VA/DoD CLINICAL PRACTICE GUIDELINE FOR MANAGEMENT OF STROKE REHABILITATION

Department of Veterans Affairs
Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and the Department of Defense (DoD) guidelines are based on the best information available at the time of publication. The guidelines are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This clinical practice guideline (CPG) is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when providers consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every health care professional using these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DoD policies. Further, inclusion of recommendations for specific testing, therapeutic interventions, or both within these guidelines does not guarantee coverage of civilian sector care.

Version 5.0 – 2024

Prepared by

Management of Stroke Rehabilitation Work Group

With support from

Office of Quality and Patient Safety, Veterans Health Administration

and

Clinical Quality Improvement Program, Defense Health Agency

Version 5.0 - 2024[a]

Based on evidence reviewed through May 2, 2023

[a] VA/DoD Clinical Practice Guideline. (2024). Management of Stroke Rehabilitation Work Group. Washington, DC: U.S. Government Printing Office.

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I. Introduction

The VA and DoD Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the VA/DoD Health Executive Committee "on the use of clinical and epidemiological evidence to improve the health of the population . . ." across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of CPG for the VA and DoD populations.(1) Development and update of VA/DoD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and wellbeing.

In 2019, VA and DoD published a CPG for Stroke Rehabilitation (2019 VA/DoD Stroke Rehabilitation CPG), which was based on evidence reviewed through 2018. Since the release of that CPG, the evidence base on Stroke Rehabilitation has expanded. Consequently, the EBPWG initiated the update of the 2019 VA/DoD Stroke Rehabilitation CPG in 2022. This updated CPG's use of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach reflects a more rigorous application of the methodology than previous iterations.(2) Therefore, the strength of some recommendations might have been modified because of the confidence in the quality of the supporting evidence (see Evidence Quality and Recommendation Strength).

This CPG provides an evidence-based framework for evaluating and managing care for adult patients, 18 years or older, who have experienced a stroke, toward improving clinical outcomes. Successful implementation of this CPG will

- Assess the patient's condition and collaborate with the patient, family, and caregivers to determine optimal management of patient care;
- Emphasize the use of patient-centered care and shared decision making;
- Minimize preventable complications and morbidity; and
- Optimize individual health outcomes and quality of life (QoL).

II. Background

A. Stroke Epidemiology and Impact in the General Population

Stroke is a pervasive medical condition, impacting nearly 800,000 individuals annually in the United States (U.S.) with approximately 75% constituting first-time occurrences and the remaining 25% being recurrent strokes.(3) It is noteworthy that roughly 3% of the U.S. population has experienced a stroke, and projections indicate a potential rise to 4% by the year 2030.(3) The intricate pathophysiologic mechanisms underlying strokes manifest across the lifespan, with an unexpected 10% of all strokes arising in individuals age 18–45.(3) Stroke stands as the fifth most prevalent cause of mortality in the United States, accounting for one out of every 21 deaths in the nation; there is a stroke-related death approximately every 3 minutes and 17 seconds.(3) One of the comorbidities

commonly associated with stroke-related mortality is pneumonia, where patients with stroke who develop pneumonia have a three-fold increase in mortality compared with stroke patients that do not develop pneumonia.(4) Furthermore, stroke is a leading contributor to long-term disability with approximately 45% of individuals age 15–50 experiencing at least moderate disability after a stroke.(5)

Sex, ethnicity, and race emerge as pivotal factors influencing variations in stroke incidence, and these distinctions extend to rehabilitative outcomes. Because of the construction of most clinical trials, most reporting of stroke epidemiology has been binary, and sex have not had information collected separately. This practice leads to the possible inclusion of impacts of both sexes on stroke risk factors, assessment, treatment, rehabilitation, and ultimate outcomes.(6, 7) Stroke is the fifth leading cause of mortality for individuals assigned male at birth, and the third leading cause in people assigned female at birth.(6) Further accentuating these disparities, individuals from non-Hispanic Black or Pacific Islander backgrounds exhibit higher rates of stroke-related mortality compared with their counterparts from non-Hispanic White, Hispanic, American Indian or Alaska Native, and Asian backgrounds.(8) The risk differentials are stark, with the likelihood of experiencing a first stroke nearly doubling for Black individuals in comparison with White individuals. Moreover, Black individuals face an elevated risk of stroke-related mortality in contrast to White individuals.(8) This complex interplay of demographic factors underscores the critical need for tailored and culturally sensitive approaches to stroke prevention, management, and rehabilitation strategies.

The repercussions of stroke transcend direct medical expenditures, encompassing indirect costs such as missed work and premature mortality. Notably, the cumulative economic burden of stroke is substantial. The annual cumulative expenses associated with stroke treatment and the economic impact of lost workdays because of strokes in the United States are approximately $56.6 billion, with the total incremental costs amounting to $35 billion, coupled with indirect costs from underemployment reaching $38.1 billion, and premature mortality costs totaling $30.4 billion per year.(9)

The spectrum of disability resulting from stroke manifests diversely, contingent on the specific area or areas affected within the central nervous system and subsequent complications from the acute stroke period (e.g., aerobic deconditioning, mood dysregulation). Typical presentations might include focal weakness and sensory disturbances, impairments in speech and swallowing, vision loss or neglect, cognitive challenges involving inattention or memory loss, and emotional difficulties such as mood disorders or anxiety. Consequently, stroke survivors require tailored and timely rehabilitative interventions, aligning with their individualized needs.(10) Acute interventions in medical or surgical stroke management play a pivotal role in mitigating disability severity, reducing the risk of subsequent complications and ameliorating potential lifelong deficits. Rehabilitative efforts aligned with the extent of injury and the patient's clinical condition are imperative to optimize functional outcomes.

Regrettably, the etiology of ischemic stroke remains elusive in approximately 30% (1 out of 3) of patients, rendering them cryptogenic, and this type of stroke is particularly prevalent among younger patients compared with the elderly.(11) In fact, 40% of ischemic strokes in young adults are cryptogenic.(12) This heightened occurrence in young adults is attributed to the relative absence of comorbidities commonly associated with stroke risk in older populations, such as uncontrolled hypertension, atrial dysrhythmias, and cerebrovascular disease.(11)

Functional outcomes assume a paramount role within the active duty military demographic, where residual deficits and the potential for recurrence bear direct consequences on mission objectives and highlight the critical need for effective rehabilitative treatment. These potential outcomes involve considerations of duty-related alterations that can influence restrictions, deployability status, and disability ratings, thereby emphasizing the interaction between the rehabilitative aftermath of strokes and the operational readiness of military personnel.

Each year, around 6,000 Veterans are admitted to VA facilities because of stroke, accompanied by approximately 60,000 stroke-related outpatient visits, highlighting the considerable impact on the Veteran population.(13) The financial commitment to their care is substantial, with the VA allocating more than $250 million annually for the management of Veterans experiencing strokes within that year.(14) Furthermore, it is crucial to acknowledge that Veterans with a history of traumatic brain injuries (TBI), ranging from mild to moderate or severe, face an elevated risk of stroke compared with their counterparts without a history of TBI.(15)

Acute medical or surgical stroke management interventions help reduce the severity of disability, decrease the risk of further complications, and lessen potentially lifelong deficits. To maximize functional outcomes, rehabilitative efforts commensurate with the degree of injury and status of the patient should start as soon as they are clinically feasible.(16)

B. Stroke Rehabilitation in the Department of Veterans Affairs Population

The VHA estimates that over 10,000 Veterans are hospitalized for stroke-related diagnoses each year. In Fiscal Year 2022, just more than 9,400 unique patients with stroke were admitted to the VA. Stroke is a leading cause of serious long-term disability and more than one-half of patients 65 years and older experience mobility deficits after stroke.(9) As of 2023, there were 53 Primary Stroke Centers, 29 limited hours Stroke Centers, 45 supporting stroke facilities, and more than 40 Commission on Accreditation of Rehabilitation Facilities accredited acute rehabilitation units in VA. There are nine CARF accredited Stroke Specialty Programs located in these acute rehabilitation units. Comprehensive outpatient neurorehabilitation programs are also located throughout VA, but many Veterans admitted to a VA medical center after surviving a stroke might find themselves in a facility that does not offer comprehensive, integrated, and coordinated

care. Additionally, Veterans might receive acute treatment for stroke in facilities outside the VHA and later present for follow-up care at their local VA facility.

C. Stroke Rehabilitation in the Department of Defense Population

Although stroke is less common than in the VA population, it does occur in active duty, retiree, and other beneficiary populations served by DoD. Military treatment facilities (MTF) can perform initial triage of patients suspected of having acute stroke. However, there are no Joint Commission certified Stroke Centers within DoD; therefore, patients with stroke are often transferred to nearby stroke centers for further care. With limited inpatient rehabilitation beds, DoD often partners with VA or civilian network providers when these services are needed. At some of the larger MTFs, comprehensive outpatient stroke rehabilitation services might be available through TBI or physical medicine and rehabilitation clinics. Survivors of stroke who live outside MTF catchment areas may access community stroke resources through the TRICARE network.

III. Scope of This Guideline

This CPG is based on published clinical evidence and related information available through May 2, 2023. It is intended to provide general guidance on best evidence-based practices (see Appendix A for additional information on the evidence review methodology). Although the CPG is intended to improve the quality of care and clinical outcomes (see Introduction), it is not intended to define a standard of care (i.e., mandated or strictly required care).

A. Guideline Audience

This CPG is intended for use by VA and DoD providers and others on the healthcare team assessing and managing patients who have experienced a stroke and are receiving rehabilitation services. Additionally, this CPG is intended for community-based providers involved in the care of Service members, beneficiaries, or Veterans who have experienced a stroke.

B. Guideline Population

This CPG is intended for adult patients (18 years and older) who have experienced a stroke and are eligible for care in the VA or DoD health care delivery systems, and those who receive care from community-based providers. This CPG includes Veterans and Service members as well as their eligible adult dependents.

IV. Highlighted Features of This Guideline

A. Highlights in This Guideline

The current document is an update to the 2019 VA/DoD Stroke Rehabilitation CPG. The major strength of this CPG is the coordination and collaboration of the multidisciplinary team ensuring a broad representation of providers engaged in the management of

stroke rehabilitation. The following significant updates make it important that providers review this version of the CPG:

- Updated algorithm and sidebars to define a clinical flow;
- Added 24 new recommendations; reviewed and replaced 19 recommendations; reviewed and amended 3 recommendations; reviewed and did not change 1 recommendation; and deleted 16 recommendations from the 2019 VA/DoD Stroke Rehabilitation CPG.

Additional updates include an initial or expanded literature search or both into complementary and integrative health (CIH), including acupuncture, non-invasive brain stimulation techniques, management of post-stroke spasticity, and technology-based modalities including virtual reality (VR).

As noted above, the methodology used in developing this CPG has been updated since the prior versions and reflects a more rigorous application of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology than previous versions. The result is a refined CPG that includes methodologically rigorous, evidence-based recommendations for the rehabilitation of stroke survivors.

This CPG also provides expanded recommendations on research needed to strengthen future guidelines.

B. Components of This Guideline

This CPG provides clinical practice recommendations for the care of patients with Stroke Rehabilitation (see Recommendations). In addition, the Algorithm incorporates the recommendations in the context of the flow of patient care. This CPG also includes Research Priorities, which list areas the Work Group identified as needing additional research.

To accompany this CPG, the Work Group also developed toolkit materials for providers and patients, including a provider summary, a patient summary, and a quick reference guide, which can be found at https://www.healthquality.va.gov/index.asp.

C. Racial and Ethnic Demographic Terminology in This Guideline

Demographic terms referring to an individual's race or ethnicity (e.g., Hispanic, Latino or Latina, Asian, Native American, Black, African American, White, Caucasian) can be ambiguously defined and understood, reflecting diverse geographies, histories, cultures, and experiences. Aligned with the recent Executive Order on Further Advancing Racial Equity and Support for Underserved Communities through the Federal Government,[a] the Work Group used terms such as Black rather than African American and White rather than Caucasian to avoid presumptions about ancestry and to promote inclusivity,

[a] Executive Order on Further Advancing Racial Equity and Support for Underserved Communities Through The Federal Government | The White House

clarity, and consistency. However, to represent accurately the evidence on which this CPG is based, the Work Group generally deferred to racial and ethnic terminology as reported in the published systematic reviews (SR), clinical trials, and other studies comprising that evidence when summarizing or otherwise referring to those studies. Consequently, usage of demographic terms in this CPG might appear inconsistent.

D. Routine Care Terminology in This Guideline

The Work Group uses various terminology, including normal rehabilitation, conventional rehabilitation, and routine rehabilitation, to represent traditional therapy throughout the CPG because it reflects the language used in the evidence. “Usual care” was used as a comparator in several of the studies in the systematic evidence review and might not have had an explicit definition. Usual care is a term used to describe the full spectrum of patient care practices in which providers have the opportunity to provide individualized care.(17)

V. Guideline Development Team

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, Defense Health Agency, identified the following three providers to serve as Champions (i.e., leaders) of this CPG’s Work Group: Blessen Eapen, MD and Johanna Tran, MD from VA; and Tyler Koehn, MD from DoD.

The Work Group comprised individuals with the following areas of expertise: primary care, pharmacy, neurology, psychology, physical therapy, speech pathology, social work, and occupational therapy. Table 1 lists the Work Group and Guideline Development Team members.

This CPG Work Group, led by the Champions, was tasked with

- Determining the scope of the CPG;
- Crafting clinically relevant key questions (KQ) to guide the systematic evidence review;
- Identifying discussion topics for the patient focus group and considering the patient perspective;
- Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence; and
- Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation.

The Lewin Team, including The Lewin Group, ECRI, Sigma Health Consulting, and Duty First Consulting, was contracted by VA to help develop this CPG.

Table 1. Guideline Work Group and Guideline Development Team

Organization	Names*
Department of Veterans Affairs	**Blessen C. Eapen, MD (Champion)**
	Johanna E. Tran, MD (Champion)
	Amy M. Donaldson, LCSW
	Andrew Buelt, DO
	Christine Matthews, CScD, CCC-SLP, BCS-S
	Frederica O'Donnell, OTD, OTR/L, LSSBB
	Jamie Basch, DHSc, OTR/L
	Jason Gleason, DNP
	Michelle Peterson, PT, DPT, NCS
	Natasha Antonovich, PharmD, BCPS
	Rebecca Ruffing, MA, CCC-SLP
	Rose Collins, PhD, LP
	Svetlana Pundik, MD, MSc
Department of Defense	**Tyler R. Koehn, MD (Champion)**
	Brian Ford, MD
	Carrie W. Hoppes, PT, PhD, NCS, OCS, ATC, CSCS
	Danielle Murray, PhD
	Jackoline Costantino, PharmD
	M. Marina LeBlanc, OTR/L
	Melissa R. Ray, CCC-SLP
	Russell J. Carroll, PsyD
	Zahari N. Tchopev, MD, MBA
VA Evidence Based Practice, Office of Quality and Patient Safety Veterans Health Administration	James Sall, PhD, FNP-BC
	Jennifer Ballard-Hernandez, DNP, RN, FNP-BC
	René Sutton, BS, HCA
	Lisa M. Wayman, PhD, RN, EBP-C
	Sarah Davis-Arnold, MSN, RN, NPD-BC, RCIS, EBP-C
Clinical Quality Improvement Program Defense Health Agency	Elaine Stuffel, MHA, BSN, RN
	Cynthia F. Villarreal, BSN, RN
	Isabella Alvarez, MA, BSN, RN
	Lynn Young, BSN, RN, CIC
	Gwen Holland, MSN, RN
The Lewin Group	Jennifer Weil, PhD
	Erika Beam, MS
	Savannah Lantz, MPH, RN
	Amanda Heinzerling, MS
	Katherine McCracken, BA

Organization	Names*
ECRI	James Reston, PhD, MPH
	Kelley Tipton, MPH
	Allison Gross, MS, MLS
Sigma Health Consulting	James G. Smirniotopoulos, MD
	Frances M. Murphy, MD, MPH
Duty First Consulting	Kate Johnson, BS
	Rachel Piccolino, BA
	Anita Ramanathan, BA
	Jake Fausnacht, BS

*Additional contributor contact information is available in Appendix H.

VI. Summary of Guideline Development Methodology

The methodology used in developing this CPG follows the *Guideline for Guidelines*, an internal document of the VA/DoD EBPWG updated in January 2019 that outlines procedures for developing and submitting VA/DoD CPGs.(18) The *Guideline for Guidelines* is available at http://www.healthquality.va.gov/policy/index.asp. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and strength, management of potential conflicts of interest [COI], interdisciplinary stakeholder involvement, use of SR and external review).(19) Appendix A provides a detailed description of the CPG development methodology.

A. Evidence Quality and Recommendation Strength

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (see Determining Recommendation Strength and Direction).(20)

1. Confidence in the quality of the evidence
2. Balance of desirable and undesirable outcomes
3. Patient values and preferences
4. Other considerations, as appropriate (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)

Using these four domains, the Work Group determined the relative strength of each recommendation (*Strong* or *Weak*). The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which incorporates the four domains.(21) A *Strong* recommendation generally indicates *High* or *Moderate* confidence in the quality of the available evidence, a clear difference in magnitude between the

benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, insufficient evidence exists on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The manner in which this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for an intervention that might be in common practice although it is unsupported by clinical evidence and particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text as shown in Table 2.

Table 2. Strength and Direction of Recommendations and General Corresponding Text

Recommendation Strength and Direction	General Corresponding Text
Strong for	We recommend . . .
Weak for	We suggest . . .
Neither for nor against	There is insufficient evidence to recommend for or against . . .
Weak against	We suggest against . . .
Strong against	We recommend against . . .

That a recommendation's strength (i.e., *Strong* versus *Weak*) is distinct from its clinical importance (e.g., a *Weak* recommendation is evidence based and still important to clinical care) is important to note. The strength of each recommendation is shown in Recommendations.

This CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations; the determination of the strength of the recommendation is more directly linked to the confidence in the quality of the evidence on outcomes that are critical to clinical decision making. The confidence in the quality of the evidence is assessed using an objective, systematic approach independent of the clinical topic of interest. Therefore, recommendations on topics for which designing and conducting rigorous studies might be inherently more difficult (e.g., randomized controlled trials [RCT]) are typically supported by lower quality evidence and, in turn, *Weak*

recommendations. Recommendations on topics for which rigorous studies can be designed and conducted might more often be *Strong* recommendations. Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2, 22) This stricter standard provides a consistent approach to determining recommendation strengths. For additional information on GRADE or CPG methodology, see Appendix A.

B. Categorization of Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, staying current typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations.(23) For example, the United States Preventative Services Task Force (USPSTF) has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every five years for either an update or reaffirmation.(24)

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England).(25, 26) Table 3 lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified, and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The 2024 CPG recommendation categories can be found in Recommendations. Appendix G outlines the 2019 VA/DoD Stroke Rehabilitation CPG's recommendation categories.

Table 3. Recommendation Categories and Definitions[a]

Evidence Reviewed	Recommendation Category	Definition
Reviewed[b]	New-added	New recommendation
	New-replaced	Recommendation from previous CPG was carried forward and revised
	Not changed	Recommendation from previous CPG was carried forward but unchanged
	Amended	Recommendation from previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted

Evidence Reviewed	Recommendation Category	Definition
Not Reviewed[c]	Not changed	Recommendation from previous CPG was carried forward but unchanged
	Amended	Recommendation from previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted

[a] Adapted from the NICE guideline manual (2012)(25) and Garcia et al. (2014)(26)

[b] The topic of this recommendation was covered in the evidence review carried out as part of the development of the current CPG.

[c] The topic of this recommendation was not covered in the evidence review carried out as part of the development of the current CPG.

Abbreviation: CPG: clinical practice guideline

C. Management of Potential or Actual Conflicts of Interest

Management of COIs for the CPGs is conducted as described in the *Guideline for Guidelines*.(18) Further, the *Guideline for Guidelines* refers to details in the VHA Handbook 1004.07 Financial Relationships between VHA Health Care Professionals and Industry (November 2014, issued by the VHA National Center for Ethics in Health Care)(27) as well as to disclosure statements (i.e., standard disclosure form completed at least twice by CPG Work Group members and the guideline development team).(18) The disclosure form inquires regarding relevant financial and intellectual interests or other relationships with, for example, manufacturers of commercial products, providers of commercial services, or other commercial interests. The disclosure form also inquires regarding any other relationships or activities that could be perceived to have influenced, or that give the appearance of potentially influencing, a respondent's contributions to the CPG. In addition, instances of potential or actual COIs among the CPG Work Group and the guideline development team were subject to random web-based identification via standard electronic means (e.g., Centers for Medicare & Medicaid Services Open Payments, ProPublica).

D. Patient Perspective

When developing a CPG, consideration should be given to patient perspectives and experiences, which often vary from those of providers.(22, 28) Focus groups can be used to help collect qualitative data on patient perspectives and experiences. VA and DoD Leadership arranged a virtual patient focus group on March 2, 2023. The focus group aimed to gain insights into patients with who are currently or were receiving stroke rehabilitation along with feedback from their caregivers and incorporate these insights into the CPG, as appropriate. Topics discussed included the patients' priorities, challenges they have experienced, information they have received regarding their care, and impacts of their care on their lives and their family members lives.

The patient focus group comprised a convenience sample of six people. There were four men and two women. Participants were mixed in where they received care

following their stroke; some received care exclusively through VA or DoD health systems and some received care from both. One participant indicated they also received care in the private sector. The time since diagnosis of stroke for the participants ranged from 9–18 months at the time of the focus group. The Work Group acknowledges this convenience sample is not representative of all individuals who are currently or were receiving stroke rehabilitation within the VA and DoD healthcare systems and, thus, findings are not generalizable and do not comprise evidence. For more information on the patient focus group methods and findings, see Appendix E. Patient focus group participants were provided the opportunity to review the final draft of this CPG and provide additional feedback.

E. External Peer Review

The Work Group drafted, reviewed, and edited this CPG using an iterative process. For more information, see Drafting and Finalizing the Guideline. Once the Work Group members completed a near-final draft, they identified experts from VA and DoD health care systems and outside organizations generally viewed as experts in the respective field to review it. The draft was sent to those experts for a 14-business-day review and comment period. The Work Group considered all feedback from the peer reviewers and modified the CPG where justified, in accordance with the evidence. Detailed information on the external peer review can be provided by the VA Office of Quality and Patient Safety.

F. Implementation

This CPG and algorithm are designed for adaptation by individual health care providers with respect to unique patient considerations and preferences, local needs, and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the care of patients who have experienced a stroke. The Work Group submits suggested performance metrics for VA and DoD to use when assessing the implementation of this CPG. Robust implementation is identified in VA and DoD internal implementation plans and policies. Additionally, implementation would entail wide dissemination through publication in the medical literature, online access, educational programs, and, ideally, electronic medical record programming in the form of clinical decision support tools at the point of care.

VII. Approach to Care in the Department of Veterans Affairs and the Department of Defense

A. Patient-Centered Care

Intended to consider patient needs and preferences, guideline recommendations represent a whole/holistic health approach to care that is patient centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning disabilities. VA/DoD CPGs encourage providers to use a patient-centered, whole/holistic health approach (i.e., individualized treatment based on patient needs,

characteristics, and preferences). This approach aims to treat the particular condition while also optimizing the individual's overall health and wellbeing.

Regardless of the care setting, all patients should have access to individualized evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in providers, and improve treatment adherence.(29, 30) A whole/holistic health approach (https://www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and wellbeing goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to sex, culture, ethnicity, and other differences.

B. Shared Decision Making

This CPG encourages providers to practice shared decision making, a process in which providers, patients, and patient care partners (e.g., family, friends, caregivers) consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(31) Shared decision making is emphasized in *Crossing the Quality Chasm,* an Institute of Medicine, now NAM, report in 2001 (32) and is inherent within the whole/holistic health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, expected outcomes, and levels or settings of care or both, especially where patient heterogeneity in weighing risks and benefits might exist. Veterans Health Administration and MHS have embraced shared decision making. Providers are encouraged to use shared decision making to individualize treatment goals and plans based on patient capabilities, needs, and preferences.

C. Patients with Co-occurring Conditions

Co-occurring conditions can modify the degree of risk, impact diagnosis, influence patient and provider treatment priorities and clinical decisions, and affect the overall approach to managing stroke rehabilitation. Many Veterans, active duty Service members, and their families have one or more co-occurring conditions. Because stroke is sometimes accompanied by co-occurring conditions, managing stroke collaboratively with other care providers is often best. Some co-occurring conditions might require early specialist consultation to determine necessary changes in treatment or to establish a common understanding of how care will be coordinated. This approach might entail reference to other VA/DoD CPGs (e.g., Major Depressive Disorder).[b]

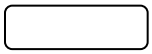
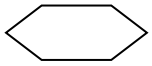
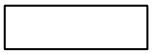
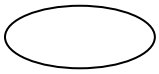
[b] The VA/DoD Clinical Practice Guidelines are available at: https://www.healthquality.va.gov/

VIII. Algorithm

This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in managing the rehabilitation of patients with stroke. This algorithm format represents a simplified flow of the management of patients post stroke and helps foster efficient decision making by providers. It includes

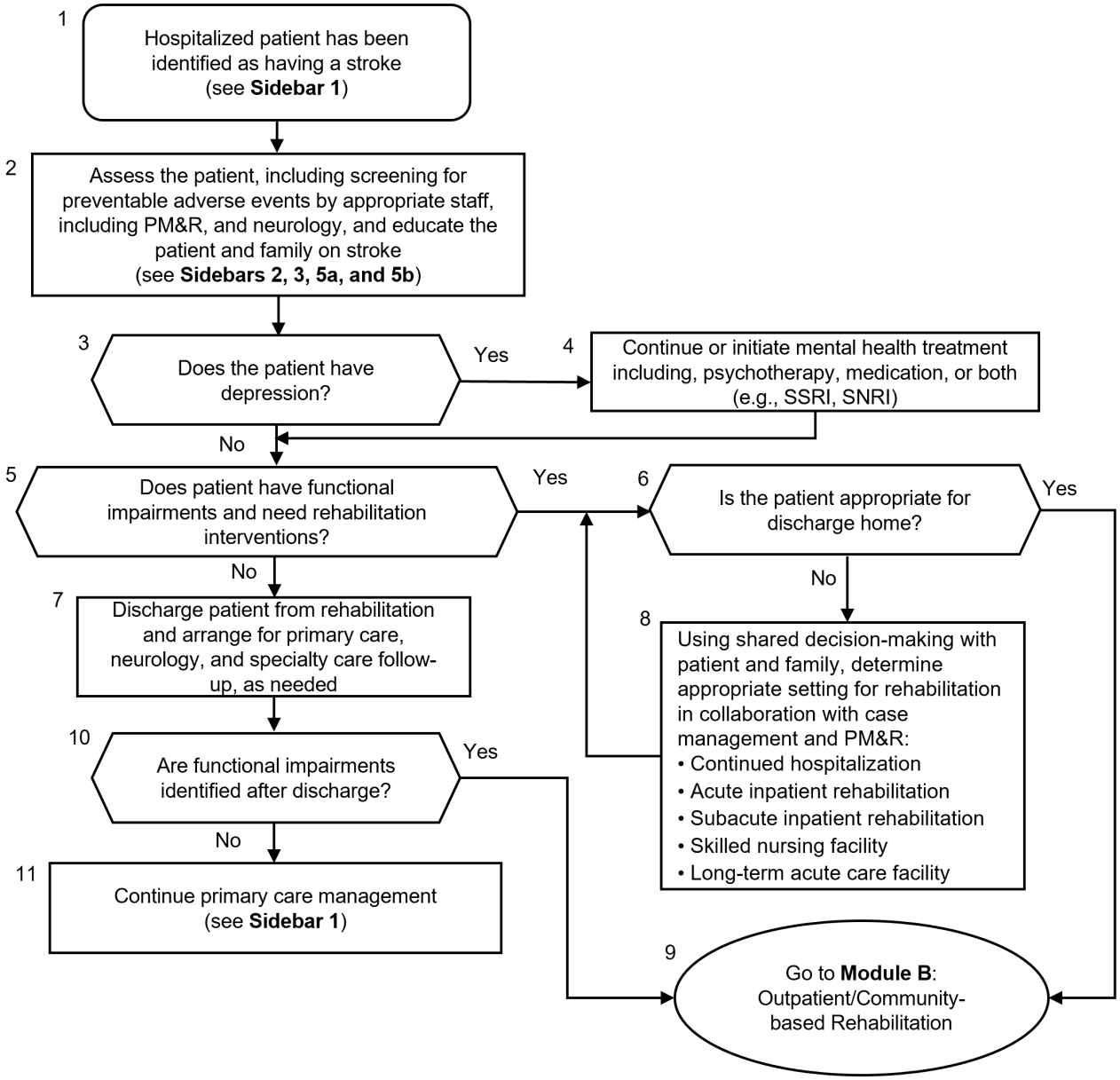
- Steps of care in an ordered sequence,
- Decisions to be considered,
- Decision criteria recommended, and
- Actions to be taken.

The algorithm is a step-by-step decision tree. Standardized symbols display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.(33) Sidebars 1–5 provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the process of care, formulated as a question that can be answered "Yes" or "No."
	Rectangles represent an action in the process of care.
	Ovals represent a link to another section within the algorithm.

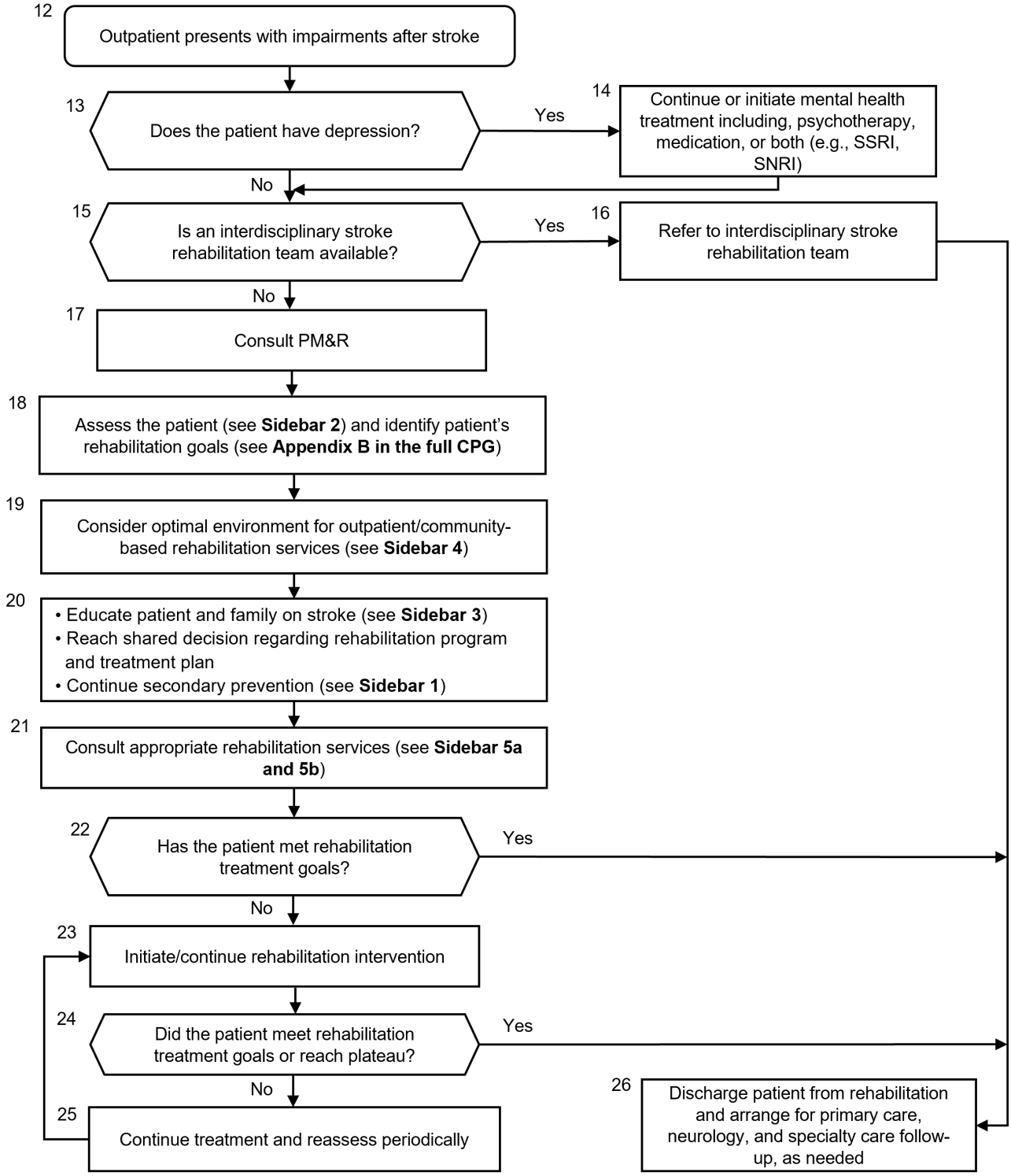
Appendix J contains alternative text descriptions of the algorithms.

A. Module A: Rehabilitation Disposition of the Inpatient with Stroke



Abbreviations: PM&R = Physical medicine and rehabilitation; SSRI = Selective serotonin reuptake inhibitor; SNRI = Serotonin–norepinephrine reuptake inhibitor

B. Module B: Outpatient/Community-Based Rehabilitation



Abbreviations: PM&R = Physical medicine and rehabilitation; SSRI = Selective serotonin reuptake inhibitor; SNRI = Serotonin–norepinephrine reuptake inhibitor

Sidebar 1: Essential Guidelines for the Medical Management of Stroke

- 2019 Update to the 2018 AHA/ASA Guidelines for the Early Management of Patients with Acute Ischemic Stroke(34)
- 2021 AHA/ASA Guidelines for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack(35)
- 2022 AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage(36)

Abbreviations: AHA: American Heart Association; ASA: American Stroke Association

Sidebar 2: Assessment of Impairments and Disabilities

- Assessment of impairments
  - Auditory/hearing
  - Bowel and bladder
  - Cognition
  - Communication
  - Emotion and behavior
  - Exercise tolerance/aerobic capacity
  - Inattention/neglect
  - Motor/mobility/balance
  - Swallowing and nutrition
  - Tactile/touch/somatosensory
  - Vision and formal visual fields
  - Vestibular
- Assessment of barriers to participation in therapy
  - Cognitive impairment
  - Communication impairment
  - Fatigue and sleep
  - Medical conditions
  - Mental health (e.g., depression)
  - Motivation
  - Pain
  - Social determinants of health (e.g., financial, employment, transportation)
- Assessment of activity and function
  - ADLs (e.g., feeding, dressing, grooming) and IADLs (e.g., finances, shopping)
  - Driving
  - Meaningful roles (e.g., parent, spouse)
  - Return to work/duty or school
  - Sexual function and intimacy
- Assessment of support system
  - Family, caregivers, community
  - Military leadership/structure, if applicable

Abbreviations: ADLs: activities of daily living; IADLs: instrumental activities of daily living

Sidebar 3: Stroke Education Topics

- Stroke signs and symptoms – BE FAST
  - Balance – Sudden difficulty with balance or coordination, dizziness, vertigo
  - Eyes – Sudden blurred, double, or loss of vision in one or both eyes
  - Face – Sudden facial droop/weakness on one side
  - Arm – Sudden weakness in one arm
  - Speech – Slurred speech, inability to speak, or difficulty understanding speech
  - Time – If any of these symptoms occur, call 911. Time is critical for stroke.
- Common causes of stroke
  - Ischemic stroke (80–90% of all strokes)
    - Heart conditions, such as atrial fibrillation
    - Atherosclerosis of the large arteries in the neck and brain
    - Small vessel disease
    - ~30% of ischemic strokes are not found to have a clear cause (cryptogenic)
  - Hemorrhagic stroke (10-20% of all strokes)
    - High blood pressure (hypertension)
    - Vascular malformations (aneurysm, cavernous malformation, fistula)
    - Amyloid angiopathy
- Risk factors for stroke
  - High blood pressure (hypertension)
  - High blood sugar (diabetes mellitus)
  - High cholesterol (hyperlipidemia)
  - Heart conditions (atrial fibrillation, heart failure)
  - Tobacco/nicotine (smoking, vaping, chewing)
  - History of previous stroke
  - Age, ethnicity, sex, race, socioeconomic status
- Nutrition
- Physical activity and falls prevention
- Continuum of care options/follow-up after discharge
- Inpatient rehabilitation
- Outpatient rehabilitation
- Therapy at home
- Adjustment and coping after stroke
- Primary care follow-up

Sidebar 4: Considerations for Outpatient/Community-Based Rehabilitation Services
• Current functional status and endurance level • Family and caregiver support • Home assessment for safety • Motivation and preferences • Necessary equipment • Resources, availability, and eligibility • Transportation

Sidebar 5a: Resources for Management of Post-Stroke Impairments/Needs[d]	
Consultants/Referrals	**Impairment/Need**
Behavioral and mental health	• Adjustment and coping • Behavioral smoking cessation • Cognition • Emotion and behavior • Family and caregiver support • Pain • Sexual function and intimacy
Case management (social work, nursing, or both)	• Community resources • Emotion and behavior • Family and caregiver support • Financial resources • Risk for abuse and neglect (e.g., emotional, financial exploitation, physical)
Dietetics	• Healthy eating and nutritional needs
Neurology	• Medication management • Optimization of secondary stroke prevention • Spasticity (medical management)
Nursing	• Bowel and bladder function • Medication administration • Patient and family education • Self-management skills, ADLs, IADLs • Skin care
Occupational therapy	• Cognition • Driving • Durable medical equipment recommendations • Home safety • Self-management skills, ADLs, IADLs • Sexual function and intimacy • Spasticity • Strength • Vision/vision perception
Ophthalmology	• Eyecare • Strabismus assessment and procedures

[d] Some impairments/needs might have multiple consultants/referrals, depending on various factors (e.g., severity).

Sidebar 5a: Resources for Management of Post-Stroke Impairments/Needs[d]		
Consultants/Referrals	**Impairment/Need**	
Optometry/visual rehabilitation	• Eyecare • Functional eye exam • Nonoperative strabismus management	• Strabismus assessment and procedures • Visual field cut/blind spot/scotoma
Physical medicine and rehabilitation (e.g., physiatry)	• Medication administration • Pain (medical management) • Prevention of post-stroke complications	• Rehabilitation management, oversight, and direction, including assistance with return to work/duty or school • Sexual function and intimacy • Spasticity (medical management)
Physical therapy	• Balance disorders and dizziness • Durable medical equipment recommendations • Exercise recommendations/ aerobic reconditioning • Home safety • Motor/mobility problems	• Pain • Sexual function and intimacy • Spasticity • Strength • Self-management skills, ADLs, IADLs
Primary care	• Management of common stroke risk factors • Hypertension • Diabetes mellitus • Hyperlipidemia	• Tobacco use • Medication management • Management of comorbidities
Recreation therapy	• Adaptive sports • Community reentry • Functional cognition	• Leisure and recreation participation • Self-management skills, ADLs, IADLs
Speech-language pathology	• Cognition • Communication	• Self-management skills, ADLs, IADLs • Swallowing
Vocational rehabilitation	• Return to work/duty or school	

Abbreviations: ADLs: activities of daily living; IADLs: instrumental activities of daily living

Sidebar 5b: Resources for Management of Post-Stroke Impairments/Needs[e]	
Impairment/Need	**Consultants/Referrals**
Adaptive sports	• Recreation therapy
Adjustment and coping	• Mental and behavioral health
Assistive technology	• Occupational therapy • Physical therapy • Rehabilitation engineers • Speech-language pathology
Balance disorders and dizziness	• Physical therapy
Behavioral smoking cessation	• Mental and behavioral health
Bowel and bladder function	• Nursing • Physical therapy
Cognition	• Behavioral, neurology, neuropsychiatry • Behavioral and mental health • Occupational therapy • Recreation therapy • Speech-language pathology
Communication	• Speech-language pathology
Community reentry	• Occupational therapy • Physical therapy • Recreation therapy • Social work
Community resources	• Case management (social work, nursing, or both)
Driving	• Occupational therapy • Recreation therapy
Durable medical equipment recommendations	• Occupational therapy • Physical therapy
Emotion and behavior	• Behavioral and mental health • Case management (social work, nursing, or both)
Eye care	• Ophthalmology • Optometry/visual rehabilitation
Family and caregiver support	• Behavioral and mental health • Case management (social work, nursing, or both)
Financial resources	• Case management (social work, nursing, or both)
Functional eye exam	• Optometry/visual rehabilitation
Healthy eating and nutritional needs	• Dietetics
Leisure/recreation participation	• Occupational therapy • Recreation therapy
Management of common stroke risk factors (e.g., Hypertension, Diabetes mellitus, Hyperlipidemia, Tobacco use)	• Primary care
Medication management	• Clinical pharmacology • Neurology • Nursing • Physical medicine and rehabilitation • Primary care

[e] Some impairments/needs might have multiple consultants/referrals, depending on various factors (e.g., severity).

Sidebar 5b: Resources for Management of Post-Stroke Impairments/Needs[e]	
Impairment/Need	**Consultants/Referrals**
Motor/mobility problems	• Occupational therapy • Physical therapy
Non-operative strabismus management	• Optometry/visual rehabilitation
Optimization of secondary stroke prevention	• Neurology • Primary care
Pain	• Behavioral and mental health • Complementary and integrative health (CIH) • Occupational therapy • Physical medicine and rehabilitation (e.g., physiatry) • Physical therapy
Patient and family education	• Behavioral and mental health • Neurology • Occupational therapy • Physical medicine and rehabilitation (e.g., physiatry) • Physical therapy • Primary care • Speech-language pathology
Prevention of post-stroke complications	
Rehabilitation management, oversight, and direction	• Case management • Physical medicine and rehabilitation (e.g., physiatry)
Return to work/duty or school	• Occupational therapy • Physical therapy • Speech-language pathology • Vocational rehabilitation
Self-management skills, ADLs, IADLs	• Nursing • Occupational therapy • Physical therapy • Recreation therapy • Speech-language pathology
Sexual function and intimacy	• Behavioral and mental health • Clinical pharmacist (drug interactions or side effects)] • Occupational therapy • Physical medicine and rehabilitation (e.g., physiatry) • Physical therapy
Skin care	• Nursing
Spasticity	• Neurology • Occupational therapy • Physical medicine and rehabilitation (e.g., physiatry) • Physical therapy
Strabismus assessment and procedures	• Ophthalmology
Strength	• Physical therapy • Occupational therapy
Swallowing	• Speech-language pathology
Vision/vision perception	• Occupational therapy • Optometry and neuro-optometry/low vision • Ophthalmology and neuro-ophthalmology
Visual field cut/blind spot/scotoma	• Optometry/visual rehabilitation

IX. Recommendations

The evidence-based clinical practice recommendations listed in Table 4 were made using a systematic approach considering four domains as per the GRADE approach (see Summary of Guideline Development Methodology). These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences, and other implications (e.g., resource use, equity, acceptability).

The Work Group uses various terminology, including normal rehabilitation, conventional rehabilitation, and routine rehabilitation, to represent traditional therapy throughout this CPG because it reflects the language used in the evidence. "Usual care" was used as a comparator in several of the studies in the systematic evidence review and might not have had an explicit definition. Usual care is a term used to describe the full spectrum of patient care practices in which providers have the opportunity to provide individualized care.(17)

Table 4. Evidence-Based Clinical Practice Recommendations with Strength and Category

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Transitions to Community		1.	We suggest using case management services at time of discharge from the acute care hospital or post-acute care facility to improve activities of daily living and functional independence.	Weak for	Reviewed, New-added
		2.	We suggest the following interventions for patients and their caregivers • Behavioral health/psychosocial interventions to improve patient and caregiver depression • Psychoeducation to improve family function, patient functional independence, and quality of life	Weak for	Reviewed, New-added
		3.	There is insufficient evidence to recommend for or against implementing transitional care rehabilitation interventions (e.g., home-based services after hospital discharge) or early supported discharge to improve activities of daily living or functional disability following stroke.	Neither for nor against	Reviewed, New-replaced
		4.	There is insufficient evidence to recommend for or against community participation interventions to improve community engagement for survivors of stroke.	Neither for nor against	Reviewed, New-added
Motor Therapy	*General*	5.	We recommend task-specific practice (also known as task-oriented practice or repetitive task practice) to improve motor function, gait, posture, and activities of daily living.	Strong for	Reviewed, Not changed
		6.	We suggest mirror therapy to improve motor outcomes and activities of daily living.	Weak for	Reviewed, New-replaced
		7.	We suggest mirror therapy to improve unilateral spatial neglect.	Weak for	Reviewed, New-added

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Motor Therapy (cont.)	*General (cont.)*	8.	There is insufficient evidence to recommend for or against body-weight support treadmill training to improve motor outcomes.	Neither for nor against	Reviewed, New-replaced
		9.	We suggest rhythmic auditory stimulation as an adjunct intervention to improve motor outcomes.	Weak for	Reviewed, New-replaced
		10.	There is insufficient evidence to recommend for or against the use of high intensity interval training over moderate intensity continuous training to enhance gait recovery.	Neither for nor against	Reviewed, New-replaced
		11.	There is insufficient evidence to recommend for or against constraint-induced movement therapy to improve upper extremity motor outcomes for individuals with some movement in the paretic limb.	Neither for nor against	Reviewed, New-replaced
		12.	There is insufficient evidence to recommend for or against selective serotonin reuptake inhibitors to improve motor outcomes in patients with or without depression.	Neither for nor against	Reviewed, New-replaced
		13.	There is insufficient evidence to recommend for or against aquatic therapy, as compared with land-based therapy, to improve mobility, balance, and activities of daily living.	Neither for nor against	Reviewed, New-added
		14.	There is insufficient evidence to recommend for or against biofeedback as an adjunct intervention to improve motor outcomes.	Neither for nor against	Reviewed, New-added
		15.	There is insufficient evidence to recommend for or against motor imagery to improve motor function.	Neither for nor against	Reviewed, New-added
		16.	There is insufficient evidence to recommend for or against acupuncture to improve motor function.	Neither for nor against	Reviewed, New-added
	Technology Assisted Physical Rehabilitation	17.	We suggest neuromuscular electrical stimulation to improve motor outcomes.	Weak for	Reviewed, New-replaced
		18.	There is insufficient evidence to recommend for or against robot-assisted therapy to improve upper or lower extremity motor outcomes.	Neither for nor against	Reviewed, New-added
		19.	There is insufficient evidence to recommend for or against virtual reality to improve balance or enhance gait recovery.	Neither for nor against	Reviewed, New-replaced
		20.	There is insufficient evidence to recommend for or against the use of virtual reality/serious gaming to improve upper extremity motor outcomes, activities of daily living, or quality of life.	Neither for nor against	Reviewed, New-added
		21.	There is insufficient evidence to recommend for or against contralaterally controlled functional electrical stimulation to improve upper extremity motor outcomes and activities of daily living.	Neither for nor against	Reviewed, New-added
		22.	There is insufficient evidence to recommend for or against non-invasive brain-computer interface to improve upper extremity motor outcomes and activities of daily living.	Neither for nor against	Reviewed, New-added
		23.	There is insufficient evidence to recommend for or against vagus nerve stimulation as an adjunct intervention for rehabilitation of acute and chronic motor deficits.	Neither for nor against	Reviewed, New-added

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Motor Therapy (cont.)	*Spasticity*	24.	We suggest botulinum toxin for patients with focal spasticity depending on patient characteristics and preferences.	Weak for	Reviewed, New-replaced
		25.	There is insufficient evidence to recommend for or against the use of acupuncture or dry needling for spasticity management.	Neither for nor against	Reviewed, New-added
		26.	There is insufficient evidence to recommend for or against whole body or localized muscle vibration for spasticity management.	Neither for nor against	Reviewed, New-added
		27.	There is insufficient evidence to recommend for or against extracorporeal shock wave therapy for spasticity management.	Neither for nor against	Reviewed, New-added
Dysphagia, Cognition, and Aphasia	*Dysphagia*	28.	We suggest chin tuck against resistance exercises for patients with dysphagia.	Weak for	Reviewed, New-replaced
		29.	We suggest respiratory muscle strength training for dysphagia in patients without a tracheostomy.	Weak for	Reviewed, New-replaced
		30.	There is insufficient evidence to recommend for or against tongue pressure resistance training for dysphagia.	Neither for nor against	Reviewed, New-replaced
		31.	There is insufficient evidence to recommend for or against neuromuscular electrical stimulation and pharyngeal electrical stimulation for dysphagia.	Neither for nor against	Reviewed, New-replaced
		32.	There is insufficient evidence to recommend for or against surface electromyography for dysphagia.	Neither for nor against	Reviewed, New-added
	Cognition	33.	There is insufficient evidence to recommend for or against the use of selective serotonin reuptake inhibitors to improve cognitive outcomes.	Neither for nor against	Reviewed, New-replaced
		34.	There is insufficient evidence to recommend for or against computer assisted cognitive rehabilitation to improve cognitive outcomes.	Neither for nor against	Reviewed, New-added
	Aphasia	35.	There is insufficient evidence to recommend for or against a specific intensity of language therapy for aphasia.	Neither for nor against	Reviewed, Amended
	Spatial Neglect Therapy	36.	There is insufficient evidence to recommend for or against hemifield eye patching in addition to traditional therapy to improve functional outcomes in patients with unilateral spatial neglect.	Neither for nor against	Reviewed, New-replaced
		37.	There is insufficient evidence to recommend for or against the use of prism adaptation therapy for patients with unilateral spatial neglect.	Neither for nor against	Reviewed, Amended
Mental Health	*Prevention of Depression*	38.	There is insufficient evidence to recommend for or against solution-focused psychological interventions (e.g., motivational interviewing, problem-solving therapy) to prevent the development of depression.	Neither for nor against	Reviewed, New-added
		39.	We suggest against the use of antidepressants for the prevention of post-stroke depression.	Weak against	Reviewed, New-replaced

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Mental Health (cont.)	*Prevention of Depression (cont.)*	40.	We suggest a selective serotonin reuptake inhibitor or a serotonin norepinephrine reuptake inhibitor for depression symptoms.	Weak for	Reviewed, Amended
		41.	We suggest psychotherapy (e.g., cognitive behavioral therapy) for depression following stroke.	Weak for	Reviewed, New-replaced
		42.	We suggest mindfulness-based therapies for treatment of depression following stroke.	Weak for	Reviewed, New-added
		43.	There is insufficient evidence to recommend for or against acupuncture, either alone or as an adjunct to pharmacotherapy, for depression following stroke.	Neither for nor against	Reviewed, New-added
Telehealth		44.	We suggest either face-to-face therapy or telerehabilitation, depending on patient characteristics and preferences.	Weak for	Reviewed, New-added
		45.	There is insufficient evidence to recommend for or against the use of telerehabilitation and technology-based interventions to improve stroke-related dysphagia or aphasia outcomes or both.	Neither for nor against	Reviewed, New-added
		46.	There is insufficient evidence to recommend for or against technology-based caregiver support/education interventions to improve caregiver quality of life.	Neither for nor against	Reviewed, New-added
Non-invasive Brain Stimulation		47.	There is insufficient evidence to recommend for or against non-invasive brain stimulation (e.g., repetitive transcranial magnetic stimulation, transcranial direct current stimulation, and continuous theta burst stimulation) for patients in stroke rehabilitation.	Neither for nor against	Reviewed, New-replaced

[a] For additional information, see Determining Recommendation Strength and Direction.

[b] For additional information, see Recommendation Categorization.

A. Transitions to Community

Recommendation

1. We suggest using case management services at time of discharge from the acute care hospital or post-acute care facility to improve activities of daily living and functional independence.
   (Weak for | Reviewed, New-added)

Discussion

In addition to medical and functional challenges resulting from stroke, many patients and their caregivers find significant challenges in negotiating the health care system to obtain the care they need. Case management is a health care process in which a professional assists a patient with planning, facilitation, care coordination, and advice to achieve the best possible health care and psychosocial outcomes while also encouraging cost effectiveness.(37) Evidence suggested that case management interventions improved activities of daily living (ADL) and independence in patients with

stroke. One SR examined eight studies (n=1,119) and showed that case management, compared with usual care, had a modest positive effect on ADLs (standardized mean difference [SMD]: 0.68; 95% confidence interval [CI]: 0.37–0.99; p<0.001), and a small positive effect on mental health (SMD: 0.26; 95% CI: 0.07–0.45; p=0.001), although the CIs for mental health outcomes were near zero. Case management did not demonstrate a positive impact on physical or social functioning.(38)

Patients shared similar preferences regarding case management. The patient focus group participants indicated that they particularly valued smooth transitions between various rehabilitation care settings and felt that case management assistance was critical to these transitions. They also noted that case management had a positive impact on their caregivers, allowing both patient and caregiver to focus on the stroke survivor's recovery rather than on allocating time to navigate complex medical systems, identify appropriate resources, and coordinate care among providers. In addition, the Work Group members noted positive experiences regarding case management and thought most providers generally value case management services. No potential harms were identified. Case management requires specially trained nurses or social workers and is widely available. Unfortunately, many settings might have too few case managers to provide the level of services needed in complex populations.

The Work Group systematically reviewed evidence related to this recommendation.(38) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including lack of blinding, allocation concealment concerns, and lack of clarity about the specific interventions.(38) The benefits of case management in improving ADLs and mental health concerns as well as decreasing perceived caregiver burden outweighed the potential harms; no potential harms were identified. Patient values and preferences were similar because patients, caregivers, and providers overwhelmingly value case management. Thus, the Work Group made the following recommendation: We suggest using case management services at time of discharge from the acute care hospital or post-acute care facility to improve activities of daily living and functional independence.

