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Section Health Technology Assessment

Health Technology Assessment (HTA)

Scoping Report

Title	Long-term physiotherapy in patients after stroke, with multiple sclerosis, or with Parkinson's disease
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Technology	Long-term physiotherapy
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Type of Technology	Medical procedure (Allied health)

Executive Summary

The Swiss Federal Office of Public Health is re-evaluating the reimbursement of long-term physiotherapy, defined as more than 36 physiotherapy sessions (4 bouts of 9 sessions each). This report aims to determine the feasibility of conducting a health technology assessment (HTA) of long-term physiotherapy in patients after stroke, with multiple sclerosis (MS), or with Parkinson's disease (PD) based on clinical, economic, legal, social, ethical and organisational data identified during the scoping phase. The comparison of interest to the policy question is long-term physiotherapy compared to short-term physiotherapy. Supplementary comparisons between long-term physiotherapy and other comparators (i.e. placebo, sham, usual care and best possible care) were also sought.

A literature search was conducted in seven biomedical databases and supplemented with searches of HTA databases and specialty websites. From the 14,878 search results, no systematic reviews or randomised controlled trials were identified that investigated the policy question (i.e. long versus short-term physiotherapy). Twelve systematic reviews comparing long-term physiotherapy to any other long-term comparator were identified, of which 10 were conducted in stroke and 2 were in PD; no reviews on long-term physiotherapy for MS were identified. The searches also identified 13 social, 2 ethical and 3 organisational-related studies. Thirteen existing economic evaluations broadly matching the PICO criteria were identified; however, their applicability to the Swiss context was limited. No legal studies were identified.

There is currently no available data to undertake an HTA on the effectiveness, safety and cost-effectiveness of long-term physiotherapy compared to short-term physiotherapy in patients after stroke, with MS or PD.

Zusammenfassung

Das Schweizer Bundesamt für Gesundheit überprüft die Rückerstattung von Langzeit-Physiotherapien mit mehr als 36 Physiotherapie-Sitzungen (4 Zyklen zu je 9 Sitzungen). Der Bericht soll die Machbarkeit einer Gesundheitstechnologiebewertung (Health Technology Assessment HTA) der Langzeit-Physiotherapie bei Patientinnen und Patienten nach einem Schlaganfall, mit Multipler Sklerose (MS) oder mit Parkinson-Erkrankung (PD) prüfen. In der Scoping-Phase werden dazu die klinischen, wirtschaftlichen, rechtlichen, sozialen, ethischen und organisatorischen Daten erhoben. Der vorliegende Bericht vergleicht Langzeit-Physiotherapie mit Kurzzeit-Physiotherapie. Ergänzende Vergleiche zwischen Langzeit-Physiotherapie und andere Komparatoren (d. h. Placebo, Scheinbehandlung, übliche Versorgung und bestmögliche Versorgung) wurden ebenfalls einbezogen.

Es wurde eine Literaturrecherche in sieben biomedizinischen Datenbanken durchgeführt und durch Recherchen in HTA-Datenbanken und auf fachspezifischen Websites ergänzt. Bei den 14 878 Suchergebnissen wurden keine systematischen Übersichten oder randomisierte kontrollierte Studien gefunden, die die politische Fragestellung (d. h. Langzeit- versus Kurzzeit-Physiotherapie) untersuchten. In 12 systematischen Übersichtsarbeiten wurde eine Langzeit-Physiotherapie mit anderen Langzeit-Therapien verglichen, von denen 10 bei Schlaganfall und 2 bei Parkinson-Erkrankung durchgeführt wurden; zur Langzeit-Physiotherapie bei MS wurden keine Übersichtsarbeiten gefunden. Weiter wurden 13 soziale, 2 ethische und 3 organisationsbezogene Studien gefunden. Zudem konnten 13 bestehende ökonomische Evaluationen identifiziert werden, die weitgehend den PICO-Kriterien entsprachen; ihre Übertragbarkeit auf den Schweizer Kontext war jedoch begrenzt. Es wurden keine juristischen Studien gefunden.

Derzeit sind keine Daten verfügbar, um ein HTA zur Wirksamkeit, Sicherheit und Wirtschaftlichkeit von Langzeit-Physiotherapien im Vergleich zu Kurzzeit-Physiotherapien bei Patientinnen und Patienten nach Schlaganfall, mit MS oder Parkinson durchzuführen.

Résumé

L'Office fédéral de la santé publique (OFSP) réévalue actuellement le remboursement de la physiothérapie de longue durée, soit au-delà de 36 séances (quatre séries de neuf séances). Sur la base de données liées aux aspects cliniques, économiques, juridiques, sociaux, éthiques et organisationnels recueillies lors de la phase de *scoping*, le présent rapport vise à déterminer s'il est possible ou non de procéder à une évaluation des technologies de la santé (ETS ou HTA pour *health technology assessment*) sur la physiothérapie de longue durée de personnes qui ont eu une attaque cérébrale ou qui sont atteintes d'une sclérose en plaques ou de la maladie de Parkinson. Il s'agit de comparer la physiothérapie de longue durée au traitement de courte durée. Des recherches sur la physiothérapie de longue durée en parallèle à d'autres comparateurs (p. ex. placebo, traitement fictif, traitement habituel et meilleur traitement possible) ont également été effectuées.

Des recherches documentaires ont été menées dans sept bases de données biomédicales, en conjonction avec des bases de données dédiées aux ETS et des sites Internet spécialisés. Parmi les 14 878 résultats de la recherche n'ont identifié aucune revue systématique et aucun essai randomisé contrôlé portant sur la politique en la matière (p. ex. comparaison entre la physiothérapie de longue durée et le traitement de courte durée). Douze revues systématiques qui comparaient la physiothérapie de longue durée à d'autres comparateurs de longue durée ont été identifiées. Parmi ces revues, dix traitaient des attaques cérébrales et deux abordaient la maladie de Parkinson. Aucune revue sur la physiothérapie de longue durée chez les personnes atteintes d'une sclérose en plaques n'a été identifiée. Par ailleurs, les recherches ont permis de repérer treize études portant sur les aspects sociaux, deux études sur les aspects éthiques et trois études sur les questions organisationnelles. Treize évaluations sur l'aspect économique répondant généralement aux critères de PICO (*Patient Intervention Comparison Outcome*) ont été identifiées. Toutefois, leur applicabilité au contexte suisse était limitée. Aucune étude traitant des aspects juridiques n'a été repérée.

Il n'existe actuellement aucune donnée qui permettrait de mener une ETS pour étudier l'efficacité, la sécurité et le rapport coût-efficacité de la physiothérapie de longue durée comparée à la physiothérapie de courte durée chez les personnes qui ont eu une attaque cérébrale ou qui sont atteintes d'une sclérose en plaques ou de la maladie de Parkinson.

Executive Summary

L'Ufficio federale della sanità pubblica sta rivalutando la rimunerazione della fisioterapia di lunga durata, ossia quella oltre le 36 sedute (4 prescrizioni di 9 sedute ciascuna). Il presente rapporto ha lo scopo di verificare la fattibilità di condurre valutazioni delle tecnologie sanitarie (HTA) concernenti la fisioterapia di lunga durata in pazienti colpiti da ictus, da sclerosi multipla o dal morbo di Parkinson, sulla base di dati clinici, economici, legali, sociali, etici od organizzativi identificati durante la fase di scoping. Per quanto riguarda i fattori relativi alla rimunerazione, si tratta di comparare la fisioterapia di lunga durata con quella di breve durata. Sono stati inoltre effettuati ulteriori paragoni tra la fisioterapia di lunga durata ed altri elementi (p. es. placebo, un trattamento simulato, il trattamento usuale e il trattamento migliore possibile).

Una ricerca bibliografica è stata condotta in sette banche dati di biomedicina ed ulteriori ricerche sono state effettuate nelle banche dati HTA e in siti web specialistici. Dai 14 878 risultati di ricerca non emergono revisioni sistematiche o studi controllati randomizzati che indagano la questione della rimunerazione (p. es. fisioterapia di lunga durata vs. fisioterapia di breve durata). Sono state ritrovate 12 revisioni sistematiche che confrontano la fisioterapia di lunga durata con ogni elemento di lunga durata, 10 delle quali condotte su pazienti colpiti da ictus e due in pazienti con il morbo di Parkinson; non sono state riscontrate revisioni sulla fisioterapia di lunga durata in malati di sclerosi multipla. Dalle ricerche sono inoltre risultati 13 studi vertenti su aspetti sociali, 2 studi su aspetti etici e 3 su aspetti organizzativi. Sono state reperite 13 valutazioni economiche che rispondono ampiamente ai criteri del modello PICO (*Patient Intervention Comparison Outcome*), ma che si applicano solo limitatamente al contesto svizzero. Non sono stati reperiti studi su aspetti legali.

Al momento non esistono sufficienti dati per effettuare una HTA sull'efficacia, la sicurezza e l'economicità della fisioterapia di lunga durata comparata a quella di breve durata in pazienti colpiti da ictus, da sclerosi multipla o dal morbo di Parkinson.

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Abbreviations and acronyms

ADL	Activities of daily living
BBS	Berg's Balance Scale
CHF	Swiss francs
CIS	Clinically isolated syndrome
CNS	Central nervous system
CT	Computed tomography
EAE	Effectiveness, appropriateness, economic efficiency
EQ-5D	EuroQol-5D
FOPH	Federal Office of Public Health
HTA	Health technology assessment
HRQoL	Health-related quality of life
MS	Multiple sclerosis
MRI	Magnetic resonance imaging
PD	Parkinson's disease
PEDro	Physiotherapy Evidence Database
PICO (EO)	Population, intervention, comparator, outcome, (economic outcomes)
PPMS	Primary progressive multiple sclerosis
QALY	Quality-adjusted life years
QoL	Quality of life
RCT	Randomised controlled trial
RRMS	Relapsing-remitting multiple sclerosis
SF-6/-12/-36	Short Form-6/-12/-36
SPMS	Secondary progressive multiple sclerosis
SR	Systematic review
TIA	Transient ischaemic attack
UK	United Kingdom
USA	United States of America
WHO	World Health Organization

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Objective of the HTA scoping report

The objective of the scoping report is to conduct a systematic literature search and to synthesize the available evidence base addressing the main health technology assessment (HTA) domains, i.e., clinical effectiveness/safety, costs/budget impact/cost-effectiveness, legal/social/ethical and organisational issues. In the report the analytical methods that are to be used when a HTA is pursued are described. Based on quantity and quality of the extracted evidence the feasibility of pursuing a HTA is judged. Analysis of the individual study outcomes is not the objective of the scoping report.

1 Policy question and context

For patients after stroke, with multiple sclerosis (MS), or with Parkinson's disease (PD), best supportive care often includes long-term physiotherapy. In Switzerland, physiotherapy is covered via mandatory health insurance for up to 36 sessions. For any patient wishing to continue physiotherapy beyond 36 sessions at the expense of mandatory health insurance, the treating physician must make a formal request for reimbursement to the medical officer of the patient's insurance company. According to the medical officers, these requests have been increasing in recent years.

Studies investigating the additional benefit of extending physiotherapy from acute and subacute care into long-term care are rare, and thus evidence about the efficacy and effectiveness for the treatment of patients after stroke or with MS or PD, is scarce. The planned HTA aims to give an overview of the existing evidence to determine whether long-term physiotherapy meets the effectiveness, appropriateness, economic efficiency (EAE) criteria required for reimbursement via mandatory health insurance in Switzerland.

2 Research question(s)

The scoping report aims to estimate the quantity and quality of relevant literature addressing the following research questions:

1) What is the clinical effectiveness, safety and cost-effectiveness of long-term physiotherapy compared to short-term physiotherapy in patients after stroke, with MS or PD?
2) What is the clinical effectiveness, safety and cost-effectiveness of long-term physiotherapy compared to best supportive care, no care, interval therapy, and unsupervised home-based therapy in patients after stroke, with MS or PD?
3) Are there any social, legal, ethical or organisational issues associated with long-term physiotherapy in patients after stroke, with MS or PD?

3 Medical background

3.1 Medical context and disease description

3.1.1 Stroke

3.1.1.1 Disease description

According to the World Health Organization (WHO), stroke is defined as: "*rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin and includes cerebral infarction, intracerebral haemorrhage and subarachnoid haemorrhage*."[1] Stroke is classified into two major types based on aetiology: ischaemic and haemorrhagic.[2] Ischaemic stroke is a neurological dysfunction episode caused by focal cerebral, spinal or retinal infarction, with symptoms persisting for more than 24 hours. Ischaemic cerebral infarction is commonly caused by atherosclerotic obstruction (i.e. main atherosclerotic lesion/thrombosis and embolism) of large cerebral and cervical arteries. Ischaemia can occur in all or part of the brain supplied by the occluded artery. Haemorrhagic stroke is caused by a rupture in the wall of blood vessels in the brain commonly caused by aneurysm and arteriovenous malformation.

Stroke is a heterogenous condition and establishing its risk factors and treatment depends on its pathogenesis. A comprehensive list of risk factors for stroke is presented in ***Table 1***.

Table 1 Risk factors for ischaemic and haemorrhagic stroke

Ischemic stroke	Haemorrhagic stroke
Modifiable risk factors*	
Alcohol consumption	Anticoagulation
Cardiac disease	Diet
Cigarette smoking	Heavy drinking
Diabetes	Hypertension
Diet	Illegal drug use (especially cocaine and crystal methamphetamine)
Hypercholesterolaemia	Thrombolytic therapy
Mitral stenosis	
Obesity and low physical activity	
Non-modifiable risk factors*	
Age/Sex	Age/Sex
Geographic location	Amyloid angiopathy
Race/ethnicity	Race/ethnicity
Hereditary/familial factors	

Source: Boehme 2017[3]; Parmar 2011[2]

Note: *Genetics is increasingly recognised as potentially modifiable either directly or through gene-environment modification

3.1.1.2 Incidence or prevalence of stroke

The lifetime risk of stroke is higher among females (20–21%) than males (14–17%).[4] As the elderly population continues to grow, it is postulated that the incidence of stroke will increase significantly.[5] Data showing the global burden of disease indicates that 24.9% of individuals aged 25 years and older carry a lifetime risk of stroke, with 18.3% at risk of ischaemic stroke and 8.2% at risk of haemorrhagic stroke.[6] A representative population survey of 19,123 households in Switzerland conducted in 2005 reported that in the previous one to two years, 6.9% were affected by stroke.[7] This imposes a high burden on health care costs, with the average cost of inpatient hospitalisation and rehabilitation estimated at CHF 62,139.[7]

3.1.1.3 Symptoms and diagnostic pathway

The most common signs and symptoms associated with ischaemic stroke are presented in ***Table 2***. Acute onset of symptoms upon waking, or otherwise, is the most common feature of ischaemic stroke, with unilateral weakness and speech disturbance the most common physical findings.[8] Sudden onset of focal neurologic deficit is likely to worsen during the first 24 hours of the event, due to increased intracranial pressure.

The diagnostic pathway for stroke typically involves neuroimaging with computed tomography (CT) scan or magnetic resonance imaging (MRI) to differentiate ischaemic stroke from intracerebral haemorrhage.[8]

Table 2 Common signs and symptoms of stroke

Symptoms	Signs
Acute onset	Arm paresis
Subjective arm weakness	Leg paresis
Subjective leg weakness	Dysphasia or dysarthria
Self-reported speech disturbance	Hemiparetic or ataxic gait
Subjective facial weakness	Facial paresis
Arm paraesthesia	Eye movement abnormality
Leg paraesthesia	Visual field defect
Headache	Dysphagia
Non-orthostatic dizziness	

Source: Yew et al. 2015[8]

3.1.2 MS

3.1.2.1 Disease description

MS is a demyelinating, inflammatory, autoimmune disease of the central nervous system (CNS) that is a major cause of chronic neurological disability in young and middle-aged adults from 18 to 50 years old.[9] [10] The pathological process in the development and progression of MS is the damage or loss of axons due to immune-mediated destruction of the myelin sheath.[11] Based on the new phenotypic classification for MS there are four main disease courses: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS).[12] The updated MS disease course description is presented in ***Table 3.***

Table 3 Description of MS disease course

Disease Course	Description	
Clinically isolated syndrome (CIS)	The first episode of CNS inflammatory demyelination that may become MS if additional activity occurs	
Relapsing-remitting MS (RRMS)	Episodes of acute deterioration of neurologic functioning (new symptoms or worsening of existing symptoms) with total or partial recovery and no apparent progression of disease	
RRMS subtypes	***Active*** evidence of new relapses, new gadolinium enhancing lesions and/or new or enlarging T2 lesions on MRI over a specified period ***Inactive*** no evidence of disease activity	***Worsening*** increased disability confirmed over a specified period following a relapse ***Stable*** no evidence of increasing disability over a specified period following a relapse
Primary progressive MS (PPMS)	Steadily worsening neurologic function from onset of symptoms without initial relapses or remissions	
PPMS subtypes	***Active*** evidence of new relapses, new gadolinium enhancing lesions and/or new or enlarging T2 lesions on MRI over a specified period ***In*active** no evidence of disease activity	***With progression*** evidence of disease worsening on an objective measure of change confirmed over a specified period, with or without relapses ***W*ithout progression** no evidence of disease worsening on an objective measure of change over a specified period
Secondary progressive MS (SPMS)	SPMS refers to the disease progressing steadily, with or without relapses, following an initial relapsing-remitting course	
SPMS subtypes	***Active*** evidence of new relapses, new gadolinium enhancing lesions and/or new or enlarging T2 lesions on MRI over a specified period ***In*active** no evidence of disease activity	***With progression*** evidence of disease worsening on an objective measure of change, confirmed over a specified period, with or without relapses ***Without progression*** no evidence of disease worsening on an objective measure of change over a specified period

Abbreviations: **CNS** = central nervous system, **MRI** = magnetic resonance imaging, **MS** = multiple sclerosis, **PPMS** = primary progressive multiple sclerosis, **RRMS** = relapsing-remitting multiple sclerosis, **SPMS** = secondary progressive multiple sclerosis.

