



What Are The Risk Factors For Chronic Pain In Different Age Groups Of Stroke Survivors? : A Systematic Review

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Article History :

Received date : 2025/03/09

Revised date : 2025/04/24

Accepted date : 2025/05/15

Published date : 2025/06/17



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E-ISSN :

ISSN 3048-1368



P-ISSN

ISSN 3048-1376



ABSTRACT

Introduction: Stroke is a leading cause of long-term disability, with chronic pain being a significant and debilitating consequence that affects survivors' quality of life. The risk factors for developing chronic post-stroke pain appear to vary with age, creating challenges for clinical management. This systematic review aims to identify and categorize the age-specific risk factors for chronic pain in young, middle-aged, and elderly stroke survivors. **Methods:** A systematic search of PubMed, Semantic Scholar, Springer, and Google Scholar was conducted using PRISMA guidelines. Inclusion criteria focused on observational studies and systematic reviews assessing risk factors for chronic pain (persisting ≥ 3 months) in stroke survivors. Out of 1,309 records identified, 18 studies were included after screening and eligibility assessment. Data on study design, sample characteristics, pain assessment, and risk factors were extracted and synthesized. **Results:** For middle-aged survivors, risk factors included stroke severity, non-thalamic stroke location, sensory and motor impairments, neglect syndrome, female gender, and longer time since stroke. In elderly survivors, older age itself and thalamic stroke location were the primary predictors of persistent pain. No specific risk factors were reported for young adult stroke survivors. Younger patients showed better pain relief in response to neuromodulation therapies. **Discussion:** The evidence indicates that risk factors are age-dependent, though findings are most robust for the middle-aged population due to the composition of study samples. The lack of data for young adults represents a significant gap in the literature. The psychosocial impact of pain is severe across all ages, necessitating integrated care. **Conclusion:** Risk factors for post-stroke chronic pain differ significantly by age group. While a clear profile exists for middle-aged and elderly survivors, there is a critical lack of information for young adults. An age-aware, personalized approach to pain management is essential, and future research must focus on closing the knowledge gap for younger survivors.

Keywords: Stroke Survivors, Post-stroke Pain, Chronic Pain, Risk Factors, Age Groups, Age-Specific

INTRODUCTION

Stroke stands as a primary cause of long-term disability worldwide, leaving many survivors to navigate a complex recovery process. A significant and often debilitating consequence of stroke is the development of chronic pain, a condition that persists for three or more months post-incident. This persistent pain profoundly impacts survivors' quality of life, leading to emotional distress, including depression, and imposing considerable limitations on their ability to perform activities of daily living. The pervasive psychosocial burden of chronic post-stroke pain underscores the critical need for a deeper understanding of its underlying mechanisms and risk factors to improve therapeutic strategies and patient outcomes across all affected populations (Sarfo et al., 2019; Lindgren et al., 2018).

The challenge in managing chronic post-stroke pain is intensified by evidence suggesting that its risk factors are not uniform across all survivors. Instead, the characteristics that predispose a stroke survivor to developing chronic pain appear to differ significantly with age. This variability presents a considerable obstacle for clinicians in predicting, diagnosing, and effectively treating pain in this diverse patient group. Acknowledging these age-specific distinctions is the first step toward developing more targeted and personalized pain management protocols that can address the unique physiological and psychosocial needs of different age demographics.

For middle-aged stroke survivors, the landscape of risk factors is multifaceted, encompassing a range of neurological and clinical variables. Studies have identified stroke characteristics as central to pain development, including the specific location of the brain lesion—with non-thalamic strokes correlating with better pain relief—and higher overall stroke severity. Furthermore, the presence of sensory disturbances, motor impairments, and neglect syndrome have been shown to be associated with increased pain intensity in this group. Demographic factors also play a crucial role, with female gender, a longer duration of time since the stroke, and poorer performance in daily activities being linked to a higher incidence and intensity of chronic pain (Aprile et al., 2020; Tanei et al., 2019; Hosomi et al., 2021; Pignolo et al., 2022; Sarfo et al., 2019;

Zhang et al., 2021).