Recommendation

2. We suggest the following interventions for patients and their caregivers.
   - Behavioral health/psychosocial interventions to improve patient and caregiver depression
   - Psychoeducation to improve family function, patient functional independence, and quality of life

   (Weak for | Reviewed, New-added)

Discussion

Stroke can dramatically alter a person's life, along with the lives of the family members and caregivers. Caregivers are intimately involved in the daily functioning and rehabilitation of survivors of stroke. Therefore, the Work Group sought to offer guidance

to enhance caregiver health and ability to participate positively in patient recovery. Based on a systematic evidence review of the most recent literature, it appears psychoeducation, participation in behavioral/psychosocial interventions, or both offered some benefit to patients and their caregivers.

An SR by Zhou et al. (2022) included 5 RCTs (n=548) that examined psychoeducation and its effect on family functioning, as assessed by the Family Assessment Device.(39) The psychoeducation interventions varied but included 1) education/information on stroke care, 2) educational support/counseling, 3) skills training (e.g., patient care, problem solving, coping strategies), and 4) social resource use. The interventions were compared with usual care, which also varied and included 1) routine care, 2) no treatment, 3) waitlist, 4) family intervention telephone tracking, and 5) strength-oriented psychoeducational programming plus routine care. There was a small effect on improving family function (weighted mean difference [WMD]: -0.13; 95% CI: -0.24– -0.01; p<0.05) favoring psychoeducational intervention. A significant difference between groups remained at 1 month post-intervention (WMD: -0.12; 95% CI: -0.18– -0.05; p<0.05) and at more than 6 months post-intervention (WMD: -0.14; 95% CI: -0.24– -0.04; p<0.05). The studies also showed that psychoeducation programming had a very small positive effect on family function as well as dyad (i.e., patient-caregiver) family function (WMD: -0.14; 95% CI: -0.84– -0.32; p<0.05).(39)

Another SR by Mou et al. (2021) included 11 RCTs (n=3,347) that compared dyadic psychoeducational interventions with usual care.(40) Outcomes included scales assessing QoL and depression. The intervention consisted of a variety of formats, including 1) face-to-face sessions mixed with telephone calls, 2) only telephone calls, 3) only face-to-face sessions, 4) a checklist to identify patient/family problems and provide tailored support for illness management, 5) an information-based workbook/package to follow up and reinforce illness self-management, and 6) structured educational sessions with follow-up consultation. The duration of the dyadic psychoeducational interventions ranged from four days to 12 months. Usual care consisted of stroke care education; complication management; secondary prevention; outpatient follow-up; information packages about stroke events, consequences, and prevention; or any combination of the aforementioned support elements. Meta-analysis (MA) suggested that dyadic interventions had a long-term (>6 months), small, positive effect on patient QoL (SMD: 0.30; 95% CI: -0.53– -0.07; p=0.01).(40) At the end of the intervention, subgroup analyses showed that dyadic psychoeducational approaches initiated while in the hospital had an immediate, small, positive effect on patient functional independence (SMD: 0.40; 95% CI: 0.08–0.72; p=0.01).(36)

With regard to behavioral health/psychosocial wellbeing, an SR by Minshall et al. (2019) analyzed 31 RCTs (n=5,715) which looked at the effectiveness of psychosocial/behavioral interventions on depressive symptoms, anxiety symptoms, and QoL in survivors of stroke as well as their caregivers.(41) The psychosocial interventions contained a psychological (behavioral health) component and a social

component and were administered face-to-face, by telephone, or online. Some interventions included a psychoeducational component, as well. More specifically, psychological components included interventions such as cognitive/behavioral support, stress/coping management, problem solving, psychoeducation counseling, cognitive behavioral therapy, motivational interviewing (MI), and other similar supportive therapies. Social components included interventions such as family/social support, community resources, health care/service links, dyad support, and peer activities. The comparison group consisted of usual care (e.g., education, counseling/active listening, waitlist, stroke education). A variety of measures were used to assess patient and caregiver depression symptoms. Results indicated that psychosocial interventions had a small effect on reducing patient depressive symptoms (SMD: -0.36; 95% CI: -0.73–0.00; p=0.05) and caregiver depressive symptoms (SMD: -0.20; 95% CI: -0.40–0.00; p=0.05); however, the CIs were on the border of statistical significance.(41)

Another SR by Pucciarelli et al. (2020), which contained 16 RCTs (n=5,184), investigated dyadic educational interventions versus usual care after stroke.(42) Interventions were heterogeneous and included behavioral therapies, caregiver support, and case management as well as education. Outcomes included patient physical functioning, ADLs, patient and caregiver depression, and patient and caregiver QoL. Results varied, though small positive effects on patient physical functioning (SMD: 0.17; 95% CI: -0.00–0.35; p=0.05), caregiver depression (SMD: -0.19; 95% CI: -0.39–0.00; p=0.05), and patient QoL (SMD: 0.17; 95% CI: 0.03–0.31; p=0.01) were found. The CIs for the effects on patient physical functioning and caregiver depression bordered on no effect.

Some variation occurs in patient preferences regarding participation in behavioral or psychosocial interventions and the willingness to receive psychoeducation. The patient focus group noted the significant burdens placed on their caregivers and expressed interest in having clearly defined support services for caregivers. Although some patients and caregivers will welcome additional educational, social, and emotional supportive services, others might prefer to avoid in these types of interventions. Some patients and caregivers might already feel overburdened by an abundance of appointments as part of their rehabilitation process and might wish to spend no additional time. Other patients limit the extent to which their caregiver can participate in their rehabilitation process; some caregivers might be reluctant or might not desire to be more involved.

Other implications to consider are the significant staffing and time that the delivery of some interventions can require. Furthermore, some patients, caregivers, or both located in more rural environments might have difficulty obtaining such services, especially telehealth services, which require reliable internet or telephone access. Lastly, not all patients have caregivers engaged in their rehabilitation.

The Work Group acknowledges the small effect sizes for the interventions in the studies discussed above. However, this recommendation places increased weight on patient

values and preferences regarding caregiver services, as expressed by the patient focus group and based on the Work Group's experience serving patients with stroke and their caregivers. Given the prospect for improved outcomes, including reduced depressive symptoms and improved family function, functional independence, and QoL, the Work Group believes that most patients and their caregivers would choose to pursue these interventions.

The Work Group systematically reviewed evidence related to this recommendation.(39-42) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including concerns around allocation concealment, blinding of outcome assessments, deviation from intended interventions, outcome measurement, and selective reporting.(39-42) The benefits of behavioral health/psychosocial interventions to improve patient and caregiver depression and participation in psychoeducation to improve family function, patient functional independence, and QoL slightly outweighed the potential harms such as the time burden for participation in additional services or concerns related to stigma. Patient values and preferences varied somewhat because although some patients and caregivers might welcome additional behavioral/psychosocial and psychoeducational services, others might prefer to avoid them. Thus, the Work Group made the following recommendation: We suggest the following interventions for patients and their caregivers.

- Behavioral health/psychosocial interventions to improve patient and caregiver depression
- Psychoeducation to improve family function, patient functional independence, and quality of life

Recommendation

3. There is insufficient evidence to recommend for or against implementing transitional care rehabilitation interventions (e.g., home-based services after hospital discharge) or early supported discharge to improve activities of daily living or functional disability following stroke.
   (Neither for nor against | Reviewed, New-replaced)

Discussion

Transitional care interventions describe patient movement between care settings (e.g. home-based services, skilled nursing facilities, subacute rehabilitation) and early supported discharge (ESD) is a discharge planning strategy that connects inpatient care with home or community services, with input from the multidisciplinary team.(43)

An SR/MA of 20 studies (n=1,735) observing ESD and transitional care found no difference in ADLs, functional disability, mortality, or caregiver strain when compared with usual care.(44) Another SR/MA with 14 studies (n=8,783) evaluated interventions to support the transition to home, excluding ESD programs.(45) These "support

interventions" were heterogeneous in terms of provider type (e.g., nurse, multidisciplinary team, social worker, physician, motivational therapist), delivery format (e.g., in-person, telephone, letter, instant messaging, virtual), and content (e.g., education, surveillance, counseling, goal-setting, problem solving, peer learning). The support interventions led to improvements in QoL for up to three months as measured by the Short Form-36 Physical Component Score (MD: 1.3; 95% CI: 0.84–1.76; no p-value provided). There were also improvements in ADLs (as measured by the Barthel Index [BI]) at three months (MD: 7.87; 95% CI: 3.93–11.81; p<0.0001) and six months (MD: 2.91; 95% CI: 0.03–5.80; p=0.05). No harms were identified. However, within this SR there were serious concerns about risk of bias and imprecision due to deviations from intended interventions, missing outcome data, and selection of reported results.

Findings in the 2019 VA/DoD Stroke Rehabilitation CPG for implementing transitional care rehabilitation interventions (e.g., home-based services after hospital discharge) or early supported discharge were inconclusive. The systematic evidence review included an SR on ESD by Langhorne et al. (2017), which included 17 trials (n=2,422).(43) No statistically significant differences between groups were found for ADLs, QoL, or hospital readmissions. Additionally, two RCTs assessed whether inter-professional home care supported improved QoL, but no statistically significant between-group differences were identified in either study.(46, 47)

Some variation occurs in patient preferences regarding this treatment. The patient focus group members did not comment specifically on ESD or specific transitional care programs. However, they did express significant frustration with transitions between care settings (e.g., inpatient rehabilitation to home care) and in navigating health care systems. They specifically appreciated care coordination. However, some patients and caregivers might not prefer multiple services or services that occur in their homes. ESD or transitional care interventions can also require intensive use of resources and care coordination. High-quality services might be unavailable in some locations. Although evidence of benefit from either ESD or transition services is lacking, they seem unlikely to cause harm.

The Work Group systematically reviewed evidence related to this recommendation(44, 45) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(43, 46, 47) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including serious risk of bias and imprecision, as discussed above. The potential benefits of transitional care interventions in possibly improving ADLs, QoL, depression, and anxiety slightly outweighed the potential harms; no potential harms were identified. Patient values and preferences vary somewhat because some patients and caregivers might not want multiple services in their homes. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against implementing transitional care rehabilitation

interventions (e.g., home-based services after hospital discharge) or early supported discharge to improve activities of daily living or functional disability following stroke.

Recommendation

4. There is insufficient evidence to recommend for or against community participation interventions to improve community engagement for survivors of stroke.
   (Neither for nor against | Reviewed, New-added)

Discussion

Lee et al. (2019) performed an SR (n=1,554) to analyze the content and effectiveness of interventions purported to enhance community participation as compared with usual care, leisure-focused interventions, and no care.(48) Broadly defined, interventions focused on high-level social engagement. The interventions variously involved education, support, or practice related to social participation, social role management, political participation or civil engagement, leisure participation in a social setting, shared religious activities, education and learning pursuits, community mobility and transportation issues, and instrumental activities of daily living (IADL) such as communication management and shopping. Specific work or employment-focused interventions were excluded from the study as were interventions with a significant caregiver component.(48) Follow-up varied across the 14 included RCTs and was conducted between eight weeks and 12 months. The results showed no statistically significant between group differences in community participation.(48) The confidence in the quality of the evidence was very low due to issues with allocation concealment, high rates of attrition, and lack of participant blinding. Serious concerns because of imprecision were also present due to vague inclusion-exclusion criteria across studies with high heterogeneity in reported treatment interventions.

Large variation occurs in patient preferences regarding community participation. Lee et al. (2019) found a trend that this type of intervention might worsen depressive symptoms in some patients.(48) The patient focus group noted that transportation issues and caregiver burden could be taxing because of increased travel time to and from various community settings. Furthermore, resource use might be a limiting factor because implementing this type of intervention requires a considerable amount of time, training, and personnel. Certain subgroups, including those with aphasia or persistent motor deficits, might be unable to participate in these types of activities.

The Work Group systematically reviewed evidence related to this recommendation.(48) Therefore, it is categorized as *Reviewed, New added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had serious limitations, including risk of bias and imprecision, as described above.(48) The benefits of community participation in improving stroke survivor community engagement slightly outweighed the potential harm of risk for increased depression, which was small. Patient values and preferences varied largely because some higher-functioning patients

might prefer this type of intervention, although others might find little to no value in it. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against community participation interventions to improve community engagement for survivors of stroke.

B. Motor Therapy

a. General

Recommendation

5. We recommend task-specific practice (also known as task-oriented practice or repetitive task practice) to improve motor function, gait, posture, and activities of daily living.
   (Strong for | Reviewed, Not changed)

Discussion

This Work Group found no new data to review and agreed with the recommendation from the 2019 VA/DoD Stroke Rehabilitation CPG.

Task-specific practice involves practice of a whole task or pre-task movements for a whole limb or limb segment, such as grasp, grip, or movement in a trajectory, to facilitate mobility or ADLs. These movements can include upper and lower limb movements, balance activities in a sitting or standing position, transfers, and functional mobility (e.g., stairs, household ambulation). The approach typically includes application of motor learning principles in regard to feedback, practice schedules, task variation, and challenge of activity.(49) These interventions were labeled differently across publications as “task-specific practice,” “task-oriented practice,” and “repetitive task practice” but appeared to have similar intervention structure in that the task or the part or segment of the task was repeated multiple times during a single therapy session. The Work Group elected to use the term “task-specific practice” for this recommendation. Exact dosing parameters and use of the motor learning principles varied, but the key concept was the repetition of the task or component of the task within the same therapy session.

An SR by French et al. (2016) that was reviewed by the 2019 Stroke Rehabilitation CPG Work Group provided moderate quality evidence to support this recommendation.(49) It compiled 32 RCTs and one quasi-RCT (n=1,853) that compared repetitive task practice with standard/usual care. Trials of repetitive activity were required to involve complex, multi-joint, functional movement patterns rather than exercise of a single joint or muscle group oriented toward strengthening of an extremity. The duration of the training ranged from 2–20 weeks. Statistically significant improvements in ADLs were found for patients at various stages post stroke when they received task-specific practice compared with usual care. This finding was maintained beyond six months follow-up and was still noted in a few studies at the four-year follow-up. In addition, Richards et al. (2004) found that the efficacy of the task-oriented approach did not depend on rehabilitation technology.(50)

The 2010 VA/DoD Stroke Rehabilitation CPG review of the literature found moderate quality evidence regarding task-specific training.(50-59) This body of evidence included 9 separate RCTs that found positive results from techniques that included training dynamic sitting balance (n=12),(52) mobility (walking over ground and on treadmill (n=23),(51) agility and balance activities (n=61),(51) (n=30),(54) (n=68),(57) walking programs (n=91),(55) body weight support treadmill training (BWSTT) (n=80),(56) backward walking (n= 25),(58) and upper limb function.(54) The 2010 VA/DoD Stroke Rehabilitation CPG also reported high-quality evidence regarding ADL training. This evidence was included in the strength of this recommendation because the studies included repetition of whole/pre-task movements. An SR by Legg et al. (2006) found task-specific training to be superior to usual or no training of ADLs.(59) This SR included nine articles (8 of them RCTs)(n=994) comparing whole ADL and pre-task movements to promote ADL training versus usual or no training. This SR addressed areas of dressing, bathing, feeding, transfers, mobility (e.g., stairs), and home tasks such as meal preparation activities.

With task-specific training, the benefits appear to outweigh the harms. Significant gains were realized in many areas maintained for at least six months. A potential risk for falls was the main concern; however, risk for falls was no greater than for other therapy interventions. This intervention can be performed in any environment (e.g., hospital room, clinic, home, community settings). Caregivers and patients can be educated in how to carry out this intervention at home. This approach requires no additional equipment beyond what is routinely found in therapy clinics or home settings. This intervention tends to be more engaging because it can be tailored to the patient's preferences and individual goals. The patient focus group members stated that they wanted to have a treatment plan tailored to their individual needs, considering their comorbidities, patient-specific goals, values, and preferences. This approach exemplifies that desire. Those who are severely impaired might require increased staff or the use of technology to assist with the safe performance of task-specific practice.

The Work Group considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(49-59) Therefore, it is categorized as *Reviewed, Not changed*. The Work Group's confidence in the quality of evidence was moderate. The body of evidence had limitations because of poor reporting of risk of bias. Other considerations for this intervention include the risk versus benefits analysis. The Work Group identified the risk for falls but did not believe that the risk was significantly greater with this approach compared with other therapy techniques. In terms of patient values and preferences, patients generally favor this technique, because it is easily individualized to address their specific goals. One of the main messages from the focus group was that patient goals and preferences should be identified and incorporated into the individualized treatment plan. Thus, the Work Group made the following recommendation: We recommend task-specific practice (also known as task-oriented

practice or repetitive task practice) to improve motor function, gait, posture, and activities of daily living.

Recommendation

6. We suggest mirror therapy to improve motor outcomes and activities of daily living.
   (Weak for | Reviewed, New-replaced)

7. We suggest mirror therapy to improve unilateral spatial neglect.
   (Weak for | Reviewed, New-added)

Discussion

Unilateral spatial neglect (USN) refers to a condition where patients do not react to various environmental stimuli originating from the contralateral side of a brain lesion in the absence of other sensory or motor deficits.(60) USN occurs much more frequently with right-side brain lesions than with left-side lesions.(61) USN causes interference with the rehabilitation process because of the profound lack of awareness of the contralesional hemispace, which results in poor functional outcomes.(62) In mirror therapy, a mirror is placed vertically in front of the patient, and the patient is instructed to perform motor activities with the unaffected limb and view the image in the mirror. Simultaneously, the patient attempts to perform the same activities with the affected limb. It is theorized that the visual feedback to the brain harnesses neuroplasticity principles as the brain perceives the affected limb as the sound one.

Mirror Therapy for Motor Outcomes

The evidence for mirror therapy for motor outcomes was reviewed in the 2019 VA/DoD Stroke Rehabilitation CPG and included 2 small RCTs (n=40 and n=36), which did not suggest a benefit with mirror therapy for improving motor function.(63, 64) In the current systematic evidence review, Thieme et al. (2018) and Morkisch et al. (2019) performed SRs, including a total of 62 RCTs (n=1,982), comparing mirror therapy to no treatment, placebo, sham, or other treatment.(65, 66) Mirror therapy was accomplished with an actual mirror or a simultaneous video or virtual setup, three to seven times per week, 15–60 minutes per session, for two to eight weeks. At the end of treatment, mirror therapy provided statistically and clinically significant benefits for several motor outcomes, including motor function, motor impairment, and ADLs. A wide variety of outcome measures were used for motor function and motor impairment, including, but not limited to, Fugl-Meyer Assessment (FMA), Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), and Berg Balance Scale (BBS). In the few RCTs that did include follow-up after six months, motor impairment was improved in the mirror therapy group, though the motor function outcome was no different between groups. These long-term follow-up sample sizes were much smaller (n=88 and n=109) compared with post-intervention sample sizes (n=1,173 and n=1,292).(65, 66) A subgroup analysis by Morkisch et al. (2019) found a trend toward larger positive effect sizes for studies using

large mirrors, studies that used unilateral movement execution versus bilateral movement execution, and studies that used exercises without objects versus exercises with objects.(66) However, none of the subgroup differences reached statistical significance. The included RCTs were considered fair quality because of several studies with incomplete outcome reporting (attrition bias) and several not reporting concealment of allocation.

Mirror Therapy for Unilateral Spatial Neglect

The evidence base for this recommendation included one SR by Zhang et al. (2022) that evaluated four RCTs (n=214).(62) There was high heterogeneity across the studies, but two studies(67, 68) used sham mirror therapy for the control condition, while one study used routine rehabilitation.(69) The fourth study used mirror therapy combined with scalp acupuncture versus scalp acupuncture alone.(70) The intensity of the intervention provided differed, from a total of fewer than 7 hours over four weeks to more than 24 hours over six weeks of therapy. The SR revealed a large effect on ADL performance (SMD: 2.09; 95% CI: 0.63–3.56; p=0.005) at the end of treatment. No adverse effects were reported in the trials within this SR.(62)

Some variation occurs in patient preferences regarding this treatment. Some patients find mirror therapy frustrating and might lose interest because of the lack of immediate effect on the paretic limb. Further, therapy staff tend to prioritize ADL treatments over mirror therapy because the more immediate goal of functional independence to speed discharge to the community seems paramount in an acute inpatient rehabilitation setting. In addition, mirror therapy requires a significant time investment on the part of the therapist for cognitively impaired patients, while cognitively intact patients can do mirror therapy asynchronously at home after initial instruction. Typically, 1 hour of mirror therapy per day is expected. The equipment needed to perform mirror therapy is inexpensive and widely available.

The Work Group systematically reviewed evidence related to these recommendations(62, 65, 66) and considered the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(63, 64) Therefore, these are categorized as *Reviewed, New-replaced* (for motor outcomes) and *Reviewed, New-added* (for USN). The Work Group's confidence in the quality of evidence was very low. The body of evidence had limitations including confounders in the analysis, such as a lack of double-blinding (although double-blinding is impossible while using mirror therapy), unclear risk for blinding of outcome assessors, and unclear allocation concealment procedures. The benefits of mirror therapy in improving motor outcomes and ADL performance slightly outweighed the potential harms, which were unidentified. Patient values and preferences vary because some patients might become frustrated with the lack of immediate effect. Thus, the Work Group made the following recommendations.

- We suggest mirror therapy to improve motor outcomes and activities of daily living.

- We suggest mirror therapy to improve unilateral spatial neglect.

Recommendation

8. There is insufficient evidence to recommend for or against body-weight support treadmill training to improve motor outcomes.
   (Neither for nor against | Reviewed, New-replaced)

Discussion

Body-weight support treadmill training is a task-specific technique for improving gait. Using a body harness, the patient is partially suspended from the ceiling or a frame to reduce (offload) the patient's relative weight and provide postural support while the patient is walking on a treadmill. The amount of offloading can gradually be decreased as the patient's control of posture and gait improves. Study results examining this intervention have been mixed. The 2019 VA/DoD Stroke Rehabilitation CPG evidence included two SRs.(71, 72) A Cochrane review by Mehrholz et al. (2017) found that stroke patients (n=3,105) who received treadmill training (TT), with or without body weight support, were not more likely to improve their ability to walk independently when compared with a variety of other rehabilitation interventions, no intervention, or sham intervention.(71) However, an SR by Ada et al. (2010) (n=549) demonstrated that BWSTT resulted in more formerly non-ambulatory patients with stroke achieving independent walking at four weeks and six months post stroke, and this difference was statistically significant.(72)

For the current systematic evidence review, Lyu et al. (2023) performed a network MA of 61 RCTs (n=2,328) examining a variety of gait interventions, including TT, BWSTT, VR, gait training, robotic-assisted gait training, overground walking training, and conventional gait training compared with usual care, sham intervention, or no exercise intervention.(73) Findings were mixed, with improvements in dynamic steady-state balance and balance test batteries with BWSTT or TT, but no difference was found for static steady-state balance or proactive balance. The authors did not specifically examine other motor outcomes, such as walking independence or walking speed. Hsu et al. (2020) performed an MA of 23 RCTs (n=1,452) comparing BWSTT to conventional overground training (COT).(74) No significant differences between the groups were found at the end of the intervention or end of follow-up for most of the outcomes, including mobility capacity, endurance/fitness, balance, and ADLs. Additionally, COT was slightly favored over BWSTT for the outcome of motor impairment at the end of the intervention, and COT was equivalent to BWSTT for the outcome of walking speed at the end of the follow-up. A subgroup analysis of non-ambulatory versus ambulatory patients, also found no significant differences in outcomes between the intervention groups.

Some variation occurs in patient preferences regarding this intervention. Treadmill training with body weight support might cause anxiety, skin abrasion or breakdown, interference with feeding tubes, and discomfort related to the harness. On the other hand, patients often like being upright and walking, regardless of the level of support

required. Among therapists, there is variation with respect to comfort level, skill, and experience with this intervention. In addition, BWSTT can be costly upfront, depending on the specific equipment used.

The Work Group systematically reviewed evidence related to this recommendation(73, 74) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(71, 72) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including inadequate randomization, allocation concealment issues, deviation from intended interventions, outcome assessor blinding issues, outcome measurement bias, missing outcome data, reporting bias, and attrition bias. The benefits were generally balanced with the potential harms, which are related to skin integrity and interference with feeding tubes. Patient values and preferences varied because of potential discomfort and anxiety, specifically with BSWTT. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against body-weight support treadmill training to improve motor outcomes.

Recommendation

9. We suggest rhythmic auditory stimulation as an adjunct intervention to improve motor outcomes.
   (Weak for | Reviewed, New-replaced)

Discussion

The 2019 VA/DoD Stroke Rehabilitation CPG suggested the use of rhythmic auditory cueing/stimulation (RAS) during gait training to help coordinate movement with timing, stimulate and incorporate overlapping brain areas, and improve walking speed. Rhythmic auditory stimulation uses an external rhythm or music to promote improvement in gait or other rhythmic movements. This therapeutic modality has been widely used in patients with stroke. The Work Group for the 2019 VA/DoD Stroke Rehabilitation CPG systematically reviewed the evidence for this intervention, and there was no new literature identified at that time that met the search criteria. Therefore, this recommendation was based on studies included in the 2010 VA/DoD Stroke Rehabilitation CPG evidence review.(75-78) Most of the included studies were small RCTs (n=20–78), with all but one demonstrating benefit in gait outcomes, albeit with low quality of evidence.

The current systematic evidence review included one SR of 22 RCTs (n=742) by Wang et al. (2022) comparing RAS plus control interventions with control interventions alone.(79) The RAS therapy group received the intervention twice per week up to twice daily, 10–60 minutes per session, for 3–12 weeks total. The control interventions were heterogeneous and included pharmacotherapies, traditional rehabilitation interventions, and treadmill training. RAS in addition to control therapies demonstrated improvement in step cadence, velocity, FMA, BBS, and overall balance index, but the control therapies varied as stated above. No long-term follow-up data were reported.

Consistent with the 2010 VA/DoD Stroke Rehabilitation CPG systematic evidence review, the included RCTs also generally had small sample sizes. The SR authors felt that future studies should use larger sample sizes with more rigorous designs to help form stronger conclusions about the benefits of RAS in patients with stroke.

Patient values and preferences regarding this intervention appear to be similar. This intervention is low-cost, easy to use, and the equipment is easily accessible. Patient factors such as hearing impairment and cognitive impairment would decrease the effectiveness of this intervention.

The Work Group systematically reviewed new evidence related to this recommendation(79) and considered the assessment of the evidence carried forward from the 2010 VA/DoD Stroke Rehabilitation CPG.(75-78) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had limitations, including unclear allocation concealment, unclear blinding of outcome assessors, and significant variation in control interventions. The benefits slightly outweigh the potential harms/burdens, which do not appear to be any greater than with conventional therapies. Patient values and preferences vary somewhat. Thus, the Work Group made the following recommendation: We suggest rhythmic auditory stimulation as an adjunct intervention to improve motor outcomes.

Recommendation

10. There is insufficient evidence to recommend for or against the use of high intensity interval training over moderate intensity continuous training to enhance gait recovery.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Cardiovascular (CV) exercise is recommended for both healthy adults as well as adults with chronic conditions or disabilities by the Centers for Disease Control and Prevention (CDC) and the Office of Disease Prevention and Health Promotion (ODPHP) within the U.S. Department of Health and Human Services.(80, 81) Guidance for dose and intensity is as follows: It is recommended that adults do at least 150 minutes–300 minutes per week of moderate-intensity aerobic physical activity, 75 minutes–150 minutes per week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic physical activity.

In the 2019 VA/DoD Stroke Rehabilitation CPG, one Cochrane SR provided guidance for physical fitness training for patients with stroke.(82) The effects of CV exercise on gait speed (both maximum and preferred), endurance, and level of functional ambulation were statistically significant when compared with resistance training as measured by the outcome measures of maximum walking speed (mean difference [MD]: 7.66 meters/minute; 95% CI: 3.65–1.68; p=0.0002), preferred walking speed

(MD: 4.47 meters/minute; 95% CI: 2.07–6.87; p=0.0003), 6-minute walk test (6MWT) (MD: 33.41 meters/6 minutes; 95% CI: 19.04–47.78; p=0.00001), and functional ambulation categories (MD: 0.53; 95% CI: 0.21–0.85; p=0.001). This information led the 2019 CPG Work Group to recommend CV exercise for the population with stroke.

The recommended guidance for CV exercise for patients with disabilities from CDC and ODPHP is considered standard of care for stroke rehabilitation. Recently, high-intensity interval training (HIIT) has been prevalent in the field. High-intensity interval training is a subtype of aerobic training that alternates periods of high intensity training (near-maximal or all-out effort) with recovery periods of lower intensity training or rest. Because of the shift toward high-intensity aerobic physical activity over moderate-intensity aerobic physical activity, the work group sought evidence to support this trend.

The 2024 VA/DoD Stroke Rehabilitation CPG systematic evidence review included two articles pertaining to HIIT. An SR by Amanzonwe et al. (2023) included 28 trials (n=1,571) evaluating the effects of aerobic training (AT) and resistance training (RT) on balance, walking, and QoL.(83) Only one study in this review evaluated effects on acute or subacute stroke; the remaining studies evaluated subjects with chronic stroke. Both AT and RT did not improve balance outcomes. AT was most effective in improving walking capacity as measured by the 6MWT (SMD: 0.37; 95% CI: 0.02–0.71; p=0.04) in comparison with RT. This finding is similar to the Cochrane SR(82) in the 2019 VA/DoD Stroke Rehabilitation CPG evidence base. Further subgroup analysis (n=426 for high dosage/n=87 for low to moderate dosage) found that a higher dosage of ≥60% heart rate reserve (HRR), rating of perceived exertion (RPE) ≥14/20 or ≥120 min/week demonstrated significantly greater effects (SMD: 0.58; 95% CI: 0.12–1.04; p=0.01) than lower dosages.

An RCT by Boyne et al. (2023) (n=55) investigated different training durations (4, 8, and 12 weeks) of HIIT versus moderate-intensity aerobic training (MAT).(84) Fifty-five participants between 40 and 80 years of age with a single stroke diagnosis that had occurred within six months to 5 years and who were able to walk at least 10 meters with or without a device at a walking speed of 1.0 m/s or less with no continuous physical assistance were enrolled in the study. Both groups performed a 3-minute warm-up of overground walking, three bouts of the MAT/HIIT protocol (10 minutes, 20 minutes, 10 minutes), and a 2-minute cooldown. The HIIT group protocol was repeated at 30-second intervals of walking at speeds targeting a mean aerobic intensity of >60% of the HRR alternating with 30- to 60-second passive recovery periods (seated or standing rest breaks). The MAT group protocol was a continuous walking format maintaining an initial target heart rate of 40% ± 5% of the HRR, progressing by 5% of the HRR every 2 weeks up to 60% of the HRR as tolerated. The HIIT group involved higher training speeds, heart rate, and RPE compared with the MAT group. However, the MAT group had a significantly higher step count. The outcome measures consisted of the 6MWT and 10-meter walk test. After 4 weeks of training, there was no significant difference between the groups on the 6MWT. After 8 weeks of training, the HIIT group showed a

statistically significant improvement on the 6MWT (MD: 29 meters; 95% CI: 5–54; p=0.02), although this result did not meet the minimally clinically important difference (MCID). After 12 weeks of training, the HIIT group did demonstrate an improvement in the 6MWT that was both statistically and clinically significant (MD: 44 meters; 95% CI: 14–74; p=0.005) when compared with the MAT group. There were statistically significant differences on the10-meter walk test at 4- (MD: 0.21; 95% CI: 0.13–0.29; p<0.0001), 8- (MD: 0.15; 95% CI: 0.05–0.25; p=0.003), and 12-week (MD: 0.20; 95% CI: 0.08–0.32; p=0.002) timeframes for the HIIT protocol. No follow-up testing assessed sustained effects. No serious adverse events and no significant differences between the groups for adverse events were found.

Some variation occurs in patient preferences regarding HIIT because obtaining high intensity thresholds can be difficult. The high intensity threshold should be further defined because 60% HRR might trend toward more moderate intensity versus near maximal effort. The overall structure of intervals allows for rest periods, which patients might like, regardless of intensity level. No harm or adverse events, such as atrial fibrillation or ventricular arrhythmias, were noted in either the HIIT or MAT groups. However, providers should consider preexisting comorbidities before recommending CV exercise interventions at any intensity. It is also important to complete screening for aerobic exercise tolerance and to monitor patient tolerance to the aerobic exercise prescription. When setting up independent programs for patients, considerations should be made for patient preferences, access to exercise facilities and equipment, neighborhood setting/safety, and local climate.

The Work Group systematically reviewed evidence related to this recommendation (83, 84) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(82) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence also had some limitations, including small sample size, incomplete outcome data, and differing sensitivity assumptions. Patient values and preferences will vary and trend toward moderate intensities over higher intensities based on the Work Group's experience, although adding intervals might improve patient tolerance of performing maximal all-out effort. The majority of the population included in these trials were in the chronic phase post stroke. Further research should focus on acute and subacute populations. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the use of high intensity interval training over moderate intensity continuous training to enhance gait recovery.

Recommendation

11. There is insufficient evidence to recommend for or against constraint-induced movement therapy to improve upper extremity motor outcomes for individuals with some movement in the paretic limb.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Constraint-induced movement therapy (CIMT) and modified constraint-induced movement therapy (mCIMT) are multicomponent interventions designed to help patients overcome learned non-use of a paretic upper extremity and increase motor function. This intervention is appropriate only for those with some movement in their paretic limb (at least 10 degrees of active extension in two fingers, the thumb, and the wrist). The 2019 VA/DoD Stroke Rehabilitation CPG defined CIMT as a neurorehabilitation technique consisting of three components: 1) immobilization of the non-paretic upper extremity to prevent its use in daily activities, 2) task-specific practice of the paretic upper extremity with frequent repetitions for about six hours per day, and 3) instruction in transfer of skills from the clinical setting to the home environment in performance of ADLs and IADLs. The main difference between CIMT and mCIMT is the number of hours of therapy per day, with CIMT requiring more than three hours per day, and mCIMT requiring three hours or fewer of therapy per day.(85)

The current systematic evidence review included one meta-analysis along with one network meta-analysis (NMA).(86, 87) Zhang et al. (2023) identified 44 RCTs (n=2,083) with the Motor Activity Log (MAL) as the primary outcome.(86) The results showed that CIMT combined with conventional rehabilitation, compared with conventional rehabilitation alone, was statistically superior in improving both the amount (MAL-Amount of Use Measure [MAL-AOU], MD: 0.46; 95% CI: 0.25–0.67) and quality of movement (MAL-Quality of Movement Measure [MAL-QOM], MD: 0.51; 95% CI: 0.28–0.73). This difference was maintained at 3 months but not at 4–12 months follow-up. However, these results did not reach the threshold for clinical significance. The FMA was analyzed as a secondary outcome. For this metric, the MCID is 10.(88) Again, statistically but not clinically significant differences between the intervention and control groups were found (MD: 2.42; 95% CI: 1.05–3.79).

An NMA by Saikaley et al. (2022) (n=6,781) compared CIMT and mCIMT with conventional rehabilitation.(87) CIMT and mCIMT were found to be relatively more effective than conventional rehabilitation for improvement in upper limb function as measured by the FMA (MD: 6.7; 95% CI: 4.3–9). Again, this finding met statistical significance but did not achieve the MCID.

Some variation occurs in patient preferences regarding this treatment. CIMT and mCIMT intervention can be burdensome to patients because the duration of treatment might average from three to six hours per day for two weeks or more. High-intensity CIMT might cause anxiety for patients, and restricting the non-paretic side for a long duration might make the rehabilitation experience less satisfactory for the patient. On the other hand, patients with a paretic dominant upper extremity might have a strong internal motivation to comply with the intensity of this intervention. Also, for the motivated patient, there is the potential for transfer of learned motor functions to the home setting, though RCTs have not documented such improvement. Of note, CIMT and mCIMT are appropriate for only those with some movement in their paretic limb.

This intervention is time intensive for providers, and the ability to provide adequate staffing might be of concern. Potential harms of this intervention could be that the constrained limb cannot be used for automatic postural reactions in the case of loss of balance and, therefore, could lead to increased risk of falls.

The Work Group systematically reviewed evidence related to this recommendation(86, 87) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(85) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including inconsistency in results, poor allocation concealment, incomplete data, and risk of bias.(86, 87) The potential benefits of CIMT and mCIMT in improving the amount and quality of arm movement slightly outweighed the potential harms of potential patient frustration or anxiety. Patient values and preferences varied because CIMT and mCIMT are time- and resource-intensive interventions with unclear benefits. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against constraint-induced movement therapy to improve upper extremity motor outcomes for individuals with some movement in the paretic limb.

Recommendation

12. There is insufficient evidence to recommend for or against selective serotonin reuptake inhibitors to improve motor outcomes in patients with or without depression.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

An SR by Su et al. (2021) examined the effect of three selective serotonin reuptake inhibitors (SSRI) (citalopram, escitalopram, and fluoxetine) on motor outcomes in non-depressed patients with subacute stroke.(89) Treatment was initiated within three weeks of stroke in all included studies. Selective serotonin reuptake inhibitors provided a significant benefit versus placebo in improving FMA scores with an average treatment difference of 17.63 points. However, changes in the modified Rankin Scale (mRS) and BI scores did not show a statistically significant improvement for the SSRI treatment groups. Another SR by Wu et al. (2023) confirmed the same trend in outcomes but included both individuals with and without depression.(90) Of note, overall patient numbers in both SRs were much lower in the FMA outcome (n=263(89) and n=287(90)) than for the mRS outcome (n=6,778(89) and n=5,431(90)) or the BI outcome (n=435(89) and n=814(90)). The result that no greater improvement in mRS and BI scores was found when more patients were evaluated might weaken the confidence that SSRIs are effective for improving motor outcomes.

In terms of time to effect of SSRIs on FMA improvement, only two of the RCTs included in Su et al.(2021) took interim evaluations of the FMA score.(89) Both studies compared treatment with fluoxetine versus placebo and were 90 days in total duration. Both

demonstrated some improvement in the interim analysis, one at day 30 and the other at day 45, but the differences between groups were not statistically significant until day 90.(91, 92) Thus, the evidence available indicates that if a significant benefit in motor impairment with SSRIs occurs, it likely takes at least three months for most patients to experience this benefit. That said, the statistical significance of individual studies might not necessarily be clinically significant given the above overall evidence from both SRs. All studies were relatively short (three to six months); therefore, assessing the durability of benefit in FMA scores is difficult.

Maintenance doses used were relatively low (fluoxetine 20 mg/day, citalopram 20 mg/day, and escitalopram 10 mg/day) and were within safe dosing limits for adults older than 60. Consistent with any medication, there are risks of side effects and drug interactions. Wu and Qin (2023) did not report significant differences in adverse events in the intervention group versus the placebo group.(90) Su et al. (2021) reported the incidence of hyponatremia (odds ratio [OR]: 2.01), seizure (OR: 1.46), and fracture (OR: 2.34) as higher in the fluoxetine group than placebo.(89) Although not reported in the SRs included in this recommendation, another rare but serious adverse effect of SSRIs is bleeding when used in combination with antithrombotic therapy. Assessment of risk should be made, particularly if the patient is on antiplatelet or anticoagulant therapy or both.(93) More common (at least 10% reported incidence) but less serious side effects of SSRIs include insomnia (most prominent with fluoxetine), anxiety (most prominent with fluoxetine), headache, diarrhea, nausea, anorexia, and dry mouth.(94-96) Thus, assessing the baseline risk of potential adverse events versus the potential benefits an SSRI might provide is important for providers considering the initiation of an SSRI in a post-stroke patient. Additional information on SSRIs is included in the 2022 VA/DoD CPG for Management of Major Depressive Disorder.[f]

Some variation occurs in patient preferences regarding this treatment. Some patients might already be prescribed an SSRI or be candidates for initiation of an antidepressant (AD). These patients might be able to obtain two benefits from one medication. On the other hand, some patients might wish to avoid taking a medication generally classified as an AD because of the stigma surrounding mental health. The Work Group also noted that patients post stroke are often started on multiple new medications, and they might not prefer adding another oral medication. SSRIs are prescription medications but are easily accessible because many health care providers are familiar with their use.

The Work Group systematically reviewed evidence related to this recommendation.(89, 90) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including small sample size and short duration. Some studies did not report whether patients were allowed to use other treatments for motor rehabilitation, although others specified that patients could be in a physical rehabilitation program or receive

[f] See: https://www.healthquality.va.gov/guidelines/MH/mdd/VADoDMDDCPGFinal508.pdf

"standard of care." As mentioned above, the only outcome that showed statistically significant benefit (FMA), was studied in a small number of patients. The mRS and BI outcomes on both SRs were studied in considerably larger numbers of patients but showed no difference between groups. This result led to an insufficient evidence conclusion.(89, 90) Overall, the potential benefits of SSRIs to improve motor outcomes were balanced with the potential harms, which were low in incidence. Patient values and preferences varied. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against selective serotonin reuptake inhibitors to improve motor outcomes in patients with or without depression.

Recommendation

13. There is insufficient evidence to recommend for or against aquatic therapy, as compared with land-based therapy, to improve mobility, balance, and activities of daily living.
    (Neither for nor against | Reviewed, New-added)

Discussion

The evidence base for this recommendation included a single SR that demonstrated mixed results for the use of aquatic therapy for improvement of motor outcomes.(97) The SR included 21 RCTs of mostly poor quality (n=961), with methodological flaws, including lack of concealed allocation and outcome assessor blinding, high attrition, and no intention-to-treat (ITT) analysis. They compared aquatic therapy with no intervention or land-based therapy. Diverse forms of water-based therapy were provided, including aquatic treadmill walking and established concepts of aquatic therapy such as Halliwick, Ai Chi, Watsu, or Bad Ragaz Ring methods. Most of these were combined with additional water-based gait or balance exercises, and all remaining trials applied mainly walking or balance-based exercises or both in a pool. The control intervention included land-based walking and balance exercises in most studies, with a small number of studies using over-ground treadmill walking, ergometer training, neuromuscular facilitation techniques, or functional motor training of the upper limb. The subjects, who were between 30 days and 3.6 years after their stroke, participated in 6–40 sessions of aquatic therapy, lasting 20–60 minutes each. The duration of treatment was unclear, and only the number of treatment sessions was reported. At the end of treatment, results were mixed, with improvement in gait and balance motor outcomes but no difference between groups for muscular function and strength of lower limbs or ADL independence. No follow-up was reported after the treatment ended.

Some variation occurs in patient preferences regarding aquatic therapy. Although patients frequently request and enjoy this therapy, it might be less available and wait times to attend can be long. As a result, practitioners must be selective about their referrals. Some patients might find aquatic therapy challenging, though it can be tailored to meet each patient's specific needs and tolerance level. Other patient subgroup

considerations, including incontinence and feeding tubes, might interfere with the patient's ability to participate in this therapy.

The Work Group systematically reviewed evidence related to this recommendation.(97) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had limitations, as described above. The benefits of aquatic therapy were balanced with the potential harms, such as slipping, falling, or drowning, which might be minimized with appropriate supervision. Patient values and preferences varied somewhat because some patients might enjoy this therapy, although others might find it overly challenging. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against aquatic therapy, as compared with land-based therapy, to improve mobility, balance, and activities of daily living.

Recommendation

14. There is insufficient evidence to recommend for or against biofeedback as an adjunct intervention to improve motor outcomes.
    (Neither for nor against | Reviewed, New-added)

Discussion

Biofeedback is a rehabilitation tool using biomechanical and physiological variables to generate visual, auditory, or tactile feedback or any combination of the aforementioned to modulate motor function and improve motor learning.(98, 99) Two SRs included in the systematic evidence review demonstrated mixed results for the use of biofeedback to improve motor outcomes.(98, 99) Bonini-Rocha et al. (2022) conducted an SR, including nine RCTs (n=323), examining biofeedback plus conventional therapy compared with conventional therapy alone.(98) The studies employed the following types of biofeedback: electromyography (EMG)/visual/auditory, EMG/visual, visual, auditory, and neurofeedback/visual, for 1–5 sessions per week, 20–60 minutes per session, over 2–48 weeks. Biofeedback resulted in statistically significant improvements in the ARAT and FMA, but these MDs were small and did not appear to be clinically significant. There was no difference between groups in the WMFT outcome. Most studies lacked blinding, allocation concealment, and ITT analysis, but attrition was low.

Bowman et al. (2021) conducted an SR including four RCTs (n=115) comparing biofeedback plus conventional therapy to conventional therapy alone for gait impairment in patients with stroke.(99) Many different wearable devices were used, with biomechanical sensors (inertial measurement units and/or pressure, electro goniometer) and physiological sensors (EMG, electroencephalography [EEG]) placed on various locations of the body. Patients completed 10–30 sessions, lasting 20–90 minutes each, over 3–6 weeks. The results showed no difference in gait outcomes between the two groups. The quality of the RCTs in this SR was poor because most had unclear risk of bias in allocation concealment, blinding of participants and personnel, blinding of outcome

assessment, incomplete outcome data, and selective reporting. They also lacked adequate randomization procedures. No long-term follow-up was reported.

There is some variation in patient preferences regarding this intervention. Some patients might embrace the use of biofeedback, which is generally safe; however, it requires specialized training and equipment that might be unavailable in many health care facilities.

The Work Group systematically reviewed evidence related to this recommendation.(98, 99) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had limitations, as described above. The benefits of biofeedback for improvement in motor outcomes were generally balanced with the potential harms; no potential harms were identified. Patient values and preferences varied somewhat because some patients might welcome the use of technology to augment their rehabilitation, although others might not. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against biofeedback as an adjunct intervention to improve motor outcomes.

Recommendation

15. There is insufficient evidence to recommend for or against motor imagery to improve motor function.
    (Neither for nor against | Reviewed, New-added)

Discussion

Motor imagery is a cognitive process in which the patient imagines the execution of a movement, without physically performing the movement. The current systematic evidence review included two SRs comparing motor imagery plus other interventions to conventional therapies.(100, 101) An SR by Monteiro et al. (2021) included 10 RCTs (n=278) comparing motor imagery in association with other interventions, including VR or conventional rehabilitation versus VR, conventional rehabilitation alone, or both. The RCTs were considered fair quality. Patients received treatment two to five times per week, for 30–180 minutes per session, for 3–10 weeks. They found no difference in gait speed or FMA scores between groups. A Cochrane SR by Silva et al. (2020) included 21 RCTs (n=762) comparing motor imagery alone or associated with other interventions, including action observation, physical activity, or functional gait training versus physical practice, mirror therapy, muscle relaxation, neuromuscular electrical stimulation (NMES), or drug treatment.(100, 101) A majority of the RCTs were poor quality and at high risk of bias because of issues with randomization, allocation concealment, lack of blinding of outcome assessors, or any combination of the aforementioned. Patients in the motor imagery group received treatment two to six times per week, 30–60 minutes per session, for a total of 2–8 weeks. Silva et al. (2020) found a statistically significant improvement in walking speed but no difference in motor function or functional mobility.(100, 101) Only a few studies in this SR assessed

outcomes at long-term follow-up from 2–18 weeks post-treatment, but the authors were unable to pool the data regarding these outcomes. In reviewing the SRs and their included RCTs for motor imagery, it appears the terms “mental practice” and “motor imagery” are often used interchangeably.

Separate from the KQ 1 evidence base, there was a Cochrane SR by Barclay et al. (2020) that included 25 RCTs (n=676) comparing mental practice plus conventional therapies with conventional therapies alone.(102) This SR was captured in the evidence base for KQ 11 regarding sensory rehabilitation interventions to improve sensory or functional outcomes or both. In the SR by Barclay et al. (2020), no difference in ADLs was found at the end of treatment.(102) However, most of the RCTs were of poor quality with a high risk of bias because of inadequate or unclear randomization, allocation concealment, and blinding of participants or personnel.

Some variation occurs in patient preferences regarding this intervention. Motor imagery might be an appealing intervention for some patients because it might be less physically demanding for them. It might also be an option for patients with minimal other therapy options, such as those with the inability to move the affected limb. Cognitive deficits might limit the ability of some patients to participate. This intervention is low-cost and relatively easy for patients to complete independently at home after education is provided.

The Work Group systematically reviewed evidence related to this recommendation.(100-102) Therefore, it is categorized as *Reviewed, New-added*. The Work Group’s confidence in the quality of the evidence was very low. The body of evidence had limitations, including issues with randomization, allocation concealment, and lack of blinding of outcome assessors. The benefits of motor imagery were balanced with the potential harms, which were unidentified. Patient values and preferences varied somewhat because some patients might prefer therapy options that are less physically strenuous and that can be performed at home, although others might not. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against motor imagery to improve motor function.

Recommendation

16. There is insufficient evidence to recommend for or against acupuncture to improve motor function.
    (Neither for nor against | Reviewed, New-added)

Discussion

Two SRs in the systematic evidence review regarding the use of acupuncture to improve motor outcomes demonstrated statistically significant benefits in the FMA, BI, and modified Barthel Index (mBI).(103, 104) Tu et al. (2022) included 27 RCTs (n=1,293) comparing various methods of acupuncture to Western medicine or rehabilitation in an Asian population. Western medicine or rehabilitation was not described in greater detail.(103, 104) Zhuo et al. (2021) included 38 RCTs (n=3,836)

comparing various methods of acupuncture to various control interventions, including surgery, drugs, rehabilitation, and symptomatic or supportive measures or both in a mostly Asian population at different stages post stroke.(103, 104) The modes of acupuncture in these SRs included scalp acupuncture, hand acupuncture, hand-foot acupuncture, tongue acupuncture, auricular acupuncture, electro-acupuncture, warm acupuncture, and nerve trunk stimulation therapy. These SRs included poor-quality RCTs that had significant flaws in methodology, including inadequate randomization methods, lack of reporting on allocation concealment and blinding, lack of double-blinding, selective outcome reporting, and incomplete outcome data.

Some variation occurs in patient preferences regarding acupuncture. Some patients might fear needles, blood, or both and might have differing preferences regarding non-traditional therapies. Acupuncture requires trained practitioners, who are less available in many health care facilities. Acupuncture is widely practiced and accepted in China, so there might be a confounding cultural expectation of benefit in these studies, which makes the results difficult to generalize to a U.S. population. Additionally, there is a wide variety of acupuncture types and techniques, and access to all of these would likely be limited.

The Work Group systematically reviewed evidence related to this recommendation.(103, 104) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had many limitations, as described above. The benefits of improved motor outcomes were balanced with the potential harms associated with a needle procedure (bleeding, bruising, infection). Patient values and preferences varied somewhat, given differing preferences regarding non-traditional therapies. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against acupuncture to improve motor function.

b. Technology Assisted Physical Rehabilitation

Recommendation

17. We suggest neuromuscular electrical stimulation to improve motor outcomes. **(Weak for | Reviewed, New-replaced)**

Discussion

The 2019 VA/DoD Stroke Rehabilitation CPG suggested the use of functional electrical stimulation (FES), NMES, or transcutaneous electrical nerve stimulation (TENS) for improvement in both upper and lower extremity motor outcomes, based on evidence from one SR and seven RCTs.(105-112) These modes of electrical stimulation are used in rehabilitation to strengthen and reeducate muscles or muscle groups. Despite the heterogeneity in trial protocols, electrical stimulation showed statistically superior results in most trials. When FES, NMES, and TENS were compared with placebo electrical stimulation or no electrical stimulation, improvements were noted in gait speed(105, 106),

functional abilities as measured by the BI, the physical function subscale of the 36-item Short Form Health Survey (SF-36)(109, 110, 112), and upper extremity motor function.(107, 109)

The current systematic evidence review identified two SRs that include 46 studies (n=1,900). (113, 114) Monte-Silva et al. (2019) concluded that electromyogram-triggered/controlled neuromuscular electrical stimulation (EMG-NMES) was effective in improving upper limb motor impairment.(114) Kristensen et al. (2022) found benefits of NMES for improvement in ADL function but less clear evidence for improvement in functional motor ability.(113) The studies had variable stimulation protocols in pulse, duration, frequency, and so forth.

The SR/MA by Monte-Silva et al. (2019) (n=782) found that EMG-NMES as an adjunct to conventional care, compared with conventional care alone, had a statistically significant effect at the end of treatment on the International Classification of Functioning, Disability, and Health body structure and function domain, as measured by Fugl-Meyer Assessment - Upper Extremity (FMA-UE), reaction time, force, and range of motion (SMD: 0.47; 95% CI: 0.21–0.72; p<0.001).(114) However, no significant effect was noted in the ICF Activity and Participation domains (Functional Independence Measure, mBI, MAL-AOU, and others). Treatment dose varied from 2–20 weeks duration, 6–168 hours of intervention, delivered one to three times per day, one to seven times per week. Only eight of the studies in this SR (approximately 1/4 of the subjects) reported long-term follow-up in any ICF domain, ranging from 5 weeks to one year. There were no differences between groups in any domain at follow-up. This SR included trials where the patient had to produce EMG activity in the affected muscle to receive the stimulation; contralaterally controlled electrical stimulation trials were excluded.

An SR/MA by Kristensen et al. (2022) (n=1,100) found that NMES, compared with control (sham NMES or no intervention), had a statistically significant effect on ADLs as measured by the BI, mBI, and Functional Independence Measure (FIM) (SMD: 0.41; 95% CI: 0.14–0.67; p=0.003).(113) Subgroup analysis revealed that this effect was primarily driven by studies of upper extremity NMES (SMD: 0.34; 95% CI: 0.04–0.64; p=0.02). No improvement in functional motor ability was noted overall. However, subgroup analyses revealed a statistically significant positive effect on functional motor ability as measured by the ARAT in patients with severe paresis (SMD: 0.41; 95% CI: 0.12–0.70; p=0.005). This SR considered only NMES studies with surface electrode delivery and documented visible muscle contraction.