Source: Lublin 2014[12]

3.1.2.2 Incidence or prevalence of MS

MS is the most common neuroimmunological disorder seen in young adults (average age of onset 30 years). The estimated number of people with MS increased from 2.1 million in 2008 to 2.3 million in 2013, with the global median prevalence increasing from 30 per 100,000 in 2008 to 33 per 100,000 in 2013.[13] The overall prevalence of MS in Switzerland was estimated to be 150 per 100,000 in 2011 rising to 190 per 100,000 in 2015, which translates to an estimated 10,000 individuals with MS in 2011 and 12,600 in 2015.[14]

3.1.2.3 Symptoms and diagnostic pathway

Symptoms of MS are highly variable and unpredictable depending on the degree and location of demyelination in the CNS. Common symptoms experienced by MS patients include discrete episodes of numbness, tingling, weakness, vision loss, gait impairment, loss of coordination, imbalance, and bowel and bladder dysfunction. Patients may be stable between attacks but may experience fatigue and heat sensitivity.[15]

No single test can determine if a person has MS. The diagnosis process involves gathering evidence from clinical examination, medical history, lab tests and MRI of the brain and spinal cord.[16] Diagnosis of MS relies on evidence of CNS lesions showing the twin tenets of dissemination in time, signifying that damage has occurred more than once, and dissemination in space, suggesting damage in more than one location in the nervous system. The lack of precision in diagnosing MS led to the development of the McDonald Criteria by the International Panel on MS Diagnosis, which involves clinical, radiographic and laboratory data to diagnose MS.[17]

3.1.3 PD

3.1.3.1 Disease description

PD is a complex neurodegenerative condition characterised by the loss of dopaminergic neurons in the substantia nigra located in the basal ganglia, and the presence of Lewy bodies.[18]

The risk factors associated with PD include elevated cholesterol, environmental toxins (carbon disulfide, cyanide, herbicides, methanol and organic solvents, pesticides), head trauma, high caloric intake, increased body mass index, inflammation associated with activation of microglia, methcathinone (manganese content), methamphetamine/amphetamine abuse, mitochondrial dysfunction, nitric oxide toxicity, oxidative stress (potent neurotoxins and formation of free radicals), post-infection state and signal mediated apoptosis.[18]

3.1.3.2 Incidence or prevalence of PD

The prevalence of PD is 100 to 200 per 100,000 people, with an annual incidence of 15 per 100,000. The disease is more common in males than females, with disease onset usually occurring between 65 to 70 years of age.[19] In Europe, the estimated prevalence of PD is 108 to 257 per 100,000, and the estimated incidence is 11 to 19 per 100,000 inhabitants per year.[20] According to a Swiss population-based epidemiological study, PD in the canton of Geneva showed an age-adjusted prevalence of 114 (105.8–122.2) per 100,000, while the age-adjusted incidence was 20.1 (16–24.3) per 100,000 inhabitants between 2009 and 2012.[20] From 1990 to 2016, deaths, prevalence and disability-adjusted life years increased in Switzerland by 13.9%, 10.3% and 10.8%, respectively.[21]

3.1.3.3 Symptoms and diagnostic pathway

The cardinal features of PD such as bradykinesia, rigidity and resting tremor are often reported as the first clinical findings of the disease and are classified as motor symptoms.[22] Postural instability affects 50% of PD patients within five years of diagnosis. Other symptoms include freezing of gait, sialorrhea (drooling or excessive salivation), amimia (inability to express ideas through gestures or signs), depression, loss of taste and sense of smell, sleep disturbance, gastrointestinal complications, constipation, anxiety, pain, fatigue, sexual dysfunction, hallucinations and psychosis, impulse control disorder, cognitive impairment and dementia.[23] [24]

Parkinsonism is defined as bradykinesia in combination with either resting tremor, rigidity or both.[25] Parkinsonism must be established before criteria from the Movement Disorder Society[25] can be applied to determine whether the patient meets the criteria for PD as the cause. However, there is no reliable test to diagnose PD, making it difficult to distinguish from other conditions with similar presentations. Therefore, this condition is mainly diagnosed by a range of classical presentations only related to PD, such as hypokinesia, bradykinesia, postural instability, rigidity and sometimes a rest tremor.[26] [27]

4 Technology

4.1 Technology description

Physiotherapy is a mode of therapy that uses physical techniques to develop, maintain and restore movement and functional ability.[28] In patients after stroke, or with MS or PD, physiotherapy is commonly performed over a long-term basis to assist in the treatment and management of these diseases through movement and exercise, manual therapy, and education. Due to the complexity of neurological diseases, physiotherapists often require additional training to specialise in the rehabilitation of patients after stroke, with MS or PD.

4.1.1 Physiotherapy for patients after stroke

The care pathway for stroke patients often includes a multidisciplinary rehabilitation team with clearly documented roles and duties. This team should work closely with the patient and the family/caregiver so that all important information can be gathered and full support to the patient and family can be provided.[29] At the time of admission, patients should be screened across the following domains: orientation, positioning, mobility level (incl. risk of fall), pressure area risk, swallowing, continence, communication, nutritional status and hydration.

The National Institutes of Health Stroke Scale,[30] and the Barthel Index[31] or Extended Barthel Index[32] are commonly used to assess functional abilities, psychological function, pain, activity restriction and other environmental factors at admission, and again at discharge.

Physiotherapy can be implemented in the acute setting, at a rehabilitation centre, in an out-patient setting, and at home or in primary care centres.

The recommended timing for physiotherapy is at the very early stage of recovery, ideally within 24 hours of stroke onset, especially for patients who are unable to maintain or change posture on their own.[33] ***Table 4*** lists physiotherapy interventions used to treat various stroke impairments.

Table 4 Physiotherapy interventions for stroke impairments

Stroke impairment	Physiotherapy intervention
Gait, balance, mobility and movement	Gait-oriented physical fitness training Balance training Repetitive task training Muscle strength training Electrical stimulation Electromechanical-assisted gait training Hydrotherapy Ankle foot orthoses Cardiorespiratory training Resistance training Circuit class training
Upper limb function	Constraint induced movement therapy Electromechanical-/robotic-assisted training Repetitive task training Splinting Mirror therapy Electrostimulation Electromyographic biofeedback Virtual reality Bilateral training
Post-stroke spasticity	Routine resting splint of upper limb Routine functional electrical stimulation Electromyographic biofeedback Robot-mediated passive therapy
Dysphagia	Muscle strengthening exercises Electrical stimulation Biofeedback
Pain	Electrical stimulation Exercise Position and supportive devices
Fatigue	Graded aerobic exercise Cognitive intervention
Other	Mental practice Motor imagery Patient and caregiver education

Source: Adapted from various guidelines[34-38]

4.1.2 Physiotherapy for patients with MS

Along with pharmacological management, physiotherapy plays an important role in the management of MS and helps to improve and maintain functional performance. Patients with MS may have problems with balance, strength, mobility and fatigue.

The optimal type of physiotherapy intervention will vary according to an individual patient's needs, depending on the stage of MS and specific functional deficits. ***Table 5*** shows the physiotherapy interventions used to treat functional defects in MS.

Table 5 Physiotherapy interventions for MS

Functional deficit	Physiotherapy intervention
Gait	Exercise interventions Functional electrical stimulation Ankle foot orthosis
Balance	Balance exercises Aquatic therapy Core strength training Vestibular exercises Dual-task training
Spasticity and flexibility	Stretching exercises Muscle strength training Electrical stimulation
Weakness	Resistance training
Coordination	Weight training Bracing/splinting
Aerobic endurance	Aerobic training Aquatic therapy
Respiratory function	Respiratory muscle training

Source: Rohrig 2018[39]

4.1.3 Physiotherapy for patients with PD

Non-pharmacological management of patients with PD targets specific areas, mainly physical capacity, transfers, manual activities, balance and falls, and gait, as well as patient-centeredness and self-management support.[40] ***Table 6*** shows the physiotherapy interventions used to treat functional deficits in PD.

Table 6 Physiotherapy interventions for PD

Functional deficit	Physiotherapy intervention
Functional mobility	Conventional physiotherapy Treadmill Tai Chi Dance
Hypokinesia	Lee Silverman voice treatment
Reciprocal movements	Recumbent bicycle Elliptical machine
Gait	Exercise Gait training
Stiffness	Stretching and flexibility
Weakness	Weight training Water resistance training
Motor disability	Aerobic training Aquatic therapy Martial arts
Respiratory function	Respiratory muscle training
Pain	Exercise Peripheral desensitisation technique Mirror therapy Cognitive strategies
Motor learning	Visual and auditory cues Cognitive strategies

Source: Adapted from European Physiotherapy Guidelines for PD[40]

4.2 Alternative technologies

Within the context of this scoping report, an alternative technology can be described as an intervention or modality of therapy, other than conventional/standard physiotherapy, that may be offered to stroke, PD and MS patients.

Various technologies can be offered as alternative or parallel treatment to physiotherapy, irrespective the length of physiotherapy treatment. For stroke, PD and MS patients, such therapies include biological therapies (e.g. stem cell treatments), acupuncture, massage, herbal therapies, Alexander technique, aromatherapy, Ayurveda, biofeedback, chiropractic treatment, diet, magnetic therapy, and yoga.[41-49]

5 PICO

5.1 Population

The eligible patient population is defined as patients diagnosed with stroke, MS or PD. Patients with transient ischemic attack (TIA), clinically and radiologically isolated MS syndrome, or juvenile onset PD were excluded.

5.2 Intervention

Long-term physiotherapy is the intervention under investigation. No definition of what constitutes "long-term" physiotherapy could be identified from existing literature and clinical practice guidelines. In Switzerland, physiotherapy is covered under mandatory health insurance for up to 36 sessions (four bouts of nine sessions each). If a patient's condition requires more than 36 sessions at the expense of mandatory health insurance, the treating physician must make a formal request for reimbursement to the medical officer of the patient's insurance company. Based on this information, long-term physiotherapy has been defined in this scoping report as continual or regular physiotherapy beyond 36 sessions for patients diagnosed with stroke, MS or PD, which translates to continuous or regular physiotherapy sessions >2 months in patients after stroke, and >6 months in patients with MS or PD. These thresholds were informed by a survey of Swiss physiotherapy practices. To allow for a degree of clinical variation, and due to the lack of certainty around this definition, these cut-offs were used as a guide rather than strict inclusion criteria.

5.3 Comparator

The primary comparison of relevance to the policy question is short-term physiotherapy compared top long-term physiotherapy. In addition, long-term physiotherapy was compared to unsupervised home-based physiotherapy, no intervention, placebo/sham, usual care and treatments other than physiotherapy (i.e. best supportive care) including pharmacological treatments, cannabis, botulinum toxin, yoga and Pilates, in patients after stroke, with MS or PD.

5.4 Outcomes

Limitations in **functional capacity and mobility** are primary concerns of patients after stroke, with MS or PD and their families. Mobility disability has a profound impact on everyday life and can affect emotional wellbeing, activities of daily living (ADL), quality of life (QoL) and autonomy. Some of the tools used to measure balance and mobility in stroke patients include the Berg's Balance Scale (BBS),[50] the Activities-Specific Balance Confidence (ABC) Scale,[51] the Functional Ambulation Classification (FAC),[52]

the Motor Assessment Scale (MAS),[53] the Rivermead Mobility Index (RMI),[54] and the Stroke Rehabilitation Assessment of Movement (STREAM).[55-58] Assessment tools used to measure functional mobility and balance in PD include the Timed Up and Go (TUG) Test,[59] the Functional Reach Test (FRT),[60] the BBS,[50] ABC Scale,[51] Mini-Balance Evaluation System Test (Mini-BEST),[61] Functional Gait Assessment (FGA),[62] and 5 Times Sit to Stand (5TST).[63 64] As disease progresses, the ability to perform ADLs is profoundly affected.[65] ADLs are classified into personal, which includes toileting, dressing, eating, grooming, ambulation and bathing, and instrumental, which involves more complex task such as communication, shopping, transportation and domestic activities (cooking, housekeeping, laundry). Validated tools used to measure ADL include the Functional Independence Measure (FIM),[66] the Barthel Index (BI),[31] and the PD ADL Scale.[67 68] Commonly used tools in assessing mobility disability among patients with MS include the Expanded Disability Status Scale (EDSS),[69] and the MS Functional Composite (MSFC).[70 71] Assessment tools used to measure dexterity include the Nine-Hole Peg Test (9HPT),[72] and the Box and Block Test (BBT),[73] which are crucial to determine finger, hand and arm function.

Walking ability is a key component of mobility, which is routinely assessed by standardised tests and scales to observe the progression of neurological conditions.[74] Walking impairment places a great burden on patients after stroke, or with MS or PD. Validated clinician- and patient-driven instruments are available to evaluate walking performance (i.e., Timed 25 Foot Walk Test (T25FW),[75] 10 Metre Walk Test (10MWT),[76] and patient self-reported 12-Item MS Walking Scale(MSWS-12)[77]) and speed (i.e., assessment of velocity in metres per second, cadence in steps per minute, stride length in metres), and to test other aspects of mobility including balance (i.e., Dynamic Gait Index (DGI),[78] Timed Up and Go (TUG) Test,[59] and Functional Gait Assessment (FGA)[62]), endurance or motor fatigue (i.e., 2- or 6-Minute Walk Test[79]). The Freezing of Gait Questionnaire (FOGQ)[80] is an additional tool for PD (scores range from 0–24 with higher scores indicating more severe freezing of gait).

Clinician-rated impairment and disability measures describe disease progression over time as observed and rated by clinicians. This includes assessment on disability, disease severity and motor and clinical impairment. For stroke patients, Modified Rankin Scale (MRS)[81] and the Glasgow Outcome Scale (GOS)[82] are considered as the gold standard for stroke outcome assessment. MRS[81] is a 6-point ordinal scale that measures global disability (0=no symptoms to 6=Dead).[83] GOS[82] is an ordinal rating scale describing disability and handicap in patients with brain injury with scores ranging from 1 (death) to 5 (good recovery).[84] The Expanded Disability Status Scale (EDSS)[69] is considered the gold standard in the clinician rated comprehensive assessment of MS related disability.[85] The clinician-rated comprehensive assessment of PD-related disability include the following: Hoehn and Yahr (H&Y)

Scale,[86] Unified PD Rating Scale (UPDRS),[87] Webster Rating Scale,[88] and the Columbia University Rating Scale (CURS)[89] (higher scores indicate greater disability).[64]

Health-related QoL (HRQoL) is critical in patients after stroke, with MS or PD to provide information on the progression of the disease, effectiveness of treatment and the management of care provided. HRQoL can be measured using a patient-reported assessment of physical, social, emotional and mental health. It also refers to the way health influences a person's ability to function, as well as their perceived physical, mental and social well-being.[90] Examples of tools used to measure HRQoL in stroke patients include the Short Form-36 and -12 (SF-36/12),[91 92] Short Form 6-Dimensions (SF-6D),[93] EuroQol-5D (EQ-5D),[94] the Stroke-Specific QoL Scale (SS-QoL),[95] the Sickness Impact Profile (SIP),[96] and the Quality of Wellbeing Scale (QWS).[97-100] HRQoL is commonly assessed using self-reported questionnaires validated for MS patients such as the MS 54-Item QoL Questionnaire (MSQoL-54),[101] the Functional Assessment of MS (FAMS)[102] Questionnaire, the Hamburg QoL Questionnaire in MS (HAQUAMS),[103] the QoL Index – MS (QLI-MS),[104] the Leeds MS QoL Scale,[105] the 29-Item MS Impact Scale (MSIS-29),[106] the Disability and Impact Profile (DIP),[107] the extension of measures of Quality-adjusted Time Without Symptoms of Disease and Toxicity of Treatment,[108] and the MS International QoL[109] Questionnaire.[10 110] In PD, QoL is commonly measured using the 39-Item PD Questionnaire (PDQ-39),[111] the PD QoL Questionnaire (PDQoL),[112] the PD Impact Scale (PIMS),[113] and the SF-36[91] or SF-12.[64 92]

Pain is a subjective experience and is often reported using the Visual Analogue Scale (VAS)[114] and the Numerical Rating Scale (NRS)[115] presented as mean differences across included patients. The VAS[114] and NRS[115] are recommended to assess pain in both stroke and MS patients. For patients with PD, the King's PD Pain Scale (KPPS)[116] is recommended for rating pain intensity, due to the insufficient validation of the VAS[115] and NRS[115] in patients with PD.[117] The KPPS Scale[116] has 14 questions that investigate the frequency and severity of different pain syndromes frequently observed in PD patients.[117] Items are scored by severity (0–3) multiplied by frequency (0–4), resulting in a subscore of 0–12, with a total possible score of 0–168.[116 117]

Fatigue is one of the most common and debilitating manifestation of MS that can significantly affect a person's functional ability at home and at work.[118] It can have socioeconomic consequences involving loss of work hours and loss of employment.[119 120] Fatigue in MS is not clearly understood. Common definition of fatigue includes: *'a sense of exhaustion, lack of energy or tiredness',* and *'subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual or desired activity.'*[119 121 122] The definition is open to a wide range of interpretation depending on the patient's cultural or educational background. Patient-reported questionnaires to quantify the severity of fatigue are commonly used for MS patients. However, this outcome can be confounded by other

conditions associated with MS, such as depression and sleep disorders.[123] Fatigue rating scales used are the Chalder Fatigue Scale (CFQ11),[124] the Krupps Fatigue Severity Scale (FSS),[125] the Modified Fatigue Impact Scale (MFIS),[126] and the Neurological Fatigue Index for MS (NFI-MS).[119 127]

Impaired cognition, muscle strength, muscle tone, sensation, coordination and gait, predispose patients after stroke, with MS or PD to increased risk of **falls**.[128-130] The falls per person year, or the standardised measure of fall occurrence, is determined by dividing the falls rate by the length of follow-up.[131-133] For patients after stroke, with MS or PD, the Falls Efficacy Scale-International (FES-I)[134] has been used to measure the patient's confidence in performing ADL (scores ranging from 1 to 10 with higher scores signifying lower levels of confidence and a total score of 70 or more denoting that the patient has a fear of falling).[64 135 136]

Poor **compliance** to physiotherapy and rehabilitation intervention can have a negative effect on overall health outcomes and on the long-term healthcare cost.[137] Compliance with physiotherapy intervention, like adherence to physical activity, might be difficult since the symptoms and impairment in patients after stroke, with MS or PD change over time.[138 139] Compliance can be measured using adherence.[140] Adherence is defined as: '*the degree to which the person's behavior corresponds with the agreed recommendation from a healthcare provider*,' and is calculated as the number of sessions the patient attended over the expected number of treatment sessions in a specific time period or duration.[138 141] The concept of adherence in physiotherapy is multidimensional and could include appointment attendance, treatment fidelity and performance of the prescribed exercises (frequency and duration).[142] The most frequently used adherence measurement methods were diaries and logbooks.[139]