In contrast, the risk factors identified for elderly stroke survivors are more narrowly defined. The primary determinants of persistent pain in this demographic are older age itself and the occurrence of a thalamic stroke. This more focused set of risk factors suggests that the mechanisms driving chronic pain in the elderly may be distinct from those affecting their middle-aged counterparts, possibly linked to age-related changes in neural plasticity and pain processing. The strong association with thalamic lesions in this age group points to the critical role of specific neural pathways in the manifestation of persistent post-stroke pain in the elderly (Xu et al., 2020).

A significant gap in the current body of research is the lack of information regarding young adult stroke survivors. Across the reviewed literature, no specific risk factors for chronic pain have been reported for this age group. This omission highlights a critical area for future investigation. While some evidence suggests that younger patients may have more favorable outcomes and better responses to certain treatments like neuromodulation, the factors that either protect them from or predispose them to chronic pain remain unknown. Understanding the unique trajectory of post-stroke pain in young adults is essential for providing comprehensive care to this growing patient population.

This review was guided by the overarching research question: What are the risk factors for chronic pain in different age groups of stroke survivors? To answer this, the objectives were to systematically identify, categorize, and synthesize findings from existing academic literature. The primary goals were to collate neurological, demographic, and clinical risk factors and to analyze how these factors are differentially represented across young, middle-aged, and elderly adult stroke survivors. A further objective was to summarize any reported age-related patterns in treatment responses and the broader psychosocial impacts of chronic pain.

The methodology for this inquiry involved a comprehensive search across a vast academic database, which retrieved 500 relevant papers for screening. Each paper was evaluated against stringent inclusion criteria, ensuring that the studies focused on chronic pain (persisting ≥ 3 months), included stroke survivors as the primary population, assessed potential risk factors, and

established a clear temporal link between those factors and pain onset. The review prioritized observational studies, systematic reviews, and meta-analyses to ensure a high standard of evidence. Data on study design, sample characteristics, pain assessment methods, and identified risk factors were systematically extracted for analysis.

Beyond identifying risk factors, this review also sheds light on the broader context of living with post-stroke pain. Treatment efficacy appears to be influenced by age, with studies on neuromodulation therapies reporting that younger patients tend to experience better pain relief. (Tanei et al., 2019; Hosomi et al., 2021). This suggests that age should be a key consideration when selecting therapeutic interventions. Regardless of age, the psychosocial consequences of chronic pain are consistently severe, marked by a significant reduction in quality of life and a heightened risk of depression. This universal burden emphasizes the need for integrated care models that screen for and address psychosocial needs in all stroke survivors suffering from chronic pain (Sarfo et al., 2019; Lindgren et al., 2018; Creamer et al., 2018).

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the risk factors for chronic pain in different age groups of stroke survivors.

Screening

We screened in papers that met these criteria:

- **Pain Duration:** Does the study examine pain that persists for 3 or more months post-stroke?
- **Population:** Does the study include stroke survivors (of any age) as the primary population?
- **Risk Factor Assessment:** Does the study assess one or more potential risk factors (demographic, clinical, psychological, or social) for post-stroke pain?
- **Temporal Relationship:** Does the study establish a clear temporal sequence between the proposed risk factors and the onset of pain?
- **Study Design:** Is the study design either an observational study (cohort, case-control, cross-sectional), systematic review, or meta-analysis?
- **Outcome Definition:** Is chronic pain clearly defined as an outcome measure in the study?
- **Pain Timing:** Does the study clearly distinguish between pre-existing pain and new onset post-stroke pain?
- **Pain Type:** Does the study examine chronic pain rather than focusing exclusively on acute pain (< 3 months)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

We asked a large language model to extract each data column below from each paper. We gave the model the extraction instructions shown below for each column.

- **Study Design:**

Identify the specific type of study design used. Look in the methods section for explicit description of the study design.

Possible designs include:

- Cross-sectional survey
- Qualitative interview study
- Observational cohort study

- Intervention study
- Retrospective analysis

If multiple design elements are present, list all. If the design is not clearly stated, write "Design not clearly specified" and note the page/section where design-related information was found.