The findings from the 2019 VA/DoD Stroke Rehabilitation CPG and the current systematic evidence review reveal that short-term improvement might occur in upper extremity motor outcomes/ADLs and lower extremity motor outcomes, but insufficient evidence exists to determine whether this improvement is sustainable.

Some variation occurs in patient preferences regarding these treatments. Neuromuscular electrical stimulation is generally well tolerated, and patients like to see paretic limbs move. A small risk of skin irritation is associated with transcutaneous electrodes. NMES devices vary from relatively inexpensive to more costly, depending on the unit features. These interventions are acceptable and feasible for providers and health care systems.

The Work Group systematically reviewed evidence related to this recommendation(113, 114) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(105-112) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including small sample sizes, lack of allocation concealment, and inadequate blinding procedures.(113, 114) The potential benefits of short-term improvement in upper limb motor function/ADLs and lower limb motor function outweighed the potential harms of skin irritation. Patient values and preferences varied somewhat because most patients like to see their paretic limbs move in this usually well-tolerated intervention. Thus, the Work Group made the following recommendation: We suggest neuromuscular electrical stimulation to improve motor outcomes.

Recommendation

18. There is insufficient evidence to recommend for or against robot-assisted therapy to improve upper or lower extremity motor outcomes.
    (Neither for nor against | Reviewed, New-added)

Discussion

Robot-assisted therapy (RAT) (e.g., exoskeleton) devices are available for use in stroke rehabilitation. Most of the devices can be programmed to perform passive, active-assistive, or resisted movements, and some can adapt automatically based on the patient's ability. The rationale for the use of RAT is to increase the amount of task-specific practice of the movement pattern or activity.

Use of RAT for Upper Extremity Motor Outcomes

The evidence was mixed for the use of RAT for improvement in upper extremity motor outcomes. Two SR/MAs found that RAT with or without usual care improved upper limb movements as measured by the FMA.(115, 116) The SR/MA by Zhang et al. (2022) included 46 RCTs (n=2,553) and also found improvement in Stroke Impact Scale and FIM scores at the end of treatment when compared with usual care alone in the short term (<3 months).(115) However, there was no difference between the interventions on the ARAT. In addition, conflicting results were found in ADL outcomes as measured by the mBI with one SR showing improvement(115) and the other not(116). Outcome durability was evaluated only in the SR/MA by Zhang et al. (2022), and there was no difference between groups at three or more months post-treatment.(115)

Use of RAT for Lower Extremity Motor Outcomes

The current systematic evidence review identified two SRs evaluating RAT for lower extremity post-stroke motor outcomes, including one SR with 15 RCTs (n=449) and another SR with 62 RCTs (n=2,440).(117, 118) These reviews evaluated a variety of robotic interventions using several different metrics. No studies found superiority of robotic-based interventions alone (i.e., without concurrent physical therapy interventions).(118) However, RAT interventions for the lower extremities combined with physical therapy did show promise for reaching some short-term goals; at follow-up assessments, however, that advantage was no longer significant.

- Electromechanical- and robot-assisted gait training with physical therapy improved Functional Ambulation Classification - Lower Extremity (FAC-LE) and gait speed more than physical therapy alone; no difference resulted in walking capacity.(117)
- Leg-driven treadmill-based exoskeleton robot training alone was inferior to conventional therapy for improving balance, but when combined with physical therapy, it showed superiority over physical therapy alone.(118) However, with or without conventional therapy, leg-driven treadmill-based exoskeleton robot training was inferior to physical therapy alone for improving FAC-LE scores, gait speed, cadence, or walking endurance.(118)
- When compared with physical therapy alone, exoskeleton with physical therapy improved FAC-LE scores but not gait speed or walking capacity.(117)
- End-effector devices combined with physical therapy improved gait speed and walking capacity more than physical therapy alone; however, no difference occurred in FAC-LE scores.(117)
- When combined with physical therapy, mobile devices for overground walking and ankle devices did not result in significant gait speed or walking capacity improvements when compared with physical therapy alone.(117)

Follow-up in the above studies using RAT for lower extremity post-stroke motor outcomes ranged from 18–22.3 weeks, although it was not reported in all cases. In domains where robot-assisted interventions showed superiority, this advantage was no longer significant at long-term follow-up. Some variation occurs in patient values and preferences regarding this treatment. Some patients might find RAT very engaging, exciting, and innovative, but other patients might find the technology intimidating. Robot-assisted therapy is less available in most clinics (because of cost and space constraints), and fewer providers might have adequate training to implement its use. The robotic system must be used frequently to maintain therapist skills and comfort with the device. Although initial setup might be time and labor intensive, once the setup is completed and the device is donned and ready, the number of staff members and time needed for safe execution of a movement-based task (such as ambulation) might be

decreased. The potential side effects or harms tend to be related to discomfort from the harnesses and skin integrity issues.

The Work Group systematically reviewed evidence related to this recommendation.(115-118) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence for upper extremity motor outcomes had some limitations, including lack of blinding of outcome assessors, possible attrition bias, and possible selective reporting.(116) Unclear blinding or unblinded interventions and unclear allocation concealment were noted in several studies of upper extremity motor outcomes.(115) The body of evidence for lower extremity motor outcomes had some limitations, including unclear allocation methods; unclear blinding or unblinded participants, staff, assessors, or any combination of the aforementioned individuals; and incomplete data.(118) Studies of lower extremity motor outcomes frequently did not indicate whether participants, staff, assessors, or any combination of the aforementioned individuals were blinded and whether concerns for selective reporting and unclear or improper randomization and allocation concealment techniques developed.(117) Patient values and preferences varied because some patients might find RAT especially exciting and innovative, although others might prefer to avoid this technology. If the availability of RAT increases to potentially include home use, patients might be more likely to continue engaging in rehabilitation and have sustained positive effects. The benefits of RAT for short-term improvements in upper limb movements as measured by the FMA only slightly outweighed the potential harms, which were minimal and related to discomfort from the harnesses and skin integrity issues. Based on the data suggesting equal efficacy of conventional therapy, the Work Group can recommend neither for nor against the use of RAT for improvement of lower extremity motor outcomes. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against robot-assisted therapy to improve upper or lower extremity motor outcomes

Recommendation

19. There is insufficient evidence to recommend for or against virtual reality to improve balance or enhance gait recovery.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Virtual reality computer-based systems allow the user to interact within a virtual multisensory environment in real time. A wide array of systems is available, from simple commercial units used primarily for home gaming or fitness to more elaborate systems designed specifically for rehabilitation. Virtual reality/gaming systems used for stroke rehabilitation, otherwise known as serious games, have an education or specific rehabilitation goal (e.g., increased involved extremity use) instead of an entertainment purpose. These systems can be non-immersive where a person interacts with a

computer screen (simple computer games) or immersive with the person having the sense of being completely within the VR environment via goggles or half-dome or dome-closed, projected environments. These systems might include haptic information through sensors in bands or robotics that increase the person's perception of being in and reactive to the simulated environment. They might also include olfactory information through scents (e.g., the smell of pine when walking in a VR forest scene).

Evidence for this recommendation is carried forward from the 2019 VA/DoD Stroke Rehabilitation CPG. The evidence used for the previous recommendation was primarily found in the 2010 VA/DoD Stroke Rehabilitation CPG which recommended considering VR for gait rehabilitation. The recommendation was based on three RCTs using VR to augment a robotic treadmill and conventional physical therapy protocol.(119-121) Sample sizes were very small (n=24, n=20, n=18), and there was significant heterogeneity among interventions. As a group, these RCTs found significantly greater improvements in the VR-augmented therapy groups compared with the control groups on a variety of gait parameters and balance measures (including, but not limited to, gait velocity, community walking speed, community ambulation, BBS, and Activities-specific Balance Confidence Scale [ABC Scale]). The quality of the evidence put forth in the 2010 VA/DoD Stroke Rehabilitation CPG was assessed as low.

The 2019 VA/DoD Stroke Rehabilitation CPG Work Group reviewed one RCT from Lee et al. (2017) (n=50) that used a non-immersive VR method for balance-related training.(122) Both the VR group and the control group exhibited significant improvement in balance as measured by the BBS (p=0.000) and Timed Up and Go cognitive test (p=0.005). Adverse events included soreness, hypertonicity, dizziness, or shoulder pain; all resolved with rest and did not carry over into subsequent sessions. The VR intervention group rated the VR experience more pleasurable than the control group intervention (p=0.027). No significant difference was observed in either group on other outcome measures (mBI for ADL ability; ABC Scale for balance confidence; and Stroke Impact Scale for QoL).

The current systematic evidence review found one SR by Zhang et al. (2021).(123) Significant inconsistencies and errors in this publication made it unsuitable to include in this evidence review.

Some variation occurs in patient values and preferences. Virtual reality system use might be inappropriate for patients who have significant cognitive or visual impairments or both. The group felt that there was no increased risk for falls, soreness, hypertonicity, or shoulder pain compared with usual care. There could be a slight increase in dizziness; these symptoms appeared to resolve quickly with rest. People have different levels of comfort with certain forms of technology. Some patients are more familiar with the commercially available VR systems used for gaming or home fitness. Virtual reality could enhance motivation to participate in therapy and increase engagement in repetitive task-specific practice. This technology is becoming more widely available. The

cost of systems varies greatly based on non-immersive and immersive qualities, with the latter being more costly. Some simple VR systems can be purchased at lower price points, whereas specific systems designed for rehabilitation can cost significantly more. Further studies to show the efficacy of the different types of systems would be beneficial. To some extent, VR is feasible in most care settings. Additional resource considerations include the need for designated space to use VR safely, provider training on the VR systems, and increased provider access related to an increased number or duration of sessions to achieve optimal outcomes. As well, there could be concerns for data and information security when using VR systems.

The Work Group systematically reviewed evidence related to this recommendation(123) and considered the assessment of the evidence put forth in the 2010 and 2019 VA/DoD Stroke Rehabilitation CPGs.(119-122) Therefore, it is categorized as *Reviewed, New-replaced*. The body of evidence for the 2024 VA/DoD Stroke Rehabilitation CPG was limited to one SR determined to be unsuitable to include in this evidence review. The 2019 VA/DoD Stroke Rehabilitation CPG evidence was limited to one small RCT that showed no difference in balance outcomes with the use of VR versus the control group. The 2010 VA/DoD Stroke Rehabilitation CPG evidence base included three very small RCTs with significant heterogeneity among interventions in the studies. The Work Group's confidence in the quality of the evidence remained low. Without additional studies to support the strength of the 2010 and 2019 VA/DoD Stroke Rehabilitation CPG recommendations for VR intervention for gait, balance, or both, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against virtual reality to improve balance or enhance gait recovery.

Recommendation

20. There is insufficient evidence to recommend for or against the use of virtual reality/serious gaming to improve upper extremity motor outcomes, activities of daily living, or quality of life.
    (Neither for nor against| Reviewed, New-added)

Discussion

Virtual reality computer-based systems allow the user to interact within a virtual multisensory environment in real time. A wide array of systems is available, from simple commercial units used primarily for home gaming or fitness to more elaborate systems designed specifically for rehabilitation. Virtual reality/serious gaming systems used for stroke rehabilitation have an education or specific rehabilitation goal (e.g., increased upper extremity use) instead of an entertainment purpose. These systems can be non-immersive where a person interacts with a computer screen (simple computer games) or immersive with the person having the sense of being completely within the VR environment via goggles or half-dome or dome-closed, projected environments. These systems might include haptic information through sensors in bands, gloves, or robotics that increase the person's perception of being in and reactive to the simulated

environment. They might also include olfactory information through scents (e.g., a floral scent when picking flowers in a VR garden scene). When used as an upper extremity rehabilitation intervention, the system supports the person in repetitive, task-specific practice to facilitate the use of the involved extremity.

This recommendation was supported by two SRs, one MA, and one NMA.(116, 124-126) The articles included in the systematic evidence review looked at VR/serious gaming interventions compared with usual care or sham VR, except for the Chen et al. (2022) review, which included studies with control groups who received no therapy.(122)

An SR by Jin et al. (2022) reviewed 40 studies (n=2,018).(124) The VR interventions varied from non-immersive to immersive. Virtual reality systems were also variable, ranging from home gaming systems to rehabilitation-specific systems. Findings showed that the VR group had a statistically significant improvement in overall arm function, motor impairment, and ADLs compared with the control group, which consisted of usual care or sham VR. The advantage over usual care was not sustained at the 4-week follow-up. There were no significant differences between groups in specific task performance or participation measures.

An MA by Doumas et al. (2021) included 42 trials (n=1,760) and focused on comparing serious gaming to conventional therapy for upper limb rehabilitation after stroke.(125) Serious gaming was defined as systems that have education or rehabilitation as the primary goal instead of entertainment. Some of these devices could adapt the difficulty level based on the patient's performance, mimic functional tasks, provide feedback during or after task completion, or any combination of the aforementioned functions. The serious gaming systems provided attentional engagement and problem-solving challenges. Treatment varied from 2–12 weeks (mean: 5 weeks). Large variation occurred in the daily dose of intervention, ranging from 30–225 minutes. There was consistency between the control and experimental groups in each study included in the SR because they had similar duration of treatment 85% of the time. Results showed that rehabilitation using serious gaming led to improved upper extremity motor function of medium effect size (SMD: 0.47; 95% CI: 0.24–0.70; p<0.0001) and significantly better improvement of small effect size for upper limb activity (SMD: 0.25; 95% CI: 0.05–0.46; p=0.02) compared with the control group of usual care. At follow-up timeframes, varying from one to six months (mean=2.3 months), VR therapy was statistically superior to control for upper limb motor function (SMD: 0.42; 95% CI: 0.05–0.79; p=0.03) but not statistically significant for upper limb activity or participation measures.

In addition to VR, Doumas et al. (2021) tracked adherence to neurorehabilitation principles in the included studies. These principles included massed practice, dosage, structured practice, task-specific practice, variable practice, multisensory stimulation, increased difficulty, explicit feedback, and implicit feedback.(125) The number of principles present in the studies ranged from 4–11. Studies were divided into the

following groups: 8 or more principles, 5–7 principles, and fewer than 5 principles. The groups that adhered to more than 8 principles had significantly better improvements in upper extremity motor function (SMD: 0.62; 95% CI: 0.33–0.92; p=0.0001) and upper limb activity (SMD: 0.42; 95% CI: 0.12–0.72; p=0.006). A large effect size was found in participation measures when comparing the subgroup of studies that contained 8 or more principles to conventional treatment (SMD: 0.66; 95% CI: 0.29–1.03; p=0.0005). Only 50% of the studies performed follow-up evaluations. The length of time for those who did perform a follow-up ranged from one to six months (mean=2.3 months). Upper extremity motor function retention showed a medium effect size for the VR group (SMD: 0.42; 95% CI: 0.05–0.79; p=0.03).

An SR by Chen et al. (2022), including 42 studies (n=1,893), examined the effect of VR on 12 rehabilitation outcomes (upper extremity motor function, grip strength, spasticity, range of motion, stroke recovery stage, muscle strength, independence in day-to-day activities, hand dexterity, arm and hand motor ability, hand motor ability, QoL, and upper extremity use in daily life).(126) Compared with usual care or no therapy, the use of VR-supported exercise showed statistically significant improvements in upper extremity motor function, range of motion, and upper extremity muscle strength. Mixed results were found in overall functional independence. Significant improvements were found in day-to-day activities as measured by the FIM (SMD: 0.23; 95% CI: 0.06–0.4; p=0.01) but not as measured by the BI or mBI. There were no significant improvements in outcomes related to participation restrictions as measured by the Stroke Impact Scale or daily use of the upper extremity via the MAL. The benefits of the VR intervention were not maintained, and the author did not provide a timeframe for follow-up.

An NMA by Zhu et al. (2023), including 101 publications (n=4,702), compared VR with a control group of usual care and each of the following interventions: rehabilitation robots, brain-computer interface (BCI) with electrical stimulation, remote rehabilitation (a model of service delivery using internet communication technology), intelligent rehabilitation (intelligent biofeedback therapy devices), and a robotic system embedded with a VR component (RT+VR).(116) Overall, the results varied based on the outcome measure used. No significant improvement resulted in upper limb motor function or ADLs with the use of VR or any of the listed modalities as measured by FMA-UE and mBI.

When dividing the FMA-UE into proximal (shoulder/elbow) and distal (wrist) foci, no significant difference was found for improvement in distal musculature. However, a significant difference in improvement in proximal musculature was found with the RT+VR intervention. There was no significant difference with VR in isolation for improvement in proximal or distal musculature. Improvement in hand function, as measured by the ARAT, was found with all interventions compared with usual care. According to the results of the surface under the cumulative ranking curve (SUCRA) analysis, the most effective intervention was RT+VR (SUCRA, 99.6%) followed by VR (SUCRA, 60.9%).

Patient values and preferences are likely to vary. Virtual reality systems would be inappropriate for a subgroup of patients who have significant cognitive or visual impairments or both. Some patients enjoy VR/games although others dislike them. Patients might be more familiar with the commercially available VR systems used for entertainment or home fitness. Virtual reality systems offer providers another tool to add variety to their treatment planning, especially as technology becomes more widely available. The use of VR in rehabilitation can enhance motivation to participate in therapy and increase engagement in repetitive task-specific practice in the clinic or as a home exercise program. The cost of VR systems varies greatly, with immersive systems typically being more costly. Some simple VR systems are less expensive, whereas systems designed specifically for rehabilitation, immersive systems, or both can cost significantly more. Virtual reality is feasible in most care settings to some extent. Additional resource considerations include the need for designated space to use VR safely, provider training on the VR systems, and the potential increased number or duration of sessions or both required for optimal outcomes. Concerns for data and information security could arise when using VR systems.

The Work Group systematically reviewed evidence related to this recommendation.(116, 124-126) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had the following limitations: prominent lack of blinding of research staff and participants, possible attrition bias and selective reporting, unclear or improper randomization and allocation concealment techniques, and lack of ITT analyses. The benefits of potential gains in upper extremity motor function and ADLs were balanced with the potential harm of intolerance, either to the VR system itself or the increased duration of treatments required to show minimal benefits. Patient values and preferences varied concerning the acceptability and familiarity with VR. This intervention would be inappropriate for patients with significant cognitive or visual impairments or both. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the use of virtual reality/serious gaming to improve upper extremity motor outcomes, activities of daily living, or quality of life.

Recommendation

21. There is insufficient evidence to recommend for or against contralaterally controlled functional electrical stimulation to improve upper extremity motor outcomes and activities of daily living.
    (Neither for nor against | Reviewed, New-added)

Discussion

Contralaterally controlled functional electrical stimulation (CCFES) allows patients to control movements in a paretic limb while wearing a command glove or sensing electrodes on the non-paretic limb and stimulating electrodes on the paretic forearm.

The volitional opening of the non-paretic hand acts as an input signal, producing a proportional intensity of stimulation to the paretic hand.

The evidence base for this recommendation included one SR of 6 RCTs (n=267).(127) Variable protocols of CCFES administration were used. Some protocols included therapist-guided functional task practice (20- to 90-minute sessions, two to six times per week, for 1–4 weeks); others consisted of self-administered home stimulation exercise (10–12 hours per week for 6–12 weeks). Motor outcome measures included FMA-UE, Box and Blocks Test (BBT), and active range of motion (AROM). As measured by the FMA-UE, results from all six studies indicated a higher level of improvement in the CCFES-treated patients (n=137) versus the NMES-treated patients (n=130) (SMD: 0.42; 95% CI: 0.07–0.76; p=not reported [NR]). As measured by the BBT, results from three studies indicated better results with CCFES (n=62) versus NMES (n=56) (SMD: 0.48; 95% CI: 0.10–0.86; p=NR). For AROM (finger extension and wrist extension), results from four studies indicated a significant improvement in the CCFES group (n=84) compared with the NMES group (n=82) (SMD: 0.54; 95% CI: 0.23–0.86; p=NR). Activities of daily living outcome measures included the mBI and the Arm Motor Abilities Test (AMAT). As measured by the mBI, results from two studies showed a significant improvement in the CCFES group (n=45) compared with the NMES group (n=44) (SMD: 0.54; 95% CI: 0.12–0.97; p=NR). As measured by the AMAT, results from three studies (n=118) indicated no significant difference between groups (SMD: 0.34; 95% CI: −0.03–0.72; p=NR). Adverse events reported in two RCTs included a few instances of numbness, tingling, and irritation of the skin at the electrode sites as well as temporary discomfort from electrical stimulation.

Patients have similar values and preferences regarding this treatment. The treatment is generally well tolerated, and patients like to see paretic limbs move. A small risk of skin irritation is associated with transcutaneous electrode sites.

The Work Group systematically reviewed evidence related to this recommendation.(127) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including large heterogeneity of subjects in terms of time post stroke and degree of impairment and lack of adequate randomization, allocation concealment, and participant blinding procedures. In addition, the evidence reviewed included only one SR of six RCTs, three of which were by the same authors. The benefits of CCFES for improvement in upper extremity motor and ADL outcomes exceeded the potential harms, which included occasional numbness, tingling, and irritation of the skin at the electrode site as well as temporary discomfort from electrical stimulation. Patient values and preferences were similar because patients are motivated to regain movement in paretic limbs. Although CCFES shows promise as a treatment for hand paresis, it is currently less available outside a research setting. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against

contralaterally controlled functional electrical stimulation to improve upper extremity motor outcomes and activities of daily living.

Recommendation

22. There is insufficient evidence to recommend for or against non-invasive brain-computer interface to improve upper extremity motor outcomes and activities of daily living.
    (Neither for nor against | Reviewed, New-added)

Discussion

Brain-computer interface is a growing area of interest in rehabilitation research. It consists of capturing the subject's brain signals via EEG obtained during a motor imagery task and converting the signal into a stimulus that provides feedback for the patient through electrical stimulation, sensory feedback (auditory/tactile/visual), or robotics. BCI can be applied non-invasively on the scalp or invasively on the cortex of the brain. The following studies included in this systematic evidence review were all non-invasive using EEG.

An NMA by Zhu et al. (2023) included 101 publications (n=4,702) that compared BCI with electrical stimulation against a control group of usual care, rehabilitation robots (RT), VR, remote rehabilitation (a model of service delivery using internet communication technology), intelligent rehabilitation (intelligent biofeedback therapy devices), and RT+VR.(116) There was no statistically significant improvement in upper limb motor function or ADLs with the use of BCI compared with usual care or the other interventions as measured by the FMA-UE (its subparts) and the mBI. There was statistically significant improvement in upper extremity distal motor function for all the listed interventions compared with usual care as measured by the ARAT. According to the results of the analysis, RT+VR (SUCRA, 99.6%) and VR (SUCRA, 60.9%) were more effective than BCI (SUCRA, 57.7%).

An SR/MA by Peng et al. (2022) included 16 RCTs (n=488) that compared BCI intervention with a control group consisting of usual care, sham BCI, motor imagery, FES, or Manus robot (Manus Robotics, Inc., Lexington, Massachusetts).(128) Frequency of interventions ranged from two to five times per week for two to eight weeks. A statistically significant difference was found in upper extremity motor function (SMD: 0.53; 95% CI: 0.26–0.80; p≤0.05) and ADLs (SMD: 1.67; 95% CI: 0.61–2.74; p≤0.05) with the use of BCI versus the respective control groups as measured by the FMA-UE and mBI. Only 6 of the 16 studies used the Modified Ashworth Scale (MAS) to address the effects of BCI on spasticity. The MA did not show a significant difference in spasticity between BCI intervention and matched control groups.

An SR by Xie et al. (2022) included 17 studies (n=410) that compared BCI intervention with control conditions of usual care, motor imagery, sham BCI, and isolated FES/robotics.(128) A statistically significant difference in motor function (SMD: 0.62;

95% CI: 0.34–0.90; p≤0.0001) was found between BCI versus control conditions as measured by the FMA-UE. Three of the studies (n=80) included in this SR found significant improvement in ADLs (SMD: 1.12; 95% CI: 0.65–1.60; p≤0.00001) as measured by mBI in the BCI intervention group versus control conditions.

As mentioned above, BCI can be applied invasively or non-invasively. Brain-computer interface systems are subject to significant risks related to the need for neurosurgical intervention to implant devices or sensors in or on the brain. The studies included in these reviews appeared to all be non-invasive (using scalp EEG). The non-invasive BCI systems used in the studies above were relatively safe with only minor adverse events and were well tolerated by the participants when sufficient rest breaks were provided. The adverse events reported were allergic reactions to electrode/electrode gel, shoulder pain, and generalized fatigue. Fatigue is a common symptom post stroke. Most of the interventions were 30 minutes or longer with one study reporting attention-related fatigue after 20–30 minutes. It was recommended that sufficient rest breaks be taken after 15 minutes and throughout the intervention application to minimize fatigue.

Large variation occurs in patient preferences regarding this treatment. Cognitive demand for this intervention is high, so the application would be limited to a subset of patients without cognitive deficits. Fatigue did appear to be an issue with this modality, and this fatigue was additive to general post-stroke fatigue. The BCI system requires setup time, which might decrease active therapy time in sessions. Some patients might dislike having to wash their hair to remove the electrode gel after sessions. Other patients might find that the overall burden is acceptable for the potential of improvement in upper extremity motor function. The potential for upper extremity improvement exists with minor adverse events, such as allergic reactions to electrode gel, shoulder pain, and generalized fatigue. Most of these systems are used for clinical research and not in mainstream clinical practice. The BCI systems are operated by knowledgeable providers who have had extensive training. These systems are specialized, and the EEG is incorporated into some type of output/feedback system. The costs of these systems are significant, especially with the addition of FES or robotics.

The Work Group systematically reviewed evidence related to this recommendation.(116, 128, 129) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including an overall small sample size specific to the BCI intervention. Furthermore, all publications had prominent methodological concerns related to lack of allocation concealment; lack of blinding of outcome assessors, subjects, or both; possible attrition bias; and possible selective reporting. Overall benefits and harms/burdens were balanced for non-invasive BCI systems using EEG. Patient values and preferences are expected to vary significantly; a subset of patients will not tolerate this intervention because of the required cognitive demand or the increased fatigue level. Thus, the Work Group made the following recommendation:

There is insufficient evidence to recommend for or against non-invasive brain-computer interface to improve upper extremity motor outcomes and activities of daily living.

Recommendation

23. There is insufficient evidence to recommend for or against vagus nerve stimulation as an adjunct intervention for rehabilitation of acute and chronic motor deficits.
    (Neither for nor against | Reviewed, New-added)

Discussion

When paired with task-specific rehabilitation, vagus nerve stimulation (VNS) is thought to modulate neural networks and increase neuroplasticity to enhance motor recovery after stroke.(130) Gao et al. (2023) reviewed seven RCTs (n=263); some studies used invasive vagus nerve stimulation, while some used transcutaneous auricular vagus nerve stimulation.(130) The intervention groups underwent active VNS therapy with task-oriented limb training, with or without a trunk exercise program, and completed at least 300 movements or at least 30 minutes per session, 3–7 sessions per week, for 9–20 total sessions. Control groups received time-, intensity-, and dose-matched rehabilitation with or without sham VNS therapy. Results suggested improvement with VNS in motor outcomes including FMA, WMFT, MAL, ARAT, Nine Hole Peg Test, grip strength, and BBT, but the authors noted their concerns regarding publication bias.(130) In addition, there are risks for patients receiving surgically implanted VNS devices, including vocal cord paresis, dysphagia, hoarseness, shortness of breath, infection, bleeding, and cardiac arrhythmia.

Some variation occurs in patient preferences regarding this treatment. Although some patients might be unwilling to undergo a surgical procedure, others might be willing to consider this option in the absence of other available interventions, especially if they have moderate to severe deficits. However, there are several other important considerations for this type of intervention. These devices require trained practitioners to use them during a patient's rehabilitation. The upfront cost for surgically implanted VNS, estimated to be in the tens of thousands of dollars, could be prohibitive for many patients, depending on insurance coverage. The implanted devices have batteries that must be replaced regularly through a surgical procedure, with the frequency of battery replacement depending on the stimulator settings and usage. There are contraindications to the use of this therapy, including arrhythmia and sleep apnea, both of which are prevalent in the stroke population. These considerations would eliminate eligibility for many patients with stroke.

The Work Group systematically reviewed evidence related to this recommendation.(130) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence was limited (one SR including a small number of RCTs, most with small sample sizes) and was notable for concerns regarding publication bias. The potential harms slightly outweighed the benefits of VNS,

considering the risks of surgery and post-operative adverse effects. Patient values and preferences vary because patients might be reluctant to undergo a surgical procedure when other non-invasive rehabilitative options are feasible and potentially effective. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against vagus nerve stimulation as an adjunct intervention for rehabilitation of acute and chronic motor deficits.

c. Spasticity

Recommendation

24. We suggest botulinum toxin for patients with focal spasticity, depending on patient characteristics and preferences.
(Weak for | Reviewed, New-replaced)

Discussion

Botulinum toxin can improve spasticity in patients with a history of stroke.(131, 132) Since the publication of the 2019 VA/DoD Stroke Rehabilitation CPG, additional evidence has become available for both upper and lower limb spasticity as well as comparative evidence to other standard treatments such as oral baclofen. An NMA by Hsu et al. (2022) (n=1,930) demonstrated significant improvement in upper and lower limb spasticity, measured by the MAS, up to the 6th week after injection of botulinum toxin compared with control (which included any of the following: saline injections, sham extracorporeal shockwave therapy, physical therapy, and oral antispastic medications).(132) The magnitude of effect waned between the 7th and 12th weeks after the intervention. Between-group differences remained statistically significant for the upper limb MAS scores; however, the singular study within the NMA that evaluated the lower limb did not show a difference between groups during this period. Overall improvements in spasticity were observed over a variety of protocols in this NMA. Toxin used varied between onabotulinumtoxinA, incobotulinumtoxinA, or abobotulinumtoxinA.

A small (n=29) RCT by Güntürk et al. (2022) compared the efficacy of botulinum toxin 100–300 IU (from a predetermined diagram for dosing) with oral baclofen 30–80 mg per day (in multiple doses titrated to effect and tolerance) on multiple upper and lower limb spasticity outcomes, including the MAS and Brunnstrom stages of recovery.(131) No significant difference was found between botulinum toxin and oral baclofen in any outcome except ankle spasticity, which favored botulinum toxin (treatment difference of 1 point on the MAS). The totality of the evidence supports botulinum toxin as an effective treatment option for spasticity but also asserts that botulinum toxin might not have a dramatically different place in therapy compared with oral antispasmodics based on efficacy alone. The Work Group determined that the use of botulinum toxin should depend on patient characteristics and preferences. For example, patients with focal spasticity that is painful, impairs function, reduces their ability to participate in rehabilitation, or compromises proper positioning or skin care might be candidates for the targeted approach that botulinum toxin treatment offers.

Some variation occurs in patient values and preferences regarding this treatment. Though some patients might prefer the non-oral medication alternative botulinum toxin injections provide, others might find traveling for repeated injections about every 12 weeks burdensome, might prefer avoiding a treatment that requires multiple injections, or both. Access to this treatment might vary, because providers need specialized training to properly administer botulinum toxin. Some initial injection site discomfort might occur with botulinum toxin injections. As a targeted treatment option, botulinum toxin allows for higher dosing in affected muscles without global limitation to the function of other muscles. Botulinum toxins also generally lack systemic side effects, whereas sedation can be a limiting side effect common with oral anti-spasticity treatments. Weakness of injected muscles is possible, and this weakness might worsen function for some patients (e.g., a patient who uses lower limb extensor spasticity to aid with standing, transfers, or ambulation). Botulinum toxin injections are contraindicated in individuals with myasthenia gravis and might be less than ideal for patients with or highly prone to skin infections. Botulinum toxin therapy, compared with oral anti-spasticity medications, results in greater resource use, including procurement costs, dedicated clinic space, trained providers, and time devoted to administering injections.

The Work Group systematically reviewed evidence related to this recommendation(131, 132) and considered the assessment put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(133-136) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including a small sample size in the comparative study to oral baclofen.(131) The benefits of botulinum toxin injections in improving spasticity slightly outweighed the potential harms of initial injection site discomfort and muscle weakness. Patient values and preferences varied somewhat based on the difference in acceptability and accessibility of an injected treatment option compared with oral anti-spasticity medications. Thus, the Work Group made the following recommendation: We suggest botulinum toxin for patients with focal spasticity, depending on patient characteristics and preferences.

Recommendation

25. There is insufficient evidence to recommend for or against the use of acupuncture or dry needling for spasticity management.
    (Neither for nor against | Reviewed, New-added)

Discussion

Acupuncture

Acupuncture is part of the ancient practice of Traditional Chinese Medicine (TCM), whose practitioners believe the human body has more than 2,000 acupuncture points connected by pathways or meridians.(137) These pathways create an energy flow through the body that is responsible for overall health. By applying acupuncture to certain points, it is thought to improve the flow of Qi, thereby improving overall health.

An SR by Xue et al. (2022) compared various types of acupuncture (manual, abdominal, scalp, eye, body needling, and electroacupuncture) alone and with conventional rehabilitation (CR) to CR alone.(138) Acupuncture alone versus CR had mixed outcomes as measured by the MAS, FMA-UE, and BI. Acupuncture showed no difference versus CR in lower limb FMA and clinical spasticity index (CSI) scores. When combined with CR, acupuncture had more consistently favorable results as measured by MAS, CSI, upper and lower limb FMA, and BI scores.(138) Because this SR pooled the outcomes from many types of acupuncture, two other studies were included in the systematic evidence review that compared different types of acupuncture. Wang et al. (2022) directly compared various types of acupuncture, including fire, filiform, warm, and electroacupuncture.(139) Across 6 studies that included MAS as an outcome (n=198), no differences were found among any types of acupuncture. Warm and fire acupuncture both showed greater improvement in FMA (14 studies, n=467) and BI scores (8 studies, n=239) than electroacupuncture. In another SR by Qui et al. (2021), fire acupuncture was compared with conventional acupuncture.(140) Fire acupuncture showed greater improvements in whole-body (12 studies, n=720) and upper limb (6 studies, n=332) MAS scores but not lower limb (2 studies, n=70) MAS scores. Fire acupuncture also showed greater improvement in FMA (7 studies, n=418) and BI scores (4 studies, n=216).

Although the overall body of evidence was large, all SRs had serious limitations, including high risk of bias and lack of blinding. Thus, the Work Group expressed concerns about the accuracy of the efficacy outcomes. Risks are also associated with acupuncture, including punctate hemorrhage, subcutaneous hematoma, subcutaneous ecchymosis, and needle syncope.(138) The Work Group also acknowledged that MAS scores tend to have a high interrater and intra-rater variation.

Dry Needling

Dry needling is a non-pharmacologic intervention in which a provider inserts needles into patients' muscles to stimulate them. It is more commonly used for the management of musculoskeletal pain; however, there has been interest recently in use for post-stroke spasticity. Fernández-De-Las-Peñas et al.'s (2021) SR of seven RCTs (n=242) suggested that dry needling improved spasticity (SMD: -1.01; 95% CI: -1.68– -0.34, p<0.001) as measured by the MAS at short-term follow-up (<4 weeks). The interventions included any form of muscle dry needling, resulting in heterogeneous treatment protocols (concerning the number and frequency of sessions). The comparator groups included dry needling with a standard rehabilitation program in five of seven RCTs and no other treatment in the remaining two. Additionally, when the results were separated into upper (four studies) and lower (three studies) limbs, only the MAS in the lower limbs was improved at short-term follow-up. In total, the three lower limb RCTs had only 42 patients in the intervention groups. There was no sustained improvement at the 4-week follow-up, and there was never any improvement in motor function (based on heterogenous scales across studies). Only two of the seven RCTs

reported adverse events, including post-needling heaviness at the shoulder and tingling at an unreported rate. Two patients had a brief loss of consciousness, 10% of patients reported local cutaneous vasodilatation and sweating, and 50% of patients reported post-needling soreness, which resolved after 48–72 hours. The concurrent use of antiplatelets or anticoagulants was not reported.(141)

Some variation occurs in patient preferences regarding these treatments. The patient focus group noted a preference for different modes of therapy as well as individualized care. Some patients might prefer a non-pharmacologic treatment option for spasticity. On the other hand, some patients might not want to try acupuncture or dry needling because of a fear of needles, travel that might be needed to visit a qualified provider, or both. Providers who would like to incorporate acupuncture or dry needling into their practice must complete a training program and dedicate time and space to perform this treatment. These requirements might present a feasibility challenge. Providers might not practice all aforementioned specialty types of acupuncture (e.g., fire, filiform, warm, electroacupuncture), which might limit the above-described treatment options for patients.

The Work Group systematically reviewed evidence related to this recommendation.(138-141) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of acupuncture evidence had some limitations, including a lack of appropriate blinding procedures and a high risk of bias.(138-140) The body of dry needling evidence was limited to one SR of seven smaller, heterogeneous RCTs.(141) The statistically significant benefits of acupuncture for spasticity slightly outweighed the potential harms of adverse events, which were infrequent and generally mild. The benefit of dry needling in improving MAS scores in the short term (<4 weeks), particularly in the lower limbs, was balanced with adverse events that were inconsistently reported in the literature. Patient values and preferences are expected to vary based on patients' willingness to try a non-pharmacologic option that involves the placement of many needles in the body. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the use of acupuncture or dry needling for spasticity management.

Recommendation

26. There is insufficient evidence to recommend for or against whole body or localized muscle vibration for spasticity management.
(Neither for not against | Reviewed, New-added)

Discussion

Whole-body vibration (WBV) is a posited therapeutic approach to address spasticity wherein the patient stands or sits on a vibratory board that emits sinusoidal oscillations that propagate through the entire body. One purported mechanism of action of WBV on spasticity is related to the interference of synaptic transmission.(142)

An SR of 11 RCTs by Zhang et al. (2023) suggested that WBV, alone or in conjunction with other intervention modalities, showed a statistically significant reduction in spasticity (SMD: -0.26; 95% CI: -0.44– -0.07; p=0.006), as measured by the MAS.(142) The 11 studies evaluated 475 patients (n=252 in the experimental group, n=233 in the control group). The experimental group included those receiving WBV alone or combined with another intervention modality, while the control group received either sham vibration or another intervention modality. The other intervention modalities were heterogeneous across studies. Nine articles included patients with lower limb spasticity and two included those with upper limb spasticity. In 2 of the studies, the patients were seated as opposed to standing. There was heterogeneity in the frequency and amplitudes of the delivered oscillations as well as in the duration and frequency of treatment. Measurement timepoints ranged anywhere from one to eight weeks, with only 2 studies reporting a follow-up of three or six months. Subgroup analysis suggested heterogeneity in response based on the chronicity of the spasticity, age of the patient, upper versus lower limb as well as vibration frequency and duration. No serious adverse events were reported in 5 studies, while the remaining studies reported fatigue, redness of the skin, mild headache, drowsiness, and knee pain.(142)

Some variation occurs in patient preferences regarding WBV. The patient focus group noted a preference for different modes of therapy as well as individualized care. Although not discussed in the patient focus group, WBV offers a non-pharmacologic option for the treatment of spasticity as part of an individualized care plan. However, some variation might occur in patient preferences because this intervention appears to require in-person therapy by an experienced provider to titrate the treatment dose, thereby limiting access for some patients. The providers must also have the space and resources to purchase and fit such a device in a clinic.

The Work Group systematically reviewed evidence related to this recommendation.(142) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had limitations because there was only one international SR of 11 smaller RCTs with heterogeneous patients and treatment protocols.(142) The potential benefits of WBV in improving spasticity, at least statistically, slightly outweighed the potential harm of adverse events, which were mild when reported. However, the low quality of the heterogeneous data and low SMD of MAS scores between treatment groups poses a limitation. Patient values and preferences varied because although some patients might prefer this non-invasive treatment option, it appears to require in-person treatment in a clinic setting. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against whole body or localized muscle vibration for spasticity management.

Recommendation

27. There is insufficient evidence to recommend for or against extracorporeal shock wave therapy for spasticity management.
(Neither for nor against | Reviewed, New-added)

Discussion

Extracorporeal shockwave therapy (ESWT) is a non-pharmacological intervention used for lithotripsy, and more recently musculoskeletal treatments, including spasticity. The two recognized forms include focused ESWT (fESWT), which uses electrohydraulic, electromagnetic, or piezoelectric energy to deliver target pressure at the treatment site, and radial ESWT (rESWT), which is generated pneumatically and disperses the pressure waves indirectly to the treatment site. ESWT is posited to have immediate effects on reducing spasticity, thereby facilitating subsequent therapy; however, the mechanism behind the effects remains relatively unclear.

Low-quality evidence from an SR of 13 RCTs by Ou-Yang et al. (2023) found that ESWT statistically improved spasticity as measured by the MAS, in the short-term (1-2 weeks after treatment), mid-term (>3 and <4 weeks after treatment), and long-term (up to 12 weeks after treatment) follow-up periods, compared with sham ESWT or conventional physiotherapy.(143) The included studies evaluated patients (n=677) who received ESWT or were in a control group of either sham ESWT or conventional physiotherapy.(143) Four studies used fESWT, 7 rESWT, and 2 did not delineate a type of ESWT. Of studies using MAS as an outcome measure, 11 were included in the short-term analysis (n=533), 9 in the mid-term analysis (n=421), and 4 in the long-term analysis (n=285). Ten studies evaluated the effects on the upper limbs, and 4 evaluated the lower limbs. Despite the reported statistical difference in MAS scores at all three timepoints, the MD at short-term (MD: -0.43; 95% CI: 0.77-0.10; p<0.01), mid-term (MD: -0.50; 95% CI: -0.81– -0.20; p<0.01), and long-term (MD: -0.81; 95% CI: -1.15– -0.47; p< 0.01) effects were interpreted by the Work Group as not clinically significant. The applied shock wave frequencies differed, as did the frequency of the therapies. The timing of therapy following the stroke was varied. The authors of the SR did not review the reported complications of the RCTs' interventions.(132, 143)

Hsu et al. (2022) performed an NMA to evaluate the comparative effectiveness of botulinum toxin and ESWT on the WMD of MAS reduction in the short- (at or before the 6th-week post-treatment) and mid-term (between the 7th- and 12th-week post-treatment).(132) Of the 33 included RCTs (n=1,930), 10 compared rESWT with control, 4 compared fESWT with control, 1 compared fESWT with rESWT, and 1 compared rESWT with botulinum toxin, while the remaining 17 compared botulinum toxin only with a control. The control groups could have consisted of sham ESWT, physical therapy, oral anti-spasticity medication, or, in the case of botulinum toxin trials, saline injection. In the short-term NMA, Hsu et al. (2022) found that botulinum toxin (WMD: -0.69; 95% CI: -0.87– -0.50), fESWT (WMD: -0.36; 95% CI: 0.69–0.03), and rESWT (WMD: -0.62;

95% CI: -0.84– -0.40) were statistically superior in reducing spasticity compared with control. At the mid-term NMA, botulinum toxin (WMD: -0.44; 95% CI: -0.62– -0.26), fESWT (WMD: -0.74; 95% CI: -1.26– -0.23), and rESWT (WMD: -0.79; 95% CI: -1.07– -0.51) were statistically superior in reducing spasticity compared with control. The Work Group felt that although these results were statistically significant, they were not clinically significant. Because of variations in ESWT dosing, the interpretation of these results has limitations. The timing of therapy following stroke was varied. Hsu et al. (2022) noted that the included studies did not specifically report rates of severe adverse effects, though the side effects of ESWT might include transient skin petechiae or localized pain.(132)

Some variation occurs in patient preferences regarding this treatment. The patient focus group noted a preference for different modes of therapy as well as individualized care. Although not discussed during the patient focus group, ESWT might be a reasonable non-pharmacologic option as part of an individualized care plan. Yet, this intervention requires the acquisition of the machine and in-person treatments by a trained provider, thereby limiting access for some clinics and patients.

The Work Group systematically reviewed evidence related to this recommendation.(132, 143) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence, including one SR and an NMA, had some limitations, including small individual RCTs. The benefits of ESWT, perhaps specifically rESWT, include statistically improved spasticity by non-pharmacologic means and slightly outweighed the potential harm of adverse events, which although inconsistently reported in these studies, appear mild. Patient values and preferences varied somewhat because although the intervention is non-pharmacologic, it requires in-person intervention by a trained provider. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against extracorporeal shock wave therapy for spasticity management.

C. Dysphagia, Cognition, and Aphasia

a. Dysphagia

Recommendation

28. We suggest chin tuck against resistance exercises for patients with dysphagia. **(Weak for | Reviewed, New-replaced)**

Discussion

Chin tuck against resistance (CTAR) is a dysphagia therapy that helps strengthen the musculature around the hyoid bone and facilitates the upward and forward movement of the hyoid. The movement of the hyoid and elevation of the larynx assist in protecting the airway and transitioning the bolus through the pharynx. Hyoid movement aids in safely moving the bolus through the pharynx by repositioning the laryngeal entrance to the airway with subsequent traction forces of the upper esophageal sphincter opening.

Numerous therapeutic modalities target this suprahyoid musculature, including CTAR, Shaker exercises, and resistive jaw opening exercises. Chin tuck against resistance is facilitated with a variety of devices, from measurement devices with quantitative feedback to rubber balls held in place by a chin tuck throughout the therapeutic exercise. Shaker exercises enable hyoid excursion by positioning. In Shaker exercises, patients are in a supine position and then lift their heads while keeping their shoulders affixed to the surface on which they are resting. Evidence suggested that CTAR decreased aspiration in patients with post-stroke dysphagia.(144) Evidence also suggested that CTAR outperformed Shaker exercises.(144)

The control condition for the evidence base included traditional dysphagia therapy. The spectrum of what is included in traditional dysphagia therapy is variable across different sites and localities. Most traditional dysphagia therapy includes limited sessions with a speech-language pathologist focusing on instrumental swallowing evaluations that assist with the identification of physiologic impairments that inform targeted exercise work in physiology restoration and aspiration prevention.

An SR by Liu et al. (2023) including five RCTs (n=247) (two of which were included in the 2019 VA/DoD Stroke Rehabilitation CPG evidence base(145, 146)) continued to show a meaningful and consistent difference in disease-oriented aspiration measures in patients instructed in CTAR.(144) The SR found an MD of -1.43 on the Penetration Aspiration Scale (PAS) (95% CI: -1.81– -1.06; $p<0.0001$), favoring CTAR compared with traditional dysphagia therapy. Some studies used adjunct modalities including transcranial direct current stimulation, oral facial massage, and thermal-tactile stimulation in the control arm, which complicates some of the external validity of this SR. A subgroup analysis of four studies that compared the effect of CTAR with Shaker exercises on PAS scores showed an MD of -0.49 (95% CI: -0.83– -0.16; $p=0.004$), favoring CTAR. This result is of debatable clinical significance. However, the poor patient perception of Shaker exercises because of significant neck discomfort during their execution was enough to remove the “Shaker or” phrasing from the 2019 VA/DoD Stroke Rehabilitation CPG recommendation. CTAR seems preferable to patients and is potentially more helpful than Shaker exercises.

One small study (n=29) by Park et al. (2018) with 4 weeks of follow-up examined a specific CTAR facilitation technique called resistive jaw opening exercise (RJOE).(145) This study found no difference in PAS scores of patients using the RJOE device compared with a sham device. This finding might be because the sham device effectively facilitated CTAR.

Some variation occurs in patient preferences regarding this treatment. Though CTAR tends to be an uncomfortable and intense therapy, it can offer protection from a time-limited but potentially life-threatening problem (i.e., severity of dysphagia and risk of aspiration decreases as patients progress out of the acute and subacute phase of many stroke syndromes). Therefore, CTAR might be acceptable to patients if required for only

a short time in return for a significant clinical benefit such as the prevention of aspiration. CTAR initially requires patient training by a speech-language pathologist or other specialist trained in dysphagia management. Once trained, patients can complete the exercises independently, without a therapist or caregiver. Also, online videos online can facilitate training in remote locations or austere circumstances where trained providers are unavailable.

The Work Group systematically reviewed evidence related to this recommendation (144) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(145, 146) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including small sample sizes, concerns about allocation concealment, and unclear randomization procedures.(144) The benefits of decreased aspiration outweighed the potential harm of patient discomfort and fatigue. Patient values and preferences vary somewhat, based on the perceived levels of annoyance, discomfort, or both that patients experience when using CTAR while eating and drinking. Thus, the Work Group made the following recommendation: We suggest chin tuck against resistance exercises for patients with dysphagia.

Recommendation

29. We suggest respiratory muscle strength training for dysphagia in patients without a tracheostomy.
    (Weak for | Reviewed, New-replaced)

Discussion

In dysphagia therapy, respiratory muscle strength training refers to any number of therapeutic techniques using a device that targets strengthening of the muscles of respiration through resistance for training the actions of inhalation, exhalation, or both. It uses a device that gives metered feedback on performance to participants who receive training from a speech-language pathologist. Evidence from an SR by Zhang et al. (2022) (n=523) suggests that respiratory muscle strength training using a device decreases aspiration in patients with dysphagia after stroke (PAS MD: 0.81; 95% CI: -1.19– -0.43; p<0.0001).(147) The control conditions in this SR were variable and included traditional dysphagia therapy or sham devices but without any respiratory muscle training. Devices used in the trials included those that focus on expiration, inspiration, or both inspiration and expiration. Though this study showed a statistically significant effect of treatment, whether this difference is clinically significant is unclear because the raw MD between groups fell just below the one-point change on the PAS, which is usually considered the MCID.(147, 148). Zhang et al. (2022) also demonstrated a number needed to treat (NNT) of 15 to reduce the risk of respiratory complications (a composite of pneumonia and other lung infections diagnosed after training had begun). Studies within this SR used traditional dysphagia therapy without respiratory muscle training and sham devices without training as controls. No single type of device was

identifiable as the most likely to result in lower respiratory complication risk. Devices included those that focus on expiration, inspiration, and both inspiration and expiration.

Some variation occurs in patient preferences regarding this treatment. This therapy can require frequent sessions (in some trials, 14 times per week for up to 13 weeks), which can be fatiguing for some patients. The intervention is performed at home and without direct caregiver support. This approach is notable insofar as the patient focus group encouraged reducing caregiver burden. The devices used in these trials have variable costs but are affordable. Some concerns about patient subpopulations exist because patients with advanced pulmonary disease, tracheostomies, or both might be unable to participate in this therapy. Of note, patients with tracheostomies might also find participation in this therapy difficult. The studies included looked at only acute and subacute stroke populations, not at patients with chronic stroke.

The Work Group systematically reviewed evidence related to this recommendation (147) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(149, 150) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including risks of bias because of problems with allocation concealment in some of the included studies. Although the SR by Zhang et al. (2022) comprised 523 patients, the heterogeneity of trial design limits the confidence of any single recommended practice. The benefits of decreased fewer respiratory tract infections and a trend toward less aspiration slightly outweighed the potential harm of patient fatigue. Patient values and preferences varied because some patients value therapies that require no travel or result in a burden on caregivers (i.e., a task that after training can be performed independently for some). However, patients might find the required frequency and intensity of this intervention burdensome. Thus, the Work Group made the following recommendation: We suggest respiratory muscle strength training for dysphagia in patients without a tracheostomy.

Recommendation

30. There is insufficient evidence to recommend for or against tongue pressure resistance training for dysphagia.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Tongue pressure resistance training is a modality in speech-language pathology that facilitates the strengthening of the tongue and the suprahyoid musculature. This therapy typically involves a portable pressure sensor in the form of an air-filled bulb to provide biofeedback. It is frequently used in the treatment of oropharyngeal dysphagia to aid with intrabolus pressure generation and to help with the clearance of food bolus from the oropharynx.

Evidence is mixed that tongue pressure against resistance training can improve swallowing and decrease aspiration in patients with oral and oropharyngeal dysphagia after stroke. The evidence base for this recommendation includes a single RCT (n=36) that evaluated intense monitored tongue pressure resistance training over four weeks compared with conventional dysphagia therapy. Conventional therapy in this study included frequent traditional swallowing rehabilitation treatment (orofacial motor control exercises, sensory stimulation of orofacial muscles, respiratory training, and airway protection manipulation) overseen by a speech-language pathologist.(151) Measures of swallowing function improved and measures of aspiration decreased significantly more in the resistance training group than in the traditional dysphagia therapy group (a difference-in-differences) as measured by the Functional Communication Measure and the Oral Motor Function Scale, maximum tongue pressure, Murray Secretion Scale, Rosenbek PAS, and presence of food residue in pyriform sinuses. Both groups showed a statistically significant improvement on the scales (except for the presence of food residue in the pyriform sinuses, for which there was no difference before and after treatment in the conventional therapy group). The difference between those parameters statistically favored the tongue pressure resistance training only in maximum tongue pressure and the Oral Motor Function Scale. These scales are disease-oriented metrics that should reflect improved physiology with a heavy oral focus on tongue pressure resistance training. Though less residue was visualized in the pyriform sinus, the small sample size decreased the Work Group's confidence in the study findings. Of note, this study included patients with dysphagia because of post-stroke oral motor dysfunction.(151) A previous RCT (n=41) evaluating tongue pressure resistance training reviewed in the 2019 VA/DoD Stroke Rehabilitation CPG failed to demonstrate a between-group difference in the PAS (groups again included conventional therapy versus conventional therapy and tongue pressure resistance training). The current systematic evidence review showed no group difference on the PAS.(152)

Some variation occurs in patient preferences regarding this treatment because of the daily and intense nature of the therapy, which could cause excessive fatigue as detailed in the included study.(151) The need for the oral pressure sensor could also be uncomfortable for some patients. Furthermore, this therapy requires daily oversight by a speech-language pathologist, which is resource intensive. The sensor device is portable and relatively inexpensive.

