decrease, p=0.40
	Zampieri (2006)[64] (n=5, crossover)	Nil data provided by study.	Nil data provided by study.	Not measured.	Change scores: T0: 0.06±0.15 vs T1: -0.05±0.27, p=0.23
	Zampieri (2006)[64] (n=10, retention)	1.07±0.37	0.87±0.18	0.90±0.23	**T0 higher than T1, p=0.04**, T1 difference to T2, p=0.45.
Swing time[67] *(s)*	**Suteera-watta-nanon (2002)**[69]	R:0.62±0.01 L:0.66±0.03	R:0.54 L: 0.56	Nil follow-up data provided by study.	%change not reported.
	Zampieri (2006)[64] (n=19)	Nil data provided by study.	T: 0.60±0.09 C: 0.76±0.21	Not measured.	Change scores: T: 0±6.35 vs C: 0.05±0.11, p=0.21 Within group comparison: T: T0 vs T1 nil significant improvement, p=.90 C: T0 vs T1 nil significant improvement, p=0.20
	Zampieri (2006)[64] (n=5, crossover)	Nil data provided by study.	Nil data provided by study.	Not measured.	**Change scores: T0: 0.10±0.11vs T1:-0.15±0.11, p=0.04**
	Zampieri (2006)[64] (n=10, retention)	0.71 ±0.20	0.62.21±0.	67±0.22	T0 higher than T1, p=0.06, T1 difference to T2, p=0.26
Step number over 3m[166]	**Suteera-watta-nanon (2002)**[69]	5.50±2.12	6.00±1.41	Nil follow-up data provided by study.	% change pre-training to post-training: 8% increase

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MOBILITY ASSESSMENTS- GAIT SPEED AND GAIT ANALYSIS MEASURES (cont):					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Heel-to-heel base of support[69] *(cm)*	**Suteera-watta-nanon (2002)**[69]	R:12.91±0.29 L:12.96±2.12	R:17.50±0.85 L:17.94±1.12	Nil follow-up data provided by study.	%change not reported.
Duration of double support[67] *(% stride)*	**Sale (2014)**[67]	15%±0.023 11%±0.030	13%±0.035 8%±0.018	Nil follow-up.	% change not reported.
VISION ASSESSMENTS:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Vertical Gaze Fixation Score (vGFS):[74]	**Zampieri (2006)**[64] (n=19)	T:0.48±0.31 C: 0.38±0.27	T: 0.30±0.23 C: 0.30±0.21	Nil follow-up	Between group T vs C: **significant main effect of test $F_{1,17}$=6.98, p=0.01, significant interaction $F_{1,17}$=2.57, p=0.001** Within group: **T: T0 higher than T1, p=0.004** C: T0 higher than T1, p=0.57
	Zampieri (2006)[64] (n=5, crossover)	0.34±0.24	0.28±0.11	Nil follow-up	T0 higher than T1, p=0.90
	Zampieri (2006)[64] (n=10, retention)	0.31±0.14	0.29±0.25	Nil follow-up	T0 higher than T1, p=0.24, T1 difference to T2, p=0.41,
Gaze Error Index:[74]	**Zampieri (2006)**[64] (n=19)	T: 64.11±8.87 C:53.15±29.16	T: 53.15±8.61 C:60.75±7.20	Nil follow-up	Between group T vs C: **significant main effect of test $F_{1,17}$=9.76, p=0.006, significant interaction $F_{1,17}$=9.56, p=0.006** Within group: **T: T0 higher than T1, p<0.001** C: T0 higher than T1, p=0.72
	Zampieri (2006)[64] (n=5, crossover)	60.18±14.00	60.74±15.53	Nil follow-up	T0 higher than T1, p= 0.72
	Zampieri (2006)[64] (n=10, retention)	Nil data provided by study.	Nil data provided by study.	Nil data provided by study.	T0 higher than T1, p= 0.06, T1 difference to T2, p=0.90

COGNITIVE/ NEURO- PSYSCHIATRIC ASSESSMENTS					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Geriatric Depression Scale (GDS)[150]	**Nicolai (2010)**[66]	4(1-11)	6(3-10)	5(2-9)	No significant differences between three assessments.
MEASURES ASSESSING MULTIPLE DOMAINS					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Progressive Supranuclear Palsy Rating Scale (PSPRS)[148]	**Di Pancrazio (2013)**[65]	Nil data provided by study.	Nil data provided by study.	Nil follow-up data provided by study.	Nil data provided by study.
	Santens (2009)[68]	See Appendix VIII	See Appendix VIII	Nil follow-up.	In 5/6 patients, the total score of the subsections improved at T1, with most prominent improvements found on the gait/midline symptoms. Repetition of the trial in one patient resulted in similar improvements on all three occasions.
Unified Parkinson's Disease Rating Scale (UPDRS)[71]	**Nicolai (2010)**[66]	33 (19-70)	41 (33-60)	39 (28-67)	No significant difference in UPDRS.
CONSEQUENCES OF SYMPTOMS:					
MEASURE:	**STUDY:**	**T0:**	**T1:**	**T2:**	**FINDINGS:**
Parkinson's Disease Questionnaire-39.[76]	**Nicolai (2010)**[66]	36.2 (28.6-55.4) See Appendix IX	26.7 (22.3-44.0) See Appendix IX	24.5 (21.3-40.1) See Appendix IX	Improved T0 to T1 but did not reach significance (p=0.25). **T0-T2 significantly improved (p=0.039).**
Activities-specific Balance Confidence (ABC)[149]	**Nicolai (2010)**[66]	13.8 (1.3-28.1)	6.9 (0.0-21.3)	16.3 (0.0-16.7)	**ABC: T0: T1 deteriorated by 50%, p=0.047** and no further changes at T2.