- **Sample Characteristics:**

Extract detailed participant demographics:

- Total sample size
- Age range or mean age
- Gender distribution
- Time since stroke
- Inclusion/exclusion criteria for stroke survivors

Look in methods section for participant recruitment and demographics. If ranges are provided, record both minimum and maximum. If mean is provided, also note standard deviation if available.

If information is incomplete, note "Partial information available" and specify what details are missing.

- **Pain Characteristics:**

Extract specific details about chronic pain:

- Type of pain (e.g., shoulder pain, central post-stroke pain)
- Pain location
- Pain intensity (if measured)
- Duration of pain
- Onset characteristics

Prioritize information from results and methods sections. If multiple pain descriptions exist, list all. Use direct quotes if precise language is important.

If pain measurement tools were used (e.g., Visual Analog Scale), note the specific tool and its scoring.

- **Risk Factors:**

Identify and extract any factors associated with chronic pain risk:

- Stroke location
- Age
- Stroke severity
- Comorbidities
- Treatment interventions

Look in results and discussion sections for statistical analyses or correlations related to pain risk. Note the statistical significance and effect sizes if reported.

If no explicit risk factors are identified, write "No specific risk factors reported".

- **Pain Treatments:**

List all pain treatments mentioned:

- Medication types
- Non-medication interventions
- Frequency of treatment use
- Self-reported effectiveness of treatments

Extract from results section, focusing on specific treatment details. If percentages of treatment use are provided, record them.

For each treatment, note:

- Percentage of participants using it
- Perceived effectiveness (if reported)
- Any comparative effectiveness data

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Stroke Survivors	Post-stroke Patients	Individuals after stroke	Patients after stroke
Intervention (I)	Risk Factors	Predictive Factors	Associated Factors	Predictors
Comparison (C)	Age Groups	Age-Specific	Age-Related Variations	Age Stratification
Outcome (O)	Chronic Pain	Post-stroke Pain	Persistent Pain	Pain Intensity

The Boolean MeSH keywords inputted on databases for this research are: (*"Stroke Survivors" OR "Post-stroke Patients" OR "Individuals after stroke" OR "Patients after stroke"*) AND (*"Risk Factors" OR "Predictive Factors" OR "Associated Factors" OR "Predictors"*) AND (*"Age Groups" OR "Age-Specific" OR "Age-Related Variations" OR "Age Stratification"*) AND (*"Chronic Pain" OR "Post-stroke Pain" OR "Persistent Pain" OR "Pain Intensity"*)

Data retrieval

Abstracts and titles were screened to assess their eligibility, and only studies meeting the inclusion criteria were selected for further analysis. Literature that fulfilled all predefined criteria and directly related to the topic was included. Studies that did not meet these criteria were excluded. Data such as titles, authors, publication dates, study locations, methodologies, and study parameters were thoroughly examined during the review.

Quality Assessment and Data Synthesis

Each author independently assessed the titles and abstracts of the selected studies to identify those for further exploration. Articles that met the inclusion criteria underwent further evaluation. Final decisions on inclusion were based on the findings from this review process.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Stroke Survivors" OR "Post-stroke Patients" OR "Individuals after stroke" OR "Patients after stroke" AND "Risk Factors" OR "Predictive Factors" OR "Associated Factors" OR "Predictors") AND ("Age Groups" OR "Age-Specific" OR "Age-Related Variations" OR "Age Stratification") AND ("Chronic Pain" OR "Post-stroke Pain" OR "Persistent Pain" OR "Pain Intensity")	21
Semantic Scholar	("Stroke Survivors" OR "Post-stroke Patients" OR "Individuals after stroke" OR "Patients after stroke") AND ("Risk Factors" OR "Predictive Factors" OR "Associated Factors" OR "Predictors") AND ("Age Groups" OR "Age-Specific" OR "Age-Related Variations" OR "Age Stratification") AND ("Chronic Pain" OR "Post-stroke Pain" OR "Persistent Pain" OR "Pain Intensity")	250
Springer	("Stroke Survivors" OR "Post-stroke Patients" OR "Individuals after stroke" OR "Patients after stroke") AND ("Risk Factors" OR "Predictive Factors" OR "Associated Factors" OR "Predictors") AND ("Age Groups" OR "Age-Specific" OR "Age-Related Variations" OR "Age Stratification") AND ("Chronic Pain" OR "Post-stroke Pain" OR "Persistent Pain" OR "Pain Intensity")	131
Google Scholar	("Stroke Survivors" OR "Post-stroke Patients" OR "Individuals after stroke" OR "Patients after stroke") AND ("Risk Factors" OR "Predictive Factors" OR "Associated Factors" OR "Predictors") AND ("Age Groups" OR "Age-Specific" OR "Age-Related Variations" OR "Age Stratification") AND ("Chronic Pain" OR "Post-stroke Pain" OR "Persistent Pain" OR "Pain Intensity")	908