The Work Group systematically reviewed evidence related to this recommendation (151) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(152) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations because it included only two small trials at single sites, and both studies lacked long-term follow-up and patient-centered metric data to suggest ongoing benefits. The benefits of aspiration reduction and swallowing improvement slightly outweighed the potential harms of patient fatigue and discomfort

from the device. Patient values and preferences varied somewhat because of the frequent and intense nature of the therapy. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against tongue pressure resistance training for dysphagia.

Recommendation

31. There is insufficient evidence to recommend for or against neuromuscular electrical stimulation and pharyngeal electrical stimulation for dysphagia. **(Neither for nor against | Reviewed, New-replaced)**

Discussion

In dysphagia therapy, NMES refers to the placement of surface electrodes on the skin overlying laryngeal and submental regions. The premise of this therapy is to elicit the contraction of oropharyngeal musculature and stimulate sensory input for swallowing. Significant debate exists as to the ability of this technology to support the physiologic action of swallowing. Variations of this technique include increased channels that address some of the perturbations in usual physiological swallowing. Specifically, concern exists that NMES therapies depress the hyolaryngeal complex without horizontal excursion, which is antithetical to the need for hyoid excursion superiorly and anteriorly to protect the airway and prevent aspiration. Four-channel NMES has theoretical advantages over older two-channel options when it comes to facilitating physiologic movements of the perihyoid musculature during swallowing.(153)

Also, largely proprietary catheter-based bipolar ring electrodes (through a nasogastric feeding tube) help trigger pharyngeal musculature contractions through a procedure called pharyngeal electrical stimulation (PES). However, the effect of PES is more than just muscular contraction as seen in NMES. In contrast, PES attempts to affect the neuroplasticity of the swallowing network, including the sensory and motor cortices of the brain responsible for the pharynx and the afferent peripheral nervous system.

The evidence suggested that NMES therapies improved swallowing and decreased aspiration during the use of the therapeutic technique but not at long-term follow-up. This result was seen in two small, variable quality trials(153, 154) and one NMA.(155) The NMA by Zhuang et al. (2023) included nine studies (n=474) evaluating NMES versus control (control condition not specified).(155) NMES was found to be superior to the control and had a SUCRA score of 28 with an OR of 0.23 (95% CI: 0.11–0.43). This SUCRA is the largest for the NMA (which included acupuncture, behavioral interventions, drug therapy, NMES, and PES), suggesting some degree of benefit. In the smaller RCTs by Zhang et al. (2022) (n=35) and Lee et al. (2021) (n=49), NMES and four-channel NMES were compared with sham, respectively.(153, 154) Both of these studies similarly showed improvement in swallowing function and reduction in aspiration as measured by the PAS at the end of treatment. There was no long-term follow-up in any of these three studies.(153-155) The only trial with long-term follow-up that continued to look for benefits outside the therapy session was an RCT by Cakmak

et al. (2023) (n=34) that showed no durable difference between patients treated with NMES compared with patients treated with traditional dysphagia therapy over a three-month follow-up period.(156) Importantly, this trial demonstrated improvement in dysphagia symptom severity and QoL in both traditional dysphagia therapy and traditional dysphagia therapy with NMES. The traditional therapy comparator included patient education, oral hygiene, diet regulation, nutritional support, and compensatory and rehabilitative approaches.

Evidence suggested that PES therapies improved dysphagia symptoms, but no compelling evidence was found that they facilitated a decrease in aspiration. In the 2019 VA/DoD Stroke Rehabilitation CPG, one small MA(157) suggested a benefit from PES, but a larger, multisite trial did not substantiate this finding.(158) New evidence reviewed included one new RCT and one NMA.(155, 159) The NMA by Zhuang et al. (2023) included six studies (n=341) comparing PES to control (control condition not specified).(155) PES was found to be superior to control (OR: 0.27; 95% CI: 0.12–0.59). The smaller RCT (n=81) failed to show a difference in PAS scores when PES was compared with sham over a two-week follow-up.(159) There was also a small multisite study included in Zhuang et al.'s (2023) NMA that evaluated the use of applied PES for early decannulation in tracheotomized stroke patients with post-stroke neurogenic dysphagia.(160) This study demonstrated an improvement in rates of decannulation of post-stroke patients after a stroke with a tracheostomy.(160)

Some variation occurs in patient preferences regarding NMES. This therapy can be uncomfortable because of the equipment itself as well as the muscular burden of frequent involuntary contractions. However, some patients with dysphagia will be highly motivated to participate in treatments that could improve their swallowing, and they will appreciate the ability to use musculature affected by the stroke that they perceived their stroke might have limited. NMES is an observed therapy that requires facilitation by a trained provider. Larger variation occurs in patient preferences regarding PES. The main driver of this increased variance is the need for a nasogastric tube to facilitate the procedure, which can be significantly uncomfortable. The other issues driving variation in patient values and preferences are similar to those with NMES, as described above.

The Work Group systematically reviewed evidence related to this recommendation (153-156, 159) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(157, 158, 161-165) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including small sample sizes, variable outcome measures, and variable experimental constructs. The benefits of improved swallowing decreased dysphagia, and decreased aspiration slightly outweighed the potential harms (e.g., patient fatigue, discomfort from the device, tingling, and itching). The concerns associated with the pathophysiology of swallowing were not detailed or meaningfully addressed in the reviewed evidence. Patient values and preferences vary somewhat because of the balance between device-related

discomfort and the potential for improved swallowing. Some patients might prefer the use of their swallowing musculature even if actualizing is difficult for them without the assistance of the therapy. However, there are also concerns about the need for a nasogastric tube for PES. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against neuromuscular electrical stimulation and pharyngeal electrical stimulation for dysphagia.

Recommendation

32. There is insufficient evidence to recommend for or against surface electromyography for dysphagia.
(Neither for nor against | Reviewed, New-added)

Discussion

Surface electromyography (sEMG) is a biofeedback tool used in dysphagia care. It involves the application of electrodes to the musculature of the mouth and pharynx to detect impulses in coordinated patterns, which helps guide the management of secretions as well as bolus challenges of different consistencies. The underlying mechanism is purported to help the patient relearn the behaviors necessary to facilitate safe swallowing.

A single small RCT (n=27) by Benfield et al. (2023) suggested that use of sEMG is neither helpful nor harmful for patients with dysphagia following stroke.(166) The authors found no difference in dysphagia severity (as measured by the Dysphagia Severity Rating Scale) or aspiration scores (as measured by the PAS) between patients who received sEMG-guided biofeedback versus usual speech-language pathology care. Usual care consisted of two to three 25-minute sessions over 2 weeks, most of which targeted assessment and only 10% of which focused on rehabilitation with techniques such as CTAR. The sEMG group received 10 one-on-one sessions with a speech-language pathologist lasting up to 45 minutes over 2 weeks. Surface electromyography facilitated biofeedback did not demonstrate a statistically significant difference in dysphagia severity or aspiration scores compared with usual care. However, in the sEMG group, there was a consistent trend toward lower dysphagia severity scores on the Dysphagia Severity Rating Scale (3.2 for sEMG biofeedback and 4.3 for usual care) and a lower risk of aspiration on the Penetration Aspiration Scale (3.2 for sEMG biofeedback and 4.4 for usual care). This trend did not reach statistical significance. Additionally, lower rates of recurrent chest infections were reported in the sEMG group (67% for sEMG biofeedback and 33% for usual care), though this difference also did not reach statistical significance.

A similarly small RCT (n=24) evaluated a technique called effortful swallow therapy, a remedial method of training swallowing-related muscles.(167) No difference was seen when this therapy was compared with usual care on the video fluoroscopic dysphagia scale scores. In a subgroup analysis, this technique demonstrated improvement in the oral phase of swallowing. The quality of this study was limited by the imprecision of

measurement (based on the degree of uncertainty around the outcome effect size as a result of the small sample size). Also, the control group was explicitly directed to not swallow forcefully, an uncommonly used technique in conventional dysphagia therapy.

Biofeedback is a commonly used technique in speech-language pathology. Some variation occurs in patient preferences regarding this modality. Most patients (92%) in the Benfield et al. (2023) trial noted that sEMG was comfortable, but approximately 25% found the sessions too frequent or too long.(166) Almost one-half (42%) of the participants felt the exercise was difficult.(166) The patient focus group members noted the importance of individualizing therapies based on where the patients are in their recovery. As a result of the relatively frequent nature of the therapy as studied and described above (10 one-on-one sessions with a speech-language pathologist lasting up to 45 minutes over 2 weeks), there was concern about resource use and equity in areas across the country in locations where speech-language pathology is less available. Similar concerns existed with effortful swallow therapy.

The Work Group systematically reviewed evidence related to this recommendation.(166, 167) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including a small sample size, single trial location, between-population recruitment differences, volume of care variation, underpowering of the study, and very serious imprecision in measurements. The benefits of facilitated biofeedback, using tools such as sEMG and techniques like effortful swallow training, slightly outweighed the potential harms which were principally limited to fatigue and discomfort, which are common difficulties in speech-language therapy. Patient values and preferences varied because of discrepancies in perceptions of the intensity of the therapies and comfort with them. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against surface electromyography for dysphagia.

b. Cognition

Recommendation

33. There is insufficient evidence to recommend for or against the use of selective serotonin reuptake inhibitors to improve cognitive outcomes.
(Neither for nor against | Reviewed, New-replaced)

Discussion

Little development has transpired in the evidence regarding the use of pharmacotherapy to enhance or improve cognitive function since the 2019 VA/DoD Stroke Rehabilitation CPG.[g] An SR by Kalbouneh et al. (2022) included four RCTs (n=216) that examined the efficacy of SSRIs for improving post-stroke cognitive outcomes.(168) Only one of the included RCTs, Cao et al. (2020), was published after the 2019 VA/DoD Stroke

[g] See: https://www.healthquality.va.gov/guidelines/Rehab/stroke/VADoDStrokeRehabCPGFinal8292019.pdf

Rehabilitation CPG. (169) Cao et al. (2020) compared treatment with escitalopram with placebo (n=100).(169) Scores on the Mini Mental Status Exam (MMSE) increased in the escitalopram treatment group, but when compared with the control group, the increase was not statistically significant. Furthermore, evidence from Nys et al. (2005), a study not included in the current evidence review and therefore not used to impact the strength of the recommendation, suggests that the MMSE is a screening measure for cognition and might be insensitive to change in the stroke population.(170) One small (n=88) RCT by Jorge et al. (2010)(171), also included in the SR by Kalbouneh et al. (2022)(171), showed statistically significant gains on the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) delayed memory subtest and improvement in the RBANS total score following the use of escitalopram compared with placebo.(171) The RBANS is also a screening measure originally developed for the assessment of dementia. No improvement was observed on several other diagnostic neuropsychological measures.(171)

Some variation occurs in patient preferences regarding this treatment. Some patients wish to minimize medication use, whereas others would be willing to try a medication for the potential benefit of improved cognition. SSRIs are relatively safe interventions, though some patients might experience side effects, most commonly gastrointestinal upset. SSRIs are low-cost and easy to administer as one pill per day.

The Work Group systematically reviewed evidence related to this recommendation(168, 169) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(171) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had several limitations, including inadequate randomization procedures and deviations from the intended interventions. The benefits of SSRIs for improving cognitive recovery slightly outweighed the potential harms, which include potential side effects of these medications (e.g., gastrointestinal upset). Patient's values and preferences varied somewhat because some patients dislike taking medications. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the use of selective serotonin reuptake inhibitors to improve cognitive outcomes.

Recommendation

34. There is insufficient evidence to recommend for or against computer-assisted cognitive rehabilitation to improve cognitive outcomes.
    (Neither for nor against | Reviewed, New-added)

Discussion

Computer Assisted Cognitive Rehabilitation (CACR) can be used as a remedial approach to train cognitive skills as part of a traditional, comprehensive rehabilitation program. In an SR by Loetscher et al. (2019), CACR was compared with variable controls, including, but not limited to, computerized activities with low attention demands

and social activities.(172) In addition, CACR varied and was either conducted in the clinic or completed at home. Significant post-intervention improvements were observed in the CACR group (n=165) as measured by the Paced Auditory Serial Addition Test (PASAT). However, the authors found no convincing effects on measures of functional abilities, including the BI, FIM, and mRS, or on other measures of attention.(172) A second SR by Gibson et al. (2022) compared computer-based interventions with paper-based interventions or traditional occupational therapy (OT) using compensatory or adaptive interventions.(173) Individual RCTs within this SR included computer-based interventions that were provider directed; however, provider presence was not specified for all trials. Statistically significant improvements were observed for visual attention overall (n=620 for short-term; n=293 for long-term), sustained visual attention (n=463 for short-term; n=171 for long-term), and selective visual attention (n=244 for short-term; n=122 for long-term). Short-term follow-ups ranged from 10 days to 12 weeks while long-term follow-ups were conducted between three and six months. Statistically significant improvements at up to 18 weeks post-treatment were observed on measures of immediate verbal memory span (n=357) and immediate spatial memory span (n=292). Statistically significant improvements at short-term follow-ups were observed for working memory (n=420), sustained visual attention (n=463), and executive function performance overall (n=550) at initial follow-up but were not sustained at longer-term follow-up. Similarly, only short-term gains were observed in non-verbal reasoning (n=224), cognitive flexibility (n=43), and delayed recall (n=184). Gibson et al. (2022) observed improvements in ADLs as measured by the FIM, but the authors noted that the change was unimportant because it was below 22 points, which did not meet the criteria for MCID for the FIM in this population. Findings were similar on global cognitive performance as measured by the Montreal Cognitive Assessment (MoCA), MMSE, or both which reached statistical but not clinical significance.(173) Therefore, similar to the SR by Loetscher et al. (2019), the authors found no convincing effects on measures of functional abilities.(172)

Some variation occurs in patient preferences regarding this treatment. Although these studies suggest that CACR might be beneficial to improve outcomes on specific cognitive measures, there was extensive heterogeneity in interventions and various modes of delivery, ranging from self-directed training at home to CACR with frequent provider interaction. Computerized cognitive rehabilitation programs are frequently developed to automatically adapt to the difficulty level based on the patient's performance. These technologies might require less direct support from providers and can be self-directed. The patient focus group noted a preference for setting, with their providers, personalized goals tailored to their hobbies and activities and noted their appreciation for outward support and immediate and direct feedback from their providers while completing therapeutic activities. The patient focus group's feedback suggests patients might prefer interventions targeting cognitive skills in functional contexts to maximize the applicability of treatment to their everyday lives and environments. Other considerations include the cost of computerized programs, access

to the programs, and willingness to engage with technology, required technological support, or both, all of which were also key concerns of the patient focus group.

The Work Group systematically reviewed evidence related to this recommendation.(172, 173) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including inadequate randomization and allocation procedures, inadequate blinding of participants and personnel, and incomplete outcome data. In addition, the individual RCTs had small sample sizes. The benefits of CACR in improving performance on some cognitive measures slightly outweighed the potential harms of requirements for extensive treatment time, frequent duration and intensity, cost, and limited access and availability of specialized providers and programs. Patient values and preferences vary somewhat because some patients welcome technology and deem computerized programs more innovative approaches to therapy, whereas others are less comfortable with technology-based interventions. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against computer-assisted cognitive rehabilitation to improve cognitive outcomes.

c. Aphasia

Recommendation

35. There is insufficient evidence to recommend for or against a specific intensity of language therapy for aphasia.
    (Neither for nor against | Reviewed, Amended)

Discussion

Resuming functional communication following stroke is an important aspect of recovery for many stroke survivors and can directly impact QoL. Unfortunately, limited evidence exists regarding the intensity of aphasia therapy that could be expected to yield maximum benefit for improved communicative effectiveness and QoL in both acute and chronic phases of stroke recovery. The evidence reviewed in the development of this recommendation included two RCTs evaluating the outcomes for patients with aphasia because of stroke who received intensive language therapy. In an RCT by Godecke et al. (2021), individuals who received rehabilitation within 14 days of aphasia onset were randomized to undergo usual aphasia therapy or higher-intensity aphasia therapy for 20 sessions.(174) Within the high-intensity group, individuals received either individualized non-prescriptive aphasia therapy (labeled "usual care–plus") or The Very Early Rehabilitation for SpEech (VERSE) treatment. The authors defined VERSE treatment as an impairment-based therapy program that prioritized error-free, verbal communication while achieving between 50–80% accuracy at each goal level. The lower intensity, usual aphasia therapy group was not standardized for duration or frequency of sessions. Participants within this group received an average of 9.5 hours (SD: 7.6) of therapy over a median of 28 days (SD: 17) with participants receiving an average of 2.3 hours of usual aphasia therapy per week. Individuals within the intense treatment cohort (both usual

care–plus and VERSE) received an average of 22.7 hours (SD: 8.4) of therapy over a median of 32 days with participants receiving an average of 5.0 hours of aphasia therapy per week. The primary outcome observed was improvement in communication on a performance-based assessment of aphasia with additional assessment of naming, content production in discourse, QoL, and depression. Outcomes showed significantly improved communicative abilities across measures at 12 and 26 weeks of follow-up for the majority of individuals in both treatment intensities with no statistically significant difference in outcomes between treatment groups.

An RCT study by Rose et al. (2022) compared two intensive interventions in addition to usual care with usual care alone in the treatment of chronic post-stroke aphasia.(175) After a 2-week intervention period, individuals were evaluated immediately and at 12-week follow-up. Individuals within the intensive treatment cohorts were allowed to continue their usual care but also received either constraint-induced aphasia therapy or multimodality aphasia therapy with treatment administered 3.0 hours per day, 5 days per week, for a total of 30.0 hours of treatment. Across all cohorts, fewer than 50% of individuals received no aphasia therapy outside the intervention provided by the researchers. The individuals who received aphasia therapy as a part of their usual care were provided a median number of 10 speech therapy sessions over the 15-week trial period. Although the primary outcome of aphasia severity was not significantly different between groups, several secondary outcomes (naming, functional communication, and communication-related QoL) had statistically significant improvement in the high-intensity groups compared with those who received only usual care at the post-intervention timepoint. However, only word retrieval benefits were maintained at the follow-up timepoint, and the difference was not clinically significant. Of note, naming was measured using the Constraint-induced or Multi-modal Personalized Aphasia Rehabilitation (COMPARE) naming battery, composed of 180 items, 80 of which were trained for individuals in both intensive treatment groups but none of which was trained for the usual care cohort. The statistically significant adjusted MD was noted for these 80 trained items but not for the untrained items.

Some variation occurs in patient preferences regarding this treatment. The patient focus group members noted their preference for stroke treatment to be individualized, which might include differing intensities of treatment. Frequent visits might be burdensome for some patients, whereas others might want to engage in as much rehabilitation as possible. Patients are generally eager to have access to various rehabilitation treatments and desire the information and opportunity to explore all potential options. The resource use associated with intensive therapy is significant, impacting staffing and physical space constraints, and potentially could impact fiscal resources. Additionally, not all individuals post stroke have the medical or mental health stability and endurance, cognitive ability, transportation access, or fiscal means necessary to participate in intensive aphasia rehabilitation.

The Work Group systematically reviewed evidence related to this recommendation.(174, 175) Therefore, it is categorized as *Reviewed, Amended*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including the quality of the outcomes and comparability of the intervention and usual care groups because these were under-specified.(174, 175) The benefits of intensive language therapy in improving outcomes of functional communication and communication-related QoL slightly outweighed the potential harm of the burden of intensive rehabilitation. Patient values and preferences varied somewhat because some patients prefer less intensive treatment. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against a specific intensity of language therapy for aphasia.

d. Spatial Neglect Therapy

Recommendation

36. There is insufficient evidence to recommend for or against hemifield eye patching in addition to traditional therapy to improve functional outcomes in patients with unilateral spatial neglect.
(Neither for nor against | Reviewed, New-replaced)

Discussion

Occurring in two-thirds of patients with acute right hemispheric stroke,(176) unilateral spatial neglect, a distressing consequence of stroke, is a condition in which patients are unaware of or fail to respond to stimuli presented on the side opposite the brain lesion. Traditional therapy for USN includes compensatory strategies directed toward the side of the deficit, including verbal cueing, visual scanning, full head turn (proprioceptive), anchoring techniques, limb activation aids, and environmental adaptations. Hemifield eye patching (HEP) has been used in addition to traditional therapy for patients with USN following stroke. It might be regarded as a remedial visual type of constraint-induced (forced use) therapy. For an individual with a right hemisphere stroke resulting in left visual field loss, left neglect, or both, typically the right half of eyeglasses are patched with dark, non-translucent tape. Hemifield eye patching has been suggested to work by reducing stimulation of the left hemisphere, thereby stimulating the right hemisphere and leading to interhemispheric rebalance.(177)

A Cochrane Review by Longley et al. (2021) analyzed the results of three RCTs(178-180) that included HEP as part of the treatment provided to the experimental group.(181) The control conditions were conventional OT or usual care. The interventions in these trials were variable. The experimental groups in the three RCTs were as follows: Fong et al. (2007) used voluntary trunk rotation in combination with HEP (30 hours of treatment);(179) Machner et al. (2012) used optokinetic stimulation (OKS) in combination with HEP (15 minutes of OKS daily and HEP all day for seven days);(178) and Wu et al. (2013) used constraint-induced movement therapy with HEP (30 hours).(180) All the trials had a relatively high risk of bias in multiple areas, especially the lack of blinding of

patients and study personnel. The study population was heterogeneous in terms of time since stroke (acute to chronic). No difference in ADL outcomes was found, as measured by the FIM and the Catherine Bergego Scale (CBS), either at the end of treatment or at long-term follow-up. The CBS is a standardized checklist used to evaluate the presence and degree of neglect during a therapy practitioner's observation of everyday tasks.

Some variability occurs in provider and patient preferences regarding HEP treatment. Some individuals reject HEP treatment simply because of discomfort. On the other hand, HEP is low-cost, instructor-led, and reinforced during therapies to improve attention to the neglected side. HEP can easily be used during ADL training, though providers must be trained regarding proper patch placement; consultation with an eye care practitioner might be needed. Potential harm includes increased fall risk if patients wear patched glasses during dynamic tasks; patched glasses are recommended for use only during static tasks.

The Work Group systematically reviewed evidence related to this recommendation(181) and considered the assessment of the evidence put forth in the 2019 Stroke Rehabilitation CPG.(178, 182) Therefore, it is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of evidence is very low. The body of evidence had limitations, including overall small sample sizes and lack of blinding of study participants and personnel. Other considerations regarding this recommendation include the balance of benefits, which are unproven, and the potential harms, which included the risk of falls. Patient values and preferences vary somewhat because some patients might be willing to try HEP, although others might not. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against hemifield eye patching in addition to traditional therapy to improve functional outcomes in patients with unilateral spatial neglect.

Recommendation

37. There is insufficient evidence to recommend for or against the use of prism adaptation therapy for patients with unilateral spatial neglect.
(Neither for nor against | Reviewed, Amended)

Discussion

Unilateral spatial neglect refers to a condition in which patients do not react to various environmental stimuli originating from the contralateral side of a brain lesion, in the absence of other sensory or motor deficits.(60) This condition occurs much more frequently with right-side brain lesions than with left-side brain lesions.(61) An important clinical problem for patients with USN is interference with the rehabilitation process by the profound lack of awareness of the contralesional hemispace, which results in poor functional outcomes.(60)

Prism adaptation (PA) is a treatment used for USN that involves brief, daily visuomotor training sessions while wearing optical prisms. PA realigns the left visual field into

attentional focus. The evidence base for this recommendation includes a new Cochrane review, two new RCTs, and two RCTs carried forward from the 2019 VA/DoD Stroke Rehabilitation CPG.(61, 181, 183-185)

A 2021 Cochrane review evaluated the effect of PA on the performance of ADLs in patients with subacute stroke and USN.(181) Participants in five RCTs (n=158) were followed up at the end of a two-week intervention, and 39 patients were followed up at six to eight weeks. The treatment typically included 15- to 20-minute sessions of PA, for a total of 10–20 sessions while performing either a pointing task or engaging in ADLs. In three of the studies, the control group patients wore sham glasses. No effect was found for PA on ADLs as measured by the CBS, either immediately after the intervention or at follow-up. A semiquantitative rating scale, the CBS is administered by a trained examiner or therapy practitioner and is used to evaluate the presence and degree of neglect during the observation of everyday tasks. One study (n=20) had a treatment arm that included the use of FES for 20-minute sessions on the affected upper extremity at an intensity that produced “sufficient” finger and wrist movements. No change in ADLs performance was found with the use of PA with or without FES in this study.(186)

A double-blind RCT (n=23) of patients with moderate to severe USN within one month of stroke compared neutral goggles with prism glasses that shifted the visual field 11.4 degrees to the ipsi-lesional side of space.(183) Of note, two of the patients in this RCT had traumatic brain injury, not stroke. Both groups completed a visuomotor task and a pointing task for 10 training sessions of 15–20 minutes each. In a per-protocol analysis, although both groups improved, there was no significant difference in ADL performance as measured by the CBS, both at the end of treatment and at two- and four-week follow-up. Similarly, a double-blind RCT (n=20) of patients with left moderate-to-severe USN at least one month following stroke compared placebo glasses with prism glasses that shifted the visual field 10.0 degrees to the right.(185) Both groups performed rapid finger-pointing to visual target tasks for 6–10 minutes daily for four weeks. Although both groups improved, no difference between groups was found on the FIM at the treatment conclusion or six-month follow-up.

In contrast, two studies showed positive findings.(61, 184) A double-blind RCT (n=74) of patients with subacute right hemispheric stroke and moderate to severe USN compared neutral goggles with prism glasses that shifted the visual field 11.4 degrees to the right.(184) Both groups performed a pointing task for 12 training sessions of 30 minutes each. At the end of treatment, the intervention group showed a significant improvement in ADLs performance as measured by the CBS (MD: -5.65; 95% CI: -8.10– -3.20; $p<0.001$). A multicenter, double-blind RCT (n=38) of patients with subacute stroke and mild to severe USN compared sham glasses with Fresnel prism glasses that shifted the visual field 12.0 degrees to the right.(61) Prism exposure was 20 minutes, twice per day for 10 days, and the groups performed a pointing task. In post-hoc analyses, significant differences were found in the total FIM score for the group with mild USN but not for the group with severe USN (graphic data only).

Some variation occurs in patient preferences regarding this treatment. Some patients do not tolerate PA because of multiple adverse effects, including headache (the most common side effect), difficulty with navigation, diplopia, optical glare/aberrations, or visual confusion.(187) A moderate amount of time is needed to train providers in PA. In addition, as well as the cost of the prism glasses themselves, PA treatment requires eye specialists with neurological training to prescribe the glasses and a vision therapist to provide the treatment. Access to PA treatment is limited for some patients because such specialists or therapists are unavailable in some geographical areas.

The Work Group systematically reviewed evidence related to this recommendation(181, 183, 184) and considered the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(61, 185, 187) Therefore, it is a *Reviewed, Amended* recommendation. The Work Group's confidence in the quality of evidence is very low. The body of evidence had limitations, including, most prominently, lack of blinding of participants, as well as confounders in the analysis, study personnel, and outcome assessors. The benefits of PA slightly outweighed the potential harm of adverse effects as noted above, most notably headaches. Patient values and preferences vary because some patients do not tolerate PA because of adverse effects. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the use of prism adaptation therapy for patients with unilateral spatial neglect.

D. Mental Health

a. Prevention of Depression

Recommendation

38. There is insufficient evidence to recommend for or against solution-focused psychological interventions (e.g., motivational interviewing, problem-solving therapy) to prevent the development of depression.
(Neither for nor against | Reviewed, New-added)

Discussion

As many as one-half of stroke survivors might develop depression within five years of their stroke.(188) The goal of solution-focused psychological interventions, such as MI and problem-solving therapy, is to identify problems, barriers, or both hindering patients' recovery, thereby empowering them to make progress toward their goals.

A Cochrane SR by Allida et. al. (2020) examined seven RCTs (n=607) comparing psychological interventions to usual care or attention control for the prevention of depression in patients with stroke.(189) Patients with diagnosed depression or anxiety at baseline were excluded. Various forms of psychological interventions were used, including problem-solving therapy, cognitive behavioral coping therapy, broadly defined home-based therapy, solution-focused brief therapy, and MI. Depression was commonly assessed using the Hamilton Depression Rating Scale (HAM-D) and the Hospital Anxiety and Depression Scale (HADS). The psychological interventions reduced the

proportion of people who developed depression (RR: 0.68; 95% CI: 0.49–0.94; p=0.02).(189) However, there were significant methodological concerns noted in the RCTs included in the SR. Specifically, there was a high risk of bias related to incomplete outcome data/attrition for several studies and an unclear risk of bias related to inadequate random sequence generation, allocation concealment, and selective reporting. Several studies also did not report on the blinding of participants and personnel. The authors of the SR concluded that inadequate evidence exists to support the routine use of psychological therapies to prevent depression after stroke.

Some variation occurs in patient values and preferences regarding psychological interventions. Some patients might dislike talk therapy or might fear the stigma associated with engaging in behavioral health services, whereas other patients might be willing to participate in such services. The time burden and resource use might even outweigh the potential benefits of these interventions, given that many stroke patients do not go on to develop depression. Resources required include staff trained and proficient in delivering solution-based therapies such as MI.

The Work Group systematically reviewed evidence related to this recommendation.(189) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had serious limitations, including various sources of high or unclear risk of bias, as discussed above.(189) Benefits of participating in solution-focused psychological interventions were balanced with the potential harms (e.g., time burden). Patient values and preferences vary somewhat because some patients like talk therapy and others do not and because some patients might wish to avoid mental health stigma. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against solution-focused psychological interventions (e.g., motivational interviewing, problem-solving therapy) to prevent the development of depression. However, the Work Group emphasizes that if patients with stroke develop symptoms of depression, they should seek mental health services. This specific recommendation applies to the prevention of depression only in patients with stroke, not those who are not already experiencing symptoms of depression. See Recommendation 42 and Recommendation 43.

Recommendation

39. We suggest against the use of antidepressants for the prevention of post-stroke depression.
    (Weak against | Reviewed, New-replaced)

Discussion

The evidence in the 2019 VA/DoD Stroke Rehabilitation CPG focused specifically on SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRI) and provided mixed results. Salter et al. (2013) and Zhang et al. (2013) demonstrated a reduced risk of post-stroke depression with prophylactic use of SSRIs or duloxetine, respectively.(190, 191) A higher-quality study by Kim (2017) did not demonstrate any difference in the

proportion of individuals with depression in the treatment (escitalopram) and placebo groups.(192) Given the mixed results, the 2019 VA/DoD Stroke Rehabilitation CPG concluded there was insufficient evidence to recommend for or against the use of SSRIs or SNRIs for the prevention of depression after stroke.

Allida et al. (2020) conducted an SR on the use of pharmacotherapy to prevent the development of depression after a stroke.(193) This was an update to a Cochrane review first published in 2004 by Anderson et al. (2004) and updated in 2008 by Hackett et al. (2008).(194, 195) Allida et al. (2020) identified 12 RCTs (n=734), consisting of 14 interventions, that examined a variety of ADs to prevent post-stroke depression. The ADs examined were common first-line ADs as well as less frequently used ADs and other medications with AD effects, including fluoxetine, sertraline, escitalopram, paroxetine, trazodone, nortriptyline, milnacipran, piracetam, maprotiline, mianserin, and methylphenidate. Pharmacotherapy was compared with placebo. The majority of participants had ischemic stroke and their mean age ranged from 55–73 years old. Studies containing mixed-etiology populations (e.g., stroke and brain injury), participants with depression at baseline, or both were excluded. The sex and race of participants were not reported. Time since stroke ranged from three days to 3 weeks, thus covering a range of stroke recovery phases. Treatment duration ranged from 4–52 weeks, with four trials using fixed dosing and eight trials using flexible or escalating dosing. The primary outcome at the end of treatment, the incidence of depression, was measured by 1) meeting standard diagnostic criteria for depression or 2) scoring above the cutoff for a depressive disorder on standard scales of depression, predominantly the HAM-D and the HADS.

Analysis of the 9 pharmacological interventions (n=734) with available outcome data indicated that those who received the pharmacological treatment were less likely to develop depression compared with those who received the placebo (RR: 0.50; 95% CI: 0.37–0.68, p=NR).(193) For the secondary outcome, the severity of depressive symptoms, there was no difference between groups. For example, in two trials (n=211), there was no significant difference in the mean change in depression scores between baseline and end of treatment in the pharmacotherapy group compared with the placebo group. Additionally, four studies (n=100) did not demonstrate any statistical difference in depression symptoms at the end of treatment between the intervention and placebo groups.

The quality of the evidence was considered poor because of unclear or high risk of bias, including selection bias (random sequence generation and allocation concealment), performance and detection biases owing to lack of blinding of participants and outcome assessors, and attrition bias. Given the very serious limitations in study quality and risk of bias, as well as serious indirectness given the variation in interventions and classes of pharmacological treatments used, the confidence in the quality of the evidence is very low.

In terms of risks and benefits of pharmacological intervention for the prevention of depression after stroke, a smaller subset of eight trials (9 interventions, n=496) reported on adverse events, and there was no difference found between the pharmacotherapy and placebo groups in risk of death or other adverse events. The FOCUS trial (2019; n=3,127) revealed potential risks of AD use in the stroke population, namely increased risk of falls and hip fractures, but, unfortunately, these potential risks were not measured, not reported in studies included in the current systematic review, or both.(196) The wide variation in treatment duration, ranging from 4–52 weeks, could also impact risks and benefits. The benefits of pharmacological treatment might not be demonstrated at 4 weeks because the full effect of ADs can take 4–8 weeks to be realized. Given the risk of falls, hip fractures, and complications of polypharmacy, the benefits of the long-term use of ADs in this population might not outweigh the risks, especially when ADs are prescribed for the prevention of a potential future illness that might not even occur. Additionally, there were no follow-up studies conducted and thus sustainability of treatment effects could not be examined. Depression can be a barrier to rehabilitation and recovery and can increase mortality after a stroke; thus, it should be assessed, monitored, and treated.(188)

Some variation occurs in patient preferences and values. In addition to the mental health stigma associated with AD use, many Service members and Veterans dislike taking medication and might be even less inclined to do so for a mental health condition they are not currently experiencing and that might or might not occur in the future. Although ADs are typically inexpensive and widely available, the acceptability of prescribing a medication with potential side effects for prophylaxis, rather than for treatment of depression, might be low for providers.

The Work Group systematically reviewed evidence related to this recommendation (193) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(190-192) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including selection, detection, performance, and attrition biases. Given the potential risks of ADs (e.g. falls, hip fractures), which slightly outweigh the benefits of preventing potential depression, and the very low quality of evidence, we do not recommend the universal, routine use of ADs for the prevention of post-stroke depression. Patient values and preferences vary somewhat because some patients do not want to take medication for a mental health condition that might or might not occur in the future. Thus, the Work Group made the following recommendation: We suggest against the use of antidepressants for the prevention of post-stroke depression.

b. Treatment of Depression

Recommendation

40. We suggest a selective serotonin reuptake inhibitor or a serotonin norepinephrine reuptake inhibitor for depression symptoms.
(Weak for | Reviewed, Amended)

Discussion

The 2019 VA/DoD Stroke Rehabilitation CPG suggested offering SSRIs or SNRIs for treatment of post-stroke depression, based on review of one NMA(197) and 1 RCT(196). The evidence base for the current recommendation consisted of one NMA and two MAs, which corroborated the findings of the 2019 VA/DoD Stroke Rehabilitation CPG.(198-200)

Li, L. et al. (2020) found that paroxetine was superior to a comparator of "routine treatment" at 4-week and 12-week follow-up in 98 patients (2 RCTs) with post-stroke depression(198-200) as measured by the HAM-D (4-week follow-up MD: -7.64; 95% CI: -10.05– -5.23; p<0.0001 and 12-week follow-up MD: -9.79; 95% CI: -16.94– -2.64; p=0.007).(199) Feng et al. (2022) found that escitalopram (mostly dosed at 5–10 mg per day) was superior to placebo at 1- to 12-month follow-up in 612 patients (7 RCTs) with or without depression at baseline as measured by the HAM-D and other measures at the end of treatment (SMD: -1.25; 95% CI: -1.82– -0.68; p<0.001).(200) Findings did not differ by depression status at baseline. Li, X. et al. (2020) performed an NMA of 15 RCTs with 5,547 patients with post-stroke depression, and measured the mean change in total HAM-D score after treatment with multiple different types of ADs.(198) These ADs included tricyclic ADs, which are not recommended for treatment of depression in the 2022 VA/DoD CPG for the Management of Major Depressive Disorder[h] because of their side effect profile. Extensive analyses included comparisons of SSRIs and SNRIs to placebo and revealed that SSRIs and SNRIs consistently outperformed placebo at 4-week follow-up, 8-week follow-up, and end of treatment. The mean change in HAM-D score consistently met the MCID for all analyses except for paroxetine at 4 weeks. However, the data in these three SRs should be interpreted with caution because of missing key information, such as time since stroke and past AD treatment.(198-200) Multiple studies included in the SRs did not explicitly delineate whether patients were diagnosed with depression at baseline or merely exhibited depressive symptoms.

The potential benefits of SSRIs and SNRIs and the risks of untreated depression must be balanced with the potential harms. Common side effects of these medications include drowsiness, dry mouth, diarrhea, nausea, restlessness, anxiety, dizziness, headache, insomnia, and reduced sexual desire or function. In a large-scale study in the stroke population, an additional side effect was identified. The FOCUS Trial Collaboration (2018) examined the effect of 6 months of fluoxetine (versus placebo) on

[h] https://www.healthquality.va.gov/guidelines/MH/mdd/

functional and mood outcomes in 3,127 acute stroke patients with persisting focal neurological impairments.(196) This large-scale study identified an additional side effect. Side effect data revealed that the risk of bone fractures in the fluoxetine group nearly doubled (difference between treatment and placebo group 1.41%, 95% CI: 0.38–2.43; p=0.007). Although the absolute number of individuals affected might be small, the potential risk must be considered in each case and weighed against the risks of untreated depression, which is associated with increased disability and death in individuals with stroke.(188) Additional information on SSRIs and SNRIs can be found in the 2022 VA/DoD CPG for the Management of Major Depressive Disorder.[f]

Some variation likely occurs in patient values and preferences regarding the treatment of post-stroke depression with medication because of mental health stigma. Some patients might prefer to avoid treatment with medication because of this stigma, and others might prefer to avoid medications in general. Other considerations include that SSRIs and SNRIs are widely available and generally affordable. Many of these medications have unique pharmacokinetic and pharmacogenomic properties that require careful attention when prescribing to optimize outcomes and mitigate the risk of adverse drug reactions.

The Work Group systematically reviewed evidence related to this recommendation (198-200) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(196, 197) Therefore, it is categorized as a *Reviewed, Amended* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, as described above. The benefits of SSRIs and SNRIs outweighed the potential harms of known side effects, which are typically mild. Patient values and preferences vary somewhat because some patients might prefer to avoid taking medications. Thus, the Work Group made the following recommendation: We suggest a selective serotonin reuptake inhibitor or a serotonin norepinephrine reuptake inhibitor for depression symptoms.

Recommendation

41. We suggest psychotherapy (e.g., cognitive behavioral therapy) for depression following stroke.
    (Weak for | Reviewed, New-replaced)

Discussion

In the general population, evidence exists of the effectiveness of a variety of psychotherapeutic interventions for the treatment of depression (e.g., behavioral therapy/behavioral activation, cognitive behavioral therapy [CBT], Acceptance and Commitment Therapy [ACT], interpersonal therapy, mindfulness-based cognitive therapy) (see the 2022 VA/DoD Major Depressive Disorder CPG[f]). Cognitive behavioral therapy is a class of interventions designed to change dysfunctional forms of thinking and behavior to directly reduce psychological suffering.(201) More simply stated, CBT is based on the idea that mental health problems are partially due to distorted thinking and

learned patterns.(201) Evidence from the 2019 VA/DoD Stroke Rehabilitation CPG suggested that psychotherapy interventions improve depressive symptoms in patients following stroke.(193, 201-207)

For the current systematic evidence review, the Work Group identified two SRs examining various psychological interventions versus usual care or alternative behavioral therapies. Ahrens et al. (2023) included 10 studies (n=672), six of which were RCTs, examining computer-based CBT or traditional CBT, with or without coping skills intervention or cognitive rehabilitation.(201) These interventions were compared with a variety of alternative behavioral therapies, including psychoeducational therapy and usual care, computerized cognitive training, computerized cognitive remediation therapy, or stress management education. The duration of intervention ranged from 8-16 weeks, with a mean duration of about 10 weeks. One of the primary outcomes was depression symptoms, which was measured by the Beck Depression Inventory in most studies. They found that CBT improved general depression symptoms immediately after intervention (SMD: 0.945; 95% CI: 0.52–1.37; p<0.000) and also at 3 months after intervention (SMD: 0.62; 95% CI: 0.097–1.46; p<0.025).(201) It is notable that Ahrens et al. (2023) included studies that used mostly group-based CBT interventions, which allowed participants to connect to peers experiencing the same difficulties, to reduce feelings of isolation and depressive symptoms. Additionally, they found that group-based interventions had similar effect sizes as individual-based CBT interventions, demonstrating the potential for increased access and cost-savings using group-based programs.(201)

Another SR by Allida et al. (2020) analyzed six RCTs (n=521) examining various psychological therapies, including structured CBT delivered by trained psychologists or nurses, MI delivered by nurses or non-clinical psychologists, psychosocial therapy delivered by psychiatric mental health nurse practitioners in person or via telephone, group psychotherapy, and psychotherapy with an ecosystem aspect.(193)These interventions were compared with usual care or attention control. The primary critical outcomes were depression prevalence and depression symptoms, as measured by the General Health Questionnaire, the HAM-D, and the HADS. The authors found that psychological therapies did result in improvement in depression prevalence (RR: 0.77; 95% CI: 0.62–0.95; p=0.01) and depression symptoms (MD: -6.2; 95% CI: -8.24–-4.16; p<0.001) at the end of treatment, there was no difference between the groups at the end of follow-up.(193) Patients were followed for up to 36 months in some studies, though the sample size at final follow-up was only 201 patients compared with 521 patients immediately following treatment.

Although the evidence supports the use of psychotherapy for depression following stroke, some variability occurs in both provider and patient preferences toward this intervention. Certain patients might seek to avoid the stigma associated with a mental health diagnosis and, therefore, might embrace psychotherapy less readily. Additionally, some individuals might be disinclined to invest the requisite time and effort that

psychotherapy demands, including engagement in homework assignments, practice, and self-reflection. Despite potential challenges posed by stroke-induced cognitive-linguistic impairments, psychotherapy demonstrates adaptability and employs techniques conducive to participation for those encountering cognitive difficulties. The present-centered orientation of psychotherapy, coupled with its structured framework involving worksheets and tangible methodologies, renders it suitable for a considerable cohort of stroke patients. It is worth noting that effective psychotherapy is administered by a social worker, psychologist, or other licensed mental health practitioner and, especially in individual sessions, might require a significant allocation of resources. It is also important to note that it is atypical for psychotherapy interventions to be delivered by nursing professionals in the United States, as was done in some of the trials included in the SRs.

The Work Group systematically reviewed evidence related to this recommendation(193, 201) and considered the assessment of the evidence put forth in the 2019 VA/DoD Stroke Rehabilitation CPG.(202-207) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations resulting in risk of bias. Some studies had a lack of adequate allocation concealment procedures; lack of blinding of participants, study personnel, or both; and incomplete outcome data.(193, 201) The benefits of psychotherapy (e.g., CBT) to treat depression following stroke slightly outweighed potential harms. Patient values and preferences varied somewhat because some patients might wish to avoid mental health treatment owing to associated stigma. Thus, the Work Group made the following recommendation: We suggest psychotherapy (e.g., cognitive behavioral therapy) for depression following stroke.

Recommendation

42. We suggest mindfulness-based therapies for treatment of depression following stroke.
    (Weak for | Reviewed, New-added)

Discussion

Mindfulness is a process of being fully present in the moment with intention and a nonjudgmental awareness. Numerous psychotherapeutic approaches use mindfulness-based techniques. Tao et al. (2022) conducted an SR/MA on the effectiveness of mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT) for post-stroke depression.(208) Both MBSR and MBCT are well researched, structured interventions that have demonstrated effectiveness when used with a wide range of populations for the treatment of depression and anxiety as well as for coping with various medical conditions.(209-214) Unlike previous studies, Tao et al. (2022) included RCTs in which MBSR and MBCT were used exclusively in patients with stroke, as opposed to patients with a range of vascular diseases.(208) The SR/MA contained seven studies (n=502) and consisted of participants with subacute to chronic stroke who

received MBSR or MBCT for post-stroke depression. Comparators were usual care, waitlist control, no-treatment control, or patient education without a mindfulness component. The mean age ranged from 51.63–64.80 years of age in the intervention group and from 50.5–67.3 years of age in the control group. Although the MA demonstrated a positive main effect of the mindfulness interventions on self-reported depression scores compared with controls (SMD: 0.93; 95% CI: -1.34– -0.53; p<0.001), three of the seven RCTs included participants in which depression was not clinically defined at baseline. One study included patients with "post-stroke mental fatigue" and two other studies did not report how post-stroke depression was defined or determined. Therefore, the Work Group's recommendation is based on the sub-analysis of the four RCTs (n=315) in which participants met the Chinese or American diagnostic criteria for depression on study inclusion and completed well-established validated measures of depression (HAM-D; Zung Self-Rating Depression Scale) at baseline and immediately post-intervention. The overall pooled results of the four trials demonstrated that post-intervention, self-reported depression scores in the MBSR and MBCT treatment group were significantly lower than those in the control group (SMD: -1.27; 95% CI: -1.71– -0.84; p<0.001). The mindfulness interventions had a large positive effect on post-stroke depression.

The confidence in the quality of evidence was very low because of a high risk of bias related to inadequate random sequence generation procedures, allocation concealment procedures, and blinding of outcome assessors. Reporting bias was felt to be likely present. The studies also had serious inconsistencies.

In terms of risk of harm, none of the trials examined safety or adverse effects; however, in general, the risks associated with psychotherapy and mindfulness are considered small and include the possibility of experiencing temporary psychological distress. Both MBSR and MBCT are intensive interventions and might be considered burdensome by some individuals. In addition to weekly two-hour group sessions for eight weeks, MBSR and MBCT include daily independent mindfulness practices, some of which include mindful movement (which can be adapted for a range of physical abilities) as well as completion of self-monitoring diaries or logs. Furthermore, these specific mindfulness protocols typically include a full-day mindfulness retreat, potentially adding to the perception of treatment burden. For participants in rural or austere environments, mindfulness-based therapies can be offered via video telehealth. The two-hour sessions and a full-day retreat could represent a staffing burden, though groups often contain approximately 20 participants, which could be considered relatively efficient.

Some variation occurs in patient preferences regarding this treatment. It is time intensive, requiring motivation and commitment to daily practice as well as weekly two-hour group sessions. Therefore, some patients might prefer a less intensive psychotherapeutic approach (e.g., CBT) or the simplicity of medication. For active duty Service members, this time commitment might be particularly burdensome. Some individuals find mindfulness challenging or feel too anxious or restless to participate in

meditation practices. Although mindfulness meditation is not a religious practice, some people might feel it is inconsistent with their own religious beliefs and practices. On the other hand, some individuals prefer a non-medication approach to the treatment of depression, are interested in learning and engaging in CIH approaches to conventional medicine, or both.

From a systems resource point of view, it should be noted that MBSR and MBCT facilitator competencies require considerable experiential training. At a minimum, practitioners should have completed their own personal MBSR program and have their regular meditation practice. Formal certification in MBSR is lengthy and expensive. However, other training options for facilitators are available, such as through the Veterans Affairs Compassionate Awareness Learning Module (VA CALM) training. Mindfulness-based techniques are also incorporated into other less intensive cognitive behavior therapies and can also be accessed through mobile technology applications, which can increase feasibility, accessibility, and acceptability.

The Work Group systematically reviewed evidence related to this recommendation.(208) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The SR by Tao et al. (2022) had some limitations because of population heterogeneity, selection bias, detection bias, performance bias, reporting bias, and inconsistency. The benefits of MBSR and MBCT for the treatment of post-stroke depression slightly outweigh the potential harms, such as temporarily experiencing emotional or physical discomfort or both. Patient values and preferences varied somewhat because of intensity and time burden and potential dislike for mindfulness meditation. Thus, the Work Group made the following recommendation: We suggest mindfulness-based therapies for treatment of depression following stroke.

Recommendation

43. There is insufficient evidence to recommend for or against acupuncture, either alone or as an adjunct to pharmacotherapy, for depression following stroke. **(Neither for nor against | Reviewed, New-added)**

Discussion

Acupuncture is a TCM technique performed by highly trained practitioners using specialized thin needles for the treatment of multiple health conditions. Acupuncture is theorized to work by stimulating various parts of the body to regulate the flow of Qi.(137) The evidence base for this recommendation included two SRs and two NMAs.(215-218)

An NMA by Li et al. (2023) of 38 RCTs (n=2,898) evaluated interventions that included various types of acupuncture plus AD versus AD alone.(215) Patients were treated for 2–13 weeks. At the end of treatment, various types of acupuncture plus ADs were found to be more effective than ADs alone as measured by a 25% or more reduction in scores on the HAM-D and by reduction in total HAM-D score. Of note, the authors also studied

acupressure or auricular pressure plus AD versus AD alone, and the results showed no difference between the two groups in the HAM-D response rate.

Wang et al. (2021) performed an SR/MA of 19 RCTs (n=1,606).(217) The intervention studied was electroacupuncture versus SSRI therapy, and patients were treated for 4–12 weeks. Incidence of depression was measured by the HAM-D. At 4 weeks, a small effect (SMD: -0.30; 95% CI: -0.58– -0.01; p=0.04) was observed in favor of electroacupuncture. However, the CI was near 0 and no difference was seen at 6- and 8-week follow-up.

An NMA conducted by Hang et al. (2021) included 51 RCTs (n=3,966).(218) The intervention was various types of acupuncture with or without AD versus conventional acupuncture, AD, or conventional acupuncture plus AD. Patients were treated for 4–12 weeks. At the end of treatment, the HAM-D response rate (greater than or equal to 25% reduction in the HAM-D total score) showed inconsistent results with no clear benefit for any particular intervention or combination of interventions.

It was observed by the Work Group that all four studies were performed in China, where acupuncture is widely accepted and is a preferred treatment for multiple conditions, including depression, with a high cultural expectation of benefit.(137) Therefore, these results might not be replicable and are unproven in the U.S. population. Other considerations include the need for trained acupuncturists. Finally, the Work Group considered the 2022 VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder,[f] which recommended neither for nor against acupuncture as an adjunct for the treatment of major depressive disorder.

Some variation occurs in patient preferences regarding this treatment. Some patients might prefer conventional medicine approaches (usually pharmacological management with or without counseling), whereas other patients might be interested in CIH approaches such as acupuncture. Some patients might dislike acupuncture because of needle phobia. Potential harms associated with acupuncture are mild and might include syncope, subcutaneous hemorrhage, pain, and nausea.

The Work Group systematically reviewed evidence related to this recommendation.(215-218) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of evidence was very low. The body of evidence had several limitations, including multiple confounders in the analysis, most prominently a lack of an adequate control group. The benefits of acupuncture in the treatment of post-stroke depression are balanced with the potential harms, which are mild and might include syncope, subcutaneous hemorrhage, pain, and nausea.(217) Patient values and preferences varied somewhat because some patients might have a strong preference for CIH approaches, although some might prefer conventional medicine approaches. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against acupuncture, either alone or as an adjunct to pharmacotherapy, for depression following stroke.

E. Telehealth

Recommendation

44. We suggest either face-to-face therapy or telerehabilitation, depending on patient characteristics and preferences.
(Weak for | Reviewed, New-added)

Discussion

Telerehabilitation uses communication technology to facilitate communication between providers and patients. Evidence suggested telerehabilitation was at least equal to usual care for improving independence in ADLs and balance in patients post stroke.(219, 220) In an SR by Tarihoran et al. (2023) (n=478), telehealth resulted in a greater ability to perform ADLs and maintain balance compared with a control group.(220) Four studies (n=318) in Tarihoran et al. (2023) noted improvement in ADLs with telehealth treatment compared with control measured by the mBI (SMD: 0.57; 95% CI: 0.13–1.01; p=0.01). Four studies (n=160) in Tarihoran et al. (2023) also noted improvement in balance with telehealth treatment compared with control measured using the BBS (SMD: 1.96; 95% CI: 1.27–2.66; p<0.001).

A Cochrane review by Laver et al. (2020) (n=1210) examined telerehabilitation services for stroke survivors post–hospital discharge; low-quality evidence among 351 patients showed no difference between telerehabilitation and in-person rehabilitation for balance, upper limb function, and independence in ADLs.(219) Similarly, low-quality evidence showed no difference between telerehabilitation and usual care in 198 patients post hospital discharge for mobility and upper limb function. Moderate quality evidence in 661 patients post–hospital discharge revealed no difference between telerehabilitation compared with usual care for independence in ADLs.(219) The heterogeneity of these studies did not allow the Work Group to decipher which specific rehabilitation techniques were most beneficial and which subgroups of patients would benefit the most from telerehabilitation. The majority of RCTs within the SR evaluated patients post stroke living in the community.(219)

Overall, the evidence suggests telerehabilitation is at least equivalent to in-person rehabilitation for motor outcomes, and it might be more accessible than in-person rehabilitation for certain stroke patients.(219, 220) The provider should consider additional factors, such as technological literacy, caregiver support, and devices and bandwidth, which might impact the patient's ability to participate in telerehabilitation.