Adverse events are critical safety outcomes in the management of patients after stroke, with MS or PD. An adverse event is defined as: '*an unexpected and undesired incident directly associated with the care or services provided to the patient*.'[143] Events that result in death, life threatening adverse experience, inpatient hospitalisation or prolongation of existing hospitalisation, disability, or permanent damage are categorised as serious adverse events.[10] Adverse events recorded include fracture, pain, muscle soreness, dizziness, and adverse reaction to exercise interventions such as pallor (skin becoming pale); excessive sweating or clamminess; sudden or excessive shortness of breath unrelated to increased activity; increased cough or wheeze; nausea or vomiting; confusion; chest heaviness, pain or tightness; angina and rapid heart rate; palpitations or irregular heartbeat.[64 144 145]

Table 7 Study selection for stroke

P:	• Patients diagnosed with stroke *Exclusion criteria:* • *Patients with transient ischaemic attack* • *Patients in the acute (1 to 7 days post-stroke) or sub-acute stage (7 days to 6 months post-stroke) of the disease*[146]

I:	• Any long-term physiotherapy interventions given to chronic stroke patients, which includes:
	  ○ Physiotherapeutic interventions: active and passive movement therapy, manual therapy, pelvic floor exercises, medical exercise therapy, movement therapy in water, cardiovascular physiotherapy, pelvic floor physiotherapy
	  ○ Physical methods/modalities: heat and cold therapy, muscle and connective tissue massage, electrotherapy, hydrotherapy
	  ○ Other interventions: breathing (respiratory) and lymphological physiotherapy, light and ultrasound therapy

C:	• Best supportive care, including pharmacologic, cannabis, botulinum toxin, yoga, Pilates • Interval therapy including short-term physiotherapy • Unsupervised home-based physiotherapy • No intervention • Placebo/sham procedure
O:	Critical clinical outcomes • Functional capacity and mobility (including activities of daily living, balance, gait) • Walking • Clinician-rated impairment and disability measures • Health-related quality of life Important clinical outcomes • Pain • Falls • Compliance Safety outcomes • Adverse events

Table 8 Study selection criteria for MS

P:	• Patients with MS (relapsing-remitting MS, which may convert to secondary-progressive MS, primary progressive MS, and progressive relapsing MS)
	Exclusion criteria:
	• *Study population with possible MS such as:*
	  ○ *Clinically isolated syndrome*
	  ○ *Radiologically isolated syndrome*

I:	• Any long-term physiotherapy interventions given to MS patients, which includes:
	  ○ Physiotherapeutic interventions: active and passive movement therapy, manual therapy, pelvic floor exercises, medical exercise therapy, movement therapy in water, cardiovascular physiotherapy, pelvic floor physiotherapy, hippotherapy
	  ○ Physical methods/modalities: heat and cold therapy, muscle and connective tissue massage, electrotherapy, hydrotherapy
	  ○ Other interventions: breathing (respiratory) and lymphological physiotherapy, light and ultrasound therapy

C:	• Best supportive care, including pharmacologic, cannabis, botulinum toxin, yoga, Pilates • Interval therapy including short-term physiotherapy • Unsupervised home-based physiotherapy • No intervention • Placebo/sham procedure
O:	Critical clinical outcomes • Functional capacity and mobility (including activities of daily living, balance, gait) • Walking • Clinician-rated impairment and disability measures • Health-related quality of life Important clinical outcomes • Pain • Fatigue • Falls • Compliance Safety outcomes • Adverse events

Abbreviations: MS = multiple sclerosis.

Table 9 Study selection criteria for PD

P:	• Patients with PD *Exclusion criteria:* • *Juvenile onset PD age <18 years old*

I:	• Any long-term physiotherapy interventions given to PD patients, which includes:
	  ○ Physiotherapeutic interventions: active and passive movement therapy, manual therapy, pelvic floor exercises, medical exercise therapy, movement therapy in water, cardiovascular physiotherapy, pelvic floor physiotherapy
	  ○ Physical methods/modalities: heat and cold therapy, muscle and connective tissue massage, electrotherapy, hydrotherapy
	  ○ Other interventions: breathing (respiratory) and lymphological physiotherapy, light and ultrasound therapy

C:	• Best supportive care including pharmacologic, cannabis, botulinum toxin, yoga, Pilates • Interval therapy including short-term physiotherapy • Unsupervised home-based physiotherapy • No intervention • Placebo/sham procedure
O:	Critical clinical outcomes • Functional capacity and mobility (including activities of daily living, balance, gait) • Walking • Clinician-rated impairment and disability measures • Health-related quality of life Important clinical outcomes • Pain • Falls • Compliance Safety outcome • Adverse events

Abbreviations: PD = Parkinson's disease.

6 HTA key questions

For the evaluation of the technology the following key questions covering the central HTA domains, as designated by the EUnetHTA Core Model (clinical effectiveness, safety, costs, cost-effectiveness, budget impact, legal, social, ethical and organisational aspects), are addressed:

1. Is long-term physiotherapy effective/efficacious compared to short-term physiotherapy in patients after stroke, with MS, or with PD?
    a) Is long-term physiotherapy effective/efficacious compared to no treatment, placebo/sham, best supportive care, unsupervised home-based physiotherapy and interval therapy in patients after stroke, with MS, or with PD?
2. Is long-term physiotherapy safe compared to short-term physiotherapy in patients after stroke, with MS, or with PD?
    a) Is long-term physiotherapy safe compared to no treatment, placebo/sham, best supportive care, unsupervised home-based physiotherapy and interval therapy in patients after stroke, with MS, or with PD?
3. What are the costs associated with long-term physiotherapy in patients after stroke, with MS, or with PD?
4. How cost-effective is long-term physiotherapy compared to other treatments in patients after stroke, with MS, or with PD?
5. What is the budget impact of limiting the indication of physiotherapy to 36 treatment sessions in patients after stroke, with MS, or with PD?
6. Are there legal, social or ethical issues related to limiting physiotherapy treatments to 36 sessions in patients after stroke, with MS, or with PD?
7. Are there organisational issues related to limiting physiotherapy treatments to 36 sessions in patients after stroke, with MS, or with PD?

7 Methodology literature search

7.1 Databases and search strategy

A scoping search strategy was created to identify published literature that addresses the research questions. Literature searches were conducted in seven biomedical databases (PubMed, Embase, Cochrane Library, EconLit, University of York Centre for Reviews and Dissemination (York CRD), International HTA database (date limited from 2015-2020)), Physiotherapy Evidence Database (PEDro)). Separate searches were conducted to identify systematic reviews (SRs) and economic evaluations up to 27 September 2020, randomised control trials (RCTs) up to 22 October 2020, and evidence for the social, legal, ethical, and organisational auxiliary domains up to 13 November 2020. Details about the bibliographic database searches are available in ***Appendix A***. Additionally, the websites of HTA agencies were searched to identify relevant HTA reports that included cost-effectiveness analyses (***Table 29***). The search strings for RCTs and SRs were verified using known publications identified through targeted searches and were peer-reviewed by an independent reviewer not affiliated with the authors prior to the searches being conducted.

The key search terms related to the population and intervention were combined with various methodological and topical search filters (SR and HTA, RCTs, cost-effectiveness, etc.), depending on the database and research question being addressed.[147] The full search strategies for each database are reported in ***Appendix A.***

Owing to the broad nature of the intervention keywords, clinical trials databases were not searched as the volume of hits could not be screened within the available time to produce this scoping report. Grey literature searches were conducted on specialty websites (***Table 28***) to highlight any relevant literature that may not have been otherwise identified.

7.2 Study selection

Results from the literature search were imported into Rayyan (bibliographic management software). Rayyan functions similarly to EndNote but allows for easy blinding of reviewers and management of study inclusion conflicts.[148] Study selection was limited to studies in English, French, German and Italian. French, German, and Italian are three of the four official languages of Switzerland. The fourth language of Romansh was not included because of the limited number of publications available.[149 150] Only studies that met the population, intervention, comparator and outcome (PICO) criteria were considered eligible for inclusion. SRs and RCTs were considered as eligible study designs to address the policy question comparing long- versus short-term physiotherapy. In addition, SRs were also included to identify

literature for the supplementary comparison of long-term physiotherapy versus other long-term comparators. As this comparison was not the focus of the policy question, but can provide some indication of the benefit of long-term physiotherapy, only SR evidence was considered to be eligible for inclusion.

Studies based in countries outside of WHO Mortality Stratum A were excluded during full-text screening because burdens of disease in these countries are not comparable to Switzerland. The following countries comprise WHO Mortality Stratum A: Andorra, Australia, Belgium, Brunei, Canada, Croatia, Cuba, Cyprus, Czech Republic (Czechia), Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, The Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom (UK) and United States of America (USA).[151]

Study selection was conducted independently by two reviewers in duplicate, in two phases. All records were screened by title and abstract. Conflicts between reviewers on study inclusion were settled via consensus. If consensus could not be reached, a third reviewer decided whether to include or exclude the study. Articles deemed potentially relevant were then reviewed in full text by both reviewers independently, with disagreements settled via the same procedure of consensus.

Study characteristics (e.g. author details, country of publication, year, setting, length of follow-up, population, intervention, comparator, outcomes, sample size) were extracted for the included studies using piloted extraction templates. All data extractions were completed by one reviewer, then checked by a second reviewer for accuracy.

8 Synthesis of evidence base

8.1 Overall search results

The results of the systematic literature searches are presented in ***Figure 1.*** Database searches (Medline, Embase, the Cochrane Library, York CRD, International HTA Database, PEDro, and EconLit) identified 14,878 studies. After the removal of duplicates, 10,309 studies were reviewed by title and abstract, of which 401 were reviewed by full text. No publications were identified that compared long-term physiotherapy to short-term physiotherapy.

Twelve publications[152-163] were included which compared long-term physiotherapy to any other long-term comparator. The searches also identified 13 social, 2 ethical and 3 organisational-related studies. Thirteen existing economic evaluations[164-176] broadly matching the PICO criteria were identified. No legal studies were identified. A complete list of articles excluded at full text review is presented in ***Appendix D***.

8.2 Evidence base pertaining to efficacy, effectiveness and safety

8.2.1 Search results

No systematic reviews or RCTs were identified that investigated the policy question of long-term physiotherapy compared to short-term physiotherapy in patients after stroke, with MS or with PD.

Due to the absence of information addressing the policy question, supplementary research questions were included comparing long-term physiotherapy to other alternative therapies. As this was not a focus of the scoping report, relevant evidence for these supplementary questions was limited to existing systematic reviews. For the supplementary comparison of long-term physiotherapy versus any other long-term comparators, 12 systematic reviews were identified,[152-163] of which 10 were conducted in stroke and 2 were in PD; no reviews on long-term physiotherapy for MS were identified.

The included studies are as follows:

- **Effectiveness**
    - 0 SRs or RCTs compared long-term physiotherapy to short-term physiotherapy.
    - 12 SRs compared long-term physiotherapy interventions to sham, placebo or no intervention.[152-163]
- **Safety**
    - 0 SRs or RCTs compared long-term physiotherapy to short-term physiotherapy.
    - 2 SRs compared long-term physiotherapy to sham, placebo or no intervention.[161 162]

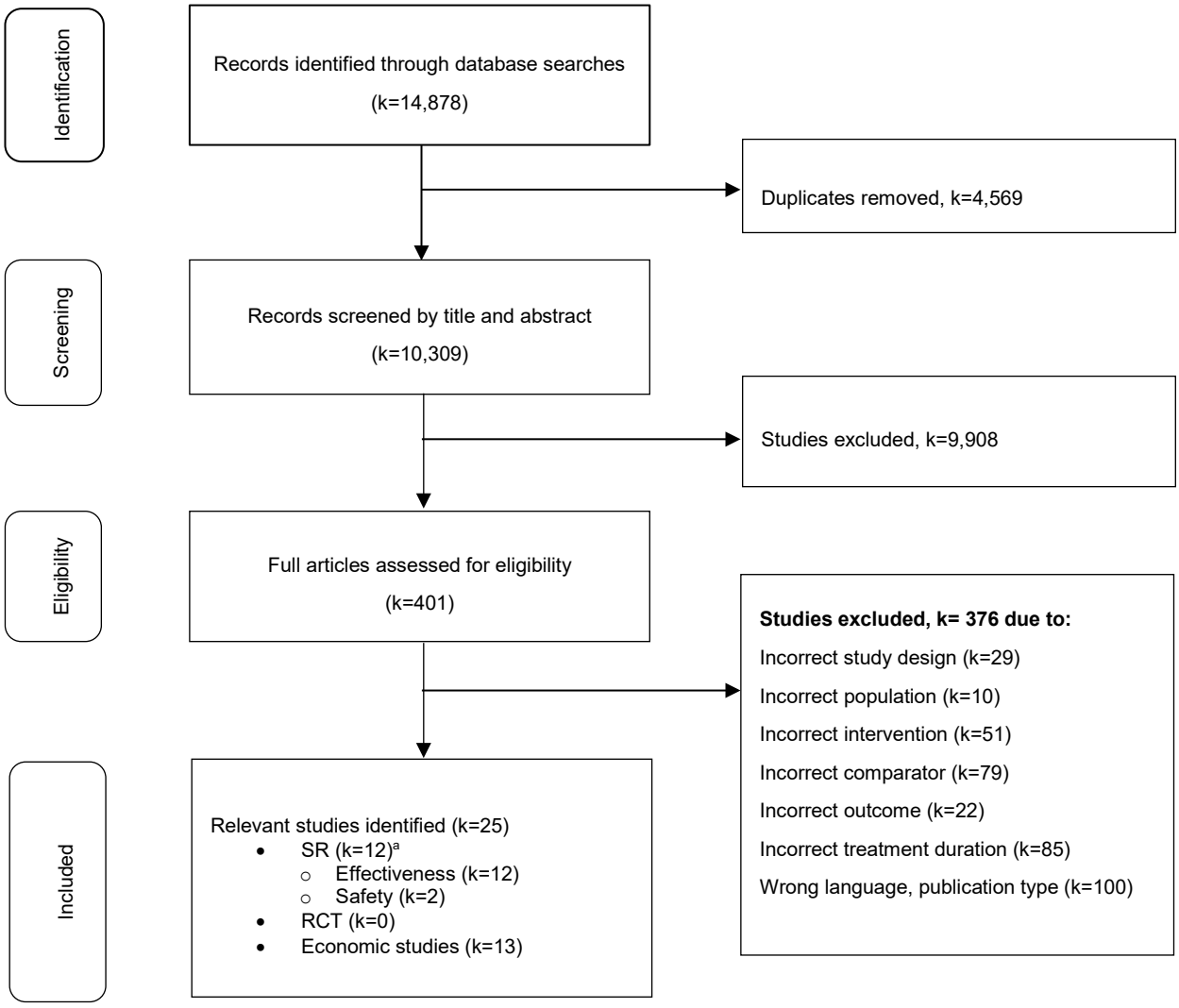

Figure 1 PRISMA flow chart for study inclusion

Abbreviations: **RCT** = randomised control trial, **SR** = systematic review.

Note: [a] = A total of 12 SRs were included: 10 studies considered effectiveness outcomes, two studies reported both safety and effectiveness data.

8.2.2 Evidence table

Detailed extraction tables reporting the characteristics of identified studies are outlined in ***Appendix B***, ***Table 30*** and ***Table 31***.

8.2.3 Findings regarding efficacy, effectiveness and safety

The 12 SRs[152-163] comparing long-term physiotherapy to any other long-term comparators included RCTs conducted across various countries, with many performed in non-stratum A countries (see ***Appendix B*** for the countries of included RCTs).

The long-term physiotherapy interventions included electrical stimulation (k=4), constrained induced movement therapy (k=1), motor rehabilitation physiotherapy interventions (k=1), cardiorespiratory and resistance training (k=1), overground physiotherapy (k=1), exercise therapy (k=2), ergometer training (k=1), and general physiotherapy interventions (k=1) compared with placebo or no intervention (k=10), sham (k=1), usual care (k=2) and treatments other than physiotherapy (k=3).

Physiotherapy in stroke is aimed to maintain functional capacity and performance in ADL. Electrical stimulation, which includes functional electrical stimulation, was the most commonly studied physiotherapy intervention (k=4) specific to patients diagnosed with stroke among the SRs included in this scoping report.

The stroke population most commonly studied included adults over 18 years of age, diagnosed at least 6 months prior to the study (k=4) with arm function of the hemiparetic/hemiplegic status after stroke (k=3). One SR included studies with participants ≥65 years of age (or mean age of participants required to be ≥65 years) regardless of stroke aetiology, type or severity.[157]

The number of studies included in the SRs ranged from 9 to 75, with sample sizes ranging from 168 to 3,617. It should be noted, however, that in the study by Stewart et al.,[157] only two of the 28 included RCTs compared electrical stimulation to sham, acupuncture or other physiotherapy interventions. There was considerable variability in the characteristics of the included SRs in terms of the type of stroke, age of the patients, and type and duration of physiotherapy interventions.

For PD, the primary goal of providing physiotherapy interventions is to enable patients to maintain the utmost level of mobility, activity and independence. This will enhance their quality of life and may prevent problems associated with the progressive nature of the disease. The number of studies included in the SRs was 25[161] and 76[162], respectively, with sample sizes of 1,181 and 1,827, respectively. The included SRs did not discriminate on duration or severity of PD, medications, falls risk, age or any duration of physiotherapy intervention.

No SRs were found that investigated the effect of long-term physiotherapy in patients with MS.

Physiotherapy interventions were most frequently compared with placebo or no intervention (k=10). Other comparators included usual care, sham and other physiotherapy interventions. It should be noted that not all of the studies included in the SRs had treatment durations greater than 2 months for stroke, or greater than 6 months for MS or PD. The duration of physiotherapy intervention ranged from 1 day to 12 months. Treatment duration, the presence of multiple physiotherapy interventions covered by the SRs and the restriction on physiotherapy intervention comparators, all limited the ability to include studies for this scoping report.

Functional capacity and mobility were the most frequently studied effectiveness outcomes (k=8 for stroke and k=2 for PD). Five studies reported on HRQoL, four studies reported on walking and ambulation, three studies investigated falls, and one study explored the clinician-rated impairment and disability measure.

In terms of safety, two SRs (one each for stroke and PD) reported on adverse events[162 163] and mortality/death.[163] Reported adverse events included recurrent non-fatal cardiovascular or cerebrovascular events, altered muscle tone, training induced injury, pain, incidence of falls and incidence of fractures. Compliance was measured by one study on PD.[162]

A summary of the studies reporting the effectiveness and safety outcomes per population is provided in ***Table 10***.

8.2.4 Quality of evidence assessment

The methodological quality of the studies included in the SRs were assessed using the PEDro scale for rating quality of RCTs and the Cochrane Collaboration's tool for assessing risk of bias. The risk of bias of the included studies varied from low to high. Two SRs only included RCTs with moderate to high quality.[154 161] One reason for the relatively low methodological quality scores relates to the difficulty in blinding the therapist providing the treatment and, to some extent, blinding of the participants on the interventions they are receiving.