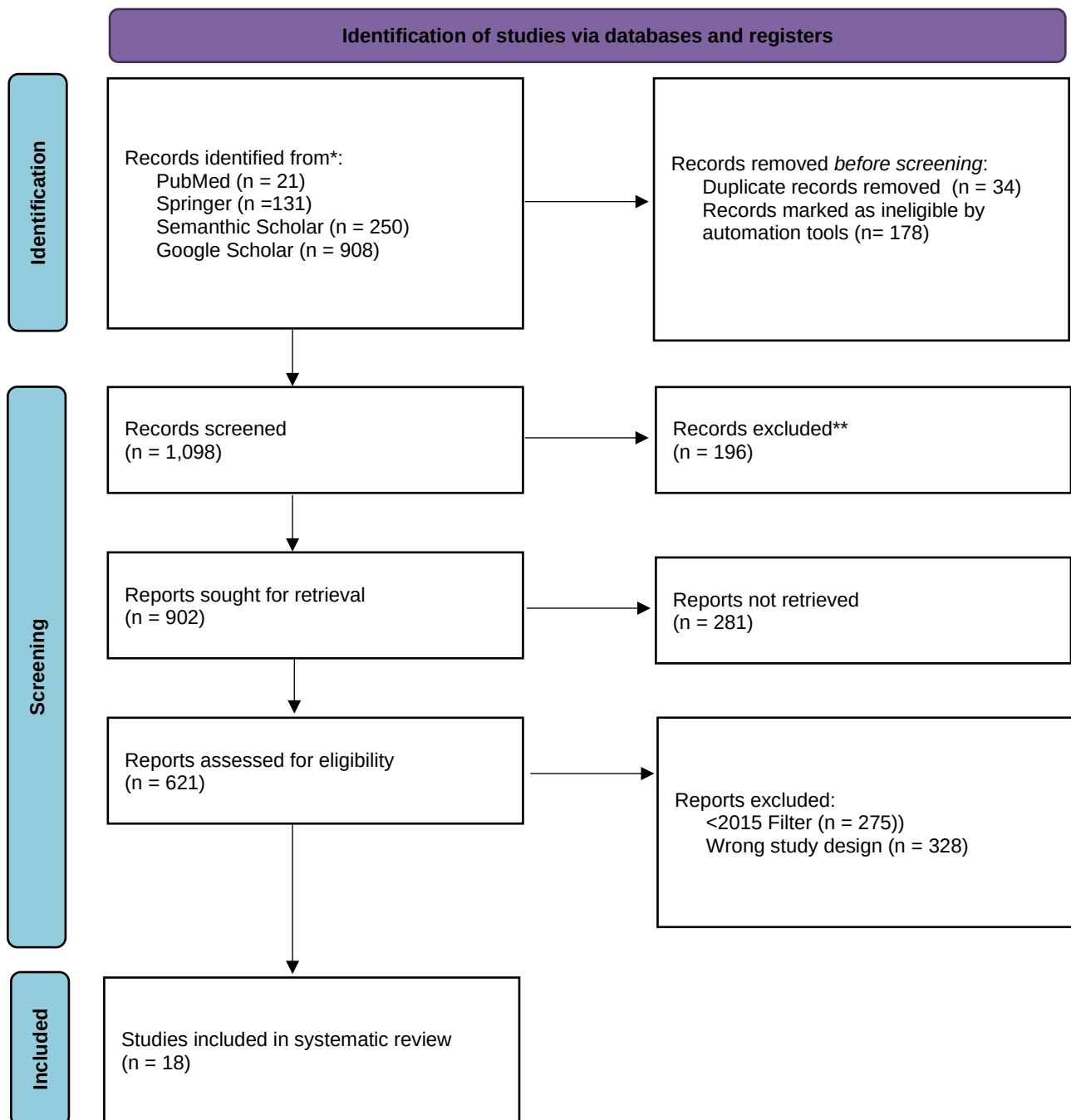


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
Adey-Wakeling et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Tanei et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Aprile et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Pignolo et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓

Haslam et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hosomi et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Lindgren et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Zhang et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kim et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Gopalakrishnan et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hosomi et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Dimyan et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Molero-Chamizo et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Creamer et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Campos et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Baik et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓

Sarfo et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Xu et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

Study	Study Design	Population Demographics	Pain Assessment Method	Primary Risk Factors Studied
Adey-Wakeling et al., 2015	Prospective observational cohort	318 stroke events in 301 individuals; age/gender not reported	Visual Analog Scale (VAS)	No mention found; focus on incidence and associations of hemiplegic shoulder pain
Tanei et al., 2019	Retrospective analysis	18 patients; mean age 63.9 (SD 8.8), 10 men/8 women; mean pain duration 4.5	Visual Analog Scale (VAS)	Age, stroke location (thalamic vs. non-thalamic)