Some variation occurs in patient preferences regarding this treatment. One study found individuals randomized to telehealth rehabilitation had slightly lower levels of satisfaction compared with those randomized to in-person rehabilitation.(219) Adverse events, most commonly arm and shoulder pain, were infrequent in incidence and similar in both the telerehabilitation and the control groups. The patient focus group noted that in-person rehabilitation can be burdensome because it requires frequent visits.

However, some individuals might be uncomfortable using technology or might prefer in-person rehabilitation. Post-stroke rehabilitation might also require special equipment, which is unavailable in some locations or in the patient's home. On the other hand, telerehabilitation might decrease the burden of travel on the patient, especially in areas with limited access to providers. With the use of telerehabilitation, providers might also find reaching more patients in need easier. One study found telehealth compared with an in-clinic program saved $654 per patient.(219)

The Work Group systematically reviewed evidence related to this recommendation.(219, 220) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including small sample sizes, lack of clear allocation concealment, and bias in patient recruitment.(219, 220) The benefits of telerehabilitation in improving stroke rehabilitation outcomes outweighed the potential harms because potential harms were unidentified. Patient values and preferences varied somewhat because some patients are uncomfortable using technology, although other patients might prefer telerehabilitation as a more convenient option. Thus, the Work Group made the following recommendation: We suggest either face-to-face therapy or telerehabilitation, depending on patient characteristics and preferences.

Recommendation

45. There is insufficient evidence to recommend for or against the use of telerehabilitation and technology-based interventions to improve stroke-related dysphagia or aphasia outcomes or both.
    (Neither for nor against | Reviewed, New-added)

Discussion

Interest in telerehabilitation and technology-based interventions has surged, particularly within post-stroke populations. This format offers an opportunity to deliver therapeutic interventions independently or alongside traditional therapy modalities. In doing so, it increases the accessibility to rehabilitation services. Telerehabilitation specifically centers on the remote delivery of these services, leveraging digital communication technologies, such as computers and mobile devices, to deliver remote stroke rehabilitative services. These telerehabilitation services aim to help patients recover, maintain, or improve their physical, cognitive, or functional abilities after a stroke. Smart applications, a tool used for telerehabilitation, aim to improve communication among health care providers, patients, and families. Health-related smart applications for stroke rehabilitation have three primary aims: task prompting, biometric measurement, and communication facilitation. Task prompting applications allow patients to self-assess blood pressure, strength, cognitive function, and other such metrics post stroke. Biometric measuring apps paired with smartwatches and other devices actively monitor a patient's stroke-related biometrics (heart rate, oxygen saturation, movement) while also screening for serious stroke-related health issues such as atrial fibrillation.

Communication facilitation apps aim to enhance real-time communication among patients, families, and their stroke rehabilitation team through video calls, text messaging, and other modalities.

The foundation of this recommendation is supported by evidence from a review of five RCTs. Trials focusing on telehealth employed various delivery formats, including synchronous, asynchronous, and hybrid models, to provide stroke rehabilitation services.(221-224)

Aphasia

An RCT by Øra et al. (2020) (n=62) included individuals with both acute and chronic aphasia.(221) The control group received in-person usual care administered by a speech-language pathologist, while the experimental group received the same in-person usual care supplemented with an additional five hours of telerehabilitation over 4 weeks. The telerehabilitation component specifically involved impairment-based methods delivered synchronously through video conferencing with a therapist. In the experimental group, statistically significant improvements were observed in key linguistic domains, specifically in the areas of repetition and sentence production, as measured by a variety of standardized measures such as the Verb and Sentence Test.(221) Of note, the experimental group received additional therapy time, which likely influenced the results.

Asynchronous delivery allows participants to practice tasks using various technological platforms (e.g., computer programs, tablet-based applications), with feedback or guidance administered remotely. This mode of delivery was implemented in three RCTs each employing distinct computerized and digital therapeutic applications.(222-224) That all three RCTs discussed below failed to clarify the qualifications or specific roles of the individuals overseeing patient check-ins and providing guidance is noteworthy. Clarifying these aspects is essential for a comprehensive understanding of the efficacy and implications of asynchronous telehealth interventions in the context of patient care. Two of the aforementioned RCTs incorporated an asynchronous model that autonomously adjusted and modified the therapeutic program based on the patient's performance during weekly or every two week check-ins with an individual.

In an RCT by Braley et al. (2021) (n=32), the experimental group underwent a rigorous treatment regimen using the digital therapeutic Constant Therapy-Research (CT-R) technique for 30 minutes per day, five days a week, for 10 weeks.(222) CT-R is a digital therapeutic software program accessible via tablet devices that includes science-based speech, language, and cognitive therapy exercises. This group's activities also included check-ins every two weeks with a provider to assess progress. The control group received usual care, which included a daily exercise routine derived from an established aphasia or cognitive rehabilitation workbook for five days a week. At the end of treatment (10 weeks), the CT-R intervention group, compared with the control group, exhibited statistically and clinically significant improvements as measured by the

Western Aphasia Battery-Aphasia Quotient (WAB-AQ). The intervention group did receive more intensive therapies, which could have influenced the results. (222)

In an RCT by Maresca et al. (2019) (n=30), an experimental linguistic treatment (ELT) was assessed using a tablet-based Virtual Reality Rehabilitation System.(223) Over 12 weeks, both the intervention and control groups engaged in identical face-to-face ELT exercises, using the tablet system and paper-and-pencil tools, respectively. Notably, all participants were inpatients during this phase. After discharge, for the following 12 weeks, the intervention group continued using the tablet-based system remotely, while the control group transitioned to conventional community-based care with in-person traditional linguistic treatment facilitated by a therapist. The experimental group had twice weekly check-ins with a neuropsychologist to monitor progress. The therapy dose for the control population was not specified. The results showed significant gains in multiple language domains for both groups. However, the experimental group, when compared with the control group, had statistically significant improvements in reading and calculation outcomes after the 6-month treatment period.(223) However, because the therapy dose for the control group was unspecified, determining whether this improvement was simply due to a greater therapy dose in the experimental group is impossible. As mentioned above, the programs used by Braley et al. (2021) and Maresca et al. (2019) independently adjusted the difficulty level as the study progressed.(222, 223)

In a larger RCT involving 278 participants by Palmer et al. (2019), individuals with chronic post-stroke aphasia underwent 6 months of computerized word-finding practice using 100 selected words (StepByStep Aphasia Software; Gloucestershire, United Kingdom) for 20-30 minutes a day.(224) The control group received usual care, which consisted of speech and language therapy face to face with a median of 5 hours and 20 minutes of therapy time over 3 months. An attention control group completed one puzzle (i.e., maze, word search) daily. Results revealed a statistically significant improvement in the experimental group in personally relevant word retrieval on a picture naming test at 6 months, with sustained improved performance at 9 and 12 months. However, no improvement was observed in conversational speech.(224) Again, the experimental group had increased total therapy time compared with the control group.

Dysphagia

In an RCT by Zhang et al. (2022), the efficacy of smart health application-based rehabilitation (n=30) versus routine rehabilitation (n=30) for 12 weeks was explored in a cohort of patients with post-stroke dysphagia.(225) Various outcome measurements, including the Water Swallow Test (WST), Standardized Swallowing Assessment (SSA), Swallow Quality-of-Life Questionnaire (SWAL-QOL), Stroke Self-Efficacy Questionnaire (SSEQ), Perceived Social Support Scale (PSSS), and nutritional indicators, were recorded in both groups. At the study's initiation, there were no significant differences in measurements between the intervention and control groups. However, following the 12-week intervention period, the intervention group exhibited statistically significant

improvements in WST and SSA scores in comparison with the control group ($p<0.01$). Furthermore, SWAL-QOL, SSEQ, and PSSS scores in the intervention group were significantly higher than those in the control group ($p<0.01$). The intervention group also demonstrated an increase in serum prealbumin levels ($p<0.01$), although no significant differences were observed in body weight, triceps skinfold thickness, total protein, or serum albumin. The findings indicate that smart health-based rehabilitation confers significant benefits in terms of swallowing function, QoL, self-efficacy, and social support for patients with post-stroke dysphagia, compared with routine rehabilitation. Nevertheless, acknowledging certain limitations inherent in the study is imperative, such as a small number of subjects, the absence of double blinding, a relatively short intervention period, and potential confounding effects related to spontaneous recovery. Additionally, the study did not independently collect data on baseline neurological impairment severity using widely available tools such as the National Institutes of Health Stroke Scale.

These studies collectively suggest that telerehabilitation and technology-based interventions have the potential to be a beneficial mode of rehabilitation service delivery for aphasia and dysphagia treatment. Further studies of telerehabilitation and technology-based interventions with standardized approaches are needed, given the existing variability in research methodologies and outcomes.

Patient preferences exhibit notable variability concerning treatment modalities. Insights from the patient focus group underscore the significance of support from health care providers, immediate feedback, and direct engagement as facilitators in goal attainment. Participants within the patient focus group expressed a preference for collaborative efforts with their providers in establishing personalized goals aligned with their hobbies and activities. This inclination toward customization should be considered when determining the mode of service delivery (e.g., synchronous, asynchronous, hybrid), considering the level of provider interaction deemed preferable or essential by the patient. Individuals within the focus group who reported residual vision and reading impairments post stroke distinctly favored in-person assistance and communication over reliance on a website or virtual platform for their care. Notably, there appears to be an overall inclination toward a relatively high level of provider interaction among patients. However, participants emphasized the importance of providers reassessing options, reconsidering intervention delivery methods, or augmenting their treatment, particularly when progress slows. In this context, telehealth and technology-based interventions emerge as a valuable avenue to augment face-to-face services, presenting increased opportunities for application in the subacute or chronic phase. This strategic integration of telehealth and technology-based interventions could be instrumental in sustaining achieved gains and increasing the potential for further gains, thereby catering to the dynamic needs of patients in the aftermath of a stroke.(222, 223) Regarding smart application usage, one major constraint is the potential cost associated with obtaining the necessary hardware for this treatment, which can be prohibitively expensive for

some. Additionally, accessibility is a concern because most applications rely on internet connectivity. Finally, patients with post-stroke cognitive, hearing, or visual impairment or any combination of the aforementioned impairments might find effectively operating such technology challenging. Despite these limitations, the Work Group recognized that telehealth, telerehabilitation, and technology-based interventions/smart applications can be helpful tools in the rehabilitation journey of patients with stroke. Further research is indicated to address existing limitations and to provide a more robust foundation for guiding clinical practice in the future.

The Work Group systematically reviewed evidence related to this recommendation.(221-225) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including small sample sizes, lack of participant blinding, increased therapy dose in the intervention groups compared with the control groups, and absence of intention-to-treat analyses.(223, 224) One RCT was notable for lack of baseline comparability of groups and also high attrition.(224) Patient values and preferences varied somewhat because some patients enjoy working with technology, whereas others do not or might have difficulty doing so because of post-stroke impairments. The benefits of telerehabilitation and technology-based interventions likely outweigh the potential harms (time burden). Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the use of telerehabilitation and technology-based interventions to improve stroke-related dysphagia or aphasia outcomes or both.

Recommendation

46. There is insufficient evidence to recommend for or against technology-based caregiver support/education interventions to improve caregiver quality of life. **(Neither for nor against | Reviewed, New-added)**

Discussion

The systematic evidence reviewed included two SR/MAs with more than 3,000 caregivers of patients with stroke (n=1,276 and n=2,003, respectively).(226, 227) Across both SR/MAs, the studies were heterogeneous in terms of intervention, format, intensity, duration, and follow-up periods. Interventions included psychoeducational, informational, supportive, and psychosocial treatments or combinations thereof. These were delivered in a variety of formats, including face-to-face, books or pamphlets, telephone, email, video, and web. The duration of the interventions ranged from 2–13 months (number of sessions not specified) with follow-up periods of 1–12 months. One SR found a small, positive effect on caregiver depression at the end of treatment for interventions that delivered technology-based structured educational programs when compared with usual care(227) (SMD: -0.27; 95% CI: -0.49– -0.05; p=0.02), but that did not hold for the other SR.(226) In addition, no differences were observed in either SR for caregiver anxiety, caregiver perceived burden, or caregiver QoL.

Some variation occurs in patient preferences regarding this treatment. The patient focus group identified caregiver support as an unmet need. However, regarding web-based interventions, some patients enjoy working with technology, whereas others do not. This type of intervention requires significant time investment, trained staff, and, in some interventions, the development of web-based tools.

The Work Group systematically reviewed evidence related to this recommendation. (226, 227) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of evidence was very low. The body of evidence had some limitations, including confounders in the analysis, most prominently lack of blinding of participants, study personnel, and outcome assessors. The benefits of technology-based caregiver support, education interventions, or both in improving caregiver QoL slightly outweighed the potential harms; no potential harms were identified. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against technology-based caregiver support/education interventions to improve caregiver quality of life.

F. Non-invasive Brain Stimulation

Recommendation

47. There is insufficient evidence to recommend for or against non-invasive brain stimulation (e.g., repetitive transcranial magnetic stimulation, transcranial direct current stimulation, and continuous theta burst stimulation) for patients in stroke rehabilitation.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Introduction

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive form of brain stimulation (NIBS) which uses a rapidly pulsed magnetic field from a coil placed over the scalp to modulate a specific part of the brain. Stimulation targets discrete anatomical regions related to specific impairments, (e.g., primary motor cortex, cortical language area [Broca's region]). Repetitive transcranial magnetic stimulation is thought to promote brain plasticity. More commonly, it is frequently administered in conjunction with rehabilitation therapy. Devices capable of performing rTMS are usually large and located at medical centers, requiring technicians to service and run them. Delivering rTMS simultaneously with motor activities is difficult; thus, rTMS is usually provided before therapy. Depending on the pattern and frequency of the repetitive pulse protocol, rTMS can either increase or decrease cortical excitability. Examples of commonly used inhibitory protocols include low frequency rTMS (1 Hz) and continuous theta burst stimulation (cTBS). Repetitive transcranial magnetic stimulation protocols that facilitate cortical excitability are high frequency rTMS (5 Hz or higher) or intermittent theta burst stimulation. Currently, rTMS has been approved by the FDA only for managing treatment-resistant major depressive disorder. In the 2022 VA/DoD CPG for Management of Major Depressive Disorder,[f] it is

suggested that rTMS be offered to patients who have demonstrated partial or no response to two or more adequate pharmacologic treatment trials.(228) Repetitive transcranial magnetic stimulation has the potential to serve as an adjunct therapy to enhance rehabilitation outcomes after stroke.

Transcranial direct current stimulation (tDCS) involves sending an electrical current to induce polarity-specific excitability changes in the brain. The specific neural mechanisms underlying tDCS are only partly understood. Devices for tDCS are of variable size, makeup, and expense, sometimes offered as a portable option and other times as a modality in an outpatient or inpatient clinical setting. Considered investigational, tDCS is currently not regulated by the FDA for the treatment of depression.

Unilateral Spatial Neglect

Unilateral spatial neglect occurs much more frequently with right-side brain lesions than with left-side lesions.(61) Unilateral spatial neglect interferes with the rehabilitation process by the profound lack of awareness of the contralesional hemispace, which results in poor functional outcomes.(62) Non-invasive brain stimulation is currently an investigational treatment for USN. The evidence base regarding NIBS for USN included one SR and two RCTs.(229-231). An SR by Yang et al. (2023) (n=83) included patients 2 to 6 weeks post-stroke and evaluated the effects of rTMS and cTBS.(231) The control conditions were sham or blank control plus rehabilitation therapy. No statistically significant differences were found at the end of treatment in neglect/ADLs performance, as measured by the CBS, except for a statistically significant effect immediately after treatment in one study (n=18, SMD: -2.29; 95% CI: -3.54– -1.03; p=0.0003) in the high-frequency rTMS (HF-rTMS) group with stimulation applied over the right posterior parietal cortex.(232) However, this relative advantage was not sustained at one-month follow-up. Minimal adverse events were reported and included mild headaches in two study participants. An RCT by da Silva et al. (2022) that included 46 patients with USN after stroke applied anodal, cathodal, or sham tDCS stimulation for fifteen 20-minute sessions, twice per week, for 7.5 weeks.(229) All participants received one hour of physical therapy immediately after the tDCS protocol. No differences were found between the experimental and control groups. Adverse effects recorded in this trial included headache in 7 patients, redness at the electrode site in 1 patient, and itching in 2 patients. There was no ITT analysis. An RCT by Nyffeler et al. (2019) of 30 patients with subacute stroke (approximately one month after stroke) and USN applied 8-train cTBS versus 16-train cTBS versus sham control over the contralesional posterior parietal cortex for two to four days.(230) At the end of treatment, there was statistically significant improvement in ADLs for both intervention groups compared with the control groups as measured by the CBS (3.46 points, p=0.04) and the FIM (3.48 points, p=0.045). The cTBS and sham protocols were well tolerated without any side effects reported. The study did not control baseline confounders, and these statistically significant improvements did not reach the threshold to be considered clinically significant.

Motor Outcomes

An SR by Chen et al. (2022) included 45 upper limb studies (n=2,064) with a wide spectrum of rTMS protocols, both inhibitory and facilitatory, targeting either ipsilesional or contralesional motor cortices.(233) Of note, acute, subacute, and chronic stroke populations were combined in this SR. For inclusion in the SR, the studies had to have at least five subjects per group. The interventions included rTMS alone or in combination with other therapies, and the control groups received sham rTMS or no rTMS. The primary outcome measure was the FMA-UE. Evidence from 45 RCTs in this SR favored rTMS over sham rTMS for improvement of upper limb mobility as measured by the FMA-UE in patients with acute, subacute, and chronic stroke. This statistically significant benefit was demonstrated at short-term follow-up (0–1 month, 14 RCTs; SMD: 0.27; 95% CI: 0.04–0.51; p=0.023) and at intermediate-term follow-up (2–5 months, 23 RCTs; SMD: 1.23; 95% CI: 0.74–1.73; p<0.01) but not at long-term follow-up (>6 months, 3 RCTs; SMD: 1.61; 95% CI: -0.43–3.65; p=0.121). The strength of evidence for this finding was moderate to high. Evidence from 17 RCTS in this SR also favored rTMS over sham rTMS for improvement in hand function as measured by the BBT. The improvement of hand function was both statistically and clinically significant (SMD: 0.38; 95% CI: 0.19–0.58; p<0.01) for patients with subacute (1–6 months post stroke, SMD: 0.69; 95% CI: 0.22–1.16; p=0.004,) and chronic (>6 months post stroke; SMD: 0.38; 95% CI: 0.07–0.69; p=0.018) stroke, but not for those with acute stroke. The strength of evidence for this finding was high.

An NMA by Xie et al. (2021) included 18 RCTs (n=943) addressing rTMS interventions to treat lower limb impairment.(234) As in the SR of upper limb studies by Chen et.al., (2022), this NMA included a wide spectrum of rTMS protocols (e.g., inhibitory, facilitatory, or both; modulating contralesional or ipsilesional motor areas or both), and this NMA combined acute, subacute, and chronic stroke populations. The rTMS group showed a statistically significant improvement in FMA-Lower Extremity scores (FMA-LE) (SMD: 0.27; 95% CI: 0.90–0.45) and gait speed (SMD: 0.63; 95% CI: 0.30–0.96).

Although these findings are promising, both SRs combined findings of various rTMS protocols targeting different brain regions (ipsilesional or contralesional motor cortices or both) and different protocols (inhibitory, facilitatory, or both), which makes developing recommendations difficult.

Regarding tDCS, based on the current systematic evidence review, there is insufficient evidence to recommend for or against tDCS for improvement in motor function and ADLs.(235-237) Chow et al. (2022) performed an SR including 31 RCTs (n=NR) comparing tDCS (with or without other intervention) to sham tDCS (with or without other intervention).(236) Patients received 1–40 tDCS treatment sessions, 10–30 minutes each session, over an unreported range of time. The other interventions studied were conventional therapy, assisted therapy, or robotic therapy. There was no benefit for motor outcomes in the tDCS standalone intervention group. The authors did find some statistically significant improvements in several motor and ADL outcomes (FMA-UE,

FMA-LE, and BI) when tDCS was combined with other interventions, but the improvements in FMA scores were small, and the SR authors felt them to be of uncertain clinical significance.(236) The authors also postulated that the benefits of tDCS for motor recovery could depend on the assessments used and associated therapies. Sun et al. (2021) performed an SR including 6 RCTs (n=134) comparing tDCS to sham tDCS.(237) Patients received 5–60 tDCS sessions, 1–60 minutes each session, over an unreported range of time. The authors found improvement in muscle strength production, for a variety of muscle actions, such as grip force, dorsiflexion strength, and plantar flexion strength. Lima et al. (2023) performed an SR with 19 RCTs (n=535) comparing tDCS to sham tDCS.(235) There was improvement in balance with tDCS but no difference in motor function. Long-term follow-up data was not reported in any of the SRs. The tDCS treatments varied in terms of session duration, number of sessions, current density, charge, charge density, total charge, total charge density, electrode size, and stimulation site.

Aphasia

The evidence base regarding tDCS for the treatment of aphasia included one NMA.(238) Ding et al. (2022) (69 RCTs, n=1,670) compared tDCS with sham or placebo and demonstrated a statistically significant difference between groups post-intervention in patients treated with the dual- and anodal (a-tDCS) tDCS in the global severity of aphasia, as measured by the Western Aphasia Battery and Aphasia Battery Chinese, and in spontaneous speech. Dual-, cathodal-, and a-tDCS treatment was also associated with statistically significant improvements in the individual domains of naming, whereas dual- and a-tDCS was associated with statistically significant improvement in the individual domain of repetition. There was no difference between treatment and control groups in the domain of comprehension. Studies included in this NMA used NIBS accompanied by speech and language therapy. However, the therapy varied, and the NIBS was sometimes nonconcurrent with speech and language therapy.(238)

Two SRs evaluated the effects of low-frequency rTMS (LF-rTMS) on aphasia outcomes.(239, 240) Zhang et al. (2021) found that LF-rTMS, when compared with sham or conventional rehabilitation, resulted in statistically significant improvement in language recovery overall as measured by the Global Scores for Aphasia Severity and WAB-AQ.(239) Improvements were also found in the individual domains of naming, repetition, and spontaneous speech. The effects of LF-rTMS on comprehension varied based on the comparator. There was no difference between the treatment and control groups on measures of expression and conversation. Yao et al. (2020) found that LF-rTMS combined with speech and language therapy when compared with sham plus speech and language therapy or speech and language therapy alone, resulted in statistically significant improvement in multiple domains of language performance, including naming, repetition, comprehension, written language, and functional communication.(240)

Dysphagia

Evidence suggested that NIBS, specifically rTMS and tDCS, might improve swallowing and decrease aspiration in patients with post-stroke dysphagia.(234, 241) For rTMS, one MA by Xie et al. (2022) of 10 studies (n=206) demonstrated statistically and clinically significant improvement in a composite of overall swallowing function (SMD: 0.76; 95% CI: -1.07– -0.46) and a reduction in aspiration as measured by the PAS (SMD: 1.03; 95% CI: -1.51– -0.55) (7 studies, n=161).(234) In this MA, the comparator was sham rTMS or traditional swallowing therapy. There was an effect on swallowing ability and reduction on a disease-oriented measure of aspiration. In addition, the treatment effect was more than that observed in many of the other modalities reviewed by the Work Group. However, the studies that yielded this data included some very low quality trials.

Xie et al. (2022) performed subgroup analyses to help parse through the considerable variability in rTMS investigations.(234) That variability consisted of the location of rTMS application, the frequency of rTMS, the frequency and duration of sessions, and the adjunct therapeutic services offered. The largest trend toward improvement was with low frequency and bilateral stimulation, though heterogeneity in studies prevents this from being declared a dominant strategy. The modeling for this SR demonstrated low to moderate heterogeneity (I^2=45% for overall swallowing function and I^2=23% for the PAS) and a fixed effect model of analysis was used. A random effect model might have allowed for closer consideration of the relatively wide quality of the included studies. Publication bias was not fully assessed in this study given the small number of trials and patients. There was also performance bias from incomplete blinding of subjects in four of the included trials.

Regarding tDCS, one SR by He et al. (2022) included 15 trials (n=787) and demonstrated improvements in swallowing function and dysphagia severity as measured by the Dysphagia Outcome and Severity Scale (DOSS), modified Mann Assessment of Swallowing Ability (MMASA), Functional Oral Intake Scale (FOIS), functional dysphagia scale (FDS), and Kubota's water drinking test (KWDT) compared with traditional dysphagia therapy or sham tDCS.(241) One smaller RCT (n=40) also evaluated aspiration risk as measured by the PAS and demonstrated a greater reduction in aspiration risk at three months in the tDCS group compared with traditional dysphagia therapy.(242) Another small RCT (n=44) compared the effects of tDCS with sham tDCS of the supramarginal gyrus on swallowing function. At one month follow-up, tDCS was statistically superior to sham tDCS as measured by the Mann Assessment of Swallowing Ability (MASA).(243)

He et al. (2022) also tried to parse out optimal characteristics for tDCS given variability in trial design.(241) Most improvement was seen with high-intensity (current up to 2mA) and bilateral stimulation, though differences were not statistically significant. The modeling for this SR demonstrated low to high levels of heterogeneity and the effect analyses were reasonably changed between fixed effects and random effects

concordant with the level of heterogeneity. These high heterogeneity numbers were sometimes a result of a few trials. In the measurement of swallowing function, when sensitivity analyses were performed with the lower heterogeneity trials, there was no discernible effect of tDCS on swallowing function as measured by the FDS. Two measures that favored tDCS for swallowing function also had high levels of heterogeneity (I^2=83% for MASA and I^2=95% for KWDT).(241) No adverse events were reported in this SR, which is unusual and might suggest inadequate documentation of the included studies, especially when compared with other studies on tDCS.

Cognitive Impairment

Two SRs evaluated the effect of tDCS on cognitive outcomes.(244, 245) An SR by Khan et al. (2022) compared tDCS versus sham intervention and showed no improvement in global cognitive function (n=132) or in suppression-type attention tasks (n=81).(244) An SR by Li et al. (2022) compared tDCS with normal rehabilitation and found statistically significant improvements on the MoCA (n=212), MMSE (n=107), and BI (n=195).(245)

Four SRs evaluated the effects of rTMS on cognitive outcomes when either compared with or paired with conventional rehabilitation.(245-248) Li et al. (2022) found statistically significant improvements in ADLs and cognitive function (MoCA n=572, MMSE n=341, and BI n=260) when rTMS was compared with normal rehabilitation.(245) Xu et al. (2022) evaluated rTMS or sham rTMS paired with conventional treatment and also found that rTMS improved ADLs and cognitive recovery (MoCA n=494, mBI n=205, and Rivermead Behavioral Memory Test [RBMT] n=415).(246) Similarly, an SR by Li et al. (2023) demonstrated statistically significant improvements on the MoCA or MMSE (n=333), mBI (n=142), RBMT (n=99), and digit symbol test (n=94) for a combination of rTMS, conventional rehabilitation and medications drugs over sham.(247) An SR by Chen et al. (2023; BI n=658, mBI n=1,464, FIM n=158) specifically evaluated HF-rTMS paired with routine rehabilitation therapy compared with sham or routine rehabilitation therapy alone and showed statistically significant improvement in the HF-rTMS group in ADLs as measured by the BI, mBI, and FIM.(248)

Depression

The current systematic evidence review for this recommendation included three SRs; two studied the effect of rTMS, and one studied the effect of tDCS, for treatment of post-stroke depression.(245, 249, 250) Liang et al. (2022) (n=2,711) compared rTMS plus an AD (primarily SSRIs and SNRIs) versus AD alone in patients diagnosed with post-stroke depression.(249) The rTMS protocols were heterogeneous and not further specified in this SR. It should be noted that 2 of the 34 RCTs included in this review used transcranial electrical stimulation (TES) rather than rTMS. In TES, scalp surface electrodes are used rather than a magnetic coil. The duration of the intervention ranged from 7–60 days. Results showed a statistically significant reduction in depression symptoms as rated on

the HAM-D in the intervention group compared with the control group (SMD: -1.44; 95% CI: -1.86– -1.03; p<0.00001). In the rTMS combined with AD group, 36 patients developed headaches compared with 4 patients in the AD alone group.

Shen et al. (2022) analyzed 7 RCTs (n=528) of rTMS in patients with chronic stroke (greater than six months post stroke, or time post stroke not recorded).(250) The rTMS protocols were heterogeneous, although most applied stimulation to the left dorsolateral prefrontal cortex for a total of 10 treatment sessions, with sham stimulation as the control condition. Two of the trials included in the SR did not describe the treatment administered to the control group. This SR found a reduction in "depression" after treatment (SMD: 4.92; 95% CI: 2.69–7.15; p<0.001); however, interpretation of the results was hampered by a lack of information on how depression and depression remission were defined and measured. Adverse events included transient headaches and local discomfort at the site of stimulation.

Li et al. (2022) analyzed 8 RCTs (n=412) of tDCS in patients with depression and subacute to chronic stroke (at least one month post stroke), 87 of whom were also diagnosed with anxiety.(245) The duration of intervention ranged from two to eight weeks and included 10–20 sessions of tDCS compared with sham stimulation in seven RCTs. The 8th RCT included music relaxation therapy along with tDCS in the intervention group, while the control group received conventional rehabilitation treatment. The anode was applied over the left dorsolateral prefrontal cortex in 6 of the RCTs and over the primary motor cortex in two studies. The results showed a reduction in general depression symptoms immediately after tDCS intervention (SMD: 1.61; 95% CI: 1.02–2.19; p<0.01) but did not show a statistically significant reduction in anxiety symptoms. No adverse events were recorded in any of the trials.

ADL and Sensory Outcomes

The evidence was mixed for the effect of NIBS on ADL and sensory outcomes, but overall the findings did not seem to indicate a clinically significant effect of NIBS intervention in these areas.(251-253) An SR by Chen at al. (2023) of 12 RCTs including a total of 639 patients with acute stroke compared LF-rTMS, HF-rTMs or LF- and HF-rTMS plus usual care with sham-rTMS, sham-rTMS in combination with other treatments, or traditional therapy.(251) ADL outcomes were measured by the BI. For LF-rTMS compared with usual care (3 RCTs, n=181), a statistically but not clinically significant effect of the intervention was found (WMD: 8.54; 95% CI: 4.14–2.93; p< 0.05). For HF-rTMS compared with usual care (3 RCTs, n=95), again a statistically but not clinically significant effect of the intervention was found (WMD: 8.01; 95% CI: 0.49–15.53; p=0.02). For LF- plus HF-rTMS compared with usual care, both a statistically and clinically significant effect of the intervention was found (WMD: 25.32; 95% CI: 14.08–35.83; p<0.05).

A small RCT by de Freitas Zanona et al. (2022) of 40 patients who were 3–24 weeks post stroke compared three different interventions: 1) rTMS with sham sensory

stimulation, 2) sensory stimulation with sham rTMS, or 3) rTMS plus sensory stimulation, with a control condition of sham rTMS and sham sensory stimulation.(252) Sensory stimulation included a combination of 20–25 minutes of active sensory training of both the paretic and non-paretic hand, 40 minutes of mirror therapy, and 45 minutes of TENS therapy on the median nerve of the paretic limb. Follow-up was at the end of 10 days of treatment, and outcome measures included FMA-UE sensory portion only (total of 12 possible points, no MCID established), Nottingham Sensory Assessment, and total FIM. For rTMS with sham sensory stimulation compared with control, a statistically but likely not clinically significant effect of the intervention was found on the FMA-UE sensory (n=20; rTMS 10.7 [1.5]; control 8.7 [1.8]; $p<0.05$). No significant difference between groups was noted on the NSA or total FIM. For sensory stimulation alone compared with control, again a statistically but likely not clinically significant effect of the intervention was found on the FMA-UE sensory (n=20; rTMS 10.5 [3.2]; control 8.7 [1.8]; $p<0.05$). No significant difference between groups was noted on the NSA or total FIM. For rTMS plus sensory stimulation compared with control, again a statistically but likely not clinically significant effect of the intervention was found on the FMA-UE sensory (n=20; rTMS 11.6 [0.8]; control 8.7 [1.8]; $p<0.05$). No significant difference between groups was noted on the NSA. However, a statistically and clinically significant effect was found on total FIM (n=20; rTMS plus sensory stimulation 16.6 [13.6]; control 3.8 [4.9]; $p<0.05$), but the CIs were wide for the intervention group, and the lower limits of the CI overlapped the control group.

A small RCT by Llorens et al. (2021) of 32 patients with chronic stroke compared 30 minutes of tDCS plus VR (apple picking task with paretic arm) plus 30 minutes of conventional physical therapy with a control condition of 30 minutes of conventional physical therapy (Note: Control group received less total therapy time).(253) At the end of treatment, no significant differences were seen between groups for the sensory outcome measure (NSA).

Summary

Although the evidence base showed statistically significant improvements in many outcomes, the Work Group considered these findings insufficient to make a specific recommendation for NIBS application because the combined studies tested different protocols (e.g., ipsilesional, contralesional, bilateral, inhibitory, facilitatory). Each of these protocols has a different effect on brain excitability, so the Work Group was unable to provide specific recommendations for application. Nonetheless, these results show promise and further research in this area is warranted.

Large variation occurs in patient preferences regarding this treatment. Some patients might favor innovative or passive interventions or both and might be desperate for treatment options and be willing to try NIBS, although others might dislike technology. Regarding depression, some patients might avoid this type of treatment because of mental health stigma. Other patients might be motivated to try NIBS because they wish to avoid medication, they are attracted to high-tech interventions, or both. Significant

resources are required to deliver NIBS, including the technology itself as well as trained staff. The burdens of this treatment include the need to travel to the treatment site repeatedly for the series of interventions. These resources are unavailable in some areas throughout the VA and DoD health care systems.

The Work Group systematically reviewed evidence related to this recommendation.(61, 62, 228-231, 233-253) Therefore, it is categorized as *Reviewed, New-replaced.* The Work Group's confidence in the quality of evidence was very low. The body of evidence had some limitations, including small sample size; confounders in the analysis, such as lack of participant, study personnel, and outcome assessor blinding; and wide heterogeneity in subject characteristics. The potential harms of NIBS, including headaches, local site irritation, and the theoretical risk of seizure, outweighed the potential benefits of NIBS. Patient values and preferences varied largely because some patients favor innovative or passive interventions or both, although others do not. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against non-invasive brain stimulation (e.g., repetitive transcranial magnetic stimulation, transcranial direct current stimulation, and continuous theta burst stimulation) for patients in stroke rehabilitation.

X. Research Priorities

During the development of the 2024 VA/DoD Stroke Rehabilitation CPG, the Work Group identified topics needing additional research, including areas requiring stronger evidence to support current recommendations and research exploring new areas to guide future CPGs.

A. Review of Stroke Rehabilitation Evidence Base

The evidence base in stroke rehabilitation is limited by the inherent difficulties in conducting research in rehabilitation in general.(254, 255) Rehabilitation research is done in the "real world," and the introduction of bias is unavoidable in most studies. For example, the stroke population is, by its nature, heterogeneous. An attempt to limit studies to more homogeneous populations (e.g., first ever left middle cerebral artery ischemic strokes) would result in very small sample sizes and limit the generalizability of study results. Several other sources of bias exist in rehabilitation research. First, difficulties might arise with recruitment because of the existence of multiple comorbidities in patients with stroke that restrict inclusion. Second, regarding randomization, study participants often hesitate to participate for fear they will be assigned to the control group, especially if the control condition includes no intervention. Third, blinding of participants and personnel is sometimes impossible because of the nature of some interventions (e.g., mirror therapy for USN), which might lead to performance bias and placebo effect. Fourth, control groups are often usual care rehabilitation, and the intervention arm often includes usual care rehabilitation. Usual care rehabilitation, by necessity, varies from patient to patient, from day to day, to

address that patient's unique condition at the time. In some studies, the control group receives no intervention at all, leading to inability to account for placebo effect. Ethical issues such as clinical equipoise are also at play because it might be rendering it unacceptable to use a control group that withholds or delays treatment. Fifth, regarding study interventions, the complexity of some interventions makes monitoring their administration difficult. Sixth, attrition can be problematic in rehabilitation research, especially in an aged population with disability because many interventions are relatively long-term. Other confounding factors in stroke rehabilitation research include difficulty identifying the true effect of the intervention versus the natural course of recovery from stroke.

Conducting inpatient stroke rehabilitation research is challenging in general. Obtaining informed consent in cognitively impaired (50%) or language impaired (30%) survivors of stroke can involve difficulties.(256) In addition, many studies exclude cognitively and language impaired patients because of anticipated difficulties participating in study metrics, which limits external validity. Post-stroke physical and emotional fatigue can impact patients' willingness and ability to participate fully in the study intervention, control condition, or both. In addition, loved ones of patients with stroke are protective and sometimes reluctant to add additional burden. On most inpatient rehabilitation units, privacy, controlled space for research, or both as well as quiet testing protocol administration are lacking as are separate areas for the intervention and control groups to be treated. Federal regulations regarding candidacy for acute inpatient rehabilitation requiring patients to participate in three hours of therapy per day might limit patient availability to participate in research studies. In addition, patients admitted to acute inpatient rehabilitation are a selected population. They must be deemed to require aggressive rehabilitation for optimal recovery but also have the physical ability to participate in three hours of therapy per day. These requirements also impact external validity. Finally, rehabilitation providers have competing opinions and priorities and might have insufficient time to support research participation, or they might even actively discourage it.

Overall, the heterogeneity in patient characteristics, recruitment issues, and difficulties with designing and implementing methodologically robust studies can lead to small sample sizes and, therefore, studies statistically underpowered to discover a treatment effect, both in the short-term and especially the long-term. Stroke rehabilitation research suffers from a relative lack of standardized, validated outcome measures, particularly those that can capture nuanced changes such as in the quality of movement.(254) This limitation makes the comparison among studies difficult and hampers study inclusion in systematic reviews and meta-analyses. In addition, the heterogeneity of the study subjects including type of stroke, clinical presentation, and time post stroke makes the performance of meta-analyses complex.(254)

All the aforementioned challenges in rehabilitation research contribute to funding disparities. In the United States in 2021, the National Institutes of Health funded $220

million in physical rehabilitation research, making it 215th out of the top 299 researched disease topics.(254)

However, research in stroke rehabilitation has many opportunities for improvement that are reasonable to implement. Random sequence generation and allocation concealment should be used to avoid selection bias. When possible, participants and study personnel should be blinded to avoid performance bias, although, as mentioned previously, sometimes this is impossible in stroke rehabilitation research. Outcome measures should be validated and specific, rather than generic measures that encompass many domains, rendering the measure insensitive. Outcome assessors should be different study personnel than the personnel who deliver the intervention, and they should be blinded to treatment allocation to avoid detection bias. Adequate reporting of study population characteristics and setting is currently poor and future clinical trials should provide a clear description of subject selection, comorbidities, function, and study setting. This approach will enhance the generalizability of clinical trials and allow inclusion in subsequent systematic reviews. Although the heterogeneity of the stroke population can be perceived as a methodological limitation, it could instead be perceived as reflecting clinical reality and should be accounted for in the statistical analysis of adequately powered trials. Finally, another opportunity for improvement would be to increase the use of the Rehabilitation Treatment Specification System (RTSS) in post-stroke therapeutic intervention research.(257) The RTSS provides a framework within which to describe ingredients (what the provider does), the proposed mechanism of action (how the intervention is expected to work), and the target (the aspect of functioning directly targeted for change). By using this model, the entire community can increase our understanding of which components of rehabilitation are most effective.

The Work Group for the current guideline effort found many of the aforementioned limitations in the stroke rehabilitation evidence base. Given these limitations, the Work Group was unable to definitively recommend for or against many interventions. This outcome should not be interpreted as guidance that these interventions are unsuccessful and rehabilitation professionals should stop performing the intervention, but rather that the evidence base is insufficient at this time to determine efficacy. Cochrane Rehabilitation Methodology meetings are ongoing, which might influence the design of future clinical trials in stroke rehabilitation.(258-260)

B. Transitions to Community

Transition points are a well-known source of difficulty for patients in general, and they can present particular challenges for survivors of stroke and their families. Issues in this area were prominent in the concerns raised by the patient focus group. However,

research in this area is extremely limited. The Work Group identified the following recommendations.

- Develop and use a standard definition for “Case Management” and “Care Coordination.”
- Conduct more research on community engagement by survivors of stroke.
- Strive to increase diversity within and among study samples with a particular focus on different nations and cultures as well as socioeconomic and demographic factors.
- Develop and evaluate educational and psychoeducational interventions for survivors of stroke and their families and caregivers or both individually and jointly.
- Explore both short- and long-term impacts of settings of care to include facility-based, home-based, and outpatient settings.
- Include short- and long-term participation and quality of life outcomes in more studies.
- Develop and evaluate the most effective interventions to support caregivers for patients with stroke.
- Develop better tools to assess readiness to drive for patients with stroke.

C. Motor Therapy

Motor outcomes are of primary importance to many survivors of stroke and their family members because deficits in these areas can have such profound effects on independence. For patients with stroke who have motor impairment, an overarching need exists for large, high-quality, randomized controlled trials, which would ideally be multicenter in nature. In most of the examined interventions for motor impairment, there were significant methodological flaws in the evidence base, hampering our ability to make firm conclusions about the effectiveness of many of these therapies. Additionally, most of the studies did not include data about long-term follow-up outcomes, so the Work Group was unable to draw further conclusions about the durability of effects that might have been achieved. The Work Group identified the following recommendations.

- Increase research on the prevention and treatment of post-stroke shoulder problems.
- Consider more systematic research evaluating utility of therapies for different levels of impairment. For example, would severely versus mildly impaired individuals benefit more from mirror therapy compared with therapy without mirror?
- Explore further non-pharmacologic interventions (e.g., vibration, ESWT) for spasticity management. Include follow-up durations of at least three to six months.

D. Technology Assisted Physical Rehabilitation

With technological advances growing and changing every day along with improving affordability of such technology, tremendous opportunities occur to improve the lives of individuals with stroke. Well-designed studies with clear protocols, adequate follow-up, and appropriate outcome measures are essential. Hospitals should attempt to collaborate with private sector entities to ensure their rehabilitation technologies are compatible within VA and DoD environments, specifically with respect to technology security restrictions. The Work Group identified the following recommendations.

a. Virtual Reality

- Clarify, when designing studies using VR, whether the VR system is the intervention or simply the format.
- Identify which patient populations benefit most from interventions using VR, considering specific deficits, time since stroke onset, age, and other factors.

b. Functional Electrical Stimulation/Neuromuscular Electrical Stimulation

- Combine FES with gait training or other challenging physical therapy activities to potentially enhance outcomes.
- Examine the effectiveness of FES and EMG-NMES at different stages post stroke.
- Improve reporting of stimulation parameters and types of applications of EMG-NMES.
- Determine the ideal EMG-NMES protocol.
- Explore further the use of contralaterally controlled FES.

c. Robot-Assisted Therapy

- Determine for which patients RAT is most helpful, including factors such as functional level, specific deficits, and time since stroke onset.
- Increase research on the role of robotics using larger sample sizes and blinding of outcome assessment.

d. Brain Computer Interface

- Determine for which patients BCI is most helpful, including factors such as functional level, specific deficits, and time since stroke onset.

e. Vagus Nerve Stimulation

- Encourage publishing of all studies examining VNS and its effect on patients with motor impairment after stroke.
- Determine the optimal parameters of VNS with respect to various patient characteristics, such as severity of motor impairment, time since stroke, and location of stroke.

E. Dysphagia, Aphasia, and Cognition

- Conduct larger studies with consistent, well-documented treatment protocols, reporting of the specific devices used, and longer-term follow-up points to assess durability of the intervention for research using non-pharmacologic interventions such as CTAR.
- Investigate the responses in acute and chronic aphasia and differentiating subtypes and severities of aphasia for studies evaluating aphasia rehabilitation.
- Investigate the effect of the intervention on functional outcomes—such as return to work or school, community participation, or both, among others—for studies evaluating aphasia or cognition.
- Use clinically relevant and validated, formal neuropsychological tests—as opposed to screening questionnaires—for studies considering neuropsychological outcomes.
- Increase research evaluating interventions that target spatial neglect.

F. Specific Interventions

a. Acupuncture

- Improve reporting of acupuncture treatment details (e.g., number of needles, insertion locations, needle depth, treatment frequency, number of treatment sessions).
- Conduct trials with more diverse populations.
- Examine the optimal timepoint to deliver acupuncture following stroke and whether it is best used as a short- or long-term treatment or both and for which outcomes.

b. Aquatic Therapy

- Examine the comparative effectiveness of different aquatic therapy methods.
- Implement consistent outcome measures to facilitate better comparison among studies.

c. Biofeedback

- Determine patient characteristics, timing, and treatment goals best suited to the use of biofeedback.
- Perform comparative studies to define the optimal type of feedback and sensor configuration.
- Implement consistent clinical and instrumental outcome measures to facilitate better comparison among studies.

d. Constraint-Induced Movement Therapy and Modified CIMT

- Ensure that the core principles of CIMT are consistently applied.

- Implement consistent outcome measures to facilitate better comparison among studies.

e. Exercise

- Develop a consistent way of defining and tracking falls.
- Design multifactorial programs to assess and address the multiple potential domains of fall risk factors (e.g., medications, visual impairment, cognitive impairment, mobility impairments).
- Provide information about disability level and the use of walking mobility aids in study participants.

f. Mirror Therapy

- Define the optimal dose, frequency, and duration of mirror therapy.
- Determine the effect of mirror therapy for patients with varying degrees of motor impairment.

g. Motor Imagery

- Consider comparing motor imagery to placebo or no intervention.
- Determine the ideal application time of motor imagery.

h. Music Therapy/Rhythmic Auditory Stimulation

- Determine the optimal type and intervention parameters (e.g., time, frequency) of RAS.

i. Repetitive Task Training

- Describe clearly the tasks that trial participants are asked to perform.
- Define the optimal dose, frequency, and duration of repetitive task training.
- Incorporate more complex tasks and examine the quality of task completion.

j. Treadmill Training

- Consider measuring the training intensity via alternative methods, such as energy expenditure, heart rate, or muscle activity, instead of basing the training intensity on number of repetitions.
- Report outcomes on multiple commonly used assessment scales.

G. Mental Health

We are beginning to understand the mental health consequences of stroke and their impact on functional outcomes. However, at this point, we still have some important

questions that merit more research. The Work Group identified the following recommendations.

- Consider including patients with stroke in samples for all depression interventions (i.e., stop using stroke as an exclusion criteria). Currently no evidence exists to suggest that the treatment of post-stroke depression should differ from the treatment of depression in other populations.
- Improve definitions and criteria for the diagnosis of post-stroke anxiety.
- Perform more research on ACT in post-stroke populations.
- Increase research on behavioral activation as a modality for treating post-stroke depression by mental health support staff.
- Explore psychotherapy interventions (e.g., CBT) for the prevention of depression post stroke.
- Conduct well-designed, prospective studies using specifically delineated groups with or without depression, when considering cognitive and motor outcomes.

H. Telemedicine

Telemedicine and technology-based interventions have grown in availability and acceptability over the last few years. These platforms offer unique opportunities to provide interventions in the home and to improve access for survivors of stroke with geographical or transportation limitations. Little is known currently about the most appropriate interventions for these modalities as well as the outcomes. The Work Group identified the following recommendations.

- Incorporate telemedicine arms into research studies whenever possible.
- Deliver the same interventions to the intervention (telerehabilitation) and control (in-person) groups for more translatable comparison when conducting studies evaluating the utility of telerehabilitation.
- Perform non-inferiority studies using rehabilitation interventions that can be delivered via both in-person and technology-based formats.
- Fine-tune the key components to an effective telehealth intervention.
- Determine the best strategies that will enhance adoption of telehealth interventions by providers, survivors of stroke, and caregivers.
- Develop a standard protocol when using videoconferencing interventions.
- Incorporate evaluation of cost effectiveness into future studies.
- Determine which types of therapies (discipline and intervention) might be best suited to telerehabilitation, unsuitable for telerehabilitation, or more effective when delivered via telerehabilitation.
- Delineate clearly, when developing technology-based studies, whether technology is used as an intervention or merely as a format. Furthermore, in

situations where technology is a format, researchers should consider adding outcomes to match hypotheses related to patient engagement. This approach might be as simple as assessing patient enjoyment of the activity or as complex as evaluating how that engagement impacted patients' continued participation and any downstream effects.

I. Pharmacologic Treatment

There are a growing number of pharmacologic and non-pharmacologic treatments for chronic sequelae of stroke that might prove beneficial. The data thus far had several limitations, including inadequate follow-up periods, incomplete reporting of safety outcomes, and exclusion criteria that eliminate large groups of patients in this population. The Work Group identified the following recommendations.

- Include for all pharmacological studies more patients with aphasia, cognitive impairment, severe strokes, or any combination of the aforementioned conditions.
- Examine the effectiveness of other commonly used AD agents above and beyond the SSRIs and SNRIs already studied.
- Gather more data on safety outcomes and adverse effects related to the use of SSRI and SNRI medications, such as hyponatremia, seizure, and fracture.
- Determine the optimal point of initiation and subsequent termination of AD therapy for the purpose of motor improvement.
- Determine the optimal point of initiation and subsequent termination of AD therapy for the purpose of cognitive improvement.
- Evaluate classes of medications beyond ADs for effectiveness in cognitive or motor improvement.

J. Non-invasive Brain Stimulation

a. Transcranial Direct Current Stimulation

- Identify the optimal dose, stimulation type, and stimulation site for tDCS, with respect to the location and stage of a patient's stroke.
- Report outcomes on multiple commonly used assessment scales.
- Determine the optimal therapies to use in combination with tDCS rather than use tDCS as a standalone therapy.
- Explore long-term follow-up for potential adverse reactions as well as treatment response when conducting studies using tDCS.

b. Repetitive Transcranial Magnetic Stimulation

- Identify the optimal dose, stimulation type, and stimulation site for rTMS, with respect to the location and stage of a patient's stroke as well as the treatment goals.

- Determine the optimal parameters of rTMS at different stages of stroke.
- Report outcomes on multiple commonly used assessment scales.
- Determine the optimal therapies to use in combination with TMS rather than use TMS as a standalone therapy.
- Explore long-term follow-up for potential adverse reactions as well as for treatment response for studies using rTMS.

Appendix A: Guideline Development Methodology

A. Developing Key Questions to Guide the Systematic Evidence Review

To guide this CPG's systematic evidence review, the Work Group drafted 12 KQs on clinical topics of the highest priority for the VA and DoD populations. The KQs followed the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework, as established by the Agency for Healthcare Research and Quality (AHRQ). Table A-1 lists and describes the PICOTS elements.

Table A-1. PICOTS (261)

PICOTS Element	Description
Population or Patients	Patients of interest. It includes the condition or conditions, populations or sub-populations, disease severity or stage, co-occurring conditions and other patient characteristics or demographics.
Intervention or Exposure	Treatment (e.g., drug, surgery, lifestyle changes), approach (e.g., doses, frequency, methods of administering treatments), or diagnostic or screening test or both used with the patient or population.
Comparator	Treatment or treatments (e.g., placebo, different drugs) or approach or approaches (e.g., different dose, different frequency, standard of care) being compared with the intervention or exposure of interest described above.
Outcomes	Results of interest (e.g., mortality, morbidity, QoL, complications). Outcomes can include short, intermediate, and long-term outcomes.
Timing, if Applicable	Duration or follow-up of interest for the particular patient intervention and outcome to occur (or not occur).
Setting, if Applicable	Setting or context of interest. Setting can be a location (e.g., primary, specialty, inpatient care) or a type of practice.

Abbreviations: PICOTS: population, intervention, comparison, outcome, timing, and setting; QoL: quality of life

Because of resource constraints, all KQs of interest to the Work Group could not be included in the systematic evidence review. Thus, the Work Group selected the 12 highest priority KQs for inclusion (see Table A-2).