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Di Pancrazio (2013)[65]: Effectiveness of a rehabilitation program combining a dynamic antigravity postural system (SPAD) and a vibration sound system (ViSS). 20 minutes, three times a week for two months. Nil follow-up.

Nicolai (2010)[66] : Effectiveness of balance and posture exercises with audio-biofeedback in improving balance. 45 minutes, three times a week for six weeks, 1:1. Follow-up at 4 weeks post.

Sale (2014)[67]: Rehabilitative program of robot-assisted walking on spatiotemporal parameters. Forty-five minutes, five times a week for four weeks.

Santens (2009)[68]: Effectiveness of repetitive transcranial magnetic stimulation (rTMS) in improving gait/midline symptoms. 1000 pulses per session, each day for five days (n=5). 1000 pulses per session, each day, for five days repeated three times with 4-week intervals (n=1).

Suteerawattananon (2002)[69]: Use of a modified body weight support treadmill training program to reduce falls and improve the balance and gait. 90 minutes, three times a week for eight weeks. Follow-up at 2-weeks post.

Zampieri (2006)[64]: Effects of balance and eye movement training compared to balance training alone on gait and gaze control. One hour, three times a week for four weeks (n=19). Following an 8-week washout period balance only group received balance+ eye exercise intervention, 3x a week for 1 hour for 4 weeks (n=5). Retention of gaze control and gait improvements 2 months post intervention (n=5).

Appendix VIII: Progressive Supranuclear Palsy Rating Scale outcome measure results in Santens (2009)[68]:

STUDY:	Baseline T0:				Post-intervention T1:				Findings:
Santens (2009)[68]: n=6	Bulbar	Supra-nuclear ocular	Limb	Gait/ Midline	Bulbar	Supra-nuclear ocular	Limb	Gait/ Midline	In 5/6 patients, the total score of the subsections improved at T1, with most prominent improvements found on the gait/midline symptoms.
Subject 1	4	13	10	9	2	13	7	5	
Subject 2	4	8	4	10	4	6	4	7	
Subject 3	5	10	10	7	5	9	10	2	
Subject 4	5	10	9	17	5	9	5	12	
Subject 5	5	9	8	5	5	9	8	5	
Subject 6	3	8	5	9	3	7	3	6	
Santens (2009)[68]: n=1, subject 1	Bulbar	Supra-nuclear ocular	Limb	Gait/ Midline	Bulbar	Supra-nuclear ocular	Limb	Gait/ Midline	Repetition of the trial in one patient resulted in similar improvements on all three occasions.
1st session	4	13	10	9	2	13	7	5	
2nd session	4	13	10	10	2	13	7	4	
3rd session	4	13	8	6	3	13	6	6	
Santens (2009)[68]: Effectiveness of repetitive transcranial magnetic stimulation (rTMS) in improving gait/midline symptoms. 1000 pulses per session, each day for five days (n=5). 1000 pulses per session, each day, for five days repeated three times with 4-week intervals (n=1).									

Appendix IX: Findings from the study that used the Parkinson's Disease Questionnaire-39[76] in Nicolai et al.[66]

Study:	T0:	T1:	T2:	Findings:
Nicolai (2010)[66] Summary Index (subtests below):	36.2 (28.6-55.4)	26.7 (22.3-44.0)	24.5 (21.3-40.1)	Improved T0 to T1 but did not reach significance (p=0.25). **T0-T2 significantly improved (p=0.039).**
Mobility	90.0 (62.5-100)	90.0 (67.5-100)	90.0 (82.5-100)	Nil comment by study.
ADL	58.3 (25.0-87.5)	54.2 (29.2-87.5)	50.0 (33.3-92.7)	Nil comment by study.
Wellbeing	8.3 (0.0-62.5)	4.2 (0.0-75.0)	4.2 (0.0-50.0)	Nil comment by study.
Stigma	0.0 (0.0-31.3)	0.0 (0.0-12.5)	0.0 (0.0-6.31)	Nil comment by study.
Social Support	0.0 (0.0-41.7)	0.0 (0.0-41.7)	0.0 (0.0-33.3)	Nil comment by study.
Cognition	37.5 (0.0-50.)	12.5 (0.0-56.3)	18.8 (0.0-31.3)	**Improved significantly T0-T2 (p=0.031).**
Communication	66.7 (50.0-75.0)	41.7 (16.7-66.7)	50.0 (25.0-66.7)	**Improved significantly T0-T1 (p=0.047)** but stayed stable T1-2.
Bodily discomfort	16.7 (0.0-25.0)	0.0 (0.0-50.0)	0.0 (0.0-37.5)	Nil comment by study.
Nicolai (2010)[66] : Effectiveness of balance and posture exercises with audio-biofeedback in improving balance. 45 minutes, three times a week for six weeks, 1:1. Follow-up at 4 weeks post.				

Appendix X: Joanna Briggs Institute Grades of Recommendations.[157]

The Joanna Briggs Institute Grades of Recommendations[157] have been developed to assist healthcare professionals when implementing evidence into practice. There are two grades of recommendation.

Grade A is a strong recommendation for a specific healthcare intervention where 1) it is clear the desirable effects outweigh the undesirable effects of the strategy, 2) there is evidence of adequate quality supporting its use, 3) there is a benefit or no impact on resource use, and 3) the values, preferences and patient experience have been taken into account.[157]

Grade B is a weak recommendation for a specific healthcare intervention where 1) the desirable effects appear to outweigh the undesirable effects of the strategy however this is not as clear, 2) there is evidence supporting its use however this may not be of high quality, 3) there is a benefit, no impact or minimal impact on resource use and 4) values, preferences and the patient experience may or may not have been taken into account.[157]

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