Table 10 Outcomes reported in SRs of physiotherapy interventions in patients after stroke, with MS or PD

Author	Effectiveness						Safety		Compliance
	Clinician-rated impairment /disability	Falls	Functional capacity and mobility	Walking	HRQoL	Pain	Adverse events	Mortality	
Stroke									
Ferrarello 2011[152]			✓						
Hakkennes 2005[153]			✓		✓				
Howlett 2015[154]			✓						
Pomeroy 2006[155]			✓						
Saunders 2020[163]			✓		✓		✓	✓	
States 2009[156]				✓					
Stewart 2019[157]					✓				
Van der Lee 2001[158]			✓						
Veldema 2020[159]		✓	✓	✓	✓				
Yang 2019[160]			✓						
Parkinson's disease									
Shen 2016[161]		✓	✓	✓					
Tomlinson 2013[162]	✓	✓	✓	✓	✓		✓		✓

Abbreviations: **HRQoL** = health-related quality of life.

8.3 Evidence base pertaining to costs, cost-effectiveness and budget impact

8.3.1 Search results

A total of 78 studies identified in the systematic literature searches (see ***Section 8.1)*** were reviewed by full text for relevancy in relation to the economic section. The study selection focused on costs and economic evaluations in line with the PICO. For inclusion, the intervention needed to be delivered or supervised by a physiotherapist. Studies comparing physiotherapy interventions to usual care, no treatment placebo or relaxation were included. No restriction was placed on the duration of physiotherapy (long- or short-term), as economic approaches relevant to the PICO could include short-

term physiotherapy interventions. Studies were excluded if they were protocols, SRs and conference abstracts, or if the intervention included robotics or electronic games (i.e. exergaming). Following full text study selection, 13 studies were considered relevant and the remaining 65 studies were excluded.

8.3.2 Evidence table

A detailed extraction table reporting the characteristics of the thirteen included studies are outlined in ***Appendix C***, ***Table 32***.

8.3.3 Findings regarding costs, cost-effectiveness, and budget impact

Physiotherapy intervention variations

The thirteen economic studies[164-176] identified in this review involved varying types of physiotherapy interventions. Ten of the studies involved physiotherapy intervention for less than three months.[164 166-168 170-174 176] Among the included studies, 11 tested the cost-effectiveness of physiotherapy against usual care,[164 165 167 169-176] one against no care,[166] and one against relaxation.[168]

Two of the studies included three physiotherapy sessions per week over 10 to 12 weeks.[168 174] One study compared higher- to lower-intensity physiotherapy.[165], the more intensive intervention involved 23 hours of treatment for stroke rehabilitation, versus a lower intensity regimen of 9 hours.

The physiotherapy interventions included a range of individual and group exercises. The longer-term study of Farag et al.[169] had varying intensities of treatments, with the intervention group receiving between 2 and 4 home visits from a physical therapist over 6 months. In the study by Chan[165] the clinical trial used for the analysis involved increased intensities of physiotherapy for stroke rehabilitation compared to the standard level of physiotherapy. The Clarke et al.[166] intervention was delivered by a therapist in 4 sessions of 58 minutes each over 8 weeks. The study by Collins et al.[168] involved fitness classes of 1 hour and 15 minutes, held 3 times per week for 12 weeks.

The interventions were delivered in many different settings including community care,[164 168 169 171 175 176] acute care and inpatient delivery,[165] outpatient clinics,[166 173 174] and primary care facilities.[172]

Economic evaluation: populations and perspectives in the studies

Six studies were associated with stroke rehabilitation,[164 165 167 168 170 171] one with MS,[176] and the remainder with PD.[166 169 172-175] Most of the stroke studies included participants aged 70–75 years. The MS study[176] included participants aged 45–46 years and the PD study included participants aged around 70–71 years.

Most of the included studies were conducted in the UK,[164 166-168 171-173 175 176] and the remainder took place in Canada,[165] Sweden,[174] Australia,[169] and New Zealand.[170] Many of the UK studies used a National Health Service government perspective. The Australian study[169] took a health system perspective, and the Swedish study[174] a societal perspective for cost-effectiveness calculations, while the New Zealand study[170] appeared to use hospital costs.

Economic evaluation: approaches

Seven of the included studies were trial-based cost-utility analyses.[166 167 169 172 174-176] Four were cost analyses,[164 170 171 173] and one a decision model.[168]

Chan[165] developed a Markov state transition model as part of the Ontario Health Technology Assessment Series. The model had a lifelong duration and employed alive and dead states for recent stroke patients. Patients transitioned from one state to another using assumptions derived from peer-reviewed journals, government reports and expert opinion from members of the Canadian Stroke Network.

Economic evaluation: costs

Costs captured in the economic evaluations generally included physiotherapist time (i.e. duration costs) and hospital cost outcomes. The studies by Beech et al.,[164] Hunter et al.,[167] Fletcher et al.,[172] Farag et al.,[169] Xin et al.,[175] Joseph et al.,[174] Tosh et al.,[176] and Clarke et al.,[166] collected costs during trials. Fletcher et al.[172] included resource use for physiotherapists involved in the delivery of the exercise. Costs of venue hire, equipment costs and travel costs incurred by physiotherapists and participants were also documented. Collins et al.[168] used costs sourced from a local community group fitness provider. In the Chan study,[165] conventional and high-intensity hours of physiotherapy duration for each arm of the model were estimated using expert opinion and the literature.

Economic evaluation: outcomes

Incremental cost per quality-adjusted life year (QALY) was reported in nine studies. Five of the studies[166 167 172 175 176] derived EQ-5D estimates of patient utility from questionnaires administered during trials, one study[174] used the SF-36 questionnaire, and one study[169] used the SF-6D questionnaire. One study[171] used a WHO QoL Index approach to estimate QoL outcomes. The Markov model study of Chan[165] sourced utility estimates from the literature, and the decision model of Collins et al.[168] used the results of a previously conducted trial. Four studies[164 170 171 173] were cost-per-patient analyses.

Economic evaluation: sensitivity analysis

The Markov modelling analysis of Chan[165] included a probabilistic sensitivity analysis, and included uncertainty of model inputs as confidence intervals or standard deviations. Univariate analyses were

conducted for duration of effect, physiotherapist wage, physiotherapy assistant cost, mortality rate, discount rate, utility value and length of inpatient stay. There were some sensitivity analyses included with trial-based studies. Tosh et al.[176] examined the impacts of differing costs of settings (private gyms or by third-party providers), disability sub-groups and wage costs, Hunter et al.[167] presented scenarios where carer costs were included and training costs excluded, Farag et al.[169] outlined scenarios for a group based program and no hospital costs, and Xin et al.[175] varied the time horizon, physiotherapist visits and numbers of sessions. The decision model of Collins et al.[168] included scenarios of different comparators, classes for 12 months and less than 7 attendees per class.

Existing systematic reviews

Two SRs undertaken to support physiotherapy HTA and economic modelling studies were identified.[177] [178] Although they were not formally included in this review, their key findings are presented as background prior to presenting results. The overarching conclusions of these two reviews were that there were limited studies that have evaluated the cost-effectiveness of physiotherapy interventions for treating neurological disorders.

- One study was conducted in Canada to support an HTA examining the effectiveness of continual long-term physiotherapy (more than 12 weeks) for patients after stroke.[177] The authors searched major databases in October 2018 and were unable to find published evidence on the clinical effectiveness of continual long-term physiotherapy for recovery post-stroke. They concluded there was a lack of available information, which prevented an assessment of cost-effectiveness.
- The review by Winser et al.[178] undertook a broader systematic search of existing evidence to identify studies examining the cost-effectiveness of physiotherapy interventions for people with neurological disorders including PD, stroke and MS. Major database searches up to July 2018 yielded 225 articles, of which 51 were duplicated studies. Following the full text screening, 10 studies were included. Three of these are included in this scoping report.[167] [169] [176] The other seven were not applicable as they related to other conditions such as complex regional pain syndrome, reflex sympathetic dystrophy, Alzheimer's disease or cerebral palsy, and interventions such as Wii™ sports games or robot-assisted therapy.

Summary

Only a limited number of economic studies were identified to assess the cost-effectiveness of physiotherapy to treat patients after stroke, with MS or PD. Most were related to stroke, and only one assessed an intervention of longer than six months. Most economic analyses were trial based. One Markov model was developed to evaluate the long-term benefit of physiotherapy; however, key

assumptions were based on limited literature which may not be relevant to Switzerland. No included study examined the cost-effectiveness of long- versus short-term physiotherapy, so assumptions are of limited applicability. Swiss cost data sourced using DRG and TARMED positions could be included in a simple decision model in the event relevant clinical outcome data were to be identified in the future.

8.4 Evidence base pertaining to legal, social and ethical issues

Searches identified 13 social and 2 ethical studies associated with physiotherapy in patients after stroke, with MS or PD. Searches did not identify any literature related to the legal implications associated with physiotherapy in patients after stroke, with MS or PD.

8.4.1 Evidence table

Relevant studies are summarised in ***Table 11***.

Table 11 List of included studies evaluating social and ethical issues

Author year Location	Condition	Study type	Outcomes
Patient and social issues			
Asplund 2009[179] Sweden	Stroke	Data from the Swedish Stroke Register (Riks-Stroke)	Patient characteristics and stroke services as determinants of patient dissatisfaction
Bulley 2011[180] UK	Stroke	Phenomenological approach using semi-structured interviews	User experiences, preferences and choices on the use of FES and AFO for foot drop
Hubbard 2012[181] Australia	Stroke	Data from the Australian audit of stroke rehabilitation practice	Adherence to recommended management and good recovery outcomes from clinical guidelines for patients after stroke
Karingen 2011[182] Norway	Stroke	Phenomenological perspective focusing on experiences of stroke survivors in rehabilitation	Long-term adherence to physiotherapy home exercise
McInnes 2008[183] UK	Stroke	Analysis of a subset of data from the Scottish Stroke Care Audit	Gender discrepancy in the use of stroke interventions
Miller 2016[184] USA	Stroke	Cross-sectional survey	Patient adherence on home exercise program as provided by physiotherapist after discharge from rehabilitation
Salbach 2009[185] Canada	Stroke	In-depth telephone interviews	Use of research evidence by physiotherapist to update clinical management of stroke patients
Skolarus 2017[186] USA	Stroke	Analysis of 2011 Medicare data for hospitalised patients diagnosed with stroke	Racial differences in rehabilitation utilisation
Wottrich 2004[187] Sweden	Stroke	Qualitative descriptive comparative study	Perspectives of patients and physiotherapist on physiotherapy session characteristics in relation to the observed behaviour

Author year Location	Condition	Study type	Outcomes
Martinkova 2018[188] Czech Republic, UK, USA, Italy, Belgium, Portugal, Norway, Croatia., Germany, Spain, Greece, Turkey, FYROM	MS	Online cross-sectional survey	Factors affecting differences in physiotherapeutic intervention application in Europe
Finlayson 2010[189] USA	MS	Cross-sectional descriptive study	Use of and need for physiotherapy services among middle-aged and older adults with MS
Allen 2015[190] Australia	PD	RCT	Predictors of adherence to fall prevention exercise program
Keus 2004[191] The Netherlands	PD	Two postal questionnaires for patients and physiotherapists	Utilisation and patient satisfaction on quality and quantity of physiotherapy care
Ethical issues			
Cherney 2006[192] USA	Stroke	Case study	Highlights the ethical issues involving the treatment of right hemisphere stroke patients
Sharp 2006[193] USA	Stroke	Case study	Highlights the ethical issues in the management of dysphagia after stroke

Abbreviations: AFO = ankle foot orthosis, **FES** = functional electrical stimulation, **FYRM** = former Yugoslav Republic of Macedonia, **MS** = multiple sclerosis, **PD** = Parkinson's disease, **RCT** = randomised control trial, **UK** = United Kingdom, **USA** = United States of America.

8.4.2 Legal results

No legal issues were identified from systematic and non-systematic searches related to physiotherapy interventions for patients after stroke, with MS or PD.

8.4.3 Social results

Thirteen studies (9 studies for stroke, 2 for MS, 2 for PD) evaluating patient, therapist or social perspectives were identified.[179-191] Most of the studies were from European countries such as UK, Norway, The Netherlands and Sweden. One study on MS examined differences in physiotherapy intervention application in the USA and Europe (Czech Republic, UK, Italy, Belgium, Portugal, Norway, Croatia, Germany, Spain, Greece, Turkey and the former Yugoslav Republic of Macedonia).[188] Eight studies sought to determine the influence of patient and physiotherapist factors on physiotherapy utilization,[179 180 183 185-189] four studies reported on adherence to physiotherapy management,[181 182 184 190] and one study described the factors influencing patient satisfaction of physiotherapy services.[191]

8.4.4 Ethical results

Two case studies highlighting the ethical issues involved in therapeutic intervention in people after stroke in the right hemisphere, and the management of dysphagia in people after stroke were identified.[192 193] While this occurred in an American context, many of the issues discussed are likely relevant to the Swiss context.

8.5 Evidence base pertaining to organisational issues

The literature search identified three studies regarding organisational issues associated with physiotherapy management.

8.5.1 Evidence table

Relevant studies are summarised in ***Table 12.***

Table 12 List of included studies evaluating organisational issues

Author year Location	Condition	Study type	Outcomes
Johnstone 2013[194] New Zealand	Stroke	Retrospective audit	Alignment of stroke management in the inpatient setting with the physiotherapy guidelines
Norris 2014[195] UK	Stroke	Qualitative methodology using semi-structured interviews	Rehabilitation ownership and the barriers in implementing self-management post-stroke
Salbach 2007[196] Canada	Stroke	Cross-sectional mail survey	Practitioner and organisational barriers to EBP among physiotherapists

Abbreviations: EBP = evidence-based practice, **UK** = United Kingdom.

8.5.2 Findings regarding organisational issues

Two studies identified the barriers in implementing a post-stroke management program and evidence-based practice among patients and physiotherapists.[194 195] One study reported on management issues associated with the alignment of physiotherapy interventions with clinical guidelines.[196]

9 Feasibility HTA

Clinical evidence

The focus of the policy question was to quantify any additional benefit of extending physiotherapy for patients after stroke, with MS or PD beyond the number of sessions currently covered under mandatory health insurance (36 sessions). The searches conducted in this scoping report did not identify any SRs or RCTs that have investigated this question directly.

The absence of direct evidence comparing long- and short-term physiotherapy was anticipated, based on the pre-scoping report and preliminary scoping searches. As such, the PICO criteria in this scoping report were broadened to include evidence comparing any long-term physiotherapy regime—where long-term was defined according to the 36-session limit covered under mandatory health insurance—to any other relevant long-term comparator. A total of 12 SRs were identified that measured the effects of long-term physiotherapy, of which 10 were on stroke and two were on PD. There were no reviews of long-term physiotherapy for MS. While this evidence provides some indication of the benefit of long-term physiotherapy, it does not inform the policy question directly. Furthermore, there is considerable heterogeneity in the type and duration of interventions reported in the existing SRs. Overall, the existing reviews can be considered to offer evidence supporting specific long-term physiotherapy subtypes, but do not cover the breadth of physiotherapy practice covered under mandatory health insurance in Switzerland.

Economic evaluation

In the absence of clinical evidence addressing the policy question, an economic evaluation of the policy question is not feasible at this time. It is technically feasible to undertake an economic analysis of long-term physiotherapy compared to other relevant long-term comparators in stroke and PD, noting that evidence exists for a range of heterogenous interventions and populations. Existing models could be used to inform the evaluation structure (most likely a decision model), but are not directly applicable to the Swiss context. In order to conduct an evaluation within the scope of the HTA program, specific physiotherapy interventions and populations with adequate clinical data would need to be prioritised.

Conclusion

No SRs or RCTs were found that compared long-term physiotherapy to short-term physiotherapy in patients after stroke, with MS, or with PD. As the primary focus of the policy question is the comparison of long-term physiotherapy versus short-term physiotherapy in patients after stroke, with MS or PD, a full HTA report on this topic is not feasible. There is currently no available data to undertake an HTA on the effectiveness, safety and cost-effectiveness of long-term physiotherapy compared to short-term physiotherapy in patients after stroke, with MS or PD.