Study	Study Design	Population Demographics	Pain Assessment Method	Primary Risk Factors Studied
		years		
Aprile et al., 2020	Secondary analysis of randomized controlled trial	224 patients; age/gender not fully reported	Numerical Rating Scale, Douleur Neuropathique 4 (DN4)	Gender, neglect syndrome, time since stroke, disability, motor function, strength, quality of life
Pignolo et al., 2022	Randomized trial protocol	118 patients; any age, both sexes; first-ever stroke within 24 hours	Visual Analog Scale (VAS), Douleur Neuropathique 4 (DN4)	Paresis, motor function, intervention (robotic vs. conventional rehabilitation)
Haslam et al., 2020	Cross-sectional survey	322; mean age 58 (SD 12), 57% female; mean 7 years post-stroke	Numeric Rating Scale (NRS)	No mention found; focus on treatment use/effectiveness
Hosomi et al.,	Retrospective	166; mean age	Pain score (0-	Age, sensory

Study	Study Design	Population Demographics	Pain Assessment Method	Primary Risk Factors Studied
2021	analysis	63.4; gender not reported	10), Patient Global Impression of Change (PGIC)	disturbance, lead location, pain region
Lindgren et al., 2018	Qualitative interview study	13; median age 65, 6 women/7 men	No mention found	No mention found; focus on lived experience
Zhang et al., 2021	Cross-sectional study	60; median age 68.5 (range 56.25-73), 39 men/21 women	Fugl-Meyer joint pain scale, Pressure Pain Threshold (PPT)	Gender, joint pain, motor function, activities of daily living (ADL)
Kim et al., 2019	Intervention study	37; age/gender not reported; mean 3.1 years post-stroke	Numeric Rating Scale (NRS), Short-form McGill Pain Questionnaire	No mention found; focus on duloxetine efficacy