Using the GRADE approach, the Work Group rated each outcome on a 1–9 scale (7–9, critical for decision making; 4–6, important, but not critical, for decision making; and 1–3, of limited importance for decision making). Critical and important outcomes were included in the evidence review (see Outcomes); however, only critical outcomes were used to determine the overall quality of evidence (see Determining Recommendation Strength and Direction).

a. Populations

The patient population of interest for this CPG is adult patients with post-stroke deficits (motor, cognitive, speech, and/or sensory) who are candidates for rehabilitation. Key question 7 is specific for adults with post-stroke dysphagia. Key question 10 is specific

for adults with spasticity following stroke. Key question 12 is specific for adults with stroke resulting in unilateral spatial neglect.

b. Interventions and Comparators

KQ	Intervention(s)	Comparator(s)
1	**Non-pharmacologic motor interventions:** • FES/NMES • CIMT • Repetitive task practice • rTMS • tDCS • Contracture prevention • Body weight supported treadmill training • Treadmill training (without partial body weight support) • Sensorimotor Training • Exercise: (HIIT, Aquatic Therapy [swimming, water aerobics, water jogging, treadmill]) • Biofeedback • VNS for upper extremity motor recovery • Acupuncture and acupressure therapy • Motor imagery training • Mirror therapy • Music therapy • Telehealth/telerehabilitation **Pharmacotherapy:** • Stimulants (methylphenidate, dexmethylphenidate, amphetamine/dextroamphetamine, amphetamine resin complex, dextroamphetamine, lisdexamfetamine, modafinil, armodafinil) • SSRIs (citalopram, escitalopram, fluoxetine, sertraline, paroxetine, fluvoxamine) • SNRIs (venlafaxine, desvenlafaxine, duloxetine, milnacipran, levomilnacipran) • Carbidopa/levodopa • Dopamine agonists (pramipexole, ropinirole, rotigotine)	• Listed interventions compared to each other • Usual care
2	**Non-pharmacologic cognitive interventions:** • rTMS • tDCS • BCI • Assistive technologies for cognition • Focused on alerting, reminding, micro-prompting, storing and displaying, and/or distracting • VR	• Listed interventions compared to each other • Usual care

KQ	Intervention(s)	Comparator(s)
2 (cont.)	**Non-pharmacologic cognitive interventions (cont.):** • "Traditional" cognitive rehabilitation interventions) ♦ Attention Process Training ♦ Chaining Technique ♦ Compensatory Strategy Training ♦ Errorless Learning ♦ Goal Attainment Scale and Goal Management Training ♦ Goal Plan Do Review ♦ Metacognitive Retraining ♦ N-Back Procedure ♦ Plan Implement Evaluate (PIE) Therapy ♦ Spaced Retrieval ♦ Systematic Instruction ♦ Time Pressure Management ♦ Training external cognitive aids ♦ Visual Imagery Training: Lighthouse Strategy • Attention training (Attention process training APT) • Speech and language/Aphasia interventions: ♦ Verb Network Strengthening Treatment ♦ Melodic Intonation Therapy ♦ Phonomotor treatment ♦ Semantic feature analysis ♦ Treatment of underlying forms ♦ Response elaboration treatment ♦ Constraint-induced language treatment ♦ Attentive reading with constrained summarization ♦ Phonologic components analysis ♦ Anagram copy treatment ♦ Copy and recall treatment ♦ Lee Silverman Voice Therapy ♦ Speak Out ♦ Speaker comprehensibility strategy training ♦ Biofeedback ♦ Listener comprehensibility strategy training ♦ Oral Reading for Language in Aphasia (ORLA) ♦ Multiple Oral Rereading (MOR) ♦ Promoting Aphasics' Communicative Effectiveness (PACE) ♦ Clinician Controlled Auditory Stimulation ♦ Object Manipulation ♦ Phonological Cuing Hierarchy ♦ Script Training ♦ Visual Action Therapy ♦ Supported conversation for adults with aphasia	

KQ	Intervention(s)	Comparator(s)
2 (cont.)	**Non-pharmacologic cognitive interventions (cont.):** • Telehealth/telerehabilitation **Pharmacotherapy:** • Including those included in 2019 evidence review • Stimulants (methylphenidate, dexmethylphenidate, amphetamine/dextroamphetamine, amphetamine resin complex, dextroamphetamine, lisdexamfetamine, modafinil, armodafinil) • SSRIs (citalopram, escitalopram, fluoxetine, sertraline, paroxetine, fluvoxamine) • SNRIs (venlafaxine, desvenlafaxine, duloxetine, milnacipran, levomilnacipran) • Amantadine • Bromocriptine • Acetylcholinesterase Inhibitors (donepezil, galantamine, rivastigmine) • Memantine	
3	**Non-pharmacologic motor interventions:** • FES/NMES • CIMT • Repetitive task practice • rTMS • tDCS • Brain computer interface • Contracture prevention • Body weight supported treadmill training (with and without partial body weight support) • Virtual Reality • Sensorimotor Training • Exercise: (HIIT, Aquatic/Aqua Therapy (swimming, water aerobics, water jogging, treadmill) • Robotics including exoskeleton • Biofeedback • VNS for upper extremity motor recovery • Early bedside arm and leg cycle ergometry • Sensory interventions • Perceptual interventions • Motor learning-based therapy	• Different duration (e.g., number of weeks), frequency (e.g., number of sessions/ week), intensity (e.g., hours/ session or hours/ day) * Including but not limited to: (1) early rehab 24-48 hours, (2) inpatient post-acute program vs. IRF, (3) home vs. center based rehab, (4) early supported discharge.

KQ	Intervention(s)	Comparator(s)
4	• Speech/language rehabilitation interventions • CIMT, Constraint Induced Aphasia Therapy (CIAT), Constraint Induced Language Therapy (CILT) for aphasia • Precision rehab for aphasia • Non-pharmacologic cognitive interventions (from KQ 2) • rTMS • tDCS • BCI • Assistive technologies for cognition ♦ Focused on alerting, reminding, micro-prompting, storing and displaying, and/or distracting • VR • "Traditional" cognitive rehabilitation interventions) ♦ APT ♦ Chaining Technique ♦ Compensatory Strategy Training ♦ Errorless Learning ♦ Goal Attainment Scale and Goal Management Training ♦ Goal Plan Do Review ♦ Metacognitive Retraining ♦ N-Back Procedure ♦ PIE Therapy ♦ Spaced Retrieval ♦ Systematic Instruction ♦ Time Pressure Management ♦ Training external cognitive aids ♦ Visual Imagery Training: Lighthouse Strategy	• Different duration (e.g., number of weeks), frequency (e.g., number of sessions/ week), intensity (e.g., hours/ session or hours/ day)

KQ	Intervention(s)	Comparator(s)
4 (cont.)	• Speech and language/Aphasia interventions: ♦ Verb Network Strengthening Treatment ♦ Melodic Intonation Therapy ♦ Phonomotor treatment ♦ Semantic feature analysis ♦ Treatment of underlying forms ♦ Response elaboration treatment ♦ Constraint-induced language treatment ♦ Attentive reading with constrained summarization ♦ Phonologic components analysis ♦ Anagram copy treatment ♦ Copy and recall treatment ♦ Lee Silverman Voice Therapy ♦ Speak Out ♦ Speaker comprehensibility strategy training ♦ Biofeedback ♦ Listener comprehensibility strategy training ♦ ORLA ♦ MOR ♦ PACE ♦ Clinician Controlled Auditory Stimulation ♦ Object Manipulation ♦ Phonological Cuing Hierarchy ♦ Script Training ♦ Visual Action Therapy ♦ SCA • Telehealth/telerehabilitation	

KQ	Intervention(s)	Comparator(s)
5	**Technology-assisted tools initiated in the subacute/chronic phase:** • Mobile apps (smartphone, tablet) • Web-based apps • Environmental control unit/smart home technology (Amazon Alexa and Apple Home) • Teaching videos (for patients and caregivers) • Orthotic Devices/FES aka functional e-stim devices (AFO-ankle foot orthosis, Bioness, Saebo, Myomo, Walkaid, thermos-plastic splint applied to wrist, fingers, and/or thumb) • BCI • VR • Augmentative and alternative communication (AAC) devices (Lingraphica (usually TouchTalk), Tobii Dynavox (commonly TD Snap), or iPad with other AAC applications (ex. Proloquo2Go, Prolquo4Text, Assistive Express, Pictello, Scene Speak), low-tech options (communication boards, navigation ring blocks) **Technology-assisted tools initiated in the subacute/chronic phase (cont.):** • Robotics including exoskeleton • Walkasins	• Usual care
6	• Exercise: treadmill • CIH: tai chi, yoga, qigong • Meditation: Mindfulness meditation, MBSR, mindful self-compassion, Mantra based meditation, loving kindness, transcendental meditation, MBCT • Relaxation practices: breathing, guided imagery • Psychotherapy • Pharmacotherapy: ♦ Antidepressants ♦ SSRIs (citalopram, escitalopram, fluoxetine, sertraline, paroxetine, fluvoxamine), SNRIs (venlafaxine, desvenlafaxine, duloxetine, milnacipran, levomilnacipran) ♦ TCAs (amitriptyline, nortriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, protriptyline) ♦ Bupropion ♦ Mirtazapine ♦ Serotonin Modulators (Trazodone, nefazodone, vilazodone, vorioxetine) ♦ MAOIs (phenelzine, selegiline)	• Usual care

KQ	Intervention(s)	Comparator(s)
6 (cont.)	• rTMS • Transcranial stimulation • tDCS • Mind-body strategies • Integrative Health • Alternative/complementary approaches • VR • Telehealth/telerehabilitation	
7	• Dysphagia exercises ♦ Oral, jaw, respiratory ♦ Vocal cord adduction ♦ CTAR ♦ Masako maneuver ♦ Lingual strengthening ♦ Shaker exercise ♦ Effortful swallow ♦ Expiratory muscle strength training • Conventional dysphagia Therapy plus head lift • TES • Deep pharyngeal neuromuscular stimulation (DPNS) • Dietary Adjustment /Modification ♦ Vitamin C ♦ Food textures/thickness ♦ National Dysphagia Diet ♦ International Dysphagia Diet Standardization Initiative (IDDSI) ♦ Thickened liquids (honey, nectar, mildly thick, moderately thick, extremely thick) ♦ Solid texture modification (mechanical soft, puree, diced, soft and bite sized, minced and moist) • rTMS • tDCS • Oral Hygiene Regimens • Biofeedback via surface EMG (sEMG) • Telehealth/telerehabilitation • Training and compensatory swallowing strategies (Chin Tuck, Head Turn, Mendelsohn Maneuver, Supraglottic Swallow Maneuver)	• Usual care

KQ	Intervention(s)	Comparator(s)
8	Case management interdisciplinary care teams; caregiver involvement (including caregiver's education and support) Interdisciplinary team may include Primary Care, PM&R, Neurology, OT, PT, Speech Therapy, Social Work, Health Coach, Care Manager, Case Manager, Caregiver, Clinical Pharmacists, Behavioral Health Team, Rehabilitation Counselor Note: Check on case navigator; include other healthcare professionals if found during the literature review	• Usual care; individual provider versus primary care team; settings compared to each other
9	• Acupuncture and acupressure • Dry needling • Extracorporeal shock wave therapy (ECSW) • Pharmacotherapy ♦ Cannabis and derivatives (including CBD) ♦ Oral muscle relaxants (baclofen, tizanidine, dantrolene, methocarbamol, cyclobenzaprine, carisoprodol) ♦ Botulinum toxins (abobotulinumtoxinA, incobotulinumtoxinA, onabotulinumtoxinA. Prabotulinumtoxina, rimabotulinumtoxinb) ♦ "Nerve block" and "Motor point block" ♦ Cyproheptadine ♦ Gabapentinoids (pregabalin, gabapentin) ♦ Clonidine ♦ Benzodiazepines (lorazepam, clonazepam, diazepam, alprazolam, temazepam, oxazepam, triazolam) • WBV • Intrathecal interventions (pumps/spinal stimulation) • Orthopedic Interventions: ♦ Tendon lengthening and tendon transfer procedures ♦ Split Anterior Tibial tendon transfer ♦ Achilles lengthening procedures • Neurosurgical Interventions: ♦ Surgical sectioning at the level of peripheral nerves and nerve rootlets ♦ Central electrical stimulators ♦ Neuroablative procedures ♦ Selective dorsal root rhizotomy • Intrathecal baclofen treatments • Telehealth/telerehabilitation	• Listed interventions compared to each other • Usual care

KQ	Intervention(s)	Comparator(s)
10	• Education • Skills training • Support groups • Peer mentors and peer groups • Respite • Care navigators • Case managers • Community Resources • Psychological support/counseling/psychotherapy • Telehealth/telerehabilitation	• Usual care
11	• Environmental enrichment (physical, cognitive, and social activities such as reading material, board and card games, gaming technology, music, artwork, and computer with internet) • Touch/texture • Massage • Vibration • Pressure • Joint position • Peripheral nerve stimulation • FES • Action observation therapy • Mirror therapy • Music therapy • Virtual reality • BCI • NIBS (rTMS, tTDCS) • Robotics • Paired association stimulation • Rehabilitation for perceptual disorders • SENSe therapy • Compressive therapy • Telehealth/telerehabilitation • Oculomotor retraining • Rhythmic auditory stimulation • Cognitive rehabilitation • Attention training • TENS • Visual scanning training • Mental practice/imagery • Cueing/feedback • Eye patch	• Usual care

KQ	Intervention(s)	Comparator(s)
11 (cont.)	• PA • Balance: Sensory Organization, Pertubation Training	
12	• Acupuncture • Neck vibration • Prisms (adaptation) • Telehealth/telerehabilitation • Visuospatial therapy • Behavioral cuing • Noninvasive brain stimulation ♦ Galvanic vestibular stimulation ♦ Continuous theta burst stimulation ♦ rTMS ♦ tDCS • VR • Robotics • Pharmacotherapy: guanfacine • Neck taping • Body position • Spatial exploration strategy • Digital practice • Computer-based cognitive rehabilitation • Hemifield eye patching • OKS optokinetic stimulation • Visual search training	• Usual care

c. Outcomes

KQ	Critical Outcomes(s)	Important Outcome(s)
1, 3, 9	• Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.) • Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.)	• Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL) • Return to work/community participation/ integration/driving (community mobility) • Neuropsychiatric testing (cognitive status [global], attention, executive function, memory, etc.) • Speech/language outcomes (communication, etc.)
2, 4	• Speech/Language Outcomes (communication, etc.) • Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.) • Neuropsychiatric testing (Cognitive status [global], Attention, Executive Function, Memory, etc.)	• Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL) • Return to work/community participation/ integration/driving (community mobility) • Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.)

KQ	Critical Outcomes(s)	Important Outcome(s)
5	• Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.) • Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.) • Speech/language outcomes (communication, etc.)	• Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL) • Return to work/community participation/ integration/driving (community mobility) • Sensory outcomes (dysesthesia, perception, proprioception, sensation, touch, etc.) • Neuropsychiatric testing (cognitive status [global], attention, executive function, memory, etc.)
6	• Anxiety • Depression	• Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL) • Return to work/community participation/ integration/driving (community mobility) • Functional outcomes (ADL, IADL [community mobility, transportation], independence, etc.) • Neuropsychiatric testing (cognitive status [global], attention, executive function, memory, etc.) • Speech/language outcomes (communication, etc.) • Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.)
7	• Decreased aspiration • Dysphagia severity/swallowing	• Adequate oral intake/nutritional status • Pneumonia • Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL, SWAL-QOL) • Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.) • Speech/language outcomes (communication, etc.)
8	• Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.) • Return to work/community participation/integration/driving (community mobility)	• Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL) • Speech/language outcomes (communication, etc.) • Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.) • Neuropsychiatric testing (cognitive status [global], attention, executive function, memory, etc.)
10	• Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.) • Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL)	• Return to work/community participation/ integration/driving (community mobility) • Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.) • Neuropsychiatric testing (cognitive status [global], attention, executive function, memory, etc.) • Speech/language outcomes (communication, etc.)

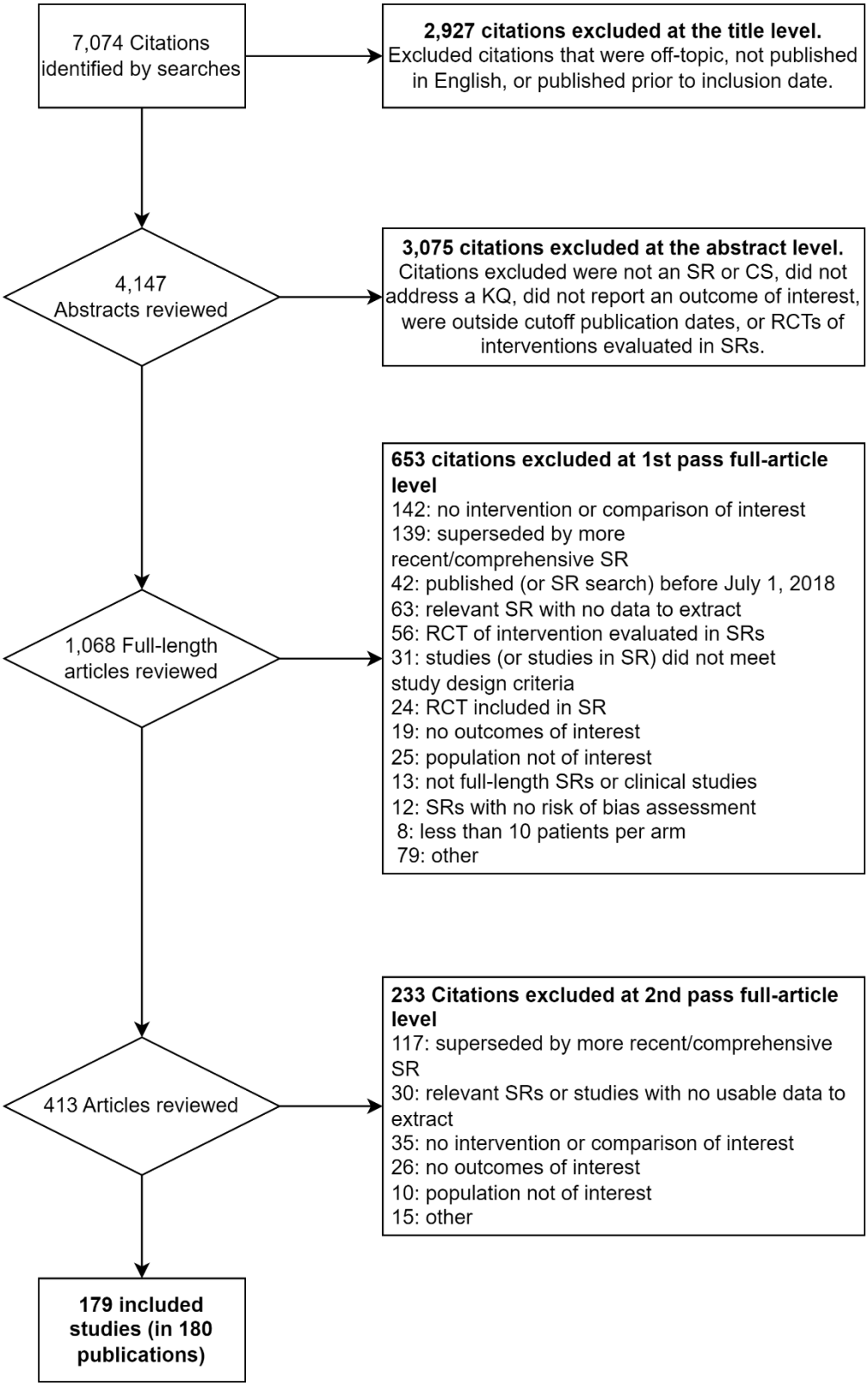
KQ	Critical Outcomes(s)	Important Outcome(s)
11	• Sensory Outcomes (dysesthesia, perception, proprioception, sensation, touch, etc.) • Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.)	• Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL) • Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.) • Return to work/community participation/ integration/driving (community mobility) • Speech/language outcomes (communication, etc.) • Neuropsychiatric testing (cognitive status [global], attention, executive function, memory, etc.)
12	• Functional Outcomes (ADL, IADL [community mobility, transportation], independence, etc.) • Neuropsych testing (Cognitive status [global], Attention, Executive Function, Memory, etc.)	• Sensory outcomes (dysesthesia, perception, proprioception, sensation, touch, etc.) • Motor Outcomes (gait speed, upper and lower extremity mobility, strength, coordination, number of falls, etc.) • Quality of Life Measures (EuroQuol [EQ-5D], SF-36, SIS, SS-QOL) • Speech/language outcomes (communication, etc.) • Return to work/community participation/ integration/driving (community mobility)

B. Conducting the Systematic Review

Based on the Work Group's decisions regarding the CPG's scope, KQs, and PICOTS statements, the Lewin Team produced a systematic evidence review protocol before conducting the review. The protocol detailed the KQs, PICOTS criteria, methodology to be used during the systematic evidence review, and the inclusion and exclusion criteria to be applied to each potential study, including study type and sample size. The Work Group reviewed and approved the protocol.

Figure A-1 below outlines the systematic evidence review's screening process (see also the General Criteria for Inclusion in Systematic Review. In addition, Table A-2 indicates the number of studies that addressed each of the questions.

Figure A-1. Study Flow Diagram



Alternative Text Description of Study Flow Diagram

Figure A-1. Study Flow Diagram is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion-exclusion process. Arrows point down to boxes that describe the next literature review step and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

1. Box 1: 7,074 citations identified by searches.
    a. Right to Box 2: 2,927 excluded at the title level. Excluded citations were off-topic, not published in English, or published prior to inclusion date.
    b. Down to Box 3.
2. Box 3: 4,147 abstracts reviewed.
    a. Right to Box 4: 3,075 citations excluded at the abstract level. Citations excluded were not an SR or CS, did not address a KQ, did not report an outcome of interest, were outside cutoff publication dates, or RCTs or interventions evaluated in SR.
    b. Down to Box 5.
3. Box 5: 1,068 full-length articles reviewed.
    a. Right to Box 6: 653 citations excluded at first pass full-article level.
        i. 142 no intervention/comparison of interest
        ii. 139 superseded by more recent/comprehensive SR
        iii. 42 published (or SR search) before July 1, 2018
        iv. 63 relevant SR with no data to extract
        v. 56 RCT of intervention evaluated in SRs
        vi. 31 studies (or studies in SR) did not meet study design criteria
        vii. 24 RCT included in SR
        viii. 19 no outcomes of interest
        ix. 25 population not of interest
        x. 13 not full-length SRs or clinical studies
        xi. 12 SRs with no risk of bias assessment
        xii. 8 less than 10 patients per arm
        xiii. 79 other
    b. Down to Box 7.

4. Box 7: 413 articles reviewed.
    a. Right to Box 8: 233 citations excluded at second pass full-article level.
        i. 117 superseded by more recent/comprehensive SR
        ii. 30 relevant SRs or studies with no usable data to abstract
        iii. 35 no intervention/comparison of interest
        iv. 26 no outcomes of interest
        v. 10 population not of interest
        vi. 15 other
5. Box 5: 179 included studies (in 180 publications)

Table A-2. Evidence Base for KQs

KQ Number	KQ	Number and Study Type
1	In adults with motor deficits following stroke, what is the comparative effectiveness of various modes of rehabilitation for motor weakness?	35 SRs (in 36 publications)
2	In adults with cognitive and/or speech and language deficits following stroke, what is the comparative effectiveness of rehabilitative and compensatory interventions for improving language and/or cognitive function?	14 SRs and 7 RCTs
3	In adults with motor deficits following stroke, what intensity and/or frequency of rehabilitation interventions improve recovery?	7 SRs and 2 RCTs
4	In adults post-stroke with cognitive and/or speech and language deficits, what intensity and/or frequency of cognitive and/or speech/language rehabilitation interventions improve recovery?	3 SRs
5	In adults following stroke, what technology-assisted tools improve functional, motor, cognitive, sensory and speech outcomes?	13 SRs and 1 NMA
6	In adults post-stroke, what interventions are effective in preventing or treating mental/behavioral health complications?	18 SRs
7	In patients with dysphagia following stroke, what treatments are effective in increasing oral intake and decreasing aspiration and/or aspiration pneumonia?	5 SRs and 13 RCTs
8	What settings and models of care (e.g., case management, and/or interdisciplinary care team approach) improve outcomes?	6 SRs and 4 RCTs
9	In adults with stroke resulting in spasticity, what is the comparative effectiveness of interventions to improve spasticity and also stroke rehabilitation outcomes?	7 SRs and 2 RCTs

KQ Number	KQ	Number and Study Type
10	What roles and/or interventions for caregivers/helpers of post-stroke patients benefit the caregivers/helpers and/or patients?	7 SRs and 3 RCTs
11	In adults following stroke, what sensory rehabilitation interventions improve sensory and/or functional outcomes?	8 SRs and 13 RCTs
12	In adults with stroke resulting in neglect, what is the comparative effectiveness of interventions to reduce neglect and improve stroke rehabilitation outcomes?	5 SRs and 6 RCTs
	Total Evidence Base	**179 studies (in 180 publications)**

Abbreviations: KQ = key question; SR = systematic review; RCT = randomized control trial; NMA = network meta-analysis

a. General Criteria for Inclusion in Systematic Evidence Review

- RCTs or SRs published on or after July 1, 2018 to May 2, 2023. If multiple systematic reviews addressed a key question, we selected the most recent and/or comprehensive review. Systematic reviews were supplemented with RCTs published after the systematic review.
- Studies had to be published in English.
- Publications must have been a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, and other publications that were not full-length clinical studies were not accepted as evidence.
- Systematic reviews must have searched MEDLINE or EMBASE for eligible publications, performed a risk of bias assessment of included studies, and assessed the quality of evidence using a recognizable rating system, such as GRADE or something comparable (e.g., the Strength of Evidence grading used by the Evidence-based Practice Centers of the AHRQ). If an existing review did not assess the overall quality of the evidence, evidence from the review must have been reported in a manner that allowed us to judge the overall risk of bias, consistency, directness, and precision of the evidence. We did not use an existing review as evidence if we were unable to assess the overall quality of the evidence in the review.
- Study must have enrolled at least 20 patients (10 per study group). Small sample size is associated with increased risk of bias, and we downgrade small studies in the GRADE domain of precision: one downgrade for imprecision of a single study with <200 patients per study arm.
- Newer Cochrane reviews already consider small sample-size in their estimation of risk of bias. In these cases, where sample size has already contributed to the assessment of the evidence, we did not downgrade those data a second time.
- Study must have reported on an outcome of interest.

- Study must have enrolled a patient population in which at least 80% of patients had experienced a stroke and were age 18 years or older. If the percentage was less than 80%, then data must have been reported separately for this patient subgroup.

b. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform, provider, or both can be found in Table A-3. See Appendix E for additional information on the search strategies, including topic-specific search terms and search strategies.

Table A-3. Bibliographic Database Information

Name		Date Limits	Platform or Provider
Bibliographic Databases	Embase (Excerpta Medica) and MEDLINE	July 1, 2018 through May 2, 2023	Elsevier
	PubMed (In-process, Publisher, and PubMedNotMedline records)	January 1, 2021 through May 2, 2023	National Library of Medicine
	PsycInfo	July 1, 2018 through May 2, 2023	OVID
Gray Literature Resources	Agency for Healthcare Research and Quality (AHRQ)	July 1, 2018 through May 7, 2023	AHRQ
	U.S. Department of Veterans Affairs (VA) Evidence Synthesis Program	July 1, 2018 through May 7, 2023	VA

c. Rating the Quality of Individual Studies and the Body of Evidence

The Lewin Team assessed the methodological risk of bias of individual diagnostic, observational, and interventional studies using the USPSTF method. Each study is assigned a rating of *Good*, *Fair*, or *Poor* based on a set of criteria that vary depending on study design. Detailed lists of criteria and definitions appear in Appendix VI of the USPSTF procedure manual.(262)

Next, the Lewin Team assessed the overall quality of the body of evidence for each critical and important outcome using the GRADE approach. This approach considers the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence. The overall quality of the body of evidence is rated as *High*, *Moderate*, *Low*, and *Very Low*.

C. Developing Evidence-Based Recommendations

In consultation with the VA Office of Quality and Patient Safety and the Clinical Quality Improvement Program, Defense Health Agency, the Lewin Team convened a 3.5 day in-person recommendation development meeting from September 19–22, 2023, to develop this CPG's evidence-based recommendations. Two weeks before the meeting, the Lewin Team finalized the systematic evidence review and distributed the report to

the Work Group; findings were also presented during the recommendation development meeting.

Led by the Champions, the Work Group interpreted the systematic evidence review's findings and developed this CPG's recommendations. The strength and direction of each recommendation were determined by assessing the quality of the overall evidence base, the associated benefits and harms, patient values and preferences, and other implications (see Determining Recommendation Strength and Direction).

a. Determining Recommendation Strength and Direction

Per GRADE, each recommendation's strength and direction is determined by the following four domains.(20) Information on each domain, questions to consider, and the resulting judgment can be found in Table A-4.

1. Confidence in the Quality of the Evidence

Confidence in the quality of the evidence reflects the quality of the body of evidence supporting a recommendation (see Rating the Quality of Individual Studies and the Body of Evidence). The options for this domain include *High*, *Moderate*, *Low*, or *Very Low*. These four ratings are a direct reflection of the GRADE ratings for each relevant critical outcome in the evidence review (see Outcomes). Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2, 22)

The recommendation strength generally aligns with the confidence in the quality of evidence. For example, *Strong* recommendations are typically supported by *High* or *Moderate* quality evidence. However, GRADE permits *Low* or *Very Low* quality evidence to support a *Strong* recommendation in certain instances (e.g., life-threatening situation).(20)

2. Balance of Desirable and Undesirable Outcomes

The balance of desirable and undesirable outcomes (i.e., benefits and harms) refers to the relative magnitudes or tradeoffs of anticipated benefits (e.g., increased longevity, reduced morbidity, improved QoL, decreased resource use) and harms (e.g., decreased longevity, increased complications, impaired QoL). The options for this domain include *benefits outweigh harms/burdens*, *benefits slightly outweigh harms/burdens*, *benefits and harms/burdens are balanced*, *harms/burdens slightly outweigh benefits*, and *harms/burdens outweigh benefits*. This domain assumes most providers will offer patients an intervention if its advantages exceed the harms. The Work Group's understanding of the benefits and harms associated with the recommendation influenced the recommendation's strength and direction.

3. Patient Values and Preferences

Patient values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life as they might apply to the intervention's potential benefits, harms, costs, limitations, and inconvenience. The options for this domain include *similar values*, *some variation*, and *large variation*. For instance, there might be *some variation* in patient values and preferences for a recommendation on the use of acupuncture because some patients might dislike needles. When patient values seem homogeneous, this domain might increase the recommendation's strength. Alternatively, when patient values seem heterogeneous, this domain might decrease a recommendation's strength. As part of this domain, the Work Group considered the findings from the patient focus group carried out as part of this CPG update (see Appendix B).

4. Other Implications

Other implications encompass the potential consequences or other impacts that might affect the strength or direction of the recommendation. The options for this domain, for example, include resource use, equity, acceptability, feasibility, and subgroup considerations. The following are example implications related to equity and subgroup considerations, respectively: some of the indicated population might be geographically remote from an intervention (e.g., complex radiological equipment); a drug might be contraindicated in a subgroup of patients.

Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgment
Confidence in the quality of the evidence	• Among the designated critical outcomes, what is the lowest quality of relevant evidence? • How likely is further research to change the confidence in the estimate of effect?	• High • Moderate • Low • Very Low
Balance of desirable and undesirable outcomes	• What is the magnitude of the anticipated desirable outcomes? • What is the magnitude of the anticipated undesirable outcomes? • Given the best estimate of typical values and preferences, are you confident that benefits outweigh harms/burdens or vice versa?	• Benefits outweigh harms/burdens • Benefits slightly outweigh harms/ burdens • Benefits and harms/burdens are balanced • Harms/burdens slightly outweigh benefits • Harms/burdens outweigh benefits
Patient values and preferences	• What are the patients' values and preferences? • Are values and preferences similar across the target population? • Are you confident about typical values and preferences?	• Similar values • Some variation • Large variation

Decision Domain	Questions to Consider	Judgment
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	• What are the costs per resource unit? • Is this intervention generally available? • What is the variability in resource requirements across the target population and settings? • Are the resources worth the expected net benefit from the recommendation? • Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?	Various considerations

b. Recommendation Categorization

A summary of the recommendation categories and definitions is available in Table 2.

1. Categorizing Recommendations with an Updated Review of the Evidence

Reviewed refers to recommendations on topics included in this CPG's systematic evidence review. *Reviewed*, *New-added* recommendations are original, new recommendations (i.e., not included in the previous CPG). These recommendations are based entirely on evidence included in the current CPG's systematic evidence review.

Reviewed, *New-replaced* recommendations were in the previous CPG but revised based on the updated evidence review. These recommendations may have clinically relevant edits. *Reviewed*, *Not changed* recommendations were carried forward from the previous CPG unchanged. *Reviewed*, *Amended* recommendations were carried forward from the previous CPG with a nominal change. This allowed for the recommendation language to reflect GRADE approach and any other not clinically meaningful edits deemed necessary. These recommendations can be based on a combination of evidence included in the current CPG's systematic evidence review and the evidence base that supported the recommendation in the previous CPG.

Reviewed, *Deleted* refers to recommendations from the previous CPG that were deleted after a review of the evidence. This may occur if the evidence supporting the recommendation is outdated (e.g., there is no longer a basis to recommend use of an intervention and/or new evidence suggests a shift in care), rendering the recommendation obsolete.

2. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous CPG without an updated review of the evidence. Given time and resource constraints, the systematic evidence review carried out for this CPG update could not cover all available evidence on stroke rehabilitation; therefore, its KQs focused on new or updated research or areas not covered in the previous CPG.

For areas in which the relevant evidence was not changed and for which recommendations made in the previous CPG were still relevant, recommendations could have been carried forward to the updated CPG without an updated review of the evidence. The evidence supporting these recommendations was thus also carried forward from the previous CPG. These recommendations were categorized as *Not reviewed*. If evidence had not been reviewed, recommendations could have been categorized as *Not changed*, *Amended*, or *Deleted*. *Not reviewed*, *Not changed* recommendations were carried forward from the previous CPG unchanged. *Not reviewed*, *Amended* recommendations were carried forward from the previous CPG with a nominal change. *Not reviewed*, *Deleted* recommendations were determined by the Work Group to not be relevant. A recommendation may not be relevant if it, for example, pertained to a topic (e.g., population, care setting, treatment) outside of the updated CPG's scope or if it was determined to be common practice.

The recommendation categories for the current CPG are noted in the Recommendations. The recommendation categories from the 2019 VA/DoD Stroke Rehabilitation CPG are noted in Appendix E.

D. Drafting and Finalizing the Guideline

The Work Group wrote, reviewed, and edited three drafts of the CPG using an iterative review process to solicit feedback on and make revisions to the CPG. The first and second drafts were posted online for 20 and 14 business days, respectively, for the Work Group to provide feedback. Draft 3 was made available for a 14-day peer review and comment (see External Peer Review). The Work Group reviewed all feedback submitted during each review period and made appropriate revisions to the CPG. Following the Draft 3 review and comment period, the Work Group reviewed external feedback and created a final draft of the CPG. The Champions then presented the CPG to the VA/DoD EBPWG for approval. The Work Group considered the VA/DoD EBPWG's feedback and revised the CPG, as appropriate, to create the final version. To accompany the CPG, the Work Group produced toolkit products, including a provider summary, quick reference guide, and patient summary. The VA/DoD EBPWG approved the final CPG and toolkit products in May 2024.

Appendix B: Identifying Patient Rehabilitation Goals

Box 18 in Module B instructs providers to, "Assess the patient and identify the patient's rehabilitation goals." A key priority in rehabilitation, goal-setting is one of the most significant factors in tailoring rehabilitation to the patient's needs. The participants in the patient focus group conducted as part of this CPG update placed significant value on setting personally meaningful goals with their provider that are modeled on the hobbies and activities in which they engaged before their stroke.

Patients with a history of stroke should have a holistic approach to their health care, with close attention paid to their current and desired levels of function. Rafsten et al. (2022) found that patient's with a history of stroke tended to self-identify with goals in the activity limitation domain of the International Classification of Functioning, Disability and Health model.(263) The most common goals reported were improving mobility outdoors, improving hand function, and being able to cook.(263) Goals should not be limited to self-care and mobility issues but should address what is required to return to active participation in one's life. This goal might require more in-depth conversations with patients and family members. Asking the following questions might help the provider understand how a stroke has impacted a person's ability to function and participate in meaningful activities, providing a steppingstone for creating collaborative, patient-centered goals.

- What things are most important for you in your life? Are you able to engage in those activities, relationships, interests, and so forth since your stroke? Would you like to do more or increase your capabilities in any of these important areas?
- Who are members of your support network, and are they available or able to help you with your current needs? Is this level of support okay with you, or do you want to work on being more independent in a certain activity?
- With what do you need help the most at home (e.g., bathing, dressing, toileting, eating)?
- Do your friends or family have concerns about your staying at home alone? For short periods? Overnight? Days or weeks at a time?
- How are you managing your medications, home therapies, or medical appointments?
- Are you concerned about your ability to pay your living expenses? Do you anticipate you will require financial assistance to pay medical expenses related to your stroke? Have you received information regarding financial assistance, resources, or both that might be available to you?
- Are you able to clean your house, manage your groceries, and prepare your meals? Are you able to maintain your yard or property?

- Have you returned to work? Why not? Do you need assistance to return to work or to obtain worksite modifications? Do you need to consider pursuing a different career?
- Do you want to return to driving? Do your friends or family have concerns about your driving?
- Have you been able to return to your leisure activities? How would you like to spend your free time? What has prevented you from doing so?
- Are you having difficulty reading or navigating from one location to another because of your vision?
- Are you having difficulties communicating or thinking clearly? Do others seem to have a hard time understanding what you are trying to tell or show them?
- Do others tell you that you repeat yourself more than you did in the past? Do you ever feel lost in conversations when talking to others?
- Do you have concerns about sex or intimacy?
- Do you have concerns regarding your bowel or bladder? Are you experiencing bladder incontinence or retention? Are you experiencing bowel incontinence, diarrhea, or constipation?
- How is your mood? Has your family communicated with you regarding changes that they have noticed with your mood? If these variations represent a big change, how are you adjusting? How is your family adjusting? Have you had thoughts that you would be better off dead or about hurting yourself in some way? Have you had thoughts about hurting others in some way?
- How are your relationships with your spouse, significant other, children, coworkers, or friends? Have you become more isolated, cut off, or irritable with others? Do you feel removed or distant from important, meaningful relationships in your life?
- How do you spend your time during the day? What is a typical day like?
- What are your biggest worries?

Remembering to communicate with the patient and the family member or caregiver in clear, non-technical terms is important as is assessing the patient's and the family member's or caregiver's understanding of the information. Patients and family members in the focus group emphasized how important communication was for them. They valued providers who listened to their perspectives and understood their experiences, challenges, and goals.

Appendix C: Additional Information on Management of Stroke

A. Education

The following websites provide additional resources on patient education.

- Centers for Disease Control and Prevention Stroke Patient Education Handouts: https://www.cdc.gov/stroke/materials_for_patients.htm
- VA Resources & Education for Stroke Caregivers' Understanding & Empowerment: https://www.cidrr8.research.va.gov/rescue/library
- American Stroke Association: https://www.strokeassociation.org/
- National Institute of Neurological Disorders and Stroke: Know Stroke | National Institute of Neurological Disorders and Stroke (nih.gov)
- NINDS, stroke prevention: Brain Basics: Preventing Stroke | National Institute of Neurological Disorders and Stroke (nih.gov)
- American Academy of Neurology: https://www.brainandlife.org/disorders-a-z/stroke/
- Veterans Health Library, Living with Stroke: https://www.veteranshealthlibrary.va.gov/LivingWith/Stroke/

B. Communication

All survivors of stroke should be screened for communication deficits. Communication deficits might impact a person's ability to understand or produce words, sentences, and discourse (two or more sentences organized to convey information). Although a range of communication deficits can occur after stroke, all these problems can impact social and occupational participation. Individuals with suspected communication difficulties should receive a formal, comprehensive assessment to determine the nature and type of their communication impairment. Assessments of communication should be performed by a speech-language pathologist or in the context of a neuropsychological evaluation in consultation with speech-language pathology.

The most commonly known communication impairment after stroke is aphasia, a language disorder which impairs one's ability to understand others' messages, speak, read, and write. Other communication deficits associated with relating communicative intent are due to a break down or lack of integration of nonverbal contextual cues, such as facial expression, body language, and prosody (intonation contours created by manipulating frequency, stress, duration, and pitch). Pragmatics, the functional use of language in context, often involves the combined use of verbal and nonverbal mechanisms to infer or relate meaning and can also be impaired following stroke.

Another class of communication impairments are motor-speech based disorders, including dysarthria and apraxia of speech. Most simply, dysarthria can be considered an impairment in *muscular control/execution* because of central or peripheral nervous

system damage, whereas apraxia of speech is an impairment in the *planning* or *programming* of the muscular movements that underly speech production, or both. Both dysarthria and apraxia of speech tend to hinder successful verbal output.

For survivors of stroke with any identified communication impairments, speech and language therapy should be provided to improve functional communication skills with treatment offered as early as it is tolerated. Education about communication impairments, etiologies, and treatment options, including multiple levels of service delivery, should be provided to the patient, caregiver, or both. Treatment plans and goals should be individualized and evidence based, and they should include the patient, caregiver, or both. Patients should be discharged from therapy only once modalities for communication have been thoroughly explored to ensure optimal level of independence or modified-independence using assisted communication.

The following websites provide additional resources on patient communication.

- A unique resource for Veterans and active duty Service members with aphasia is VA Pittsburgh's Program for Intensive Residential Aphasia Treatment & Education (PIRATE). Program participants can attend virtually or in-person at the Pittsburgh VA as they receive services from an integrated team of speech pathology clinical providers, educators, and scientist-practitioners dedicated to improving the functioning and wellbeing of people with aphasia. For additional information: PIRATE – Veterans Health Foundation
- American Speech Language Hearing Association: https://www.asha.org/Evidence-Maps/
- The Aphasia Institute: https://www.aphasia.ca/
- National Aphasia Association: https://www.aphasia.org/
- The Academy of Aphasia: http://www2.academyofaphasia.org/
- Veterans Affairs Assistive Technology: https://www.prosthetics.va.gov/AssistiveTechnology/index.asp

C. Dysphagia

Dysphagia, or difficulty swallowing, is common after stroke with incidence estimates in the literature as much as 78%.(264) All survivors of stroke should be screened for dysphagia by a speech-language pathologist or other trained health care providers. Individuals with suspected dysphagia should have their swallowing abilities formally evaluated given the risk for dehydration, malnutrition, pneumonia, and even death associated with dysphagia. Individuals identified with dysphagia might benefit from rehabilitative exercises, compensatory strategy use during oral intake, food or liquid texture alterations, or any combination of the aforementioned adjustments to ensure safety with oral intake.

As of 2020, the national VA Health Care System implemented new diet texture terminology adapted from the International Dysphagia Diet Standardization Initiative.(265) This framework consists of a continuum of numbers representing complexity levels for food and liquid texture modifications. The goal of implementation is to standardize terminology and definitions of texture modifications for patients, services, and facilities nationwide. The IDDSI framework includes the following complexity levels.

Exhibit C-1. International Dysphagia Diet Standardization Initiative Framework

IDDSI 2.0 | July 2019

For further description of the framework, see http://IDDSI.org.

D. Pseudobulbar Affect

Pseudobulbar affect (PBA) is characterized by involuntary, sudden, and intense emotional outbursts, often involving laughing or crying, that are judged to be incongruent with an individual's underlying emotional state. These episodes tend to be time limited and have little to no discernable relationship to the immediate context in which they occur. For example, a survivor of stroke might be enjoying being with friends only to start crying uncontrollably after seeing a picture of a cute puppy. These events

tend to generate considerable distress for individuals, caregivers, family members, coworkers, and friends alike. Without early and effective intervention, PBA might lead to increased social avoidance and withdrawal from meaningful activities. Early in treatment, however, providers might have difficulty determining whether these behaviors are consistent with the onset of clinically significant post-stroke anxiety or depression.

Since the 2019 VA/DoD Stroke Rehabilitation CPG, research into PBA has increasingly viewed these difficulties as changes in the regulatory, control processes in the brain (not a primary psychiatric disorder). PBA likely involves a breakdown in the connections between cerebro-ponto-cerebellar circuits in the brain, though more specific mechanisms of PBA remain unknown.(266, 267) As a difficulty with modulation, PBA can be seen as over- or under-responding to a seemingly low valence stimulus, with behaviors that appear disproportionate, out of context, or out of touch with one's more immediate experiences. As such, this condition might be socially disabling and interfere with the rehabilitation process itself. It can be potentially dangerous in a patient with dysphagia if it occurs during eating. In a 2016 SR and MA of more than 3,000 patients with stroke, PBA was found to affect 17% of patients less than one month post stroke, 20% of patients one to six months post stroke, and 12% of patients greater than six months post stroke.(268, 269)

Though no formal recommendation is made based on review of the current evidence base, SSRIs appear to improve symptoms in patients with PBA following stroke.(270-273) Hackett et al. (2010), in a Cochrane Database SR of five trials (n=213), concluded that ADs can reduce the frequency and severity of crying or laughing episodes. Of note, this review included not only RCTs of SSRIs but also tricyclic ADs (TCA).(270) A double-blind placebo-controlled trial in patients with stroke and PBA conducted by Choi-Kwon et al. (2007) (n=152) showed a significant reduction in excessive inappropriate crying after three months of treatment with 20 mg of fluoxetine daily.(273)

Medical treatment for PBA with SSRIs is widely available and inexpensive, and the benefits of PBA treatment outweigh potential harms (see Recommendation 40 for further information on potential adverse events). The patient and loved ones often desire medical treatment for this disabling condition, though some individuals prefer no pharmacological therapy.

Dextromethorphan 20 mg/quinidine 10 mg (DM/Q) is currently the only FDA-approved medication for the treatment of PBA. The PRISM II trial included patients with PBA from various etiologies and was an open label trial. The outcomes for the cohort with stroke were reported in an article by Zorowitz et al (2018).(274) The cohort with stroke enrolled 113 patients. On a primary outcome measure (Center for Neurologic Study-Liability Scale, CNS-LS), the DM/Q cohort had a significant reduction (7.6 points) from baseline at 90 days. This open label study, however, was funded by the manufacturer of DM/Q, so a possibility for bias exists as well as a lack of acknowledgement of a possible placebo effect. Furthermore, AD doses had only to be "stable" at baseline, so the effect

AD use had on the results of this study are unknown. With no generic availability at this time, DM/Q is a costly medication, which might pose a financial burden to the patient. Tolerance of DM/Q seems to be favorable in the population with post-stroke PBA.

In PRISM II's cohort with stroke, most of the adverse events were mild to moderate with the most common adverse events being diarrhea, headache, constipation, and dizziness. However, there are significant warnings and contraindications regarding QT prolongation, drug-drug interactions, risk of serotonin syndrome, hepatotoxicity, hypersensitivity reactions, and anticholinergic effects that might limit DM/Q's use post stroke.(275)

Appendix D: Caregiver Resources

Caregiver engagement is an active partnership among patients, families, and health care providers at various levels to improve health outcomes. Because of the high levels of cost associated with rehabilitative care, many services are transferred to the community after initial hospitalization and rehabilitative efforts. In these circumstances, a caregiver might have to assist with personal hygiene care, health and illness monitoring, medication administration, and finance management. Caregivers benefit from education and support to adequately prepare them for such experiences, and highly engaged caregivers offer continuity of care for Service members and Veterans. Caregivers might play an essential role in assisted or surrogate decision making, depending on the capacity of the Service member or Veteran experiencing the stroke.

Providers should consider involving caregivers in care for any Service member or Veteran who requires assistance with ADLs and IADLs, has social issues that preclude health care center-based rehabilitative efforts, has a higher risk of recurrent stroke, or is at a transitional point in life and needs social support. Providers are encouraged to consider a continuum of care in deciding how caregivers can be integrated into treatment. Contraindications to caregiver involvement might include one or more of the following: Service members' or Veterans' preference not to include family, history of caregiver abuse or trauma, baseline functional abilities of the caregiver. Individual circumstances surrounding sensitive clinical and legal issues should be carefully explored to avoid potential damage to, or exploitation of, the Service member or Veteran.

Engaging family members in care begins with the Service member or Veteran. Motivational interviewing techniques (an evidence-based approach to communication about change and growth) can engage Service members and Veterans in discussing caregiver services by exploring the role they want their caregivers to play in their recovery and their preferences about caregiver participation. This engagement handout was designed to engage Veterans in Behavioral Family Therapy, but it can be used to engage Veterans in any family service. More information is available at https://www.mirecc.va.gov/visn22/familyconsultation_veteran_engagement.pdf.

The **VA Caregiver Support Program** is a national repository of information and resources dedicated to assisting family members serving as caregivers of Veterans. It offers certain benefits and clinical support services to caregivers of eligible and covered Veterans enrolled in the VA health system. The mission of the Caregiver Support Program is to promote—through education, resources, support and services—the health and wellbeing of family caregivers who care for the Nation's Veterans. Services and support are offered within two programs: the Program of General Caregiver Support Services and the Program of Comprehensive Assistance for Family Caregivers. Every VA Medical Center has a Caregiver Support Program team to assist with information and referrals. The VA Caregiver Support Line is available at **1-855-260-3274** https://www.caregiver.va.gov/support/Respite.asp.

A variety of caregiver-centered educational handouts are available from the **American Stroke Association** with information on optimizing self-care, a caregiver guide for stroke patients, and information on finance management. More information is available at https://www.stroke.org/en/help-and-support/resource-library/resources-for-caregivers--family-and-friends.

The **Family Caregiver Alliance (FCA)** seeks to improve the quality of life for caregivers through education, services, research, and advocacy. Through its National Center on Caregiving, the FCA offers information on current social, public policy, and caregiving issues and provides assistance in the development of public and private programs for caregivers. More information is available via the following links.

Services by State: https://www.caregiver.org/connecting-caregivers/services-by-state/

Classes: https://www.caregiver.org/connecting-caregivers/events-classes/

CareNav to help navigate caregiving resources and responsibilities: https://www.caregiver.org/connecting-caregivers/fca-carenav/

The **American Stroke Foundation** is a free online repository of caregiving tips, resources, and webinars for interacting with patients who have had functional changes in the context of a stroke. More information is available at https://americanstroke.org/category/caregiver/.

The **Caregiver Action Network** includes a toolbox for family caregivers along with a message board functionality to share experiences and questions with other members of the caregiving community. More information is available at https://www.caregiveraction.org/family-caregiver-toolbox.

Appendix E: Patient Focus Group Methods and Findings

A. Methods

VA and DoD Leadership recruited six participants for the focus group, with support from the Champions and other Work Group members, as needed. Although participant recruitment focused on eliciting a range of perspectives likely relevant and informative in the CPG development process, the patient focus group participants were not intended to be a representative sample of VA and DoD patients. The participants were not incentivized for participation or reimbursed for travel expenses. The Work Group, with support from the Lewin Team, identified topics on which patient input was important to consider in developing the CPG. The Lewin Team developed, and the Work Group approved, a patient focus group guide covering these topics. The focus group facilitator led the discussion, using the guide to elicit patient perspectives about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, some questions were not addressed.

B. Patient Focus Group Findings

a. Participants want their stroke rehabilitation treatment to be based on individualized goals. Participants value providers who listen to their perspectives and assist them in maximally achieving their goals.

- Participants indicated that they prefer to set personalized goals with their providers, tailored to their favorite individual hobbies and activities in which they were able to engage before their stroke.
- Participants expressed high levels of motivation toward progress in their recovery and noted that outward support from their providers could help them achieve their goals.
- Participants relied on various forms of therapy (e.g., physical therapy, occupational therapy, and speech therapy) in various settings (in-home, inpatient, outpatient) to achieve their goals and had varied preferences toward each type.

b. Participants emphasized the importance of care coordination by providers of various specialties, within and across health care systems (VA, DoD, their community).

- Participants appreciated a smooth transition of care between different facilities and treatment modalities.
- Participants experienced a wide array of comorbid conditions, both related to their stroke and from preexisting conditions, and recognized the importance of care coordination between their various specialists and primary care physician.
- Participants valued multidisciplinary clinics that centralized their stroke care.

c. *Participants value clear, non-technical, and open communication with their providers.*

- Participants expressed sometimes having difficulty in understanding the technical language their providers used.
- Some participants noted that they had trouble communicating their long-term goals.

d. *Participants desire increased accessibility to services and support for their caregivers.*

- Participants noted the significant burdens placed on their caregivers and expressed interest in having clearly defined support services for their caregivers.

e. *Participants indicated that stroke rehabilitation support groups can provide helpful tips, information on community resources and health care benefits, and encouragement.*

- Participants engaged in peer support through various methods: their nuclear family, religious organizations, peer support groups, and social media.
- Participants expressed that support groups are beneficial for their emotional health and stroke recovery.

f. *Some participants recognized challenges in navigating the health care system and highlighted the need for assistance in accessing rehabilitation programs and services.*

- Participants had varying experiences in knowing the types of rehabilitation programs and services for which they are eligible.
- Some participants highlighted challenges using both VA and DoD health care systems and community health care systems.

Appendix F: Evidence Table

Table F-1. Evidence Table[a,b,c]

#	Recommendation	2019 Strength of Recommendation	Evidence	2024 Strength of Recommendation	2024 Recommendation Category
1.	We suggest using case management services at time of discharge from the acute care hospital or post-acute care facility to improve activities of daily living and functional independence.	NA	(38) **Additional reference** (37)	Weak for	Reviewed, New-added
2.	We suggest the following interventions for patients and their caregivers. • Behavioral health/psychosocial interventions to improve patient and caregiver depression • Psychoeducation to improve family function, patient functional independence, and quality of life	NA	(39-42)	Weak for	Reviewed, New-added
3.	There is insufficient evidence to recommend for or against implementing transitional care rehabilitation interventions (e.g., home-based services after hospital discharge) or early supported discharge to improve activities of daily living or functional disability following stroke.	Neither for nor against	(43-47)	Neither for nor against	Reviewed, New-replaced

[a] Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference had to be identified through a systematic evidence review carried out as part of the development of this CPG. The second set of references in the evidence column (called "Additional References") includes references that provide additional information related to the recommendation but that were unidentified through the systematic evidence review. These references were, therefore, not included in the evidence base for the recommendation and did not influence the strength and direction of the recommendation.

[b] Strength of Recommendation column: The VA/DoD Stroke Rehabilitation CPG was developed using the GRADE approach to determine the strength of each recommendation. Refer to the Determining Recommendation Strength and Direction section for more information.

[c] Recommendation Category column: Refer to the Recommendation Categorization section for more information on the description of the categorization process, the categories, and their definitions.