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11 Appendix A: Search results (databases)

11.1 Search results

Table 13 Summary of database search results for SRs and economic studies (27 September 2020)

Source	Results
PubMed and Embase	3,716
The Cochrane Library (incl. CENTRAL)	168
York CRD	1,198
INAHTA HTA database	146
EconLit	3
PEDro	883
Total	**6,114**

Table 14 Summary of database search results RCTs (from inception to 22 October 2020)

Source	Results
PubMed and Embase	7,341
The Cochrane Library (incl. CENTRAL)	367
PEDro	1,056
Total	**8,764**

11.2 Search strings

Table 15 Embase and Medline search for SRs and economic analyses (from inception to 27 September 2020)

Database(s): Embase 1974 to 2020 October 21, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present		
#	**Searches**	**Results**
1	exp Physical Therapy Modalities/ use ppez	154232
2	Physiotherapy/ use oemezd	85622
3	Constraint Induced Therapy/ use oemezd	564
4	Electrotherapy/ use oemezd	1499
5	Electrostimulation/ use oemezd	69540
6	Hippotherapy/ use oemezd	370
7	Home Physiotherapy/ use oemezd	325
8	exp Kinesiotherapy/ use oemezd	79299
9	Cryotherapy/	23455

10	exp Hyperthermia, Induced/ use ppez	32322
11	Thermotherapy/ use oemezd	2784
12	exp Massage/	20607
13	exp Ultrasonic Therapy/ use ppez	12161
14	exp Ultrasound Therapy/ use oemezd	16353
15	exp Phototherapy/	132230
16	(manual therap* or physiotherap* or physio-therap* or (physic* adj therap*) or CIMT or mCIMT or FES or NMES).tw,kf,kw,dv.	161647
17	((aerobic* or aquatic? or balance or bilateral or bi-lateral or breathing or cardiovascular or cardio-vascular or dualtask or dual-task or electromechanical assist* or electro-mechanical assist* or endurance or equine-assisted or exercise? or exercising or fitness or gait or horseback rid* or horse-back rid* or lower extremit* or lower limb* or mirror? or mobility or mobilisation or mobilization or motion? or movement? or muscle stretch* or physical or resistance or respiratory muscle? or strength or strengthening or taskoriented or task-oriented or task specific or treadmill* or tread-mill* or upper extremit* or upper limb*) adj2 (rehabilitat* or retraining or re-training or program* or therap* or training)).tw,kf,kw,dv.	299700
18	(ammotherap* or (biostimulat* adj2 laser*) or cryotherap* or cryo-therap* or cryotherm* or cryo-therm* or cryotreatment? or cryo-treatment? or ((induc* or local*) adj (hyperthermi* or hyper-thermi* or hypothermi* or hypo-thermi*)) or (manual* adj (lymph* adj2 drain*)) or ((lowlevel? laser? or low-level? laser? or lowpower* laser? or low-power* laser?) adj2 (irradiat* or therap*)) or massotherap* or masso-therap* or phototherap* or photo-therap* or thermotherap* or thermo-therap* or ((cold or cryogenic* or fever* or heat or hyperthermia? or hyper-thermia? or infrared or infra-red or light? or massag* or photobiomodulat* or photo-biomodulat* or ultrasonic* or ultrasound?) adj2 (therap* or treatment?))).tw,kf,kw,dv.	157043
19	(aquatherap* or aqua-therap* or hydrotherap* or hydro-therap*).tw,kf,kw,dv.	3004
20	((electric* adj3 stimulation) or electrostimul* or electro-stimul* or electrotherap* or electro-therap* or galvanostimulation or galvano-stimulation).tw,kf,kw,dv.	146128
21	(hippotherap* or hippo-therap*).tw,kf,kw,dv.	482
22	medical training therap*.tw,kf,kw,dv.	59
23	exp Exercise/	542917
24	(rehabilitat* or retraining or re-training or program* or therap* or training).mp.	17746222
25	(exercis* adj3 (rehabilitat* or retraining or re-training or program* or therap* or training)).ti,kf,kw.	40784
26	(23 and 24) or 25	296946
27	or/1-22,26 [Physiotherapeutic Interventions]	1181329
28	*Nervous System Diseases/ use ppez	30234
29	*Neurologic Disease/ use oemezd	32999
30	((neurologic* or nervous system?) adj2 (disease? or disorder?)).ti,kf,kw.	32294
31	exp *Multiple Sclerosis/	137737
32	*Demyelinating Autoimmune Diseases, CNS/ use ppez	362
33	(multiple adj (scleros#s or scleroti*)).ti,kf,kw.	136386
34	MS.ti. and (multiple adj (scleros#s or scleroti*)).ab.	7395
35	(MS adj10 (scleros#s or scleroti*)).ti,kf,kw.	3530
36	((disseminated or insular or multiplex) adj (scleros#s or scleroti*)).ti,kf,kw.	773
37	((PPMS or PRMS or RPMS or SPMS) adj10 (progressive or relaps* or remit* or scleros#s or scleroti*)).ti,kf,kw.	137
38	((ARMS or RMS or RRMS) adj10 (relaps* or remit* or scleros#s or scleroti*)).ti,kf,kw.	535

39	(encephalomyelit* adj2 disseminat*).ti,kf,kw.	2756
40	exp *Parkinson Disease/	157019
41	((Parkinson* adj disease?) or Primary Parkinsonism or Paralysis Agitans).ti,kf,kw.	157978
42	PD.ti. and Parkinson*.ab.	2709
43	*Brain Ischemia/	118294
44	exp *Intracranial Hemorrhages/ use ppez	51162
45	exp *Brain Hemorrhage/ use oemezd	54436
46	exp *Stroke/ use ppez	102506
47	exp *Cerebrovascular Accident/ use oemezd	82827
48	*Stroke Rehabilitation/	12170
49	(stroke* or poststroke? or post-stroke? or CVA or CVAs).ti,kf,kw.	320040
50	((cerebrovascular* or cerebro-vascular* or cerebral vascular*) adj2 (apoplex* or accident* or infarct*)).ti,kf,kw.	6027
51	((brain or cerebral or intracerebral or intra-cerebral or arachnoid or subarachnoid or sub-arachnoid or intracranial* or intra-cranial* or cranial*) adj2 (infarct* or isch?emi* or h?emorrhag*)).ti,kf,kw.	147137
52	((postacute or post-acute or chronic) adj5 (stroke* or poststroke? or post-stroke?)).tw,kf,kw.	18341
53	(((postacute or post-acute or chronic) adj5 (hemipare* or paretic or paresis or phase? or stage? or state? or condition? or paraly* or spastic*)) and (stroke* or poststroke? or post-stroke?)).tw,kf,kw.	9732
54	or/28-53 [Population for SR/Econ]	985945
55	Meta-Analysis.pt.	120152
56	Meta-Analysis/ or Systematic Review/ or Meta-Analysis as Topic/ or "Meta Analysis (Topic)"/ or "Systematic Review (Topic)"/ or exp Technology Assessment, Biomedical/ or Network Meta-Analysis/	648544
57	(meta-analy* or metaanaly* or met-analy* or metanaly*).tw,kf,kw.	426047
58	(systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or rapid review* or "review of reviews" or umbrella review?).tw,kf,kw.	501853
59	(technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).tw,kf,kw.	23569
60	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).tw,kf,kw.	24650
61	((integrative adj3 (research or review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).tw,kf,kw.	68709
62	(meta regression* or metaregression*).tw,kf,kw.	20984
63	(systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.	560637
64	(cochrane or (health adj2 technology assessment) or evidence report or systematic review?).jw.	54282
65	((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).tw,kf,kw.	9109
66	(multi* adj3 treatment adj3 comparison*).tw,kf,kw.	590
67	(multi* adj2 paramet* adj2 evidence adj2 synthesis).tw,kf,kw.	35
68	(multiparamet* adj2 evidence adj2 synthesis).tw,kf,kw.	35
69	(multi-paramet* adj2 evidence adj2 synthesis).tw,kf,kw.	29
70	or/55-69 [SR/MA/HTA filter]	1003662
71	Economics/	266491
72	exp "Costs and Cost Analysis"/	591273

73	Economics, Nursing/	35143
74	Economics, Medical/	41161
75	Economics, Pharmaceutical/	10331
76	exp Economics, Hospital/	879730
77	Economics, Dental/	34968
78	exp "Fees and Charges"/	70717
79	exp Budgets/	43183
80	Economics/	266491
81	Cost/	107552
82	exp Health Economics/	855030
83	Budget/	40783
84	budget*.tw,kf,kw.	69800
85	(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf,kw.	518789
86	(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2	711482
87	(cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf,kw.	399910
88	(value adj2 (money or monetary)).tw,kf,kw.	5787
89	exp Models, Economic/	17421
90	Statistical Model/	253972
91	economic model*.ab,kf,kw.	8376
92	Markov Chains/	20313
93	Probability/	165068
94	markov.tw,kf,kw.	53077
95	Monte Carlo Method/	69497
96	monte carlo.tw,kf,kw.	101048
97	exp Decision Theory/	13877
98	Decision Tree/	24584
99	(decision* adj2 (tree* or analy* or model*)).tw,kf,kw.	60423
101	or/71-99 [Econ Eval filter]	2523287
102	(Case Reports/ or letter.pt.) not ((Case Reports/ or letter.pt.) and randomized controlled trial.pt.)	4147557
103	Conference Abstract/	974462
104	102 or 103 [Conference abstracts, etc not of interest]	5122017
105	27 and 54 and 70	3449
106	(27 and 54 and 70) not 104 [SRs]	3296
107	limit 106 to (english or french or german or italian)	3232
108	remove duplicates from 107 [Final SR set]	2186
109	27 and 54 and 101	2063
110	(27 and 54 and 101) not 104 [Econ Evals]	1936

111	limit 110 to (english or french or german or italian)	1908
112	remove duplicates from 111 [Final Econ Eval set]	1530

Table 16 Cochrane library search strategy (from inception to 27 September 2020)

Search string | CDSR | 168 results
exp Physical Therapy Modalities
Cryotherapy
exp Hyperthermia, Induced
exp Massage
exp Ultrasonic Therapy
exp Phototherapy
manual therap* OR physiotherap* OR physio-therap* OR (physic* NEXT therap*) OR CIMT OR mCIMT OR FES OR NMES =ti,ab,kw
(aerobic* OR aquatic* OR balance OR bilateral OR bi-lateral OR breathing OR cardiovascular OR cardio-vascular OR dualtask OR dual-task OR electromechanical assist* OR electro-mechanical assist* OR endurance OR equine-assisted OR exercise* OR exercising OR fitness OR gait OR horseback rid* OR horse-back rid* OR lower extremit* OR lower limb* OR mirror* OR mobility OR mobilisation OR mobilization OR motion* OR movement* OR muscle stretch* OR physical OR resistance OR respiratory muscle* OR strength OR strengthening OR taskoriented OR task-oriented OR task specific OR treadmill* OR tread-mill* OR upper extremit* OR upper limb*) NEAR/2 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training) =ti,ab,kw
ammotherap* OR (biostimulat* NEAR/2 laser*) OR cryotherap* OR cryo-therap* OR cryotherm* OR cryo-therm* OR cryotreatment* OR cryo-treatment* OR ((induc* OR local*) NEXT (hyperthermi* OR hyper-thermi* OR hypothermi* OR hypo-thermi*)) OR (manual* NEXT (lymph* NEAR/2 drain*)) OR ((lowlevel* laser* OR low-level* laser* OR lowpower* laser* OR low-power* laser*) NEAR/2 (irradiat* OR therap*)) OR massotherap* OR masso-therap* OR phototherap* OR photo-therap* OR thermotherap* OR thermo-therap* OR ((cold OR cryogenic* OR fever* OR heat OR hyperthermia* OR hyper-thermia* OR infrared OR infra-red OR light* OR massag* OR photobiomodulat* OR photo-biomodulat* OR ultrasonic* OR ultrasound*) NEAR/2 (therap* OR treatment*)) =ti,ab,kw
aquatherap* OR aqua-therap* OR hydrotherap* OR hydro-therap* =ti,ab,kw
(electric* NEAR/3 stimulation) OR electrostimul* OR electro-stimul* OR electrotherap* OR electro-therap* OR galvanostimulation OR galvano-stimulation =ti,ab,kw
hippotherap* OR hippo-therap* =ti,ab,kw
medical training therap* =ti,ab,kw
exp Exercise
rehabilitat* OR retraining OR re-training OR program* OR therap* OR training =all
exercis* NEAR/3 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training) =.ti
Nervous System Diseases
(neurologic* OR nervous system*) NEAR/2 (disease* OR disorder*) =.ti
exp Multiple Sclerosis
multiple NEXT (scleros#s OR scleroti*) =.ti
MS NEAR/10 (scleros#s OR scleroti*) =.ti
(disseminated OR insular OR multiplex) NEXT (scleros#s OR scleroti*) =.ti
(PPMS OR PRMS OR RPMS OR SPMS) NEAR/10 (progressive OR relaps* OR remit* OR scleros#s OR scleroti*) =.ti
((ARMS OR RMS OR RRMS) NEAR/10 (relaps* OR remit* OR scleros#s OR scleroti*)) OR (encephalomyelit* NEAR/2 disseminat*) =.ti
exp Parkinson Disease
(Parkinson* NEXT disease*) OR Primary Parkinsonism OR Paralysis Agitans =.ti
Brain Ischemia
exp Intracranial Hemorrhages
exp Stroke

Stroke Rehabilitation stroke* OR poststroke* OR post-stroke* OR CVA OR CVAs =.ti (cerebrovascular* OR cerebro-vascular* OR cerebral vascular*) NEAR/2 (apoplex* OR accident* OR infarct*) =.ti (brain OR cerebral OR intracerebral OR intra-cerebral OR arachnoid OR subarachnoid OR sub-arachnoid OR intracranial* OR intra-cranial* OR cranial*) NEAR/2 (infarct* OR isch*emi* OR h*emorrhag*) =.ti (postacute OR post-acute OR chronic) NEAR/5 (stroke* OR poststroke* OR post-stroke*) =.ti,ab,kf. ((postacute OR post-acute OR chronic) NEAR/5 (hemipare* OR paretic OR paresis OR phase* OR stage* OR state* OR condition* OR paraly* OR spastic*)) and (stroke* OR poststroke* OR post-stroke*) =.ti,ab,kf.

Table 17 PEDro search strategy (from inception to 27 Sep 2020)

#	Searches	Results
1	Multiple Sclero*	123
2	Parkinson* Disease*	148
3	stroke*	520
4	poststroke*	30
5	post-stroke*	54
6	cerebrovascular* apoplex*	0
7	cerebro-vascular* apoplex*	0
8	cerebral vascular* apoplex*	0
9	cerebrovascular* accident*	4
10	cerebro-vascular* accident*	0
11	cerebral vascular* accident*	2
12	cerebrovascular* infarct*	1
13	cerebro-vascular* infarct*	0
14	cerebral vascular* infarct*	1
15	brain infarct*	6
16	brain ischaemi*	1
17	brain ischemi*	5
18	brain haemorrhag*	0
19	brain hemorrhag*	0
20	cerebral infarct*	1
21	cerebral ischaemi*	0
22	cerebral ischemi*	0
23	cerebral haemorrhag*	0
24	cerebral hemorrhag*	0
25	intracerebral infarct*	0
26	intracerebral ischaemi*	0
27	intracerebral ischemi*	0
28	intracerebral haemorrhag*	0
29	intracerebral hemorrhag*	2
30	intra-cerebral infarct*	0
31	intra-cerebral ischaemi*	0
32	intra-cerebral ischemi*	0
33	intra-cerebral haemorrhag*	0
34	intra-cerebral hemorrhag*	0

35	arachnoid infarct*	0
36	arachnoid ischaemi*	0
37	arachnoid ischemi*	0
38	arachnoid haemorrhag*	0
39	arachnoid hemorrhag*	0
40	subarachnoid infarct*	0
41	subarachnoid ischaemi*	0
42	subarachnoid ischemi*	0
43	subarachnoid haemorrhag*	1
44	subarachnoid hemorrhag*	0
45	sub-arachnoid infarct*	0
46	sub-arachnoid ischaemi*	0
47	sub-arachnoid ischemi*	0
48	sub-arachnoid haemorrhag*	0
49	sub-arachnoid hemorrhag*	0
50	intracranial* infarct*	0
51	intracranial* ischaemi*	0
52	intracranial* ischemi*	0
53	intracranial* haemorrhag*	0
54	intracranial* hemorrhag*	0
55	intra-cranial* infarct*	0
56	intra-cranial* ischaemi*	0
57	intra-cranial* ischemi*	0
58	intra-cranial* haemorrhag*	0
59	intra-cranial* hemorrhag*	0
60	cranial* infarct*	0
61	cranial* ischaemi*	0
62	cranial* ischemi*	0
63	cranial* haemorrhag*	0
64	cranial* hemorrhag*	0
65	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64	883

Table 18 York CRD search strategy (from inception to 27 Sep 2020)

#	Search	Results
1	MeSH DESCRIPTOR Physical Therapy Modalities EXPLODE ALL TREES	2401
2	MeSH DESCRIPTOR Cryotherapy EXPLODE ALL TREES	136
3	MeSH DESCRIPTOR Hyperthermia, Induced EXPLODE ALL TREES	226
4	MeSH DESCRIPTOR Massage EXPLODE ALL TREES	96
5	MeSH DESCRIPTOR Ultrasonic Therapy EXPLODE ALL TREES	121
6	MeSH DESCRIPTOR Phototherapy EXPLODE ALL TREES	316

7	(manual therap* OR physiotherap* OR physio-therap* OR (physic* ADJ therap*) OR CIMT OR mCIMT OR FES OR NMES):TI OR ((aerobic* OR aquatic* OR balance OR bilateral OR bi-lateral OR breathing OR cardiovascular OR cardio-vascular OR dualtask OR dual-task OR electromechanical assist* OR electro-mechanical assist* OR endurance OR equine-assisted OR exercise* OR exercising OR fitness OR gait OR horseback rid* OR horse-back rid* OR lower extremit* OR lower limb* OR mirror* OR mobility OR mobilisation OR mobilization OR motion* OR movement* OR muscle stretch* OR physical OR resistance OR respiratory muscle* OR strength OR strengthening OR taskoriented OR task-oriented OR task specific OR treadmill* OR tread-mill* OR upper extremit* OR upper limb*) ADJ2 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training)):TI OR (ammotherap* OR (biostimulat* ADJ2 laser*) OR cryotherap* OR cryo-therap* OR cryotherm* OR cryo-therm* OR cryotreatment* OR cryo-treatment* OR ((induc* OR local*) ADJ (hyperthermi* OR hyper-thermi* OR hypothermi* OR hypo-thermi*)) OR (manual* ADJ (lymph* ADJ2 drain*)) OR ((lowlevel* laser* OR low-level* laser* OR lowpower* laser* OR low-power* laser*) ADJ2 (irradiat* OR therap*)) OR massotherap* OR masso-therap* OR phototherap* OR photo-therap* OR thermotherap* OR thermo-therap* OR ((cold OR cryogenic* OR fever* OR heat OR hyperthermia* OR hyper-thermia* OR infrared OR infra-red OR light* OR massag* OR photobiomodulat* OR photo-biomodulat* OR ultrasonic* OR ultrasound*) ADJ2 (therap* OR treatment*))):TI	1115
8	(aquatherap* OR aqua-therap* OR hydrotherap* OR hydro-therap*):TI OR ((electric* ADJ3 stimulation) OR electrostimul* OR electro-stimul* OR electrotherap* OR electro-therap* OR galvanostimulation OR galvano-stimulation):TI OR (hippotherap* OR hippo-therap* OR medical training therap*):TI	216
9	MeSH DESCRIPTOR Exercise EXPLODE ALL TREES	1137
10	(rehabilitat* OR retraining OR re-training OR program* OR therap* OR training)	45576
11	#9 AND #10	903
12	(exercis* ADJ3 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training)):TI	315
13	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #11 OR #12	3928
14	MeSH DESCRIPTOR Nervous System Diseases EXPLODE ALL TREES	10135
15	((neurologic* OR nervous system*) ADJ2 (disease* OR disorder*)):TI	30
16	MeSH DESCRIPTOR Multiple Sclerosis EXPLODE ALL TREES	294
17	MeSH DESCRIPTOR Demyelinating Autoimmune Diseases, CNS EXPLODE ALL TREES	299
18	(multiple ADJ (scleros* OR scleroti*)):TI OR (MS ADJ10 (scleros* OR scleroti*)):TI OR ((disseminated OR insular OR multiplex) ADJ (scleros* OR scleroti*)):TI	311
19	((ARMS OR RMS OR RRMS) ADJ10 (relaps* OR remit* OR scleros* OR scleroti*)):TI OR (encephalomyelit* ADJ2 disseminat*):TI	1
20	MeSH DESCRIPTOR Parkinson Disease EXPLODE ALL TREES	243
21	((Parkinson* ADJ disease*) OR Primary Parkinsonism OR Paralysis Agitans):TI	273
22	MeSH DESCRIPTOR Brain Ischemia EXPLODE ALL TREES	326
23	MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES	258
24	MeSH DESCRIPTOR Stroke EXPLODE ALL TREES	1354
25	MeSH DESCRIPTOR Stroke Rehabilitation EXPLODE ALL TREES	1
26	(stroke* OR poststroke* OR post-stroke* OR CVA OR CVAs):TI OR ((cerebrovascular* OR cerebro-vascular* OR cerebral vascular*) ADJ2 (apoplex* OR accident* OR infarct*)):TI OR ((brain OR cerebral OR intracerebral OR intra-cerebral OR arachnoid OR subarachnoid OR sub-arachnoid OR intracranial* OR intra-cranial* OR cranial*) ADJ2 (infarct* OR ischaemi* OR ischemi* OR haemorrhag* OR hemorrhag*)):TI	1354
27	((postacute OR post-acute OR chronic) ADJ5 (stroke* OR poststroke* OR post-stroke*)):TI OR (((postacute OR post-acute OR chronic) ADJ5 (hemipare* OR paretic OR paresis OR phase* OR stage* OR state* OR condition* OR paraly* OR spastic*)) AND (stroke* OR poststroke* OR post-stroke*)):TI	17
28	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	10490
29	#13 AND #28	1198