Study	Study Design	Population Demographics	Pain Assessment Method	Primary Risk Factors Studied
Gopalakrishnan et al., 2018	Randomized controlled trial	10; age/gender not reported	No mention found	No mention found; focus on deep brain stimulation (DBS) effects
Hosomi et al., 2024	Post hoc analysis of phase 3 study	94; mean age 65.3 (SD 11.1), 66 male; 6 months post-stroke	Short-form McGill Pain Questionnaire Visual Analog Scale (SF-MPQ VAS)	Stroke type/location, motor weakness, time since stroke
Dimyan et al., 2022	Intervention study	No mention found; chronic stroke (6 months)	Questionnaires on pain, expectancy	No mention found; focus on predictors of response
Molero-Chamizo et al., 2021	Pilot intervention (crossover)	3; ages 43, 57, 72; 2 women/1 man; 9-15 months post-stroke	Anchored Visual Analog Scale (AVAS)	No mention found; focus on transcranial direct current stimulation (tDCS) effects

Study	Study Design	Population Demographics	Pain Assessment Method	Primary Risk Factors Studied
Creamer et al., 2018	Randomized controlled trial	60; age/gender not reported	Numeric Pain Rating Scale	No mention found; focus on intrathecal baclofen (ITB) vs. conventional medical management (CMM)
Campos et al., 2024	Randomized controlled trial pilot	20; mean age 57.8, 47% male; mean 26 months post-stroke	Numeric Rating Scale (NRS, 0-10)	No mention found; focus on Scrambler Therapy
Baik et al., 2023	Randomized controlled trial pilot	22; age/gender not reported	No mention found	Lesion location (influence on transcranial direct current stimulation (tDCS) response)
Sarfo et al.,	Prospective	No mention	Hamilton	National

Study	Study Design	Population Demographics	Pain Assessment Method	Primary Risk Factors Studied
2019	cohort/randomized controlled trial	found; mean age 55.1 (SD 12.7), 65% male	Depression Rating Scale (pain as covariate)	Institutes of Health Stroke Scale (NIHSS, stroke severity), pain
Xu et al., 2020	Case report	1; 71-year-old man	No mention found	Stroke location (thalamic), age, comorbidities

Study Design:

- Five studies used a randomized controlled trial design (including pilot and protocol studies).
- Two studies used a cohort design (prospective or observational).
- Two studies used a retrospective analysis.
- Two studies used a cross-sectional design.
- Three studies were intervention studies (including pilot/crossover).
- Two studies were secondary or post hoc analyses.
- One study was qualitative.
- One was a case report.
- One was a protocol (not yet reporting results).
- Some studies fit more than one category.

Pain Assessment Methods:

- Numeric Rating Scale (NRS, including Numeric Pain Rating Scale) was used in six studies.

- Visual Analog Scale (VAS, including Short-form McGill Pain Questionnaire Visual Analog Scale) was used in four studies.
- Douleur Neuropathique 4 (DN4) was used in two studies.
- Fugl-Meyer joint pain scale and Pressure Pain Threshold (PPT) were each used in one study.
- Short-form McGill Pain Questionnaire and Anchored Visual Analog Scale (AVAS) were each used in one study.
- Patient Global Impression of Change (PGIC) was used in one study.
- Hamilton Depression Rating Scale (pain as covariate) was used in one study.
- Questionnaires (pain, expectancy) were used in one study.
- We did not find a specified pain assessment method in four studies.

Primary Risk Factors Studied:

- Motor function, weakness, paresis, or strength were studied in five studies.
- Stroke location, type, or lesion location were studied in four studies.
- Age was studied in three studies.
- Gender was studied in two studies.
- Time since stroke was studied in two studies.
- Other risk factors (each in one study): neglect syndrome, disability, quality of life, sensory disturbance, lead location, pain region, joint pain, activities of daily living (ADL), intervention/treatment, stroke severity (National Institutes of Health Stroke Scale), pain (as covariate), comorbidities.
- We did not find a specified risk factor analysis in nine studies; these focused on incidence, treatment, or lived experience rather than risk factors.