#	Recommendation	2019 Strength of Recommendation	Evidence	2024 Strength of Recommendation	2024 Recommendation Category
4.	There is insufficient evidence to recommend for or against community participation interventions to improve community engagement for survivors of stroke.	NA	(48)	Neither for nor against	Reviewed, New-added
5.	We recommend task-specific practice (also known as task-oriented practice or repetitive task practice) to improve motor function, gait, posture, and activities of daily living.	NA	(49-59)	Strong for	Reviewed, Not changed
6.	We suggest mirror therapy to improve motor outcomes and activities of daily living.	Neither for nor against	(63-66) **Additional references** (60, 61)	Weak for	Reviewed, New-replaced
7.	We suggest mirror therapy to improve unilateral spatial neglect.	NA	(62) **Additional references** (60, 61, 67-70)	Weak for	Reviewed, New-added
8.	We suggest treadmill training (with or without body weight support) to improve balance.	Weak for	(71-74)	Weak for	Reviewed, New-replaced
9.	We suggest rhythmic auditory stimulation as an adjunct intervention to improve motor outcomes.	Weak for	(75-79)	Weak for	Reviewed, New-replaced
10.	There is insufficient evidence to recommend for or against the use of high intensity interval training over moderate intensity continuous training to enhance gait recovery.	Strong for	(82-84) **Additional References** (80, 81)	Neither for nor against	Reviewed, New-replaced
11.	There is insufficient evidence to recommend for or against constraint-induced movement therapy to improve upper extremity motor outcomes for individuals with some movement in the paretic limb.	Weak for	(85-87) **Additional Reference** (88)	Neither for nor against	Reviewed, New-replaced

#	Recommendation	2019 Strength of Recommendation	Evidence	2024 Strength of Recommendation	2024 Recommendation Category
12.	There is insufficient evidence to recommend for or against selective serotonin reuptake inhibitors to improve motor outcomes in patients with or without depression.	Neither for nor against	(89, 90) **Additional References** (91-96)	Neither for nor against	Reviewed, New-replaced
13.	There is insufficient evidence to recommend for or against aquatic therapy, as compared with land-based therapy, to improve mobility, balance, and activities of daily living.	NA	(97)	Neither for nor against	Reviewed, New-added
14.	There is insufficient evidence to recommend for or against biofeedback as an adjunct intervention to improve motor outcomes.	NA	(98, 99)	Neither for nor against	Reviewed, New-added
15.	There is insufficient evidence to recommend for or against motor imagery to improve motor function	NA	(100-102)	Neither for nor against	Reviewed, New-added
16.	There is insufficient evidence to recommend for or against acupuncture to improve motor function.	NA	(103, 104)	Neither for nor against	Reviewed, New-added
17.	We suggest neuromuscular electrical stimulation to improve motor outcomes.	Weak for	(105-114)	Weak for	Reviewed, New-replaced
18.	There is insufficient evidence to recommend for or against robot-assisted therapy to improve upper or lower extremity motor outcomes.	NA	(115-118)	Neither for nor against	Reviewed, New-added
19.	There is insufficient evidence to recommend for or against virtual reality to improve balance or enhance gait recovery.	Weak for	(119-123)	Neither for nor against	Reviewed, New-replaced
20.	There is insufficient evidence to recommend for or against the use of virtual reality/serious gaming to improve upper extremity motor outcomes, activities of daily living, or quality of life.	NA	(116, 124-126)	Neither for nor against	Reviewed, New-added

#	Recommendation	2019 Strength of Recommendation	Evidence	2024 Strength of Recommendation	2024 Recommendation Category
21.	There is insufficient evidence to recommend for or against contralaterally controlled functional electrical stimulation to improve upper extremity motor outcomes and activities of daily living.	NA	(127)	Neither for nor against	Reviewed, New-added
22.	There is insufficient evidence to recommend for or against non-invasive brain-computer interface to improve upper extremity motor outcomes and activities of daily living.	NA	(116, 128, 129)	Neither for nor against	Reviewed, New-added
23.	There is insufficient evidence to recommend for or against vagus nerve stimulation as an adjunct intervention for rehabilitation of acute and chronic motor deficits.	NA	(130)	Neither for nor against	Reviewed, New-added
24.	We suggest botulinum toxin for patients with focal spasticity, depending on patient characteristics and preferences.	Strong for	(131-136)	Weak for	Reviewed, New-replaced
25.	There is insufficient evidence to recommend for or against the use of acupuncture or dry needling for spasticity management.	NA	(138-141)	Neither for nor against	Reviewed, New-added
26.	There is insufficient evidence to recommend for or against whole body or localized muscle vibration for spasticity management.	NA	(142)	Neither for nor against	Reviewed, New-added
27.	There is insufficient evidence to recommend for or against extracorporeal shock wave therapy for spasticity management.	NA	(132, 143)	Neither for nor against	Reviewed, New-added
28.	We suggest chin tuck against resistance exercises for patients with dysphagia.	Weak for	(144-146)	Weak for	Reviewed, New-replaced
29.	We suggest respiratory muscle strength training for dysphagia in patients without a tracheostomy.	Weak for	(147, 149, 150) **Additional Reference** (148)	Weak for	Reviewed, New-replaced

#	Recommendation	2019 Strength of Recommendation	Evidence	2024 Strength of Recommendation	2024 Recommendation Category
30.	There is insufficient evidence to recommend for or against tongue pressure resistance training for dysphagia.	Neither for nor against	(151, 152)	Neither for nor against	Reviewed, New-replaced
31.	There is insufficient evidence to recommend for or against neuromuscular electrical stimulation and pharyngeal electrical stimulation for dysphagia.	Neither for nor against	(153-159, 161-165) **Additional Reference** (160)	Neither for nor against	Reviewed, New-replaced
32.	There is insufficient evidence to recommend for or against surface electromyography for dysphagia.	NA	(166, 167)	Neither for nor against	Reviewed, New-added
33.	There is insufficient evidence to recommend for or against the use of selective serotonin reuptake inhibitors to improve cognitive outcomes.	Neither for nor against	(168, 169, 171) **Additional Reference** (170)	Neither for nor against	Reviewed, New-replaced
34.	There is insufficient evidence to recommend for or against computer-assisted cognitive rehabilitation to improve cognitive outcomes.	NA	(172, 173)	Neither for nor against	Reviewed, New-added
35.	There is insufficient evidence to recommend for or against a specific intensity of language therapy for aphasia.	Neither for nor against	(174, 175)	Neither for nor against	Reviewed, Amended
36.	There is insufficient evidence to recommend for or against hemifield eye patching in addition to traditional therapy to improve functional outcomes in patients with unilateral spatial neglect.	Neither for nor against	(178, 181, 182) **Additional References** (176, 177, 179, 180)	Neither for nor against	Reviewed, New-replaced
37.	There is insufficient evidence to recommend for or against the use of prism adaptation therapy for patients with unilateral spatial neglect.	Neither for nor against	(61, 181, 183-185, 187) **Additional References** (60, 186)	Neither for nor against	Reviewed, Amended

#	Recommendation	2019 Strength of Recommendation	Evidence	2024 Strength of Recommendation	2024 Recommendation Category
38.	There is insufficient evidence to recommend for or against solution-focused psychological interventions (e.g., motivational interviewing, problem-solving therapy) to prevent the development of depression.	NA	(189) **Additional Reference** (188)	Neither for nor against	Reviewed, New-added
39.	We suggest against the use of antidepressants for the prevention of post-stroke depression.	Neither for nor against	(190-193) **Additional References** (194, 195)	Weak against	Reviewed, New-replaced
40.	We suggest a selective serotonin reuptake inhibitor or a serotonin norepinephrine reuptake inhibitor for depression symptoms.	Weak for	(196-200) **Additional Reference** (188)	Weak for	Reviewed, Amended
41.	We suggest psychotherapy (e.g., cognitive behavioral therapy) for depression following stroke.	Weak for	(193, 201-207)	Weak for	Reviewed, New-replaced
42.	We suggest mindfulness-based therapies for treatment of depression following stroke.	Weak for	(208) **Additional References** (209-214)	Weak for	Reviewed, New-added
43.	There is insufficient evidence to recommend for or against acupuncture, either alone or as an adjunct to pharmacotherapy, for depression following stroke.	NA	(215-218) **Additional Reference** (137)	Neither for nor against	Reviewed, New-added
44.	We suggest either face-to-face therapy or telerehabilitation, depending on patient characteristics and preferences.	NA	(219, 220)	Weak for	Reviewed, New-added

#	Recommendation	2019 Strength of Recommendation	Evidence	2024 Strength of Recommendation	2024 Recommendation Category
45.	There is insufficient evidence to recommend for or against the use of telerehabilitation and technology-based interventions to improve stroke-related dysphagia or aphasia outcomes or both.	NA	(221-225)	Neither for nor against	Reviewed, New-added
46.	There is insufficient evidence to recommend for or against technology-based caregiver support/education interventions to improve caregiver quality of life.	NA	(226, 227)	Neither for nor against	Reviewed, New-added
47.	There is insufficient evidence to recommend for or against non-invasive brain stimulation (e.g., repetitive transcranial magnetic stimulation, transcranial direct current stimulation, and continuous theta burst stimulation) for patients in stroke rehabilitation.	Neither for nor against	(61, 62, 228-253)	Neither for nor against	Reviewed, New-replaced

Appendix G: 2019 Recommendation Categorization Table

Table G-1. 2019 Stroke Rehabilitation CPG Recommendation Categorization Table[a,b,c,d,e,f]

2019 CPG Recommendation #	2019 CPG Recommendation Text	2019 CPG Strength of Recommendation	2019 CPG Recommendation Category	2024 CPG Recommendation Category	2024 CPG Recommendation #
1.	We recommend a team-based approach in an organized inpatient unit that encompasses comprehensive rehabilitation in order to improve likelihood of discharge to home after acute stroke.	Strong for	Reviewed, Amended	Reviewed, Deleted	NA
2.	We recommend that rehabilitation therapy should start as soon as medical stability is reached.	Strong for	Not reviewed, Amended	Not reviewed, Deleted	NA
3.	There is insufficient evidence to recommend for or against implementing very early mobilization (within 24-48 hours) to improve functional outcomes.	Neither for nor against	Reviewed, New-added	Not reviewed, Deleted	NA
4.	There is insufficient evidence to recommend for or against early supported discharge.	Neither for nor against	Reviewed, Amended	Reviewed, New-replaced	3

[a] 2019 CPG Recommendation # column: This indicates the recommendation number of the recommendation in the 2019 VA/DoD Stroke Rehabilitation CPG.
[b] 2019 CPG Recommendation Text column: This contains the wording of each recommendation from the 2019 VA/DoD Stroke Rehabilitation CPG.
[c] 2019 CPG Strength of Recommendation column: The 2019 VA/DoD Stroke Rehabilitation CPG used the GRADE approach to determine the strength of each recommendation.
[d] 2019 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2019 VA/DoD Stroke Rehabilitation CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.
[e] 2024 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2024 VA/DoD Stroke Rehabilitation CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.
[f] 2024 CPG Recommendation # column: For recommendations that were carried forward to the 2019 VA/DoD Stroke Rehabilitation CPG, this column indicates the new recommendation(s) to which they correspond.

2019 CPG Recommendation #	2019 CPG Recommendation Text	2019 CPG Strength of Recommendation	2019 CPG Recommendation Category	2024 CPG Recommendation Category	2024 CPG Recommendation #
5.	We recommend task-specific practice (also known as task oriented practice or repetitive task practice) for improving upper and lower extremity motor function, gait, posture, and activities of daily living.	Strong for	Reviewed, New-replaced	Reviewed, Not changed	5
6.	We recommend cardiovascular exercise to increase maximum walking speed after stroke.	Strong for	Reviewed, New-replaced	Reviewed, New-replaced	10
7.	We suggest offering body-weight support treadmill training as an adjunct to gait training in the non-ambulatory patient.	Weak for	Reviewed, Amended	Reviewed, New-replaced	8
8.	We suggest offering rhythmic auditory cueing as a modality to include in multimodal interventions to improve walking speed.	Weak for	Reviewed, Amended	Reviewed, New-replaced	9
9.	We suggest offering Constraint-Induced Movement Therapy or modified Constraint-Induced Movement Therapy for individuals with at least 10 degrees of active extension in two fingers, the thumb, and the wrist.	Weak for	Reviewed, Amended	Reviewed, New-replaced	11
10.	There is insufficient evidence to recommend for or against mirror therapy for improvements in limb function.	Neither for nor against	Reviewed, Amended	Reviewed, New-replaced	6
11.	We suggest offering functional electrical stimulation, neuromuscular electrical stimulation, or transcutaneous electrical nerve stimulation as an adjunctive treatment to improve upper and lower extremity motor function.	Weak for	Reviewed, New-replaced	Reviewed, New-replaced	17
12.	We suggest offering functional electrical stimulation to manage shoulder subluxation.	Weak for	Not reviewed, Amended	Reviewed, Deleted	NA
13.	For patients with foot drop, we suggest offering either functional electrical stimulation or traditional ankle foot orthoses to improve gait speed, as both are equally effective.	Weak for	Reviewed, New-added	Reviewed, Deleted	NA

2019 CPG Recommendation #	2019 CPG Recommendation Text	2019 CPG Strength of Recommendation	2019 CPG Recommendation Category	2024 CPG Recommendation Category	2024 CPG Recommendation #
14.	We suggest offering robot-assisted movement therapy as an adjunct to conventional therapy in patients with deficits in upper limb function to improve motor skill.	Weak for	Reviewed, Amended	Reviewed, Deleted	NA
15.	There is insufficient evidence to recommend for or against the use of robotic devices during gait training.	Neither for nor against	Reviewed, Amended	Reviewed, Deleted	NA
16.	We suggest offering virtual reality to enhance gait recovery.	Weak for	Reviewed, Amended	Reviewed, New-replaced	19
17.	There is insufficient evidence to recommend for or against the use of virtual reality for improving activities of daily living and non-gait motor function.	Neither for nor against	Reviewed, New-replaced	Reviewed, Deleted	NA
18.	There is insufficient evidence to recommend for or against the use of transcranial direct current stimulation to improve activities of daily living.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	47
19	There is insufficient evidence to recommend for or against repetitive transcranial magnetic stimulation to improve upper or lower extremity motor function.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	47
20.	In patients with motor deficits, there is insufficient evidence to recommend for or against starting a selective serotonin reuptake inhibitor within 30 days of stroke to improve motor recovery and functional outcomes.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	12
21.	We recommend botulinum toxin for patients with focal spasticity that is painful, impairs function, reduces the ability to participate in rehabilitation, or compromises proper positioning or skin care.	Strong for	Not reviewed, Amended	Reviewed, New-replaced	24
22.	We suggest offering intrathecal baclofen treatments for patients with severe chronic lower extremity spasticity that cannot be effectively managed by other interventions.	Weak for	Not reviewed, Amended	Reviewed, Deleted	NA

2019 CPG Recommendation #	2019 CPG Recommendation Text	2019 CPG Strength of Recommendation	2019 CPG Recommendation Category	2024 CPG Recommendation Category	2024 CPG Recommendation #
23.	We suggest offering Shaker or chin tuck against resistance exercises in addition to conventional dysphagia therapy.	Weak for	Reviewed, New-replaced	Reviewed, New-replaced	28
24.	We suggest offering expiratory muscle strength training for treatment of dysphagia in patients without a tracheostomy.	Weak for	Reviewed, New-replaced	Reviewed, New-replaced	29
25.	There is insufficient evidence to recommend for or against tongue to palate resistance training for treatment of dysphagia.	Neither for nor against	Reviewed, New-replaced	Reviewed, New-replaced	30
26.	There is insufficient evidence to recommend for or against neuromuscular electrical stimulation for treatment of dysphagia.	Neither for nor against	Reviewed, New-replaced	Reviewed, New-replaced	31
27.	There is insufficient evidence to recommend for or against pharyngeal electrical stimulation for treatment of dysphagia.	Neither for nor against	Reviewed, New-replaced	Reviewed, New-replaced	31
28.	In patients with dysphagia in the post-acute phase of stroke who require tube feeding, we suggest offering gastrostomy tube over nasogastric tube for maintenance of optimal nutrition.	Weak for	Reviewed, New-replaced	Reviewed, Deleted	NA
29.	There is insufficient evidence to recommend for or against the use of any specific cognitive rehabilitation methodology or pharmacotherapy to improve cognitive outcomes.	Neither for nor against	Reviewed, New-replaced	Reviewed, New-replaced	33
30.	There is insufficient evidence to recommend for or against the use of intensive language therapy for aphasia.	Neither for nor against	Reviewed, New-added	Reviewed, Amended	35

2019 CPG Recommendation #	2019 CPG Recommendation Text	2019 CPG Strength of Recommendation	2019 CPG Recommendation Category	2024 CPG Recommendation Category	2024 CPG Recommendation #
31.	There is insufficient evidence to recommend for or against hemifield eye patching in addition to traditional therapy for patients with unilateral spatial neglect following stroke.	Neither for nor against	Reviewed, New-replaced	Reviewed, New-replaced	36
32.	Among patients with unilateral spatial neglect, there is insufficient evidence to recommend for or against the use of prisms.	Neither for nor against	Reviewed, New-replaced	Reviewed, Amended	37
33.	Among patients with hemianopsia, there is insufficient evidence to recommend for or against the use of prisms or visual search training.	Neither for nor against	Reviewed, New-replaced	Reviewed, Deleted	NA
34.	For the prevention of post-stroke depression, there is insufficient evidence for or against the universal use of a selective serotonin reuptake inhibitor or a serotonin norepinephrine reuptake inhibitor due to the risk of fractures.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	39
35.	We suggest offering a selective serotonin reuptake inhibitor or a serotonin norepinephrine reuptake inhibitor for treatment of post-stroke depression.	Weak for	Reviewed, New-replaced	Reviewed, Amended	40
36.	We suggest offering cognitive behavioral therapy for treatment of post-stroke depression.	Weak for	Reviewed, New-added	Reviewed, New-replaced	41
37.	There is insufficient evidence to recommend for or against treatment with a combination of pharmacotherapy (selective serotonin reuptake inhibitor/serotonin norepinephrine reuptake inhibitor) and psychotherapy (cognitive behavioral therapy) for treatment of post-stroke depression.	Neither for nor against	Reviewed, New-added	Reviewed, Deleted	NA
38.	There is insufficient evidence to recommend for or against pharmacotherapy or psychotherapy for the treatment of post-stroke anxiety.	Neither for nor against	Reviewed, New-added	Reviewed, Deleted	NA

2019 CPG Recommendation #	2019 CPG Recommendation Text	2019 CPG Strength of Recommendation	2019 CPG Recommendation Category	2024 CPG Recommendation Category	2024 CPG Recommendation #
39.	We suggest offering exercise as adjunctive treatment for post-stroke depression or anxiety symptoms.	Weak for	Reviewed, New-replaced	Reviewed, Deleted	NA
40.	We suggest offering mind-body exercise (e.g., tai chi, yoga, qigong) as adjunctive treatment for post-stroke depression or anxiety symptoms.	Weak for	Reviewed, New-added	Reviewed, New-added	NA
41.	There is insufficient evidence to recommend for or against any specific assessments or interventions regarding return to work.	Neither for nor against	Reviewed, Amended	Reviewed, Deleted	NA
42.	There is insufficient evidence to recommend for or against using any specific assessments or interventions to facilitate return to driving.	Neither for nor against	Reviewed, Amended	Reviewed, Deleted	NA

Appendix H: Participant List

Natasha Antonovich, PharmD, BCPS
Program Manager, Pharmacy Benefits Management (PBM)
Orlando, Florida

Jamie K. Basch, DHSc, OTR/L
Staff Occupational Therapist,
Cincinnati VA Medical Center,
Cincinnati, Ohio

Andrew Buelt, DO
Hospitalist, Bay Pines Veteran's Affairs Healthcare System
Bay Pines, Virginia

Russell J. Carroll, PsyD
Clinical Neuropsychologist, Brain Injury Rehabilitation Service, Department of Rehabilitation Medicine, Brooke Army Medical Center (BAMC)
San Antonio, Texas

Rose Collins, PhD, LP
Staff Rehabilitation Psychologist, Minneapolis VA Health Care System
Minneapolis, Minnesota

Jackoline Costantino, PharmD
Chief, Clinical Pharmacy Coordinator, Brooke Army Medical Center (BAMC)
San Antonio, Texas

Amy M. Donaldson, LCSW
Social Work Project Assistant,
National Project Coordinator,
Department of Veteran Affairs National Social Work Program
Tulsa, Oklahoma

Blessen C. Eapen, MD
Chief, Physical Medicine and Rehabilitation Service
Council Co-Chair, Rehabilitation and Acute Clinical Ancillaries
VHA, Office of Electronic Health Record Modernization (OEHRM)
Los Angeles, California

LCDR Brian Ford, MD
Assistant Professor, Uniformed Services University of the Health Sciences, Department of Family Medicine and the Department of Military and Emergency Medicine
Bethesda, Maryland

Jason Gleason, DNP
Primary Care Provider, Montana VA at Great Falls CBOC,
Montana State DPHHS Stroke Council
Founder, Annual Rocky Mountain Stroke Conference
Great Falls, Montana

LTC Carrie W. Hoppes, PT, PhD, NCS, OSC, ATC, CSCS
Professor, Army-Baylor University Doctoral Program in Physical Therapy
San Antonio, Texas

Maj. Tyler R. Koehn, MD
Vascular Neurologist, 959 Medical Operations Squadron (959 MDOS), U.S. Air Force,
Department of Neurology, Brooke Army Medical Center (BAMC)
San Antonio, Texas

M. Marina LeBlanc, OTR/L
Occupational Therapy, Brain Injury Rehabilitation Service, Department of Rehabilitation Medicine (TBI), Brooke Army Medical Center (BAMC)
San Antonio, Texas

Christine Matthews, CScD, CCC-SLP, BCS-S
Audiology and Speech Pathology Service Chief, VA Pittsburgh Healthcare System
Pittsburgh, Pennsylvania

Danielle Murray, PhD
Staff Psychologist, Brain Injury Rehabilitation Service, Department of Rehabilitation Medicine, Brooke Army Medical Center (BAMC)
San Antonio, Texas

Frederica O'Donnell, OTD, OTR/L, LSSBB
National Occupational Therapy Discipline Lead, VHA Rehabilitation and Prosthetic Services VACO
Tampa, Florida

Michelle Peterson, PT, DPT, NCS
Physical Therapist, Minneapolis VA HealthCare System
Minneapolis, Minnesota

Svetlana Pundik, MD, MSc
Neurologist, Associate Professor, CWRU School of Medicine,
VA Northeast Ohio Healthcare System
Cleveland, Ohio

Rebecca Ruffing, MA, CCC-SLP
Speech-Language Pathologist, VA Pittsburgh Healthcare System
Pittsburgh, PA

Melissa R. Ray, CCC-SLP
CCC-SLP - DoD Speech Pathology/ Speech-Language Pathologist, Brain Injury Rehabilitation Service, Brooke Army Medical Center (BAMC)
San Antonio, Texas

Capt. Zahari Tchopev, MD, MBA
Neurology & Sleep Medicine,
59th Medical Wing, U.S. Air Force,
Wilford Hall Ambulatory Surgical Center
San Antonio, Texas

Johanna E. Tran, MD
Medical Director, Comprehensive Integrated Inpatient Rehabilitation Program (CIIRP),
James A. Haley Veteran's Hospital
Tampa, Florida

Appendix I: Literature Review Search Terms and Strategy

Table G-1. EMBASE and MEDLINE in EMBASE.com Syntax

KQ	Set #	Description	EMBASE Search String
KQ 1	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain* OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3
	#5	Population subgroup – adults with motor dysfunction	'apraxia'/de OR 'motor activity'/de OR 'motor dysfunction'/exp OR 'muslce contracture' OR 'physical mobility'/de OR 'physical performance'/exp OR 'spasticity'/de OR (((balance OR gait OR locomot* OR mobility OR motor OR movement OR stand OR standing OR walk*) NEAR/3 (deficien* OR deficit* OR disab* OR disorder* OR disturb* OR dysfunction* OR impair* OR imped* OR limit* OR perform* OR problem* OR trouble* OR weak*)):ti,ab) OR (((muscle* OR muscular) NEAR/5 contract*):ti,ab) OR spastic*:ti,ab
	#6	Population final	#4 AND #5
	#7	Interventions: Device-related, stimulation	'biofeedback'/exp OR 'biofeedback software'/de OR 'biofeedback therapy'/de OR 'biofeedback training'/de OR 'brain computer interface'/de OR 'constraint induced therapy'/de OR 'direct current stimulation'/de OR 'electrostimulation'/de OR 'electrostimulator'/de OR 'exoskeleton (rehabilitation)'/exp OR 'functional electrical stimulation'/de OR ('muscle contracture'/de AND ('prevention'/lnk OR 'rehabilitation'/lnk)) OR 'neuromuscular electrical stimulation'/exp OR 'rehabilitation robot'/de OR 'robotics'/de OR 'sensorimotor integration'/de OR 'transcranial electrical stimulation'/de OR 'transcranial electrical stimulator'/exp OR 'transcranial magnetic stimulation'/exp OR 'vagus nerve stimulation'/de OR 'vagus nerve stimulator'/de OR 'virtual reality'/de
	#8		((anodal OR cathode OR 'direct current' OR electr* OR 'functional electr*' OR neuromuscular OR transcranial OR vagal OR vagus) AND stim*):ti,ab OR (biofeedback OR 'brain machine interface' OR 'brain computer interface' OR ('constraint induced' NEAR/2 therap*) OR 'electr* muscle stimulat*' OR estim OR 'e stim' OR electrostim* OR ekso* OR exoskeleton OR lokomat OR 'functional electr* stimulat*' OR 'functional electrostimulat*' OR (('functional task*' OR 'repetitive task*') NEAR/2 (practice OR train*)) OR neurobiofeedback OR neurofeedback OR robot* OR sensorimotor OR 'virtual reality' OR CIMT OR FES OR NMES OR rTMS OR tDCS):ti,ab
	#9	Motor therapy	'functional training'/de OR 'motor learning'/de OR 'motor recovery'/de OR 'motor rehabilitation'/de OR ((motor OR movement) NEAR/5 (learn* OR 're learn*' OR 're train*' OR recover* OR rehab* OR therap* OR train* OR treat*)):ti,ab OR (motor NEAR/3 (function* OR performance OR intervention*)):ti,ab OR mobilization:ti,ab OR 'recovery of function':ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 1 (cont.)	#10	Exercise	'aquatic therapy'/de OR 'body weight supported treadmill training'/de OR 'exercise'/exp/mj OR 'high intensity interval training'/de OR 'hydrotherapy'/exp OR 'kinesiotherapy'/exp OR 'physiotherapy'/de OR 'stroke rehabilitation/de' OR 'swimming'/de OR 'treadmill'/de OR 'water aerobics'/de
	#11		((aquatic* OR pool OR water) AND (aerobic* OR class* OR exercise* OR jog* OR laps OR sport* OR therap*)):ti,ab OR exercise*:ti. OR ('high intensity interval training' OR hiit OR 'physical therap*' OR physiotherap* OR swim* OR treadmill):ti,ab
	#12	Pharmacotherapy	'cerebrovascular accident'/mj/dm_dt OR (('cerebrovascular accident'/mj OR 'stroke patient'/mj) AND 'drug therapy'/mj) OR drug*:ti OR medicat*:ti OR medicin*:ti OR pharma*:ti OR prescribe*:ti OR prescription*:ti)
	#13	Stimulant	'psychostimulant agent'/exp OR ((amphetamine NEAR/3 (dexamphetamine OR dextroamphetamine)):ti,ab) OR (amphetamine* OR 'amphetamine resin complex' OR armodafinil OR dexmethylphenidate OR dexamphetamine* OR dextroamphetamine* OR lisdexamfetamine* OR methylphenidate OR modafinil OR 'psycho stimulant*' OR psychostimulant* OR stimulant*):ti,ab
	#14	SSRI	'serotonin uptake inhibitor'/exp OR SSRI* OR 'serotonin reuptake inhibitor*' OR citalopram OR escitalopram OR fluvoxamine OR fluoxetine OR paroxetine OR sertraline
	#15	SNRI	'serotonin noradrenalin reuptake inhibitor'/exp OR SNRI* OR 'serotonin norepinephrine reuptake inhibitor*' OR 'serotonin and norepinephrine reuptake inhibitor*' OR desvenlafaxine OR duloxetine OR levomilnacipran OR milnacipran OR venlafaxine
	#16	Dopamine	'dopamine receptor stimulating agent'/exp OR 'carbidopa levodopa' OR 'carbidopa plus levodopa' OR 'dopamine agonist*' OR pramipexole OR ropinirole OR rotigotine
	#17	Rehabilitation	'stroke rehabilitation'/de OR (('rehabilitation'/de OR 'rehabilitation care'/de OR 'rehabilitation':lnk OR rehab*:ti) AND ('cerebrovascular accident'/mj OR stroke:ti))

KQ	Set #	Description	EMBASE Search String
KQ 1 (cont.)	#18	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR consult* OR health OR medical OR medicine OR monitor* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
	#19	Other interventions	'acupuncture'/exp OR acupuncture OR 'acu puncture' OR acupressure OR 'acu pressure'
	#20		'mirror image'/de OR 'mirror therapy'/de OR 'motor imagery'/de OR 'music therapy'/exp OR ((mirror* OR music*) NEAR/3 therap*) OR ((mental* OR motor*) NEAR/2 (imagery OR practice* OR train* OR rehears*)):ti,ab
	#21	Combine interventions	#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
	#22	Combine population and interventions	#6 AND #21
	#23	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))

KQ	Set #	Description	EMBASE Search String
KQ 1 (cont.)	#24	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#25	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#26	Combine exclusions	#23 OR #24 OR #25
	#27	Remove exclusions	#22 NOT #26
	#28	English language	#27 AND [english]/lim
	#29	Publication year	#28 AND [2018-2023]/py
	#30	Entry date	#29 AND [01-07-2018]/sd NOT [03-05-2023]/sd
	#31	Systematic reviews and meta-analyses	#30 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#32	Randomized controlled trials	#30 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#33	Final set	#31 OR #32
KQ 2	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain* OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3

KQ	Set #	Description	EMBASE Search String
KQ 2 (cont.)	#5	Speech/language dysfunction	'aphasia'/exp OR 'apraxia of speech'/de OR 'dysarthria'/exp OR 'dysphasia'/de OR 'speech disorder'/de OR 'language disability'/de OR 'post stroke aphasia'/de OR (((articulat* OR communicat* OR language OR phonetic OR phonolog* OR sound OR speech) NEAR/3 (difficult* OR disabilit* OR disorder* OR disturbance OR dysfunction* OR impair*)):ti,ab) OR anomia:ti,ab OR anomic:ti,ab OR aphasia*:ti,ab OR ((apraxia NEAR/2 speech):ti,ab) OR dysarthria:ti,ab OR dysphas*:ti,ab
	#6	Cognitive dysfunction	'attention disturbance'/de OR 'cognition'/exp OR 'cognitive defect'/de OR 'memory'/exp OR 'vascular cognitive impairment'/de OR (('attention'/exp OR 'cognition'/exp OR 'memory'/exp) AND (defect*:ti OR disorder*:ti)) OR (((attention* OR cognit* OR memory) NEAR/3 (defect* OR deficit* OR difficult* OR disabilit* OR disorder* OR disturbance OR dysfunction* OR function* OR impaired OR impairment*)):ti) OR cognition:ti OR comprehen*:ti OR confusion:ti OR 'executive function*':ti OR 'executive dysfunction':ti OR 'vascular cognitive impairment':ti OR (((concentration OR cognitive) NEAR/3 (accessibility OR dissonance OR structure OR symptom* OR task* OR thinking OR remembering)):ti)
	#7		#5 OR #6
	#8	Population final – stroke and cognitive or speech dysfunction	#4 AND #7
	#9	Interventions: Cognitive non-pharma	'cognitive rehabilitation'/de OR 'neurorehabilitation'/exp/mj OR 'stroke rehabilitation'/de OR 'neuro rehabilitation':ti,ab OR 'neurolog* rehabilitation':ti,ab OR neurorehab*:ti,ab OR (((cognitive OR cognition) NEAR/3 (train* OR treat* OR therap* OR rehab* OR intervention* OR recover*)):ti,ab)
	#10	Speech/language non-pharma	'speech and language rehabilitation'/exp OR (((language OR speech) NEAR/3 (intervention* OR path* OR recover* OR rehab* OR remediat* OR therap* OR train* OR treat*)):ti,ab)
	#11		(((anomia OR anomic OR aphasi* OR dysphasi* OR language* OR linguistic OR response OR speech OR vocal* OR voice) NEAR/5 (therap* OR train* OR rehabilitat* OR treat* OR remediat* OR intervention*)):ti,ab) OR ((acoustic:ti,ab OR audio*:ti,ab OR auditory:ti,ab OR sound:ti,ab) AND stim*:ti,ab) OR anagram OR 'attentive reading' OR 'augmentative communication' OR comprehensibil* OR 'constraint induced' OR (copy NEAR/1 recall) OR 'facilitated communication' OR (melodic NEAR/2 analysis) OR (('multiple oral' NEAR/2 (read* OR 're read' OR reread*)):ti,ab) OR 'oral reading for language in aphasia' OR orla OR phonologic* OR phonomotor OR 'promoting aphasics' OR 're read*' OR reread* OR script OR 'semantic feature analysis' OR ((silverman NEAR/3 (vocal* OR voice* OR speech)):ti,ab) OR 'speak out' OR 'speech generating device*' OR 'supported conversation*' OR 'systematic instruction' OR 'verb network' OR 'visual action'
	#12	Assistive technology	'assistive technology'/de OR 'assistive technology device'/exp OR 'self help'/de OR (alarm* OR alert* OR 'assistive technolog*' OR distract* OR 'micro prompt' OR prompt* OR remind OR reminder):ti,ab OR ((display OR store OR stored OR storing) AND memor*):ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 2 (cont.)	#13	Device-related, stimulation	'biofeedback'/exp OR 'biofeedback software'/de OR 'biofeedback therapy'/de OR 'biofeedback training'/de OR 'brain computer interface'/exp OR 'constraint induced therapy'/de OR 'direct current stimulation'/de OR 'electrostimulation'/de OR 'electrostimulator'/de OR 'exoskeleton (rehabilitation)'/exp OR 'functional electrical stimulation'/de OR ('muscle contracture'/de AND ('prevention'/lnk OR 'rehabilitation'/lnk)) OR 'neuromuscular electrical stimulation'/exp OR 'rehabilitation robot'/de OR 'robotics'/de OR 'sensorimotor integration'/de OR 'transcranial electrical stimulation'/exp OR 'transcranial electrical stimulator'/exp OR 'transcranial magnetic stimulation'/exp OR 'vagus nerve stimulation'/de OR 'vagus nerve stimulator'/de OR 'virtual reality'/de
	#14		((anodal OR cathode OR 'direct current' OR electr* OR 'functional electr*' OR neuromuscular OR transcranial OR vagal OR vagus) AND stim*):ti,ab OR (biofeedback OR 'brain machine interface' OR 'brain computer interface' OR ('constraint induced' NEAR/2 therap*) OR 'electr* muscle stimulat*' OR estim OR 'e stim' OR electrostim* OR ekso* OR exoskeleton OR lokomat OR 'functional electr* stimulat*' OR 'functional electrostimulat*' OR (('functional task*' OR 'repetitive task*') NEAR/2 (practice OR train*)) OR neurobiofeedback OR neurofeedback OR robot* OR sensorimotor OR 'virtual reality' OR CIMT OR FES OR NMES OR rTMS OR tDCS):ti,ab
	#15	Pharmacotherapy	'cerebrovascular accident'/mj/dm_dt OR 'aphasia'/mj/dm_dt OR (('aphasia'/mj OR 'cerebrovascular accident'/mj OR 'stroke patient'/de) AND ('drug therapy'/mj OR drug*:ti OR medicat*:ti OR medicin*:ti OR pharma*:ti OR prescribe*:ti OR prescription*:ti))
	#16	Acetylcholinesterase Inhibitors	'cholinesterase inhibitor'/exp OR ('acetylcholintesterase OR cholinesterase) NEAR/2 inhibitor*') OR donepezil OR galantamine OR memantine OR rivastigmine
	#17	Stimulants	'psychostimulant agent'/exp OR ((amphetamine NEAR/3 (dexamphetamine OR dextroamphetamine)):ti,ab) OR (amphetamine* OR 'amphetamine resin complex' OR armodafinil OR dexmethylphenidate OR dexamphetamine OR dextroamphetamine OR lisdexamfetamine* OR methylphenidate OR modafinil OR 'psycho stimulant*' OR psychostimulant* OR stimulant*):ti,ab
	#18	SSRI	'serotonin uptake inhibitor'/exp OR SSRI* OR 'serotonin reuptake inhibitor*' OR citalopram OR escitalopram OR fluvoxamine OR fluoxetine OR paroxetine OR sertraline
	#19	SNRI	'serotonin noradrenalin reuptake inhibitor'/exp OR SNRI* OR 'serotonin norepinephrine reuptake inhibitor*' OR 'serotonin and norepinephrine reuptake inhibitor*' OR desvenlafaxine OR duloxetine OR levodopa OR levomilnacipran OR milnacipran OR venlafaxine
	#20	Other pharmacotherapy	'amantadine'/de OR 'bromocriptine'/de OR amantadine OR bromocriptine
	#21	Stroke rehabilitation, general	'stroke rehabilitation'/de OR (('rehabilitation'/de OR 'rehabilitation care'/de OR 'rehabilitation':lnk OR rehab*:ti) AND ('cerebrovascular accident'/mj OR stroke:ti))

KQ	Set #	Description	EMBASE Search String
KQ 2 (cont.)	#22	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'teletherapy'/de OR 'telerehabilitation'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR psycholog* OR psychotherap* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
	#23	Traditional interventions	'attention training'/de OR 'attention training technique'/de OR 'cognitive rehabilitation'/de OR 'goal attainment'/mj OR 'neurorehabilitation'/exp OR 'time management'/de OR 'visual imagery'/de
	#24		((attention OR compensatory OR goal OR metacognitive OR 'visual imagery') NEAR/3 (train* OR 're train*' OR retrain* OR therap* OR treat*)) OR ((cognitive OR cognition) NEAR/3 (intervention* OR recover* OR rehab* OR therap* OR treat*)) OR 'chaining technique':ti,ab OR 'cognitive aid*':ti,ab OR 'errorless learning':ti,ab OR 'goal attainment':ti,ab OR 'goal plan*':ti,ab OR 'lighthouse strategy':ti,ab OR 'neuro rehabilitation':ti,ab OR neurorehab*:ti,ab OR 'plan implement evaluate':ti,ab OR (respons* NEAR/3 elab*):ti,ab OR 'spaced retrieval':ti,ab OR 'systematic instruction':ti,ab OR (time NEAR/2 manage*):ti,ab
	#25	Interventions	#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
	#26	Population and interventions	#8 AND #25
	#27	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))

KQ	Set #	Description	EMBASE Search String
KQ 2 (cont.)	#28	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#29	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#30	Combine exclusions	#27 OR #28 OR #29
	#31	Remove exclusions	#26 NOT #30
	#32	English language	#31 AND [english]/lim
	#33	Publication year	#32 AND [2018-2023]/py
	#34	Entry date	#33 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#35	Systematic reviews and meta-analyses	#34 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#36	Randomized controlled trials	#34 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#37	Final set	#35 OR #36
KQ 3	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4	Population final set	#1 OR #2 OR #3

KQ	Set #	Description	EMBASE Search String
KQ 3 (cont.)	#5	Interventions: Device-related, stimulation	'biofeedback'/exp OR 'biofeedback software'/de OR 'biofeedback therapy'/de OR 'biofeedback training'/de OR 'brain computer interface'/de OR 'constraint induced therapy'/de OR 'direct current stimulation'/de OR 'electrostimulation'/de OR 'electrostimulator'/de OR 'exoskeleton (rehabilitation)'/exp OR 'functional electrical stimulation'/de OR ('muscle contracture'/de AND ('prevention'/lnk OR 'rehabilitation'/lnk)) OR 'neuromuscular electrical stimulation'/exp OR 'rehabilitation robot'/de OR 'robotics'/de OR 'sensorimotor integration'/de OR 'transcranial electrical stimulation'/de OR 'transcranial electrical stimulator'/exp OR 'transcranial magnetic stimulation'/exp OR 'vagus nerve stimulation'/de OR 'vagus nerve stimulator'/de OR 'virtual reality'/de
	#6		((anodal OR cathode OR 'direct current' OR electr* OR 'functional electr*' OR neuromuscular OR transcranial OR vagal OR vagus) AND stim*):ti,ab OR (biofeedback OR 'brain machine interface' OR 'brain computer interface' OR ('constraint induced' NEAR/2 therap*) OR 'electr* muscle stimulat*' OR estim OR 'e stim' OR electrostim* OR ekso* OR exoskeleton OR lokomat OR 'functional electr* stimulat*' OR 'functional electrostimulat*' OR (('functional task*' OR 'repetitive task*') NEAR/2 (practice OR train*)) OR neurobiofeedback OR neurofeedback OR robot* OR sensorimotor OR 'virtual reality' OR CIMT OR FES OR NMES OR rTMS OR tDCS):ti,ab
	#7	Exercise	'aquatic therapy'/de OR 'body weight supported treadmill training'/de OR 'exercise'/exp/mj OR 'high intensity interval training'/de OR 'hydrotherapy'/exp OR 'kinesiotherapy'/exp OR 'physiotherapy'/de OR 'stroke rehabilitation/de' OR 'swimming'/de OR 'treadmill'/de OR 'water aerobics'/de
	#8		((aquatic* OR pool OR water) AND (aerobic* OR class* OR exercise* OR jog* OR laps OR sport* OR therap*)):ti,ab OR ('high intensity interval training' OR hiit OR 'physical therap*' OR physiotherap* OR swim* OR treadmill):ti,ab OR exercise*:ti.
	#9	Motor therapy	‘arm movement’/de OR ‘functional training’/de OR ‘motor control’/exp OR ‘motor learning/de’ OR ‘motor recovery’/de OR ‘motor rehabilitation’/de OR (((motor OR movement) NEAR/5 (learning OR ‘re learn’ OR ‘re train*’ OR recovery OR rehab* OR train* OR therap* OR treatment* OR recovery OR rehab* OR learning)) OR (motor NEAR/3 (function OR performance OR intervention*)) OR mobilization OR ‘recovery of function’):ti,ab
	#10	Sensory	‘object manipulation’/de OR ‘perception’/exp OR ‘sensorimotor function’/exp OR 'sensory feedback'/exp OR ‘sensory stimulation’/exp/mj
	#11		((object* NEAR/3 manipulation*):ti,ab) OR (((auditory OR proprioceptive OR sensorimotor OR sensory OR tactile OR visual) NEAR/3 feedback):ti,ab) OR (perception* OR perceptual OR sensorimotor OR sensory):ti,ab
	#12	Combine interventions	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11

KQ	Set #	Description	EMBASE Search String
KQ 3 (cont.)	#13	Duration/intensity	'duration'/de OR 'time factor'/mj/exp OR 'treatment duration'/de OR (((early OR earlier OR initiat*) NEAR/3 rehab*):ti,ab) OR duration:ti OR frequen*:ti OR intensity:ti OR ((number NEAR/3 sessions):ti,ab) OR 'time factor':ti,ab OR (((duration OR frequency OR length OR intens* OR time OR timing) NEAR/3 (therap* OR treatment OR rehab*)):ti,ab) OR 'very early rehabilitation':ti,ab
	#14	Combine interventions and duration	#12 AND #13
	#15	Combine population and interventions and duration	#4 AND #14
	#16	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#17	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#18	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#19	Combine exclusions	#16 OR #17 OR #18
	#20	Remove exclusions	#15 NOT #19
	#21	English language	#20 AND [english]/lim
	#22	Publication year	#21 AND [2018-2023]/py
	#23	Entry date	#22 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#24	Systematic reviews and meta-analyses	#23 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)

KQ	Set #	Description	EMBASE Search String
KQ 3 (cont.)	#25	Randomized controlled trials	#23 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#26	Final set	#24 OR #25
KQ 4	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3
	#5	Population subgroup – Post stroke cognitive dysfunction	'attention disturbance'/de OR 'cognition'/exp OR 'cognitive defect'/de OR 'memory'/exp OR 'vascular cognitive impairment'/de OR ((‘attention’/exp OR ‘cognition’/exp OR ‘memory’/exp) AND (defect* OR disorder*):ti) OR ((attention* OR cognit* OR memory) NEAR/3 (defect* OR deficit* OR difficult* OR disabilit* OR disorder* OR disturbance OR dysfunction* OR function* OR impairment* OR impaired)):ti OR (cognition OR comprehen* OR confusion OR 'executive function*' OR 'executive dysfunction' OR 'vascular cognitive impairment'):ti OR (((concentration OR cognitive) NEAR/3 (accessibility OR dissonance OR structure OR symptom* OR task* OR thinking OR remembering)):ti
	#6	Population subgroup - Speech/language dysfunction	‘aphasia’/exp OR 'apraxia of speech'/de OR 'dysarthria'/exp OR ‘dysphasia’/de OR 'speech disorder'/de OR 'language disability'/de OR 'post stroke aphasia'/de OR (((articulat* OR communicat* OR language OR phonetic OR phonolog* OR sound OR speech) NEAR/3 (difficult* OR disabilit* OR disorder* OR disturbance OR dysfunction* OR impair*)):ti,ab) OR (anomia OR anomic OR aphasia* OR (apraxia NEAR/2 speech) OR dysarthria OR dysphas*):ti,ab
	#7	Population	#4 AND (#5 OR #6)
	#8	Interventions: Cognitive non-pharmacotherapy	'cognitive rehabilitation'/de OR 'neurorehabilitation'/exp/mj OR 'sentence comprehension'/de OR 'sentence processing'/de OR 'social participation'/mj OR 'stroke rehabilitation'/de OR ('neuro rehabilitation' OR 'neurolog* rehabilitation' OR neurorehab*):ti,ab OR ((cognitive OR cognition) NEAR/3 (train* OR treat* OR therap* OR rehab* OR intervention* OR recover*)):ti,ab
	#9		'attention training'/de OR 'attention training technique'/de OR 'cognitive rehabilitation'/de OR 'goal attainment'/mj OR 'neurorehabilitation'/exp OR 'time management'/de OR 'visual imagery'/de

KQ	Set #	Description	EMBASE Search String
KQ 4 (cont.)	#10		((Attention OR compensatory OR goal OR metacognitive OR 'visual imagery') NEAR/3 (train* OR 're train*' OR retrain* OR therap* OR treat*)) OR ((cognitive OR cognition) NEAR/3 (intervention* OR recover* OR rehab* OR therap* OR treat*)) OR 'chaining technique':ti,ab OR 'cognitive aid*':ti,ab OR 'errorless learning':ti,ab OR 'goal attainment':ti,ab OR 'goal plan*':ti,ab OR 'lighthouse strategy':ti,ab OR 'neuro rehabilitation':ti,ab OR neurorehab*:ti,ab OR 'plan implement evaluate':ti,ab OR (respons* NEAR/3 elab*):ti,ab OR 'spaced retrieval':ti,ab OR 'systematic instruction':ti,ab OR (time NEAR/2 manage*):ti,ab
	#11	Speech/Language non-pharmacotherapy	'speech and language rehabilitation'/exp OR 'speech rehabilitation'/exp OR 'speech therapy'/de OR ((language OR speech) NEAR/3 (intervention* OR path* OR recover* OR rehab* OR remediat* OR therap* OR train* OR treat*)):ti,ab
	#12		'aphasia rehabilitation'/de OR ('aphasia'/exp/mj AND 'stroke rehabilitation'/exp/mj) OR 'comprehensibility'/de OR 'comprehension'/de OR 'constraint induced therapy'/de OR 'constraint induced language therapy'/de OR 'constraint induced aphasia therapy'/de OR 'conversation'/de OR 'language ability'/mj OR 'language therapy'/mj OR 'melodic intonation therapy'/de OR 'object manipulation'/de OR 'phonetics'/de OR 'semantics'/mj OR 'semantic feature analysis'/de OR 'speech intelligibility'/mj OR 'speech'/mj OR 'speech generating device'/de
	#13		((anomia OR anomic OR aphasi* OR dysphasi* OR language* OR linguistic OR response OR speech OR vocal* OR voice) NEAR/5 (intervention* OR rehab* OR remediat* OR therap* OR treat* OR train*)):ti,ab OR ((acoustic OR audio* OR auditory OR sound) AND stim*):ti,ab OR ((anagram OR 'attentive reading' OR 'augmentative communication' OR comprehensibil* OR 'constraint induced' OR (copy NEAR/1 recall) OR elaborate* OR semantic*):ti,ab AND (rehab* OR therap* OR treat*)):ti,ab OR 'facilitated communication' OR (melodic NEAR/2 analysis) OR ('multiple oral' NEAR/2 (read* OR 're read' OR reread*)):ti,ab OR 'Oral Reading for Language in Aphasia' OR ORLA OR phonologic* OR phonomotor OR 'promoting aphasics' OR 're read*' OR reread* OR script OR 'semantic feature analysis' OR (silverman NEAR/3 (speech OR vocal* OR voice*)):ti,ab OR 'speak out' OR 'speech generating device*' OR 'supported conversation*' OR 'systematic instruction' OR 'verb network' OR (verbal NEXT/3 strengthen*):ti,ab OR 'visual action'
	#14	Assistive technology	'assistive technology'/de OR 'assistive technology device'/exp OR 'self help'/de OR (alarm* OR alert* OR 'assistive technolog*' OR distract* OR 'micro prompt' OR prompt* OR remind*):ti,ab OR ((display OR store OR stored OR storing) AND memor*):ti,ab
	#15	Device-related, stimulation	'biofeedback'/exp OR 'biofeedback software'/de OR 'biofeedback therapy'/de OR 'biofeedback training'/de OR 'brain computer interface'/de OR 'direct current stimulation'/de OR 'electrostimulation'/de OR 'electrostimulator'/de OR 'functional electrical stimulation'/de OR 'transcranial electrical stimulation'/de OR 'transcranial electrical stimulator'/exp OR 'transcranial magnetic stimulation'/exp OR 'vagus nerve stimulation'/de OR 'vagus nerve stimulator'/de OR 'virtual reality'/de

KQ	Set #	Description	EMBASE Search String
KQ 4 (cont.)	#16		((anodal OR cathode OR 'direct current' OR electr* OR 'functional electr*' OR neuromuscular OR transcranial OR vagal OR vagus) AND stim*):ti,ab OR (biofeedback OR 'brain machine interface' OR 'brain computer interface' OR estim OR 'e stim' OR electrostim* OR neurobiofeedback OR neurofeedback OR 'virtual reality' OR rTMS OR tDCS):ti,ab
	#17	Rehabilitation (general)	'stroke rehabilitation'/de OR (('rehabilitation'/de OR 'rehabilitation care'/de OR 'rehabilitation':lnk OR rehab*:ti)
	#18	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'teletherapy'/de OR 'telerehabilitation'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR psycholog* OR psychotherap* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
	#19	Combine Interventions	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
	#20	Duration/Intensity	'duration'/de OR 'time factor'/mj/exp OR 'treatment duration'/de OR (((early OR earlier OR initiat*) NEAR/3 rehab*):ti,ab) OR duration:ti OR frequen*:ti OR intensity:ti OR ((number NEAR/3 sessions):ti,ab) OR 'time factor':ti,ab OR (((duration OR frequency OR length OR time OR intens* OR timing) NEAR/3 (therap* OR treatment OR rehab*)):ti,ab) OR 'very early rehabilitation':ti,ab
	#21	Combine interventions and duration	#19 AND #20
	#22	Combine population and interventions and duration	#7 AND #21