Table 19 International HTA database search strategy (2015 up to 27 Sep 2020)

#	Searches	Results
1	(Physical Therapy Modalities)[mh] OR (Cryotherapy)[mh] OR (Hyperthermia, Induced)[mh] OR (Massage)[mh] OR (Ultrasonic Therapy)[mh] OR (Phototherapy)[mh] OR (manual therap* OR physiotherap* OR physio-therap* OR physical therap* OR CIMT OR mCIMT OR FES OR NMES OR aerobic* OR aquatic* OR balance OR bilateral OR bi-lateral OR breathing OR cardiovascular OR cardio-vascular OR dualtask OR dual-task OR electromechanical assist* OR electro-mechanical assist* OR endurance OR equine-assisted OR exercise* OR exercising OR fitness OR gait OR horseback rid* OR horse-back rid* OR lower extremit* OR lower limb* OR mirror* OR mobility OR mobilisation OR mobilization OR motion* OR movement* OR muscle stretch* OR physical OR resistance OR respiratory muscle* OR strength OR strengthening OR taskoriented OR task-oriented OR task specific OR treadmill* OR tread-mill* OR upper extremit* OR upper limb* OR ammotherap* OR laser* OR cryotherap* OR cryo-therap* OR cryotherm* OR cryo-therm* OR cryotreatment* OR cryo-treatment* OR hyperthermi* OR hyper-thermi* OR hypothermi* OR hypo-thermi* OR lymph* drain* OR massotherap* OR masso-therap* OR phototherap* OR photo-therap* OR thermotherap* OR thermo-therap* OR cold OR cryogenic* OR fever* OR heat OR hyperthermia* OR hyper-thermia* OR infrared OR infra-red OR light* OR massag* OR photobiomodulat* OR photo-biomodulat* OR ultrasonic* OR ultrasound* OR aquatherap* OR aqua-therap* OR hydrotherap* OR hydro-therap* OR electric* stimulation OR electrostimul* OR electro-stimul* OR electrotherap* OR electro-therap* OR galvanostimulation OR galvano-stimulation OR hippotherap* OR hippo-therap* OR medical training therap*)[Title]	--
2	(Nervous System Diseases)[mh] OR (Multiple Sclerosis)[mh] OR (Parkinson Disease)[mh] OR (Brain Ischemia)[mh] OR (Intracranial Hemorrhages)[mh] OR (Stroke)[mh] OR (Stroke Rehabilitation)[mh] OR (neurologic disease* OR neurologic disorder* OR nervous system disease* OR nervous system disorder* OR Multiple Sclerosis OR Parkinson* Disease* OR Brain Ischemi* OR Intracranial Hemorrhag* OR Stroke* OR Stroke Rehabilitation OR poststroke* OR post-stroke*)[Title]	-
3	1 AND 2	146

Table 20 EconLit search strategy (from inception to 27 Sep 2020)

#	Searches	Results
1	SU (Physical Therapy Modalities OR Cryotherapy OR Hyperthermia OR Massage OR Ultrasonic Therapy OR Phototherapy) OR TI (manual therap* OR physiotherap* OR physio-therap* OR (physic* N1 therap*) OR CIMT OR mCIMT OR FES OR NMES) OR AB (manual therap* OR physiotherap* OR physio-therap* OR (physic* N1 therap*) OR CIMT OR mCIMT OR FES OR NMES) OR TI ((aerobic* OR aquatic* OR balance OR bilateral OR bi-lateral OR breathing OR cardiovascular OR cardio-vascular OR dualtask OR dual-task OR electromechanical assist* OR electro-mechanical assist* OR endurance OR equine-assisted OR exercise* OR exercising OR fitness OR gait OR horseback rid* OR horse-back rid* OR lower extremit* OR lower limb* OR mirror* OR mobility OR mobilisation OR mobilization OR motion* OR movement* OR muscle stretch* OR physical OR resistance OR respiratory muscle* OR strength OR strengthening OR taskoriented OR task-oriented OR task specific OR treadmill* OR tread-mill* OR upper extremit* OR upper limb*) N2 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training)) OR AB ((aerobic* OR aquatic* OR balance OR bilateral OR bi-lateral OR breathing OR cardiovascular OR cardio-vascular OR dualtask OR dual-task OR electromechanical assist* OR electro-mechanical assist* OR endurance OR equine-assisted OR exercise* OR exercising OR fitness OR gait OR horseback rid* OR horse-back rid* OR lower extremit* OR lower limb* OR mirror* OR mobility OR mobilisation OR mobilization OR motion* OR movement* OR muscle stretch* OR physical OR resistance OR respiratory muscle* OR strength OR strengthening OR taskoriented OR task-oriented OR task specific OR treadmill* OR tread-mill* OR upper extremit* OR upper limb*) N2 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training)) OR TI (ammotherap* OR (biostimulat* N2 laser*) OR cryotherap* OR cryo-therap* OR cryotherm* OR cryo-therm* OR cryotreatment* OR cryo-treatment* OR ((induc* OR local*) N1 (hyperthermi* OR hyper-thermi* OR hypothermi* OR hypo-thermi*)) OR (manual* N1 (lymph* N2 drain*)) OR ((lowlevel* laser* OR low-level* laser* OR lowpower* laser* OR low-power* laser*) N2 (irradiat* OR therap*)) OR massotherap* OR masso-therap* OR phototherap* OR photo-therap* OR thermotherap* OR thermo-therap* OR ((cold OR cryogenic* OR fever* OR heat OR hyperthermia* OR hyper-thermia* OR infrared OR infra-red OR light* OR massag* OR photobiomodulat* OR photo-biomodulat* OR ultrasonic* OR ultrasound*) N2 (therap* OR treatment*))) OR AB (ammotherap* OR (biostimulat* N2 laser*) OR cryotherap* OR cryo-therap*	1,431

	OR cryotherm* OR cryo-therm* OR cryotreatment* OR cryo-treatment* OR ((induc* OR local*) N1 (hyperthermi* OR hyper-thermi* OR hypothermi* OR hypo-thermi*)) OR (manual* N1 (lymph* N2 drain*)) OR ((lowlevel* laser* OR low-level* laser* OR lowpower* laser* OR low-power* laser*) N2 (irradiat* OR therap*)) OR massotherap* OR masso-therap* OR phototherap* OR photo-therap* OR thermotherap* OR thermo-therap* OR ((cold OR cryogenic* OR fever* OR heat OR hyperthermia* OR hyper-thermia* OR infrared OR infra-red OR light* OR massag* OR photobiomodulat* OR photo-biomodulat* OR ultrasonic* OR ultrasound*) N2 (therap* OR treatment*))) OR TI (aquatherap* OR aqua-therap* OR hydrotherap* OR hydro-therap* OR (electric* N3 stimulation) OR electrostimul* OR electro-stimul* OR electrotherap* OR electro-therap* OR galvanostimulation OR galvano-stimulation OR hippotherap* OR hippo-therap* OR medical training therap*) OR AB (aquatherap* OR aqua-therap* OR hydrotherap* OR hydro-therap* OR (electric* N3 stimulation) OR electrostimul* OR electro-stimul* OR electrotherap* OR electro-therap* OR galvanostimulation OR galvano-stimulation OR hippotherap* OR hippo-therap* OR medical training therap*) OR TX (exercis* N3 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training))	
2	SU (Nervous System Diseases OR Multiple Sclerosis OR Demyelinating Autoimmune Diseases, CNS OR Parkinson Disease OR Brain Ischemia OR Intracranial Hemorrhages OR Stroke OR Stroke Rehabilitation) OR TI ((neurologic* OR nervous system*) N2 (disease* OR disorder*)) OR TI (multiple N1 (scleros* OR scleroti*)) OR TI (MS N10 (scleros* OR scleroti*)) OR TI ((disseminated OR insular OR multiplex) N1 (scleros#s OR scleroti*)) OR TI ((PPMS OR PRMS OR RPMS OR SPMS) N10 (progressive OR relaps* OR remit* OR scleros* OR scleroti*)) OR TI ((ARMS OR RMS OR RRMS) N10 (relaps* OR remit* OR scleros#s OR scleroti*)) OR TI encephalomyelit* N2 disseminat* OR TI ((Parkinson* N1 disease*) OR Primary Parkinsonism OR Paralysis Agitans) OR TI (stroke* OR poststroke* OR post-stroke* OR CVA OR CVAs) OR TI ((brain OR cerebral OR intracerebral OR intra-cerebral OR arachnoid OR subarachnoid OR sub-arachnoid OR intracranial* OR intra-cranial* OR cranial*) N2 (infarct* OR ischaemi* OR ischemi* OR haemorrhag* OR hemorrhag*)) OR TI ((postacute OR post-acute OR chronic) N5 (stroke* OR poststroke* OR post-stroke*))	251
3	TI ((postacute OR post-acute OR chronic) N5 (hemipare* OR paretic OR paresis OR phase* OR stage* OR state* OR condition* OR paraly* OR spastic*)) AND (stroke* OR poststroke* OR post-stroke*)	0
4	1 AND 2	3

Table 21 Search strings for RCTs (from inception to 22 October 2020)

Database(s): Embase 1974 to 2020 October 21, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present		
#	**Searches**	**Results**
1	exp Physical Therapy Modalities/ use ppez	154861
2	Physiotherapy/ use oemezd	86194
3	Constraint Induced Therapy/ use oemezd	573
4	Electrotherapy/ use oemezd	1531
5	Electrostimulation/ use oemezd	69790
6	Hippotherapy/ use oemezd	378
7	Home Physiotherapy/ use oemezd	327
8	exp Kinesiotherapy/ use oemezd	79945
9	Cryotherapy/ [both]	23555
10	exp Hyperthermia, Induced/ use ppez	32436
11	Thermotherapy/ use oemezd	2861
12	exp Massage/ [both]	20720
13	exp Ultrasonic Therapy/ use ppez	12213
14	exp Ultrasound Therapy/ use oemezd	16691
15	exp Phototherapy/ [both]	133074

16	(manual therap* or physiotherap* or physio-therap* or (physic* adj therap*) or CIMT or mCIMT or FES or NMES).tw,kf,kw,dv.	162852
17	((aerobic* or aquatic? or balance or bilateral or bi-lateral or breathing or cardiovascular or cardio-vascular or dualtask or dual-task or electromechanical assist* or electro-mechanical assist* or endurance or equine-assisted or exercise? or exercising or fitness or gait or horseback rid* or horse-back rid* or lower extremit* or lower limb* or mirror? or mobility or mobilisation or mobilization or motion? or movement? or muscle stretch* or physical or resistance or respiratory muscle? or strength or strengthening or taskoriented or task-oriented or task specific or treadmill* or tread-mill* or upper extremit* or upper limb*) adj2 (rehabilitat* or retraining or re-training or program* or therap* or training)).tw,kf,kw,dv.	301872
18	(ammotherap* or (biostimulat* adj2 laser*) or cryotherap* or cryo-therap* or cryotherm* or cryo-therm* or cryotreatment? or cryo-treatment? or ((induc* or local*) adj (hyperthermi* or hyper-thermi* or hypothermi* or hypo-thermi*)) or (manual* adj (lymph* adj2 drain*)) or ((lowlevel? laser? or low-level? laser? or lowpower* laser? or low-power* laser?) adj2 (irradiat* or therap*)) or massotherap* or masso-therap* or phototherap* or photo-therap* or thermotherap* or thermo-therap* or ((cold or cryogenic* or fever* or heat or hyperthermia? or hyper-thermia? or infrared or infra-red or light? or massag* or photobiomodulat* or photo-biomodulat* or ultrasonic* or ultrasound?) adj2 (therap* or treatment?))).tw,kf,kw,dv.	157995
19	(aquatherap* or aqua-therap* or hydrotherap* or hydro-therap*).tw,kf,kw,dv.	3015
20	((electric* adj3 stimulation) or electrostimul* or electro-stimul* or electrotherap* or electro-therap* or galvanostimulation or galvano-stimulation).tw,kf,kw,dv.	146613
21	(hippotherap* or hippo-therap*).tw,kf,kw,dv.	486
22	medical training therap*.tw,kf,kw,dv.	59
23	exp Exercise/ [both]	546972
24	(rehabilitat* or retraining or re-training or program* or therap* or training).mp.	17834932
25	(exercis* adj3 (rehabilitat* or retraining or re-training or program* or therap* or training)).ti,kf,kw.	41048
26	(23 and 24) or 25	299355
27	or/1-22,26 [Physiotherapeutic Interventions]	1188593
28	exp *Multiple Sclerosis/ [both]	138497
29	*Demyelinating Autoimmune Diseases, CNS/ use ppez	364
30	(multiple adj (scleros#s or scleroti*)).ti,kf,kw.	137290
31	MS.ti. and (multiple adj (scleros#s or scleroti*)).ab.	7474
32	(MS adj10 (scleros#s or scleroti*)).ti,kf,kw.	3570
33	((disseminated or insular or multiplex) adj (scleros#s or scleroti*)).ti,kf,kw.	773
34	((PPMS or PRMS or RPMS or SPMS) adj10 (progressive or relaps* or remit* or scleros#s or scleroti*)).ti,kf,kw.	140
35	((ARMS or RMS or RRMS) adj10 (relaps* or remit* or scleros#s or scleroti*)).ti,kf,kw.	541
36	(encephalomyelit* adj2 disseminat*).ti,kf,kw.	2768
37	exp *Parkinson Disease/ [both]	158007
38	((Parkinson* adj disease?) or Primary Parkinsonism or Paralysis Agitans).ti,kf,kw.	159259
39	PD.ti. and Parkinson*.ab.	2738
40	*Brain Ischemia/ [both]	119234
41	exp *Intracranial Hemorrhages/ use ppez	51338
42	exp *Brain Hemorrhage/ use oemezd	54944
43	exp *Stroke/ use ppez	103074
44	exp *Cerebrovascular Accident/ use oemezd	83515
45	*Stroke Rehabilitation/ [both]	12305

46	(stroke* or poststroke? or post-stroke? or CVA or CVAs).ti,kf,kw.	322785
47	((cerebrovascular* or cerebro-vascular* or cerebral vascular*) adj2 (apoplex* or accident* or infarct*)).ti,kf,kw.	6069
48	((brain or cerebral or intracerebral or intra-cerebral or arachnoid or subarachnoid or sub-arachnoid or intracranial* or intra-cranial* or cranial*) adj2 (infarct* or isch?emi* or h?emorrhag*)).ti,kf,kw.	148033
49	((postacute or post-acute or chronic) adj5 (stroke* or poststroke? or post-stroke?)).tw,kf,kw.	18531
50	(((postacute or post-acute or chronic) adj5 (hemipare* or paretic or paresis or phase? or stage? or state? or condition? or paraly* or spastic*)) and (stroke* or poststroke? or post-stroke?)).tw,kf,kw.	9812
51	or/28-50 [Population]	917276
52	Longitudinal Studies/ use ppez	138571
53	Longitudinal Study/ use oemezd	146559
54	Time/	334516
55	Time Factors/ use ppez	1192802
56	Time Factor/ use oemezd	36573
57	"Duration of Therapy"/ use ppez	161
58	Treatment Duration/ use oemezd	235452
59	(duration? or (long* adj term?) or long-term* or longterm* or longitudinal* or time*).tw,kf,kw.	11721146
60	or/52-59 [Long-term Study filter]	12786464
61	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Adaptive Clinical Trial or Equivalence Trial or Clinical Trial, Phase III or Clinical Trial, Phase IV).pt.	609009
62	Randomized Controlled Trial/	1143841
63	exp Randomized Controlled Trials as Topic/	329993
64	"Randomized Controlled Trial (topic)"/	189427
65	Controlled Clinical Trial/	559356
66	exp Controlled Clinical Trials as Topic/	343002
67	"Controlled Clinical Trial (topic)"/	11168
68	(random* or sham or placebo*).tw,kf,kw.	3105376
69	((singl* or doubl*) adj (blind* or dumm* or mask*)).tw,kf,kw.	417514
70	((tripl* or trebl*) adj (blind* or dumm* or mask*)).tw,kf,kw.	2469
71	((adaptive or control* or equivalence) adj3 (study or studies or trial* or group*)).tw,kf,kw.	2426253
72	(quasi-random* or quasirandom*).tw,kf,kw.	10688
73	"allocated to".tw.	155236
74	((open label or open-label) adj5 (study or studies or trial*)).tw,kf,kw.	101220
75	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).tw,kf,kw.	20928
76	(pragmatic study or pragmatic studies).tw,kf,kw.	1043
77	((pragmatic or practical) adj3 trial*).tw,kf,kw.	9657
78	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).tw,kf,kw.	18628
79	trial.ti,kf,kw.	583819
80	(phase adj3 (III or "3" or IV or "4") adj3 (study or studies or trial*)).tw,kf,kw.	131029
81	or/61-80 [RCT Filter]	5259637
82	exp animals/	49787816

83	exp animal experimentation/ or exp animal experiment/	2630293
84	exp models animal/	2002835
85	nonhuman/	6362133
86	exp vertebrate/ or exp vertebrates/	48451569
87	or/82-86	51664560
88	exp humans/	40330743
89	exp human experimentation/ or exp human experiment/	534778
90	or/88-89	40333169
91	87 not 90	11333047
92	81 not 91	4491753
93	27 and 51 and 60 and 92 [Interventions + Populations + LT Studies + RCTs, Human NOT Animals]	7957
94	(case reports.pt. or *Case Report/ or letter.pt.) not ((case reports.pt. or *Case Report/ or letter.pt.) and randomized controlled trial.pt.)	4181175
95	Conference Abstract/	1001442
96	or/94-95 [Publication Types not of Interest]	5182615
97	93 not 96 [RCTs, [Publication Types not of Interest removed]	7592
98	limit 97 to (english or french or german or italian) [Final results, limited to languages of interest]	7341

Table 22 The Cochrane Library searches for RCTs (from inception 22 October 2020)

Search string | 367 results
exp Physical Therapy Modalities
Cryotherapy
exp Hyperthermia, Induced
exp Massage
exp Ultrasonic Therapy
exp Phototherapy
manual therap* OR physiotherap* OR physio-therap* OR (physic* NEXT therap*) OR CIMT OR mCIMT OR FES OR NMES =ti,ab,kw
(aerobic* OR aquatic* OR balance OR bilateral OR bi-lateral OR breathing OR cardiovascular OR cardio-vascular OR dualtask OR dual-task OR electromechanical assist* OR electro-mechanical assist* OR endurance OR equine-assisted OR exercise* OR exercising OR fitness OR gait OR horseback rid* OR horse-back rid* OR lower extremit* OR lower limb* OR mirror* OR mobility OR mobilisation OR mobilization OR motion* OR movement* OR muscle stretch* OR physical OR resistance OR respiratory muscle* OR strength OR strengthening OR taskoriented OR task-oriented OR task specific OR treadmill* OR tread-mill* OR upper extremit* OR upper limb*) NEAR/2 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training) =ti,ab,kw
ammotherap* OR (biostimulat* NEAR/2 laser*) OR cryotherap* OR cryo-therap* OR cryotherm* OR cryo-therm* OR cryotreatment* OR cryo-treatment* OR ((induc* OR local*) NEXT (hyperthermi* OR hyper-thermi* OR hypothermi* OR hypo-thermi*)) OR (manual* NEXT (lymph* NEAR/2 drain*)) OR ((lowlevel* laser* OR low-level* laser* OR lowpower* laser* OR low-power* laser*) NEAR/2 (irradiat* OR therap*)) OR massotherap* OR masso-therap* OR phototherap* OR photo-therap* OR thermotherap* OR thermo-therap* OR ((cold OR cryogenic* OR fever* OR heat OR hyperthermia* OR hyper-thermia* OR infrared OR infra-red OR light* OR massag* OR photobiomodulat* OR photo-biomodulat* OR ultrasonic* OR ultrasound*) NEAR/2 (therap* OR treatment*)) =ti,ab,kw
=ti,ab,kw
(electric* NEAR/3 stimulation) OR electrostimul* OR electro-stimul* OR electrotherap* OR electro-therap* OR galvanostimulation OR galvano-stimulation =ti,ab,kw
aquatherap* OR aqua-therap* OR hydrotherap* OR hydro-therap* OR hippotherap* OR hippo-therap* OR medical training therap* =ti,ab,kw
exp Exercise

rehabilitat* OR retraining OR re-training OR program* OR therap* OR training =all
exercis* NEAR/3 (rehabilitat* OR retraining OR re-training OR program* OR therap* OR training) =.ti

exp Multiple Sclerosis
multiple NEXT (scleros#s OR scleroti*) =.ti
exp Parkinson Disease
(Parkinson* NEXT disease*) OR Primary Parkinsonism OR Paralysis Agitans =.ti
Brain Ischemia
exp Intracranial Hemorrhages
exp Stroke
Stroke Rehabilitation
stroke* OR poststroke* OR post-stroke* OR CVA OR CVAs =.ti
(cerebrovascular* OR cerebro-vascular* OR cerebral vascular*) NEAR/2 (apoplex* OR accident* OR infarct*) =.ti
(brain OR cerebral OR intracerebral OR intra-cerebral OR arachnoid OR subarachnoid OR sub-arachnoid OR intracranial* OR intra-cranial* OR cranial*) NEAR/2 (infarct* OR isch*emi* OR h*emorrhag*) =.ti
(postacute OR post-acute OR chronic) NEAR/5 (stroke* OR poststroke* OR post-stroke*) =.ti
((postacute OR post-acute OR chronic) NEAR/5 (hemipare* OR paretic OR paresis OR phase* OR stage* OR state* OR condition* OR paraly* OR spastic*)) and (stroke* OR poststroke* OR post-stroke*) =.ti

Longitudinal Studies
Time
Time Factors
duration? OR (long* NEXT term?) OR long-term* OR longterm* OR longitudinal* OR time* =.ti,ab,kf.

Table 23 PEDro searches for RCTs (from inception to 22 October 2020)

#	Searches	Results
1	duration OR long-term OR longterm OR longitudinal OR time	1056

11.2.1 Supplementary searches for auxiliary domains and grey literature sources

The search strings reported below are not included in the PRISMA flow diagram because they are not considered to be sensitive enough to be classified as a systematic literature search.

Table 24 Search strings for legal considerations (PubMed and Embase) [from inception to 13 November 2020]

Number	Query	PubMed	Embase
1	Personal autonomy [mh]	17,214	14,346
2	Human rights [mh]	144,007	267,735
3	Human rights[tiab]	10,628	9,803
4	(free will)	70,468	14,772
5	(self determination)	31,166	18,639
6	Parental consent [mh]	3,269	5,252
7	Third-party consent [mh]	6,007	18,772
8	Presumed consent [mh]	549	443

Number	Query	PubMed	Embase
9	Informed consent by minors [mh]	137	9100
10	Consent [tiab]	64,638	132,781
11	Privacy [tw]	21,311	19,310
12	Confidentiality [mh]	53,434	33,765
13	Confidentiality[tiab]	11,577	14,195
14	Personally identifiable information [mh]	44	69
15	Health record, personal [mh]	2,007	3,248
16	(personal information)	41,504	2,931
17	Jurisprudence [mh]	205,822	52,736
18	Law enforcement [mh]	3,766	13,821
19	Law[tiab]	92,588	107,851
20	Laws[tiab]	30,612	35,831
21	Legislation as topic [mh]	162,492	118,636
22	Legislation[tiab]	37,600	44,761
23	Civil rights [mh]	24,302	27,242
24	Authority[tiab]	23,365	31,317
25	Legal case [pt]	11,029	4,853
26	Legal guardians [mh]	3,674	1,087
30	Legal [tiab]	92,665	108,549
31	Liability, legal [mh]	15,695	16,744
32	Legal services [mh]	31	366
33	Access to information [mh]	7,664	24,183
34	Social justice [mh]	12,277	11,892
35	Health equity [mh]	1,428	1,658
36	Human rights abuses [mh]	1,399	504
37	Patient rights [mh]	78,478	167543
39	Ownership [mh]	22,754	62,909
40	Intellectual property [mh]	11,581	8,172
41	Intellectual property[tiab]	2,267	3,066
42	Licensure [mh]	17,673	8,710
43	License[tiab]	7,852	12,425
44	Liability, legal [mh]	15,695	6,677
45	Liability [tiab]	19,480	24,866
46	Legislation[mh]	162,492	157,903
47	Legislation as topic [mh]	162,492	98,020
48	Medical device legislation [mh]	249	449
49	Conflict of interest [mh]	10,552	13,087
50	Guaranty[tiab]	126	235
51	Regulation[tiab]	861,687	1,055,636
52	Acquisition	164,250	204,886
53	Conflict of interest[tiab]	4,216	6,227
54	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 PR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32	1,802,195	2,697,538

Number	Query	PubMed	Embase
	OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58		
55	54 AND (((Mutiple sclerosis [MeSH] OR Parkinson disease [MeSH] OR stroke [MeSH]) OR (Multiple sclerosis)) OR (Stroke)) OR (Parkinson's disease)	7,088	50,903
56	55 AND ((Physical Therapy Modalities [MeSH]) OR (Physical therapy)) OR (Physiotherapy)	283	137

Table 25 Search strings for organisational issues (PubMed and Embase) [from inception to 13 November 2020]

Search	Query	PubMed	Embase
1	Information storage and retrieval [mh]	186,964	1,169
2	(information management)	365,405	39,527
3	Health information systems [mh]	1,328	7,971
4	Health information management [mh]	1,719	21,921
5	Health information exchange [mh]	901	21,885
6	Information literacy [mh]	6,307	542
7	Health equity [mh]	1,428	3,614
8	(work process)	210,734	422,829
9	(work flow)	65,466	24,474
10	Medical Education[mh]	167,137	238,197
11	Education, professional, retraining [mh]	1,242	32,287
12	Education, public health professional [mh]	788	345,333
13	Health information interoperability[mh]	172	321
14	Communication [mh]	313,409	560,361
15	Health communication [mh]	2,476	78,120
16	Quality assurance, health care [mh]	332,438	246,318
17	Implementation science [mh]	518	1,479
18	Organization culture [mh]	39,781	1,967
19	(human skills)	196,826	768,692
20	Sustainability[tiab]	25,481	154,667
21	(system structure)	461,170	888
22	Acceptance[tiab]	71,174	100,879
23	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23	2,152,000	1,769,086
24	23 AND (((Multiple sclerosis [MeSH] OR Parkinson disease [MeSH] OR stroke [MeSH]) OR (Multiple sclerosis)) OR (Stroke)) OR (Parkinson's disease)	391,656	15807
25	24 AND ((Physical Therapy Modalities [MeSH]) OR (Physical therapy)) OR (Physiotherapy)	794	365

Table 26 Search strings for ethical considerations (PubMed and Embase) [from inception to 13 November 2020]

Search	Query	PubMed	Ovid
1	Ethics[mh]	147,473	231,837
2	Medical ethics[tiab]	6,439	51,474
3	Ethical theory [mh]	3,395	1,027
4	Bioethics[mh]	11,003	20,555
5	Morals[mh]	170,632	862
6	Morality[tiab]	4,532	43,104
7	Ethical theory[tiab]	302	1,027
8	Principle-based ethics[mh]	29,943	24,454
9	Patient rights [mh]	78,489	14,369
10	Patient autonomy[tiab]	2,393	5,897
11	Personal autonomy [mh]	17,216	14,346
12	Autonomy[tiab]	30,218	51,299
13	Social justice [mh]	12,280	11,892
14	Ethical issues [tiab]	12,180	14,884
15	Normative [tiab]	30,044	39,252
16	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15	287,812	358,615
17	16 AND (((Multiple sclerosis [MeSH] OR Parkinson disease [MeSH] OR stroke [MeSH]) OR (Multiple sclerosis)) OR (Stroke)) OR (Parkinson's disease)	2,678	6,617
	18 AND ((Physical Therapy Modalities [MeSH]) OR (Physical therapy)) OR (Physiotherapy)	164	153

Table 27 Search string for social considerations (PubMed and Embase) [from inception to 13 November 2020]

Search	Query	PubMed	Embase
1	Patient experience[tiab]	6,495	11,654
2	Quality of life [mh]	199,770	486,701
3	Social aspects of [tiab]	2,389	5,410
4	Medical decision-making process [mh]	10,166	28,374
5	Patient education as topic [mh]	86,063	123,244
6	Patient education[tiab]	19,645	27,640
7	Patient attitude[tiab]	163	206
8	Patient preference [tiab]	4,658	7,048
9	Patient decision[tiab]	1,734	2,690
10	Patient acceptance[tiab]	2,963	4,039
11	Patient satisfaction [tiab]	37,758	53,376
12	Patient-focused [tiab]	1,659	2,363
13	Patient-centred [tiab]	6,450	8,299
14	Patient advocacy [tiab]	1,442	2,076

Search	Query	PubMed	Embase
15	Consumer satisfaction [tiab]	779	900
16	Consumer participation [tiab]	401	407
17	Consumer preference [tiab]	433	407
18	Consumer attitude[tiab]	51	51
19	Self-perception	153,179	98,033
20	Self-care	199,125	68,568
21	Self-efficacy	65,382	107,348
22	Attitude to health	550,627	117,989
23	Health education	731,148	351,412
24	Health knowledge	335,543	119,987
25	Informed choice	51,123	112,313
26	Shared decision making	12,970	15,104
27	Empowerment	13,467	19,741
28	Quality of Life	414,116	618,854
29	Adaptation, psychological	136,317	61,157
30	Coping	167,261	103,241
31	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30	2,016,054	1,450,858
32	Focus group	121,456	264,368
33	verbal communication	30,365	17,014
34	qualitative	301,688	348,887
35	survey	1,502,714	1,418,325
36	32 OR 33 OR 34 OR 35	1,857,896	1,957,915
37	31 AND 36	610,540	251,464
38	37 AND (((Multiple sclerosis [MeSH] OR Parkinson disease [MeSH] OR stroke [MeSH]) OR (Multiple sclerosis)) OR (Stroke)) OR (Parkinson's disease)	13,472	7,863
39	38 AND ((Physical Therapy Modalities [MeSH]) OR (Physical therapy)) OR (Physiotherapy)	1,841	280

Table 28 Specialty websites literature search (18 November 2020)

Society	Website	Search term: Physiotherapy or Physical therapy	Total Relevant
Stroke			
American Academy of Neurology	https://www.aan.com/	11	0
American Stroke Association	https://www.stroke.org/	58	0
European Academy of Neurology	https://www.ean.org/	3	0
Stroke Association	https://www.stroke.org.uk/	13	0
Stroke Society of Australasia	http://www.strokesociety.com.au/	1	0
World Federation of Neurology	https://wfneurology.org/	1	0
World Stroke Organization	https://www.world-stroke.org/	0	0
Multiple sclerosis			

European Committee for Treatment and Research in Multiple Sclerosis	https://www.ectrims.eu/	0	0
European Multiple Sclerosis Platform	http://www.emsp.org/	2	0
Italian Multiple Sclerosis Society	https://www.aism.it/	1	0
MS Research Australia	https://msra.org.au/	0	0
Multiple Sclerosis Society UK	https://www.mssociety.org.uk/	2	0
MS International Federation	https://www.msif.org/	0	0
National Multiple Sclerosis Society	https://www.nationalmssociety.org/	5	0
Parkinson's disease			
American Academy of Neurology	https://www.aan.com/	3	0
American Parkinson Disease Association	https://www.apdaparkinson.org/research/	0	0
European Parkinson's Disease Association	https://www.epda.eu.com/	9	0
Parkinson's Australia	https://www.parkinsons.org.au/	0	0
Parkinson Canada	https://www.parkinson.ca/	0	0
Parkinson's Foundation	https://www.parkinson.org/	0	0
Parkinson's UK	https://www.parkinsons.org.uk/research	3	0
The Michael J. Fox Foundation for Parkinson's Research	https://www.michaeljfox.org/	0	0

Table 29 HTA agency websites literature search (18 November 2020)

Society	Website	Search terms: Physiotherapy or Physical therapy AND			Total relevant
		Stroke	MS	PD	
International					
National Information Centre of Health Services Research and Health Care Technology (NICHSR)	https://www.nlm.nih.gov/hsrph.html	154	97	95	0
National Library of Medicine Health Services/Technology Assessment Texts (HSTAT)	https://www.ncbi.nlm.nih.gov/books/NBK16710/	125	62	65	0
Australia					
National Health and Medical Research Council	https://www.nhmrc.gov.au/	3	0	0	0
Australian Safety and Efficacy Register of New Interventional Procedures—Surgical (ASERNIP-S)	https://www.surgeons.org/research-audit/research-evaluation-inc-asernips	0	0	0	0
Austria					
Institute of Technology Assessment / HTA unit	https://www.oeaw.ac.at/ita/publikationen/	0	2	0	0
Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA)	https://hta.lbg.ac.at/page/publikationen/en	2	0	0	0

Society	Website	Search terms: Physiotherapy or Physical therapy AND			Total relevant
		Stroke	MS	PD	
Belgium					
Scientific Institute of Public Health (IPH)	https://www.wiv-isp.be/en	0	0	0	0
Belgian Health Care Knowledge Centre (KCE)	http://kce.fgov.be	3	0	0	0
Canada					
Institute of Health Economics (IHE)	http://www.ihe.ca	0	0	0	0
Institut National d'Excellence en Santé et en Services (INESSS)	https://www.inesss.qc.ca/en/home.html	0	0	0	0
The Canadian Agency for Drugs and Technologies in Health (CADTH)	http://www.cadth.ca/	3	2	0	0
Denmark					
Danish National Institute of Public Health	https://www.sdu.dk/en/sif/forskning	0	0	0	0
Finland					
National Institute for Health and Welfare (THL)	https://www.thl.fi	0	0	0	0
Finnish Coordinating Center for Health Technology Assessment (FinCCHTA)	https://www.ppshp.fi/Tutkimus-ja-opetus/FinCCHTA/Sivut/HTA-julkaisuja.aspx	0	0	0	0
France					
French National Authority for Health (Haute Autorité de Santé; HAS)	http://www.has-sante.fr/	0	0	0	0
Germany					
Institute for Quality and Efficiency in Health Care (IQWiG)	http://www.iqwig.de	1	0	0	0
Ireland					
Health Information and Quality Authority (HIQA)	http://www.hiqa.ie	0	0	0	0
Norway					
The Norwegian Institute of Public Health (NIPHNO)	http://www.fhi.no/	2	0	0	0
Sweden					
Swedish Council on Technology Assessment in Health Care (SBU)	http://www.sbu.se/en/	2	0	0	0
Switzerland					
Swiss Federal Office of Public Health (FOPH)	http://www.bag.admin.ch/hta	0	0	0	0

Society	Website	Search terms: Physiotherapy or Physical therapy AND			Total relevant
		Stroke	MS	PD	
Swiss Network on Health Technology Assessment (SNHTA)	http://www.snhta.ch/	-	-	-	-
United Kingdom					
Healthcare Improvement Scotland (HIS)	http://www.healthcareimprovementscotland.org	0	0	0	0
National Health Service Health Technology Assessment (UK) / National Coordinating Centre for Health Technology Assessment (NCCHTA)	https://www.nihr.ac.uk/	0	0	0	0
National Institute for Clinical Excellence (NICE)	http://www.nice.org.uk/	7	0	5	0
National Institute for Health Research (NIHR), including HTA programme	http://www.nets.nihr.ac.uk/programmes/hta	0	0	0	0
United States					
Institute for Clinical and Economic Review (ICER)	http://www.icer-review.org/	0	0	0	0