KQ	Set #	Description	EMBASE Search String
KQ 4 (cont.)	#23	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#24	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#25	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#26	Combine exclusions	#23 OR #24 OR #25
	#27	Remove exclusions	#22 NOT #26
	#28	English language	#27 AND [english]/lim
	#29	Publication year	#28 AND [2018-2023]/py
	#30	Entry date	#29 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#31	Systematic reviews and meta-analyses	#30 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#32	Randomized controlled trials	#30 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#33	Final set	#31 OR #32
KQ 5	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 5 (cont.)	#4		#1 OR #2 OR #3
	#5	Interventions: Assistive devices	'augmentative and alternative communication'/de OR 'augmentative communication system'/exp OR ((alternat* OR assist* OR augment* OR AAC OR facilitat*) AND (device* OR system* OR tech*) AND communicat*):ti,ab
	#6		('assistive express' OR (communicat* NEAR/2 board*) OR Lingraphica OR 'navigation ring block*' OR pictello OR Proloquo2Go OR Prolquo4Text OR 'scene speak' OR 'touch talk' OR TouchTalk OR 'Tobii Dynavox' OR 'TD Snap'):ti,ab
	#7	Orthotic/FES devices	'electrostimulation'/de OR 'electrostimulator'/de OR 'functional electrical stimulation'/de OR 'neuromuscular electrical stimulation'/exp
	#8		(functional NEAR/2 (electric* OR 'e stim' OR e-stim OR electrostim* OR practice OR stim* OR task OR training)):ti,ab OR ((neuromuscular OR 'neuro muscular') NEAR/2 stim*):ti,ab
	#9		'exoskeleton'/exp OR 'orthosis'/de OR orthosis:ti OR orthotic*:ti OR ((exoskelet* OR ortho*) NEAR/3 (ankle OR arm OR gait OR hand OR leg OR robot*)):ti,ab OR ((finger* OR thumb OR wrist) AND splint*):ti,ab OR (bioness OR myomo OR saebo OR walkaid OR walkasin*):ti,ab
	#10	Smart home	'home environment'/de OR ((environment* NEAR/3 control*) OR (smart NEAR/3 (home* OR hous*)) OR ((alexa OR apple) AND (home OR hous*)):ti,ab)
	#11	Technology-assisted tools	'brain computer interface'/exp/mj OR 'internet'/mj OR 'mobile application'/exp/mj OR 'mobile health'/mj OR 'mobile phone'/exp/mj OR 'personal digital assistant'/mj OR 'social media'/mj OR 'text messaging'/mj OR 'videorecording'/exp/mj OR 'virtual reality'/mj
	#12	Telehealth	(app OR apps OR 'apple watch' OR applewatch OR 'cell* phone*' OR cellphone* OR device* OR internet OR 'I pad' OR ipad OR online OR phone* OR smartphone* OR 'smart phone*' OR smartwatch* OR 'smart watch' OR technolog* OR telephone* OR web):ti OR (('apple watch' OR applewatch OR 'cell* phone*' OR cellphone* OR device* OR 'I pad' OR ipad OR online OR phone* OR smartphone* OR 'smart phone*' OR smartwatch* OR 'smart watch*' OR technolog* OR telephone* OR web) NEAR/1 (application* OR based OR intervention* OR program* OR therap*)):ab OR ((brain OR cerebellum OR cerebral OR neural) NEAR/1 interface*):ti,ab OR ((digital* OR internet OR mobile OR online OR web) NEAR/1 (application* OR based OR intervention* OR program* OR therap*)):ti OR ((mobile NEAR/2 health) OR mhealth OR 'm health' OR ehealth OR 'e health' OR emental OR 'e mental'):ti OR (('mobile health' OR mhealth OR 'm health' OR ehealth OR 'e health' OR emental OR 'e mental') NEAR/2 (application* OR based OR device* OR intervention* OR program* OR therap*)):ab OR (mobile* NEAR/1 (based OR application* OR device* OR intervention* OR technolog*)):ti OR ('personal digital assist*' OR skype OR 'social media' OR 'smart device*' OR 'wearable device*'):ti,ab OR (imessag* OR 'instant messag*' OR 'text message*' OR twitter OR video* OR 'virtual reality'):ti

KQ	Set #	Description	EMBASE Search String
KQ 5 (cont.)	#13	Stroke rehab (general)	('stroke rehabilitation'/de OR (stroke*:ti AND ('rehabilitation'/de OR 'rehabilitation care'/de OR 'rehabilitation':lnk OR rehab*:ti,ab))) AND tech*:ti
	#14	Combine interventions	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
	#15	Population and interventions	#4 AND #14
	#16	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#17	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#18	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#19	Combine exclusions	#16 OR #17 OR #18
	#20	Remove exclusions	#15 NOT #19
	#21	English language	#20 AND [english]/lim
	#22	Publication year	#21 AND [2018-2023]/py
	#23	Entry date	#22 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#24	Systematic reviews and meta-analyses	#23 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#25	Randomized controlled trials	#23 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#26	Final set	#24 OR #25

KQ	Set #	Description	EMBASE Search String
KQ 6	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3
	#5	Post stroke: Anxiety	'anxiety'/exp OR 'anxiety disorder'/exp OR (anxieties OR anxiety OR anxious):ti,ab OR (panic NEAR/2 (attack* OR disorder*)):ti,ab OR phobi*:ti,ab OR ('post stroke' AND (anxiety OR anxious)):ti,ab
	#6	Post Stroke: Behavioral health issues	'behavior disorder'/exp OR (((behavior* OR behaviour*) NEAR/2 (aberrant OR crisis OR disorder* OR disturb*)):ti,ab) OR ('post stroke':ti,ab AND (behavior*:ti,ab OR behaviour*:ti,ab) AND disorder*:ti,ab)
	#7	Post stroke: Depression	'depression'/exp OR 'major depression'/de OR 'post-stroke depression'/de OR (depress* OR dysthymi*):ti,ab OR ('post stroke' NEAR/2 depression)
	#8	Population	#4 AND (#6 OR #7 OR #8)
	#9	Interventions: Behavioral health	'behavioral health'/de OR 'behavioral health care'/de OR 'behavior therapy'/de OR 'cognitive behavioral therapy'/exp/mj OR 'cognitive therapy'/de OR 'group therapy'/de OR 'guided imagery'/de OR 'hypnosis'/de OR 'mindfulness'/de OR 'meditation'/exp/mj OR 'muscle relaxation'/de OR ((behavi* NEXT/2 (health OR therap*)):ti,ab) OR breath*:ti OR 'cognitive behaviour*':ti OR 'cognitive behavior*':ti OR 'guide* imagery':ti OR hypnosis:ti OR meditat*:ti OR 'mind* body':ti OR mindful*:ti OR mindfulness:ti OR relax*:ti OR visual*:ti OR mbct:ti,ab OR mbsr:ti,ab OR mbt:ti,ab OR micbt:ti,ab
	#10	Biofeedback	'biofeedback'/exp OR 'biofeedback therapy'/de OR 'biofeedback training'/exp OR 'neurofeedback'/de OR 'neurofeedback therapy'/de OR 'neurofeedback training'/de OR ('bio feed back*' OR 'bio feedback*' OR 'biofeed back*' OR biofeedback* OR feedback* OR myobiofeedback* OR myofeedback* OR neurobiofeedback* OR neurofeedback* OR 'psychophysiolog* feedback'):ti,ab
	#11	Complementary and integrative health	'alternative medicine'/exp OR 'integrative medicine'/de OR 'complement* integrat* health':ti,ab OR ((alternat* OR complement*) NEXT/5 (care OR health* OR intervent* OR medicine OR therap*)):ti,ab OR 'functional medicine':ti,ab OR ((integrated OR integrative) NEAR/2 health)
	#12		'acupuncture'/exp OR 'dry needling'/de OR 'massage'/exp OR ('dry needl*' OR acupressure OR acupuncture OR electroacupuncture OR 'electro acupuncture' OR massage*):ti,ab
	#13		'qigong'/de OR 'tai chi'/de OR 'yoga'/exp OR 'chi kung':ti,ab OR 'ch i kung':ti,ab OR chigung:ti,ab OR 'qi gong':ti,ab OR 'tai chi':ti,ab OR 't ai chi':ti,ab OR taichi:ti,ab OR 'tai ji':ti,ab OR taiji*:ti,ab OR yoga*:ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 6 (cont.)	#14	Exercise	'exercise'/exp OR 'kinesiotherapy'/exp OR 'physiotherapy'/de OR 'physical therap*' OR exercis* OR physiotherap* OR treadmill*
	#15	Pharmacotherapy	'cerebrovascular accident'/mj/dm_dt OR (('cerebrovascular accident'/mj OR 'stroke patient'/de) AND ('drug therapy'/mj OR drug*:ti OR medicat*:ti OR medicin*:ti OR pharma*:ti OR prescribe*:ti OR prescription*:ti))
	#16	Antidepressants	'antidepressant agent'/exp OR 'anxiolytic agent'/exp OR ((('anti anxiety' OR antianxiety) NEAR/2 (agent* OR drug* OR medication* OR prescri*)):ti,ab) OR antidepress*:ti,ab OR 'anti depress**':ti,ab OR 'serotonin modulator*':ti,ab OR 'mirtazapine'/de OR mirtazapine
	#17	Bupropion	'amfebutamone'/de OR bupropion
	#18	iMAOis	'monoamine oxidase inhibitor'/exp OR maoi OR 'monoamine oxidase inhibitor*' OR phenelzine OR selegiline
	#19	SNRIs	'serotonin noradrenalin reuptake inhibitor'/exp OR snri* OR ssnri OR 'selective serotonin noradrenalin reuptake inhibitor' OR 'serotonin and noradrenaline reuptake inhibitor*' OR 'serotonin and noradrenalin uptake inhibitor*' OR 'serotonin norepinephrine reuptake inhibitor*' OR 'serotonin and norepinephrine reuptake inhibitor*' OR desvenlafaxine OR duloxetine OR levodopa OR levomilnacipran OR milnacipran OR venlafaxine
	#20	SSRIs	'serotonin uptake inhibitor'/exp OR ssri* OR 'serotonin reuptake inhibitor*' OR citalopram OR escitalopram OR fluvoxamine OR fluoxetine OR paroxetine OR sertraline
	#21	Serotonin modulators	nefazodone OR vilazodone OR vorioxetine OR 'serotonin modulator*' OR trazodone
	#22	TCAs	amitriptyline OR amoxapine OR clomipramine OR desipramine OR doxepin OR imipramine OR nortriptyline OR protriptyline OR tca
	#23	Psychotherapy	'psychotherapy'/exp OR psychotherap*:ti,ab OR (((behavior* OR behaviour* OR group* OR psycho* OR socio*) NEAR/5 (intervention* OR therap* OR train*)):ti,ab)
	#24	Transcranial stimulation	'transcranial direct current stimulation'/de OR 'transcranial electrical stimulation'/exp OR 'transcranial magnetic stimulation'/exp OR rtms:ti,ab OR tdcs:ti,ab OR ((transcranial NEAR/2 stimulat*):ti,ab)

KQ	Set #	Description	EMBASE Search String
KQ 6 (cont.)	#25	Telehealth	('e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'telepsychiatry'/de OR 'telepsychology'/de OR 'telepsychotherapy'/de OR 'telerehabilitation'/de OR 'teletherapy'/de OR 'text messaging'/de OR 'video consultation'/de OR 'videoconferencing'/de) AND 'web-based intervention'/de OR 'wireless communication'/de OR 'virtual reality'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR psychiatr* OR psycholog* OR psychotherap* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telepsych*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR 'virtual reality':ti OR web:ti OR website*:ti OR zoom:ti
	#26	Combine interventions	#9 OR #10 #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
	#27	Combine population and interventions	#4 AND #26
	#28	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#29	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))

KQ	Set #	Description	EMBASE Search String
KQ 6 (cont.)	#30	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#31	Combine exclusions	#28 OR #29 OR #29
	#32	Remove exclusions	#27 NOT #31
	#33	English language	#32 AND [english]/lim
	#34	Publication year	#33 AND [2018-2023]/py
	#35	Entry date	#34 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#36	Systematic reviews and meta-analyses	#35 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#37	Randomized controlled trials	#35 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#38	Final set	#36 OR #37
KQ 7	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3
	#5	Dysphagia	'aspiration pneumonia'/de OR 'dysphagia'/exp OR 'malnutrition'/de OR (aphagopraxia OR 'aspiration pneumonia' OR ((deglutition OR swallow*) NEAR/2 (difficult* OR disorder*)) OR dysphag* OR malnourish* OR malnutrition OR odynophagia OR undernourish* OR undernutrition OR under-nutrition):ti,ab
	#6	Population	#4 AND #5
	#7	Interventions: General rehabilitation	'stroke rehabilitation'/de OR 'rehabilitation'/de OR 'rehabilitation care'/de OR 'rehabilitation':lnk OR rehab*:ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 7 (cont.)	#8	Device, stimulation	'biofeedback'/exp OR 'biofeedback software' OR 'biofeedback therapy'/de OR 'biofeedback training'/de OR 'direct current stimulation'/de OR 'electrostimulation'/de OR 'electrostimulator'/de OR 'electrotherapy'/de OR 'functional electrical stimulation'/de OR 'pharyngeal electrical stimulation'/de OR 'surface electromyography'/de OR 'transcranial direct current stimulation'/de OR 'transcranial direct current stimulator'/de OR 'transcranial electrical stimulation'/exp OR 'transcranial electrical stimulator'/de OR 'transcranial magnetic stimulation'/exp/mj OR 'transcutaneous electrical nerve stimulation'/de OR 'vagus nerve stimulation'/de OR 'vagus nerve stimulator'/de
	#9		biofeedback*:ti,ab OR estim*:ti,ab OR 'e stim*':ti,ab OR electrostim*:ti,ab OR electrotherap*:ti,ab OR 'electro therap*':ti,ab OR 'functional electr* stimulat*':ti,ab OR 'functional electrostimulat*':ti,ab OR ((surface NEAR/2 (emg OR electromyograph*)):ti,ab) OR dpns:ti,ab OR fes:ti,ab OR nmes:ti,ab OR rtms:ti,ab OR semg:ti,ab OR tdcs:ti,ab
	#10		(anodal:ti,ab OR cathode:ti,ab OR 'direct current':ti,ab OR electr*:ti,ab OR 'functional electr*':ti,ab OR pharyngeal*:ti,ab OR transcranial*:ti,ab OR vagal:ti,ab OR vagus:ti,ab) AND stim*:ti,ab
	#11	Exercises for swallowing	('dysphagia'/exp OR 'swallowing'/exp/mj) AND 'rehabilitation':lnk OR 'swallowing therapy'/de OR 'chin tuck' OR 'effortful swallow*' OR 'expiratory muscle strength training' OR headlift OR 'head lift' OR headturn* OR 'head turn*' OR 'lingual strengthen*' OR respir* OR 'submental emg' OR 'swallow strong' OR swallowstrong* OR (((dysphagia OR masako OR mendelsohn OR shaker OR swallow*) NEAR/2 (aid* OR device* OR exercise* OR instrument* OR intervention* OR maneuver* OR therap*)):ti,ab)
	#12	Nutrition	'diet supplementation'/de OR 'enteric feeding'/de OR 'nutritional support'/de OR 'parenteral nutrition'/exp/mj OR (((diet* OR food* OR fluid* OR hydrat* OR nutrition*) NEAR/2 (adjust* OR modif* OR supplement*)):ti,ab) OR (((enteral OR enteric OR intragastric* OR intraintestinal OR nasogastric OR 'naso gastric' OR nasojejunal OR nose OR sip OR tube) NEAR/2 (diet* OR feed* OR nutrition*)):ti,ab) OR ((diet*:ti,ab OR food*:ti,ab OR liquid*:ti,ab OR solid*:ti,ab) AND ('bite size*':ti,ab OR dice:ti,ab OR diced:ti,ab OR dicing:ti,ab OR mince*:ti,ab OR moist*:ti,ab OR puree:ti,ab OR soft:ti,ab OR texture*:ti,ab OR thick*:ti,ab)) OR ((texture NEAR/2 modif*):ti,ab) OR ((dysphagia NEAR/2 diet*):ti,ab) OR 'iddsi':ti,ab OR 'ascorbic acid':ti,ab OR diet*:ti,ab OR mineral*:ti,ab OR nutrition*:ti,ab OR supplement*:ti,ab OR vitamin*:ti,ab
	#13	Oral hygiene	'mouth hygiene'/de OR 'oral health care'/de OR ((dental:ti,ab OR mouth:ti,ab OR oral:ti,ab) AND (care:ti,ab OR health*:ti,ab OR hygien*:ti,ab)) OR jaw*:ti,ab OR pharynx:ti,ab OR throat*:ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 7 (cont.)	#14	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'teletherapy'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
	#15	Combine interventions	#7 OR #8 OR #9 OR #10 OR #11 #12 OR #13 OR #14
	#16	Combine population and interventions	#6 AND #15
	#17	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#18	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#19	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)

KQ	Set #	Description	EMBASE Search String
KQ 7 (cont.)	#20	Exclusions	#17 OR #18 OR #19
	#21	Remove exclusions	#16 NOT #20
	#22	English language	#21 AND [english]/lim
	#23	Publication year	#22 AND [2018-2023]/py
	#24	Entry date	#23 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#25	Systematic reviews and meta-analyses	#24 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#26	Randomized controlled trials	#24 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#27	Final set	#25 OR #26
KQ 8	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3
	#5	Interventions: Caregiver education	'caregiver support'/de OR (caregiver* AND (educat* OR empower* OR support*)):ti,ab
	#6	Case management	'Case management'/de OR 'case manager'/de OR ((care OR case) NEAR/5 (coordinat* OR manage* OR navigator*)):ti,ab) OR 'coordinated care':ti,ab OR 'co ordinated care':ti,ab OR 'stroke coordinator*':ti,ab
	#7	Health care delivery	('health care delivery'/exp/mj OR (healthcare*:ti AND (deliver*:ti OR mode*:ti OR setting*:ti))) AND ('stroke rehabilitation'/de OR (stroke*:ti AND rehabilitation:lnk))
	#8		'healthcare delivery'/exp OR 'patient care planning'/de OR 'treatment planning'/de OR (((medical* OR patient*) NEAR/3 care*) OR ('health care' OR healthcare OR rehab* OR service* OR therap* OR treat*)):ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 8 (cont.)	#9	Health care personnel	'caregiver'/de OR 'health care personnel'/exp OR (aide* OR 'behavior* health team' OR 'behaviour* health team*' OR caregiver* OR 'care giver*' OR 'care manager*' OR 'case manager*' OR clinician* OR counselor* OR doctor* OR 'health coach' OR neurologist* OR nurse* OR physician* OR practitioner* OR 'primary care' OR professional* OR provider* OR 'rehab* counselor' OR (therapist* NEAR/2 (occupational OR physical OR speech)) OR 'social work*' OR (stroke NEAR/2 team*) OR worker*):ti,ab)
	#10	Collaborative care	'collaborative care team'/de OR 'interprofessional collaboration'/de OR 'integrated health care system'/de OR 'multidisciplinary team'/de OR 'patient care team'/de OR 'teamwork'/de OR ('care team' OR collaborat* OR 'collaborative care' OR integrat* OR interdisciplin* OR 'inter disciplin*' OR interprofessional* OR multidisciplin* OR 'multi disciplin*' OR multiprofession* OR 'multi profession*' OR team OR teams OR teaming OR teamwork OR 'team work' OR 'team based'):ti,ab
	#11	Combine healthcare delivery or personnel and collaborative care	(#7 OR #8 OR #9) AND #10
	#12	Combine interventions	#5 OR #6 OR #11
	#13	Combine population and interventions	#4 AND #12
	#14	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#15	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#16	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#17	Exclusions	#14 OR #15 OR #16
	#18	Remove exclusions	#13 NOT #17
	#19	English language	#18 AND [english]/lim
	#20	Publication year	#19 AND [2018-2023]/py

KQ	Set #	Description	EMBASE Search String
KQ 8 (cont.)	#21	Entry date	#20 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#22	Systematic reviews and meta-analyses	#21 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#23	Randomized controlled trials	#21 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#24	Final set	#22 OR #23
KQ 9	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3
	#5	Population subgroup spasticity	'spasticity'/de OR reflex OR spastic OR spasticism OR spascticity OR torque
	#6	Population	#4 AND #5
	#7	Interventions: Acupuncture	'acupuncture'/exp OR 'dry needling'/de OR acupuncture OR 'acu puncture' OR acupressure OR 'acu pressure' OR 'dry needl*'
	#8	Device	'shock wave therapy'/de OR 'whole body vibration'/de OR 'extracorporeal shockwave*' OR 'extracorporeal shock wave*' OR ESWT OR rESWT OR ECSW OR (shockwave* OR 'shock wave*'):ti,ab OR (('whole body' OR wholebody) AND vibrat*):ti,ab
	#9	Intrathecal, spinal stimulation	'intrathecal drug administration'/de OR 'intrathecal pump'/exp OR 'spinal cord stimulation'/de OR (('electrostimulation'/de OR 'electrostimulator'/de OR 'nerve stimulation'/exp OR electrostim*:ti,ab) AND (intrathecal:ti,ab OR 'intra thecal':ti,ab OR spinal:ti,ab OR spine:ti,ab OR subarachnoid:ti,ab)) OR (((intrathecal OR 'intra thecal' OR spinal OR spine OR subarachnoid) NEAR/3 (baclofen OR drug OR inject* OR pump OR stimulat*)):ti,ab)
	#10	Neurosurgical	'dorsal rhizotomy'/de OR 'neurosurgery'/exp/mj OR 'vagus nerve stimulation'/de OR (('ablation therapy'/exp/mj OR 'surgery'/exp/mj OR ablat*:ti OR surg:ti) AND ('peripheral nervous system'/exp/mj OR nerve*:ti)) OR 'dorsal root':ti,ab OR ((dorsal OR posterior) NEAR/2 rhizotom*):ti,ab OR (ablat* AND (nerve* OR neuro*)):ti,ab OR neuroablat*:ti,ab OR (neurosurg* AND nerve*):ti,ab OR ((electric* OR vagal OR vagus OR nerve*) NEAR/3 stim*):ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 9 (cont.)	#11	Orthopedic	'orthopedic surgery'/exp OR 'tendon lengthening'/de OR 'tendon transfer'/de OR (orthoped* NEAR/2 (procedure* OR surg*)) OR ((achilles OR tendon*) NEAR/3 (lengthen* OR transfer))
	#12	Pharmacotherapy	'drug therapy'/mj OR (Drug* OR medication* OR pharma* OR prescribe* OR prescription*):ti
	#13		'benzodiazepines'/exp OR 'botulinum toxin'/de OR 'cannabinoid'/exp OR 'cyproheptadine'/de OR 'gabapentinoid'/de OR 'muscle relaxant agent'/exp OR 'nerve block'/exp OR abobotulinumtoxinA:ti,ab OR 'abobotulinumtoxin A':ti,ab OR Alprazolam:ti,ab OR Baclofen:ti,ab OR benzodiazepine*:ti,ab OR cannabinoid*:ti,ab OR cannabinol:ti,ab OR cannabis:ti,ab OR CBD:ti,ab OR carisoprodol:ti,ab OR clonidine:ti,ab OR clonazepam:ti,ab OR cyclobenzaprine:ti,ab OR cyproheptadine:ti,ab OR dantrolene:ti,ab OR diazepam:ti,ab OR gabapentin:ti,ab OR gabapentinoid*:ti,ab OR incobotulinumtoxinA:ti,ab OR 'incobotulinumtoxin A':ti,ab OR lorazepam:ti,ab OR methocarbamol:ti,ab OR 'motor point block*' OR 'muscle relax*':ti,ab OR 'nerve block*':ti,ab OR onabotulinumtoxinA:ti,ab OR 'onabotulinumtoxin A':ti,ab OR oxazepam:ti,ab OR Prabotulinumtoxina:ti,ab OR 'Prabotulinumtoxin a':ti,ab OR pregabalin:ti,ab OR rimabotulinumtoxinb:ti,ab OR 'rimabotulinumtoxin b':ti,ab OR temazepam:ti,ab OR tizanidine:ti,ab OR triazolam:ti,ab OR ((autonomic OR conduction) NEAR/2 block*):ti,ab OR ((botulinium OR botulinus OR botulism) AND toxin*):ti,ab
	#14	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'teletherapy'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti

KQ	Set #	Description	EMBASE Search String
KQ 9 (cont.)	#15	Combine interventions	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
	#16	Combine population and interventions	#6 AND #15
	#17	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#18	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#19	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#20	Exclusions	#17 OR #18 OR #19
	#21	Remove exclusions	#16 NOT #20
	#22	English language	#21 AND [english]/lim
	#23	Publication year	#22 AND [2018-2023]/py
	#24	Entry date	#23 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#25	Systematic reviews and meta-analyses	#24 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#26	Randomized controlled trials	#24 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#27	Final set	#25 OR #26
KQ 10	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab

KQ	Set #	Description	EMBASE Search String
KQ 10 (cont.)	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4		#1 OR #2 OR #3
	#5	Population subgroup caregiver	'caregiver'/de OR 'caregiver support'/de OR 'caregiver burden'/de OR 'family'/exp OR caregiver*:ti,ab OR 'care giver*':ti,ab OR carepartner*:ti,ab OR 'care partner*':ti,ab OR carer*:ti,ab OR family:ti,ab OR partner*:ti,ab OR spous*:ti,ab
	#6	Population	#4 AND #5
	#7	Interventions: Education and skills training	'health education'/exp OR 'health program'/exp OR 'patient education'/de OR 'self care'/exp OR 'skill'/de OR 'skills training'/de OR 'care need*':ti,ab OR 'health education':ti,ab OR psychoeducation:ti,ab OR 'pscyho education':ti,ab OR selfcare:ti,ab OR 'self care':ti,ab OR 'self efficacy':ti,ab OR 'self help':ti,ab OR 'self manag*':ti,ab OR ((skill* NEAR/2 train*):ti,ab) OR educat*:ti OR teach*:ti OR train*:ti
	#8	Nurses/peer support	'respite care'/de OR 'support group'/exp OR ((care OR case OR nurse) AND (navigat* OR manag*)) OR (((peer OR peers) NEAR/2 (based OR befriend* OR coach* OR group* OR leader* OR mentor* OR support*)):ti,ab) OR ((respite NEAR/2 (care OR program* OR service*)):ti,ab) OR 'support group*':ti,ab
	#9	Psychotherapy	'cognitive behavioral therapy'/de OR 'emotional support'/de OR 'psychological care'/exp OR 'psychosocial care'/de OR 'psychotherapy'/exp OR ((behavior*:ti,ab OR behaviour*:ti,ab) AND (intervention*:ti,ab OR therap*:ti,ab OR treatment*:ti,ab)) OR cope:ti,ab OR coping:ti,ab OR psychoeducation*:ti,ab OR psychologic*:ti,ab OR 'psycho social':ti,ab OR psychosocial:ti,ab OR 'pscyho therap*':ti,ab OR psychotherap*:ti,ab OR 'psycho socio* emotion*':ti,ab OR 'psychosocio* emotion*':ti,ab
	#10	Resources/community	'community care'/exp OR 'community mental health center'/mj OR 'social support'/exp/mj OR 'social work'/mj OR ((community NEXT/3 ('mental health' OR partner* OR program* OR resource* OR service* OR support*)):ti) OR 'community based':ti,ab OR ((social NEXT/1 (service* OR support* OR work*)):ti)

KQ	Set #	Description	EMBASE Search String
KQ 10 (cont.)	#11	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'telepsychiatry'/de OR 'telepsychology'/de OR 'telepsychotherapy'/de OR 'teletherapy'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR psychiatr* OR psycholog* OR psychotherap* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telepsych*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
	#12	Combine Interventions	#7 OR #8 OR #9 OR #10 OR #11
	#13	Combine population and interventions	#6 AND #12
	#14	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#15	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))

KQ	Set #	Description	EMBASE Search String
KQ 10 (cont.)	#16	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#17	Exclusions	#14 OR #15 OR #16
	#18	Remove exclusions	#13 NOT #17
	#19	English language	#18 AND [english]/lim
	#20	Publication year	#19 AND [2018-2023]/py
	#21	Entry date	#20 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#22	Systematic reviews and meta-analyses	#21 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#23	Randomized controlled trials	#21 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#24	Final set	#22 OR #23
KQ 11	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4	Population	#1 OR #2 OR #3
	#5	Interventions: Cognitive/behavior	'attention training'/de OR 'mental imagery'/de OR ((attention OR cognitive) AND (train* OR therap* OR rehab* OR)):ti OR ((behavior OR behaviour) AND (cue OR cues OR cuing OR prompt* OR redirect OR 're direct' OR signal)):ti OR 'mental imagery':ti
	#6	Device-related, including computer interface	'brain computer interface'/exp OR 'functional electrical stimulation'/de OR 'prism'/de OR 'rehabilitation robot'/de OR 'rhythmic auditory stimulation'/de OR 'robotics'/de OR 'sensorimotor integration'/de OR 'transcranial direct current stimulation'/de OR 'transcranial direct current stimulator'/de OR 'transcranial magnetic stimulation'/exp OR 'virtual reality'/de

KQ	Set #	Description	EMBASE Search String
KQ 11 (cont.)	#7		(auditory:ti OR 'direct current':ti OR 'functional electr*':ti OR peripheral:ti OR transcranial:ti) AND stim*:ti OR 'brain machine interface':ti OR 'brain computer interface':ti OR 'electr* muscle stimulat*':ti OR estim:ti OR 'e stim':ti OR electrostim*:ti OR exoskeleton:ti OR 'functional electr* stimulat*':ti OR 'functional electrostimulat*':ti OR 'paired associative':ti OR prism:ti OR prisms:ti OR robot*:ti OR sensorimotor:ti OR 'virtual reality':ti OR fes:ti OR nmes:ti OR rtms:ti OR tdcs:ti OR tens:ti
	#8	Environment enrichment	'environmental enrichment'/de OR 'mirror imagery' OR 'music therapy'/exp OR ((enrich* NEXT/2 environment*):ti) OR ((cognit*:ti OR physical:ti OR social:ti) AND (activities:ti OR activity:ti OR engagement:ti)) OR (((mirror OR music) NEAR/2 therap*):ti)
	#9	Physical/motor	'action observation therapy'/de OR 'action observation training'/de OR 'compression therapy'/exp/mj OR 'massage'/mj OR 'perturbation'/de OR 'touch therapy'/de OR 'action observation':ti,ab OR 'joint position':ti,ab OR perturbation:ti,ab OR (((compression OR massage* OR pressure OR sense OR sensory OR touch OR vibrat*) NEAR/2 therap*):ti,ab) OR 'music* stimulat*':ti,ab OR 'pulse* rhythm*':ti,ab OR 'rhythmic auditory stimulat*':ti,ab OR (((sens* OR somatosens*) NEAR/2 (organization OR therap*)):ti,ab)
	#10	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'teletherapy'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
	#11	Vision	(('eye movement disorder'/exp/mj OR 'perception disorder'/exp OR 'vision'/exp/mj) AND 'rehabilitation'/exp/mj OR 'vision therapy'/de) OR ((eye:ti OR eyes:ti OR oculomotor:ti OR optic*:ti OR perception:ti OR vision:ti OR visual:ti) AND (rehab*:ti OR retrain*:ti OR 're train*':ti OR therap*:ti OR train*:ti))

KQ	Set #	Description	EMBASE Search String
KQ 11 (cont.)	#12	Combine interventions	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
	#13	Combine population and interventions	#4 AND #12
	#14	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))
	#15	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#16	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#17	Exclusions	#14 OR #15 OR #16
	#18	Remove exclusions	#13 NOT #17
	#19	English language	#18 AND [english]/lim
	#20	Publication year	#19 AND [2018-2023]/py
	#21	Entry date	#20 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#22	Systematic reviews and meta-analyses	#21 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#23	Randomized controlled trials	#21 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#24	Final set	#22 OR #23

KQ	Set #	Description	EMBASE Search String
KQ 12	#1	Stroke	'cerebrovascular accident'/exp OR 'stroke patient'/de OR 'post stroke':ti,ab OR poststroke:ti,ab OR stroke*:ti,ab
	#2		((ischaemi* OR ischemi*) NEAR/3 attack*):ti,ab
	#3		((brain OR cerebral OR 'cerebro vasc*' OR cerebrovasc*) NEAR/3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)):ti,ab
	#4	Population	#1 OR #2 OR #3
	#5	Neglect	'asomatognosia'/exp OR 'perception disorder'/de OR 'unilateral spatial neglect'/de OR 'spatial orientation'/de OR (percept*:ti,ab AND (defect*:ti,ab OR disorder*:ti,ab OR distortion*:ti,ab OR disturbance*:ti,ab)) OR ((hemispatial*:ti,ab OR spatial*:ti,ab) AND (aware*:ti,ab OR inattention:ti,ab OR perception:ti,ab OR recogn*:ti,ab)) OR neglect:ti,ab
	#6	Population subgroup	#4 AND #5
	#7	Interventions: Acupuncture	'acupuncture'/exp OR acupressure:ti,ab OR 'acu pressure':ti,ab OR acupuncture:ti,ab OR 'acu puncture':ti,ab
	#8	Behavioral cuing/prompting	(behavior*:ti,ab OR behaviour*:ti,ab OR verbal:ti,ab OR vision:ti,ab OR visual:ti,ab) AND (cue:ti,ab OR cues:ti,ab OR cuing:ti,ab OR prompt*:ti,ab OR redirect:ti,ab OR 're direct':ti,ab OR signal:ti,ab)
	#9	Device	'augmented reality'/de OR 'computer-based cognitive training' OR 'prism'/de OR 'prism adaptation'/de OR 'robotics'/exp OR 'virtual reality'/de OR ((('computer based' OR 'computer simulat*') NEAR/3 'cognitive rehab*'):ti,ab) OR 'augmented reality':ti,ab OR prism:ti,ab OR prisms:ti,ab OR robotic*:ti,ab OR 'virtual reality':ti,ab
	#10	Non-invasive brain stimulation	'transcranial direct current stimulation'/de OR 'transcranial direct current stimulator'/de OR 'transcranial magnetic stimulation'/exp OR ((('continuous theta burst' OR 'galvanic vestibular') NEAR/2 stimulat*):ti,ab) OR (((direct OR magnetic OR noninvasive OR 'non invasive' OR transcranial) NEAR/5 'brain stimulat*'):ti,ab) OR rtms:ti,ab OR tdcs:ti,ab
	#11	Pharmacotherapy	'guanfacine' OR intuniv
	#12	Physical interventions	'body position'/exp OR 'head movement'/exp OR 'body position':ti,ab OR 'digital practice':ti,ab OR ((head NEAR/2 (movement OR tilt*)):ti,ab) OR (neck:ti,ab AND (tape:ti,ab OR taping:ti,ab OR vibrat*:ti,ab))

KQ	Set #	Description	EMBASE Search String
KQ 12 (cont.)	#13	Telehealth	'e therapy'/de OR 'internet'/de OR 'mobile application'/exp OR 'mobile phone'/exp OR 'podcast'/de OR 'self care'/exp OR 'self-care software'/exp OR 'short message service'/de OR 'social media'/de OR 'tablet computer'/de OR 'teleconsultation'/exp OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/de OR 'teletherapy'/de OR 'telerehabilitation'/de OR 'text messaging'/de OR 'web-based intervention'/de OR 'wireless communication'/de OR 'video consultation'/de OR 'videoconferencing'/de OR (((distance OR mobile OR remote OR tele OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR automat*:ti OR chat*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR 'face tim*':ti OR facetim*:ti OR instagram*:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR podcast*:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR 'store and forward':ti OR synchronous*:ti OR teams:ti OR technolog*:ti OR tele:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telerehab* OR teletherapy:ti OR televisit*:ti OR texting*:ti OR 'tik tok*':ti OR tiktok* OR tweet*:ti OR twitter*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
	#14	Visual	'depth perception'/exp OR 'eye patching'/de OR 'vision'/exp OR 'depth perception':ti,ab OR 'eye patch*':ti,ab OR 'optokinetic stimulation':ti,ab OR 'spatial exploration strategy':ti,ab OR 'visual perception':ti,ab OR 'visual search training':ti,ab OR (((visuospatial* OR 'visual spatial*') NEAR/2 (therap* OR train*)):ti,ab) OR (((vision OR visual) NEAR/5 (rehab* OR therap*)):ti,ab)
	#15	Combine interventions	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
	#16	Combine population and interventions	#6 AND #15
	#17	Animals	[animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))

KQ	Set #	Description	EMBASE Search String
KQ 12 (cont.)	#18	Undesired publications	'book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR (book:pt NOT series:pt) OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti))
	#19	Children and adolescents	(adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti)
	#20	Exclusions	#17 OR #18 OR #19
	#21	Remove exclusions	#16 NOT #20
	#22	English language	#21 AND [english]/lim
	#23	Publication year	#22 AND [2018-2023]/py
	#24	Entry date	#23 AND ([01-07-2018]/sd NOT [03-05-2023]/sd)
	#25	Systematic reviews and meta-analyses	#24 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab*" OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science")) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR "review protocol" OR "scoping review"):ti)
	#26	Randomized controlled trials	#24 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	#27	Final set	#25 OR #26

Table I-2: Pubmed Syntax (All Key Questions)

Set #	Description	PubMed Search String
#1	Stroke	stroke[ti] OR poststroke[ti] OR “post stroke”[ti]
#2		"ischaemic attack"[Title:~2] OR "ischemic attack"[Title:~2] OR "ischaemic attacks"[Title:~2] OR "ischemic attacks"[Title:~2]
#3		((brain[ti] OR cerebral[ti] OR "cerebro vasc*"[ti] OR cerebrovasc*[ti] OR intracerebral[ti] OR intra-cerebral[ti] OR intracranial[ti] OR intra-cranial[ti] OR subarachnoid[ti] OR sub-arachnoid[ti]) AND (accident*[ti] OR arrest[ti] OR attack*[ti] OR disease*[ti] OR haemorrhage*[ti] OR hemorrhage*[ti] OR infarct*[ti] OR insufficiency[ti] OR insult*[ti] OR ischaemi*[ti] OR ischemi*[ti] OR lesion*[ti] OR vasculopathy[ti]))
#4	Population	#1 OR #2 OR #3
#5	Animals	((animal[ti] OR animals[ti] OR canine*[ti] OR dog[ti] OR dogs[ti] OR feline[ti] OR hamster*[ti] OR lamb[ti] OR lambs[ti] OR mice[ti] OR monkey[ti] OR monkeys[ti] OR mouse[ti] OR murine[ti] OR pig[ti] OR piglet*[ti] OR pigs[ti] OR porcine[ti] OR primate*[ti] OR rabbit*[ti] OR rat[ti] OR rats[ti] OR rodent*[ti] OR sheep*[ti] OR swine[ti] OR veterinar*[ti] OR (vitro[ti] NOT vivo[ti])) NOT (human*[ti] OR patient*[ti]))
#6	Undesired publications	(booksdocs[Filter] OR "case report"[ti] OR comment*[ti] OR editorial[ti] OR letter[ti] OR news[ti] OR ((protocol[ti] AND (study[ti] OR trial[ti])) NOT ("therapy protocol*"[ti] OR "treatment protocol*"[ti])))
#7	Children and adolescents	((adolescen*[ti] OR babies[ti] OR baby[ti] OR boy[ti] OR boys[ti] OR child*[ti] OR girl*[ti] OR infancy[ti] OR infant*[ti] OR juvenile*[ti] OR neonat*[ti] OR newborn*[ti] OR nurser*[ti] OR paediatric*[ti] OR pediatric*[ti] OR preschool*[ti] OR "school age*"[ti] OR schoolchildren*[ti] OR teen*[ti] OR toddler*[ti] OR youth*[ti]) NOT (adult*[tiab] OR father*[ti] OR matern*[tiab] OR men[tiab] OR mother*[ti] OR parent*[ti] OR patern*[tiab] OR women[tiab]))
#8	Exclusions	#5 OR #6 OR #7
#9	Remove exclusions	#4 NOT #8
#10	English language	english[la]
#11	Publication year	2021:2023[pdat]
#12	Entry date	"2021/01/01"[Date - Create] : "2023/05/02"[Date - Create]
#13	Unprocessed	(Inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
#14	Combine Inclusions	#9 AND #10 AND #11 AND #12 AND #13
#15	Systematic reviews and meta-analyses	#14 AND (("cochrane database syst rev"[ta] OR systematic*[ti] OR cochrane*[tiab] OR "meta analy*"[tiab] OR metaanaly*[tiab] OR (search*[tiab] AND (cinahl*[tiab] OR databases[tiab] OR ebsco*[tiab] OR embase*[tiab] OR psychinfo*[tiab] OR psycinfo*[tiab] OR "science direct*"[tiab] OR sciencedirect*[tiab] OR scopus*[tiab] OR systematic*[tiab] OR "web of knowledge*"[tiab] OR "web of science*"[tiab])) OR (systematic*[tiab] AND review*[tiab])) NOT ((protocol[ti] AND review[ti]) OR "review protocol"[ti] OR "scoping review"[ti]))
#16	Randomized controlled trials	#14 AND ("phase 3"[tw] OR "phase iii"[tw] OR random*[tw] OR RCT[tw])
#17	Final set	#15 OR #16

Table I-3. PsycInfo in Ovid Syntax (All Key Questions)

Set #	Description	PsycInfo Search String
#1	Adults with stroke	cerebrovascular accidents/ or (stroke or poststroke or post-stroke).tw.
#2		((ischaemi* OR ischemi*) adj3 attack*).ti,ab.
#3		((brain OR cerebral OR cerebro-vasc* OR cerebrovasc* OR intracerebral OR intra-cerebral OR intracranial OR intra-cranial OR subarachnoid OR sub-arachnoid) adj3 (accident* OR arrest OR attack* OR disease* OR haemorrhage* OR hemorrhage* OR infarct* OR insufficiency OR insult* OR ischaemi* OR ischemi* OR lesion* OR vasculopathy)).ti,ab.
#4		1 OR 2 OR 3
#5	Undesired publications	(chapter or "column/opinion" or "comment/reply" or dissertation or editorial or letter or review-book).dt. or (book or encyclopedia or "dissertation abstract").pt. or ("case report" or comment* or editorial or letter or news).ti. or ((protocol and (study or trial)) not ("therapy protocol*" or "treatment protocol*")).ti.
#6	Children and adolescents	(adolescen* or babies or baby or boy* or child* or girl* or infancy or infant* or juvenile* or neonat* or newborn* or nurser* or paediatric* or pediatric* or preschool* or "school age*" or schoolchildren* or teen* or toddler* or youth*).ti. not (adult*.ti,ab. or father*.ti. or matern*.ti,ab. or men.ti,ab. or mother*.ti. or parent*.ti. or patern*.ti,ab. or women.ti,ab.)
#7	Medline records	(1* or 2* or 3* or 4* or 5* or 6* or 7* or 8* or 9*).pm.
#8	Exclusions	5 OR 6 OR 7
#9	Remove exclusions	4 NOT 8
#10	English language	limit 9 to english language
#11	Publication year	Limit 10 to yr="2018 - 2023"
#12	Entry date	Limit 11 to up=20180701-20230502
#13	Systematic reviews and meta-analyses	12 AND ((meta analysis or systematic review).md. or meta analysis/ or systematic review/ or systematic.ti. or (cochrane* or meta analy* or metaanaly* or (search* and (cinahl* or databases or ebsco* or embase* or psychinfo* or psycinfo* or science direct* or sciencedirect* or scopus* or systematic* or "web of knowledge*" or "web of science*")) or (review* adj3 systematic*) or (systematic* adj3 review*)).ti,ab.) not ((protocol adj3 review) or review protocol or scoping review).ti.
#14	Randomized controlled trials	12 AND (exp randomized controlled trials/ or random sampling/ or (phase 3 or phase iii or random* or RCT).ti,ab.)
#15	Final set	13 OR 14

Appendix J: Alternative Text Descriptions of Algorithm

The following outline narratively describes the Management of Stroke Rehabilitation Algorithm. An explanation of the purpose of the algorithm and description of the various shapes used within the algorithm can be found in the Algorithm section. The sidebars referenced within this outline can also be found in the Algorithm section.

Module A: Rehabilitation Disposition of the Inpatient with Stroke

1. Module A begins with Box 1, in the shape of a rounded rectangle: "Hospitalized patient has been identified as having a stroke (see **Sidebar 1**)"
2. Box 1 connects to Box 2, in the shape of a rectangle: "Assess the patient, including screening for preventable adverse events by appropriate staff, PM&R, and neurology, and educate patient and family on stroke (see **Sidebars 2, 3, 5a, and 5b**)"
3. Box 2 connects to Box 3, in the shape of a hexagon, and asks the question, "Does the patient have depression?"
    a. If the answer is "Yes" to Box 3, then Box 4, in the shape of a rectangle: "Continue or initiate mental health treatment, including psychotherapy, medication, or both (e.g., SSRI, SNRI)"
    b. If the answer is "No" to Box 3, then Box 5, in the shape of a hexagon, asks the question, "Does patient have functional impairments and need rehabilitation interventions?"
        i. If the answer is "Yes" to Box 5, then Box 6, in the shape of a hexagon, asks the question, "Is the patient appropriate for discharge home?"
            a. If the answer is "Yes" to Box 6, then Box 9, in the shape of an oval: "**Go to Module B**: Outpatient/Community-Based Rehabilitation"
            b. If the answer is "No" to Box 6, then Box 8, in the shape of a rectangle: "Using shared decision-making with patient and family, determine appropriate setting for rehabilitation in collaboration with case management and PM&R:
                - Continued hospitalization
                - Acute inpatient rehabilitation
                - Subacute inpatient rehabilitation
                - Skilled nursing facility
                - Long-term acute care facility"

ii. If the answer is “No” to Box 5, then Box 7, in the shape of a rectangle: “Discharge patient from rehabilitation and arrange for primary care, neurology, and specialty care follow-up, as needed”

4. Box 7 connects to Box 10, in the shape of a hexagon, and asks the question, “Are functional impairments identified after discharge?”
    a. If the answer is “Yes” to Box 10, then Box 9, in the shape of an oval: “Go to **Module B**: Outpatient/Community-based Rehabilitation”
    b. If the answer is “No” to Box 10, then Box 11, in the shape of a rectangle: “Continue primary care management (see **Sidebar 1**)”

Module B: Outpatient/Community-based Rehabilitation

1. Algorithm B begins with Box 12, in the shape of a rounded rectangle: “Outpatient presents with impairments after stroke”
2. Box 12 connects to Box 13, in the shape of a hexagon, and asks the question, “Does the patient have depression?”
    a. If the answer is “Yes” to Box 13, then Box 14, in the shape of a rectangle: “Continue or initiate mental health treatment, including psychotherapy, medication, or both (e.g., SSRI, SNRI)”
        i. Box 14 connects to Box 15, in the shape of a hexagon, and asks the question, “Is an interdisciplinary stroke rehabilitation team available?”
            1. If the answer is “Yes” to Box 15, then Box 16, in the shape of a rectangle: “Refer to interdisciplinary stroke rehabilitation team”
                a. Box 16 connects to Box 26, in the shape of an oval: “Discharge patient from rehab and arrange for primary care, neurology, and specialty care follow-up, as needed”
            2. If the answer is “No” to Box 15, then Box 17, in the shape of a rectangle: “Consult PM&R”
    b. If the answer is “No” to Box 13, then Box 15, in the shape of a hexagon, asks the question, “Is an interdisciplinary stroke rehabilitation team available?”
        i. If the answer is “Yes” to Box 15, then Box 16, in the shape of a rectangle: “Refer to interdisciplinary stroke rehabilitation team”
            1. Box 16 connects to Box 26, in the shape of an oval: “Discharge patient from rehabilitation and arrange for primary care follow-up, as needed”

ii. If the answer is “No” to Box 15, then Box 17, in the shape of a rectangle: “Consult PM&R”

3. Box 17 connects to Box 18, in the shape of a rectangle: “Assess the patient (see **Sidebar 2**) and identify patient’s rehabilitation goals (see **Appendix B**)”
4. Box 18 connects to Box 19, in the shape of a rectangle: “Consider optimal environment for outpatient/community-based rehabilitation services (see **Sidebar 4**)”
5. Box 19 connects to Box 20, in the shape of a rectangle:
    - “Educate patient and family on stroke (see **Sidebar 3**)
    - Reach shared decision regarding rehabilitation program and treatment plan
    - Continue secondary prevention (see **Sidebar 1**)”
6. Box 20 connects to Box 21, in the shape of a rectangle: “Consult appropriate rehabilitation services (see **Sidebar 5a and 5b**)”
7. Box 21 connects to Box 22, in the shape of a hexagon, and asks the question, “Has the patient met rehabilitation treatment goals?”
    a. If the answer is “Yes” to Box 22, then Box 26, in the shape of a rectangle: “Discharge patient from rehabilitation and arrange for primary care, neurology, and specialty care follow-up, as needed”
    b. If the answer is “No” to Box 22, then Box 23, in the shape of a rectangle: “Initiate or continue rehabilitation intervention”
8. Box 23 connects to Box 24, in the shape of a hexagon, and asks the question, “Did patient meet rehabilitation treatment goals or reach plateau?”
    a. If the answer is “Yes” to Box 24, then Box 26, in the shape of a rectangle: “Discharge patient from rehabilitation and arrange for primary care, neurology, and specialty care follow-up, as needed”
    b. If the answer is “No” to Box 24, then Box 25, in the shape of a rectangle: “Continue treatment and reassess periodically”
9. Box 25 connects to Box 23, in the shape of a rectangle: “Initiate/continue rehabilitation intervention”

Appendix K: Abbreviations

Abbreviation	Definition
6MWT	6-minute walk test
ABC Scale	Activities-specific Balance Confidence Scale]
ACT	Acceptance and Commitment Therapy
AD	Antidepressant
ADL	activities of daily living
AHRQ	Agency for Healthcare Research and Quality
AMAT	Arm Motor Abilities Test
APT	Attention Process Training
ARAT	Action Research Arm Test
AROM	active range of motion
AT	aerobic training
BBS	Berg Balance Scale
BBT	Box and Blocks Test
BCI	brain-computer interface
BI	Barthel Index
BWSTT	body weight support treadmill training
CACR	Computer Assisted Cognitive Rehabilitation
CBS	Catherine Bergego Scale
CBT	cognitive behavioral therapy
CCFES	contralaterally controlled functional electrical stimulation
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CIH	complementary and integrative health
CIMT	constraint-induced movement therapy
COI	conflict of interest
COMPARE	Constraint-induced or Multi-modal Personalized Aphasia Rehabilitation
COT	conventional overground training
CPG	clinical practice guideline
CR	conventional rehabilitation
CSI	clinical spasticity index
CTAR	chin tuck against resistance
cTBS	continuous theta burst stimulation
CT-R	Constant Therapy-Research

Abbreviation	Definition
CV	Cardiovascular
DoD	Department of Defense
DOSS	Dysphagia Outcome and Severity Scale
EBPWG	Evidence-Based Practice Work Group
EEG	Electroencephalography
ELT	experimental linguistic treatment
EMG	Electromyography
EMG-NMES	electromyogram-triggered/controlled neuromuscular electrical stimulation
ESD	early supported discharge
ESWT	extracorporeal shockwave therapy
FAC-LE	Functional Ambulation Classification-Lower Extremity
FDS	functional dysphagia scale
FES	functional electrical stimulation
fESWT	focused extracorporeal shockwave therapy
FIM	Functional Independence Measure
FMA	Fugl-Meyer Assessment
FMA-LE	Fugl-Meyer Assessment-Lower Extremity
FMA-UE	Fugl-Meyer Assessment-Upper Extremity
FOIS	Functional Oral Intake Scale
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HADS	Hospital Anxiety and Depression Scale
HAM-D	Hamilton Depression Rating Scale
HEP	hemifield eye patching
HF-rTMS	high frequency repetitive transcranial magnetic stimulation
HIIT	high-intensity interval training
HRR	heart rate reserve
IADL	instrumental activities of daily living
ITT	intention-to-treat
KQs	key questions
KWDT	Kubota's water drinking test
LF-rTMS	low-frequency repetitive transcranial magnetic stimulation
MA	meta-analysis
MAL	Motor Activity Log
MAL-AOU	Motor Activity Log - Amount of Use Measure
MAL-QOM	Motor Activity Log - Quality of Movement Measure

Abbreviation	Definition
MAS	Modified Ashworth Scale
MASA	Mann Assessment of Swallowing Ability
MAT	moderate-intensity aerobic training
MBCT	mindfulness-based cognitive therapy
mBI	modified Barthel Index
MBSR	mindfulness-based stress reduction
MCID	minimal clinically important difference
mCIMT	modified constraint-induced movement therapy
MD	mean difference
MHS	Military Health System
MI	motivational interviewing
MMASA	modified Mann Assessment of Swallowing Ability
MMSE	Mini Mental Status Exam
MoCA	Montreal Cognitive Assessment
MOR	Multiple Oral Rereading
mRS	modified Rankin Scale
MTF	military treatment facility
NIBS	non-invasive form of brain stimulation
NMA	network meta-analysis
NMES	neuromuscular electrical stimulation
NNT	number needed to treat
NR	not reported
NSA	Nottingham Sensory Assessment
ODPHP	Office of Disease Prevention and Health Promotion
OKS	optokinetic stimulation
OR	odds ratio
ORLA	Oral Reading for Language in Aphasia
PA	prism adaptation
PACE	Promoting Aphasics' Communicative Effectiveness
PAS	Penetration Aspiration Scale
PASAT	Paced Auditory Serial Addition Test
PBA	Pseudobulbar affect
PES	pharyngeal electrical stimulation
PICOTS	population, intervention, comparison, outcome, timing, and setting
PIE	Plan Implement Evaluate Therapy

Abbreviation	Definition
PSSS	Perceived Social Support Scale
QoL	quality of life
RAS	rhythmic auditory cueing/stimulation
RAT	robot-assisted therapy
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
RBMT	Rivermead Behavioral Memory Test
RCT	randomized controlled trial
rESWT	radial extracorporeal shockwave therapy
RJOE	resistive jaw opening exercise
RPE	rating of perceived exertion
RT	rehabilitation robots
RT	resistance training
RTSS	Rehabilitation Treatment Specification System
RT+VR	rehabilitation robots and virtual reality
rTMS	repetitive transcranial magnetic stimulation
sEMG	surface electromyography
SF-36	36-item Short Form Health Survey
SMD	standardized mean difference
SNRI	serotonin-norepinephrine reuptake inhibitor
SR	systematic review
SSA	Standardized Swallowing Assessment
SSEQ	Stroke Self-Efficacy Questionnaire
SSRI	selective serotonin reuptake inhibitor
SUCRA	surface under the cumulative ranking curve
SWAL-QOL	Swallow Quality-of-Life Questionnaire
TBI	traumatic brain injury
TCA	tricyclic antidepressant
TCM	Traditional Chinese Medicine
tDCS	transcranial direct current stimulation
TENS	transcutaneous electrical nerve stimulation
TES	transcranial electrical stimulation
TT	treadmill training
U.S.	United States
USN	unilateral spatial neglect
USPSTF	United States Preventative Services Task Force

Abbreviation	Definition
VA	Department of Veterans Affairs
VERSE	The Very Early Rehabilitation for SpEech
VHA	Veterans Health Administration
VNS	vagus nerve stimulation
VR	virtual reality
WAB-AQ	Western Aphasia Battery-Aphasia Quotient
WBV	whole-body vibration
WMD	weighted mean difference
WMFT	Wolf Motor Function Test
WST	Water Swallow Test

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