12 Appendix B: Characteristics of included trials

12.1 Efficacy studies

Table 30 List of included systematic reviews for effectiveness outcomes

Author; year	Number of studies (country of studies); sample size	Inclusion and exclusion criteria	Intervention; Comparator	Treatment duration	Relevant outcomes
Stroke					
Ferrarello 2011[152]	RCT = 15 (Canada x3, Taiwan x3, USA x2, UK x2, Brazil x1, Australia x1, Sweden x1, Hong Kong x1, New Zealand x1) N = 700	**Inclusion criteria** • RCT performed at least 6 months after stroke onset, enrolling 5 or more adults in each group, randomised to an active physiotherapy intervention aimed either at improving mobility and ADL independence or at controlling treatment (placebo or no intervention) • Interventions that represent standard practice in stroke rehabilitation **Exclusion criteria** • Physiotherapy prescribed <6 months from stroke event • Interventions that are highly innovative or uncommonly used in practice	Motor rehabilitation and physiotherapy interventions; Placebo or no intervention	10 to 120 min, 1 to 5 times per week from 4 to 26 weeks	• Mobility • ADL independence
Hakkennes 2005[153]	RCT = 14 (USA x9, UK x1, Thailand x1, Saudi Arabia x1, Canada x1, The Netherlands x1) N = 292	**Inclusion criteria:** • Trial participants >18 years old reduced functional use of an upper extremity due to stroke • study design either RCT or quasi-RCT including cross-over designs or a systematic review of RCTs	Constrained-induced muscle treatment; No treatment	12 days to 10 weeks	• ADL • Patient satisfaction • QoL

Author; year	Number of studies (country of studies); sample size	Inclusion and exclusion criteria	Intervention; Comparator	Treatment duration	Relevant outcomes
Howlett 2015[154]	RCT = 18 (Finland x3, UK x2, USA x2, Denmark x2, Australia x1, Slovenia x1, Taiwan x1, Japan x1, Korea x1, Switzerland x1, Saudi Arabia x1, Hong Kong x1, India x1) N = 168	**Inclusion criteria:** • Adults 18+ • Moderate- to high-quality (PEDro >4) randomised or controlled trials of adults with stroke using FES	FES; Placebo/nil	2 to 12 weeks, with the total dose ranging from 5 to 90 hours	• Measures of activity limitation
Pomeroy 2006[155]	RCT and quasi RCT = 24 (USA x10, UK x4, Sweden x2, Slovenia x1, Australia x1, Italy x1, China x1, Denmark x1, Turkey x1, Hong Kong x1, could not determine x1) N = 888	**Inclusion criteria:** • Participants with diagnosis of either ischaemic stroke or haemorrhagic stroke at any time after stroke **Exclusion criteria** • Trials which investigated an experimental condition that differed from the control condition by combining electrostimulation with other interventions (e.g. splints)	Electrostimulation; Placebo, no treatment	Up to three months	• Functional motor ability • Ability to undertake ADL • Motor impairment • Normality of movement (voluntary movement control)

Author; year	Number of studies (country of studies); sample size	Inclusion and exclusion criteria	Intervention; Comparator	Treatment duration	Relevant outcomes
Saunders 2020[163]	RCT = 75 (USA x9, UK x9, Korea x9, China x8, Australia x6, Ireland x4, Canada x4, Sweden x3, The Netherlands x3, Belgium x3, Turkey x2, Japan x2, Israel x2, Portugal x1, Brazil x1, Iran x1, Norway x1, France x1, Germany x1, Italy x1, Switzerland x1, Jamaica x1, South Africa x1, Norway x1, New Zealand x1) N = 3617	**Inclusion criteria** • All studies described as RCTs that examined the effects of cardiorespiratory, resistance or mixed training • Studies in which controls were exposed to either physical activity occurring during usual care or no training or usual care • Full text reports of published and unpublished studies	Cardiorespiratory training, resistance training, mixed training; Usual care, no intervention	12 weeks or less	• Death • Dependence • Disability • Adverse events • Vascular risk factors • Physical fitness, mobility • Physical function • Health status and QoL • Mood • Cognitive function
States 2009[156]	RCT = 9 (Canada x4, Taiwan x3, UK x2) N = 499	**Inclusion criteria** • Adults (>18 years) who had a stroke and mobility deficits at least 6 months prior to inclusion in study **Exclusion criteria** • Studies that only used treadmill training, only used technologically demanding forms of gait training like body weight-supported treadmill training, only used progressive resistance training without gait-oriented exercises, or only included home-care programmes	Overground physical therapy; No intervention or control intervention (other rehabilitative techniques that do not include gait training)	1 to 3 sessions per week for 4 to 19 weeks	• Gait function

Author; year	Number of studies (country of studies); sample size	Inclusion and exclusion criteria	Intervention; Comparator	Treatment duration	Relevant outcomes
Stewart 2019[157]	RCT = 28 (for nerve stimulation 2 studies) (UK x1, Australia x4, Sweden x3, Canada x3, USA x2, Norway x1, Holland x1, Brazil x1, Taiwan x1, and Italy x1) N = 326	**Inclusion criteria** • Participants ≥65 years of age, or mean age of participants ≥65 years of age • All aetiologies, types and severity of stroke/stroke symptoms	Nerve stimulation (TENS), physiotherapy interventions; Sham, acupuncture, other physiotherapy interventions	30 min, 2x a week for 10 weeks	• QoL
van der Lee 2001[158]	RCT = 13 (USA x7, The Netherlands x2, UK x2, Belgium x1, Canada x1) N = 939	**Inclusion criteria** • Studies concerning exercise therapy aimed at amelioration of motor function of hemiparetic/hemiplegic arm in stroke patients • Studies designed and reported as RCTs • Outcomes measured at impairment and/or disability level • Separate results presented for affected arm • Published full-length articles • English, German, French or Dutch language • Published after 1966. **Exclusion criteria** • Studies concerning pharmacological interventions, biofeedback techniques or electrical stimulation	Exercise therapy; Other rehabilitation intervention, usual care, no treatment	5 to 2 hours/day; 3 to 6 times a week; for 2 to 20 weeks	• Arm function

Author; year	Number of studies (country of studies); sample size	Inclusion and exclusion criteria	Intervention; Comparator	Treatment duration	Relevant outcomes
Veldema 2020[159]	RCT = 28 (Korea x8, China x3, Canada x2, Israel x2, Italy x2, Denmark x2, USA x2, Taiwan x2, Egypt x1, Ireland x1, Australia x1, Germany x1, The Netherlands x1) N = 1,115	**Inclusion criteria** • Human studies • Prospective studies • English language	Ergometer training; No intervention	Between 15 and 365 intervention sessions with follow-up over 8 weeks and 12 months in 2 studies	• Cardiorespiratory fitness • Motor function and muscle force of lower limbs • Independence in ADLs • Glucose metabolism • Predictive force accuracy • Cognitive abilities • Walking abilities • Balance ability • Postural control • Health relevant physiological indicators • Multidimensional stroke outcome • Health related QoL
Yang 2019[160]	RCT = 59 (USA x14, UK x6, Korea x6, Japan x5, Turkey x5, China x4, Taiwan x3, Brazil x2, Canada x2, The Netherlands x2, Italy x2, Germany x2, Egypt x1, Spain x1, Thailand x1, Sweden x1, Hong Kong x1, Australia x1) N=1,712	**Inclusion criteria** • RCTs reporting the effects of ES on arm function after stroke **Exclusion criteria** • Articles with only protocols, conference papers or animal studies • RCTs that investigated the effect of a combined treatment, where the effects of electrical stimulation cannot be isolated • Crossover studies with no isolated outcomes before the crossover	ES; Placebo	20 minutes to 12 hours; treatment frequency of 3 times per week to 3 times per day; treatment duration of 1 day to 5 months	**Primary outcome** • Body function **Secondary outcome** • Activity assessment
Parkinson's Disease					

Author; year	Number of studies (country of studies); sample size	Inclusion and exclusion criteria	Intervention; Comparator	Treatment duration	Relevant outcomes
Shen 2016[161]	RCT = 25 (USA x5, Australia x4, Italy x3, Germany, x2, Hong Kong x2, Taiwan x2, UK x2, Canada x1, China x1, The Netherlands x1, Sweden x1, USA & The Netherlands x1) N =1,181	**Inclusion criteria** • RCTs for PD with outcomes related to balance, gait and/or falls **Exclusion criteria** • Interventions did not involve any gait, balance or strengthening exercises • Control group had balance, gait or strengthening exercises for the LE • Low-quality studies	Exercise (balance, gait, strength training); Control group that did not receive any intervention or placebo training that did not include balance, gait, or strengthening exercises	2 to 24 weeks	• Falls • Balance • Gait Ability
Tomlinson 2013[162]	RCT = 76 RCTs from 39 studies (USA x9, could not determine x8, Canada x4, UK x4, Australia x2, India x2, The Netherlands x2, Turkey x2, Austria x1, Germany x1, Hong Kong x1, Iran x1, Poland x1, USA & Netherlands x1) N = 1,827	**Inclusion criteria** • RCTs comparing physiotherapy intervention with no physiotherapy intervention including placebo control • Participants of any age, duration of PD, drug therapy and any duration of physiotherapy treatment	Physiotherapy intervention; No physiotherapy intervention (including placebo control); trials in which the no-intervention arm used an active or credible placebo, as long as no physiotherapy was delivered to this group	4 weeks to 12 months	• Gait • Functional mobility and balance • Falls • Clinician-rated impairment and disability • Patient rated QoL • Adverse events • Compliance • Economic analysis

Abbreviations: **ADL** = activities of daily living, **ES** = electrical stimulation, **FES** = functional electrical stimulation, **LE** = lower extremity, **Min** = minutes, **PEDro** = Physiotherapy Evidence Database, **PD** = Parkinson's disease, **QoL** = quality of life, **RCT** = randomised controlled trials, **TENS** = transcutaneous electrical nerve stimulation, **UK** = United Kingdom, **USA** = United States of America.

12.2 Safety studies

Table 31 List of included systematic reviews for safety outcomes

Author; year; country	Number of studies; country of studies; sample size	Inclusion and exclusion criteria	Intervention; Comparator	Treatment duration	Relevant outcomes
Stroke					
Saunders 2020[163]	RCT = 75 (USA x9, UK x9, Korea x9, China x8, Australia x6, Ireland x4, Canada x4, Sweden x3, The Netherlands x3, Belgium x3, Turkey x2, Japan x2, Israel x2, Portugal x1, Brazil x1, Iran x1, Norway x1, France x1, Germany x1, Italy x1, Switzerland x1, Jamaica x1, South Africa x1, Norway x1, New Zealand x1) N = 3,017	**Inclusion criteria** • All studies described as RCTs which examined the effects of cardiorespiratory, resistance or mixed training • Studies in which controls were exposed to either physical activity occurring during usual care or no training or usual care • Full text reports of published and unpublished studies	Cardiorespiratory training, resistance training, mixed training; Usual care, no intervention	12 weeks or less	• Adverse events • Death
Parkinson's disease					
Tomlinson 2013[162]	RCT = 76 RCTs from 39 studies (USA x9, could not determine x8, Canada x4, UK x4, Australia x2, India x2, The Netherlands x2, Turkey x2, Austria x1, Germany x1, Hong Kong x1, Iran x1, Poland x1, USA & Netherlands x1) N = 1,827	**Inclusion criteria** • RCTs comparing physiotherapy intervention with no physiotherapy intervention including placebo control • Participants of any age, duration of PD, drug therapy and any duration of physiotherapy treatment	Physiotherapy intervention; No physiotherapy intervention (including placebo control); trials in which the no-intervention arm used an active or credible placebo, as long as no physiotherapy was delivered to this group.	4 weeks to 12 months	• Adverse events

Abbreviations: PD = Parkinson's disease, **RCT** = randomised control trial, **UK** = United Kingdom, **USA** = United States of America.

13 Appendix C: Economic evaluation study extraction

Table 32 Evidence table for included studies on health economic evaluations

Study	Country	Treatment regimen, duration	Costing Year	Model time horizon	Study Perspective	Patients	Approach	Health State Costs and sources	Sensitivity Analysis	Discount rate	Source	QoL Measure	Evaluation Outcome
Stroke													
Beech et al 1999[164]	UK	-Community-based rehabilitation for stroke -Conventional care -Planned program for 3 months	1997	12 months	Government	Early stroke discharge	Cost analysis	Physician, GP and social service costs obtained using a questionnaire	Overhead rate	Nil	RCT	NR	Average annual cost per patient
Chan 2015[165]	Canada	- Higher-intensity physiotherapy for stroke rehabilitation (23 hours) -Lower intensity (9.2 hours)	2014	Lifelong	Government	Recent stroke patients	Markov model	Times spent by physiotherapists were multiplied by federal wages. Average bed costs and rehabilitation time from literature	-Duration of effect -Physiotherapist wage -Physiotherapy assistant -Mortality rate -Discount rate -Utility value -Inpatient stay	5%	Literature review	EQ-5D	Cost per QALY

Study	Country	Treatment regimen, duration	Costing Year	Model time horizon	Study Perspective	Patients	Approach	Health State Costs and sources	Sensitivity Analysis	Discount rate	Source	QoL Measure	Evaluation Outcome
Collins et al 2018[168]	UK	-Fitness programme (3 times/week for 12 weeks). - Each class 1 hour and 15 minutes -Relaxation	2014	7 months	Societal	Stroke	Decision model	Costs provided by local community group fitness provider	Comparing to usual care, classes for 12 months, less than 7 attendees per class	Nil	Previous RCT	SF-36	Cost per QALY
Faulkner et al 2017[170]	NZ	-Short-term exercise and education -Usual care	2015	3·5 years	Hospital	Transient ischemic attack or minor stroke	Costing model	Hospital costs estimated using unit costs based on disease groupings	Nil	Nil	Hospital records	Nil	Cost per patient
Harrington et al 2010[171]	UK	-16 sessions (1 hour exercise and 1 hour education) for 8 weeks -Standard care	2004	1 year	Societal	Stroke	Cost comparison	Resource use collected prospectively using diaries. Intervention costs included venue hire, staff costs, transport, and disposable items	Nil	Nil	RCT	WHO QOL Index	Cost per patient

Study	Country	Treatment regimen, duration	Costing Year	Model time horizon	Study Perspective	Patients	Approach	Health State Costs and sources	Sensitivity Analysis	Discount rate	Source	QoL Measure	Evaluation Outcome
Hunter et al 2018[167]	UK	- Conventional physical therapy plus functional strength training for upper limb for 90 min/day, 5 days/week for 6 weeks - Conventional physical therapy plus movement performance therapy for 60 min/day, 5 days/week	2015	6 months	Health system	Stroke	Trial based cost utility analysis	A log of equipment, and training costs was used to cost the intervention. Patients were asked to provide details of health service use at follow-up which were valued using reference costs.	Including carer cost and excluding training costs	Nil	RCT	EQ-5D	Cost per QALY
PD													
Clarke et al 2016[166]	UK	-Physiotherapy & occupational therapy tailored to individual patient requirements. Median therapy dose 4 sessions of 58 minutes over 8 weeks -No therapy	2012	15 months	Government	Mild to moderate PD	Trial based cost utility analysis	GP and practice nurse visits, hospital inpatient stays, outpatient visits and accident attendances costed using a resource-utilisation questionnaire	Missing values	Nil	RCT	EQ-5D	Cost per QALY

Study	Country	Treatment regimen, duration	Costing Year	Model time horizon	Study Perspective	Patients	Approach	Health State Costs and sources	Sensitivity Analysis	Discount rate	Source	QoL Measure	Evaluation Outcome
Farag et al 2016[169]	Australia	-Monthly exercise class & 2–4 home visits from physical therapist over 6 months -Usual care	2012	6 months	Health system	PD	Trial-based cost utility analysis	Implementation costs from records of service delivery and travel. Monthly calendars used for health service utilisation	Nil	Nil	RCT	SF-6D	Cost per QALY
Fletcher et al 2012[172]	UK	-10-week group exercise programme with supplementary home exercises -Usual care	2008	20 weeks	Societal	PD and self-reported history of 2 or more falls in preceding 12 months	Trial based cost-utility analysis	Physiotherapist time input was recorded by research team. Reference costs used for valuing services	Nil	Nil	RCT	EQ-5D	Cost per QALY
Gage et al 2006[173]	UK	-1 day/week for 6 consecutive weeks, 2 hours exercise	2000	6 weeks	Societal	PD	Cost comparison	Costs derived from protocol and hospital financial managers	Nil	Nil	Cohort analysis	Nil	Cost analysis
Joseph et al 2019[174]	Sweden	-10-week (3 times/week), group-based, progressive balance training program, led by 2 physical therapists -Usual care	2013	10 weeks	Societal	Mild to moderate PD	Trial based cost utility analysis	Costs included physiotherapist education, participants' and therapists' costs during assessments, and facilities use. Mean wages applied to retrospective data	Nil	Nil	RCT	SF-36	Cost per QALY

Study	Country	Treatment regimen, duration	Costing Year	Model time horizon	Study Perspective	Patients	Approach	Health State Costs and sources	Sensitivity Analysis	Discount rate	Source	QoL Measure	Evaluation Outcome
Xin et al 2020[175]	UK	-12 x 1-hour sessions of physiotherapist-delivered fall prevention programme -Usual care	2016	12 months	Government	PD, history of fall	Trial based cost utility analysis	Questionnaires used by participants to collect resource use for primary, hospital, medicines and social services	Time horizon, physiotherapist visits and numbers of sessions	Nil	RCT	EQ-5D	Cost per QALY
MS													
Tosh et al 2014[176]	UK	-18 supervised and 18 home exercise sessions over 12 weeks -Usual care	2011	6 months	Health system	MS	Trial-based cost-utility analysis	Questionnaires used to cost health services	Private gyms or by third-party providers. Personal costs and time off work	Nil	RCT	EQ-5D	Cost per QALY

Abbreviations: EQ-5D = EuroQol-5D, **GP**= general practitioner, **MS** = multiple sclerosis, **NR** = not reported, **NZ** = New Zealand, **PD** = Parkinson's disease, **RCT** = randomised control trial, **QALY** = quality-adjusted life year, **QoL** = quality of life, **SF-6D/-36** = short form-6D/-36, **UK** = United Kingdom, **WHO** = World Health Organisation

14 Appendix D: List of excluded trials at full text

14.1 Wrong study design

1. Ashburn A, Pickering R, McIntosh E, et al. Exercise-and strategy-based physiotherapy-delivered intervention for preventing repeat falls in people with parkinson's: The PDSAFE RCT. 2019;23(36):1-147.
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14.4 Wrong comparator

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14.6 Wrong intervention/comparator treatment duration

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