Risk Factors Across Age Groups

Neurological Factors

Risk Factor Category	Young Adults	Middle-Aged	Elderly	Strength of Association
Stroke location (thalamic vs. non-thalamic)	No mention found	Non-thalamic location associated with better pain relief (Tanei et al., 2019)	Thalamic location associated with persistent pain (Xu et al., 2020)	Moderate (Tanei et al., 2019; Xu et al., 2020)
Stroke severity (National Institutes of Health Stroke Scale)	No mention found	Higher severity associated with pain and depression (Sarfo et al., 2019)	No mention found	Strong (Sarfo et al., 2019)
Sensory disturbance	No mention found	Less sensory disturbance associated with better spinal cord stimulation outcomes (Hosomi et al.,	No mention found	Moderate (Hosomi et al., 2021)

Risk Factor Category	Young Adults	Middle-Aged	Elderly	Strength of Association
		2021)		
Motor impairment/paresis	No mention found	Paresis increases risk for pain (Pignolo et al., 2022)	No mention found	Moderate (Pignolo et al., 2022)
Neglect syndrome	No mention found	Associated with higher pain intensity (Aprile et al., 2020)	No mention found	Moderate (Aprile et al., 2020)

- All five risk factors (stroke location, stroke severity, sensory disturbance, motor impairment/paresis, and neglect syndrome) were reported for middle-aged adults.
- Only one risk factor (stroke location) was reported for elderly adults.
- We did not find any risk factors reported for young adults.
- For each risk factor:
 - Stroke location was reported for two age groups (middle-aged and elderly).
 - The other four risk factors were reported only for middle-aged adults.
- Four risk factors (stroke location, sensory disturbance, motor impairment/paresis, neglect syndrome) were reported with moderate associations.
- One risk factor (stroke severity) was reported with a strong association.

Demographic and Clinical Factors

Risk Factor Category	Young Adults	Middle-Aged	Elderly	Strength of Association
Age	Younger age associated with better pain relief (Tanei et al., 2019; Hosomi et al., 2021)	Most samples are middle-aged; better pain relief than elderly	Older age associated with persistent pain (Xu et al., 2020)	Moderate (Tanei et al., 2019; Hosomi et al., 2021; Xu et al., 2020)
Gender	No mention found	Female gender associated with higher pain intensity (Aprile et al., 2020; Zhang et al., 2021)	No mention found	Moderate (Aprile et al., 2020; Zhang et al., 2021)
Time since stroke	No mention found	Longer time since stroke associated with higher pain	No mention found	Moderate (Aprile et al., 2020)

Risk Factor Category	Young Adults	Middle-Aged	Elderly	Strength of Association
		intensity (Aprile et al., 2020)		
Disability/Activities of Daily Living	No mention found	Higher disability and lower activities of daily living associated with higher pain (Aprile et al., 2020; Zhang et al., 2021)	No mention found	Moderate (Aprile et al., 2020; Zhang et al., 2021)
Comorbidities	No mention found	Dystonia, depression, anxiety as consequences of pain (Xu et al., 2020)	No mention found	Weak (Xu et al., 2020)

- All five risk factor categories were reported in middle-aged adults, but only age was reported for young adults and elderly.
- For age, three studies reported that younger age was associated with better pain relief, while older age was associated with persistent pain.

- For gender, two studies in middle-aged adults found that female gender was associated with higher pain intensity; we did not find data for young adults or elderly.
- For time since stroke, one study in middle-aged adults found that longer time since stroke was associated with higher pain intensity; we did not find data for young adults or elderly.
- For disability/activities of daily living, two studies in middle-aged adults found that higher disability and lower activities of daily living were associated with higher pain; we did not find data for young adults or elderly.
- For comorbidities, one study in middle-aged adults found dystonia, depression, and anxiety as consequences of pain; we did not find data for young adults or elderly.
- The strength of association was rated as moderate for age, gender, time since stroke, and disability/activities of daily living, and weak for comorbidities.
- We did not find reporting for gender, time since stroke, disability/activities of daily living, or comorbidities in young adults or elderly.

Thematic Analysis

Age-Specific Pain Manifestations

Theme	Key Findings	Age-Related Variations	Clinical Implications
Pain type and location	Shoulder pain, central post-stroke pain, spasticity-related pain are common	Most studies focus on middle-aged/elderly; age-specific differences not well reported	Need for age-stratified pain assessment and management
Pain intensity and duration	Moderate to severe pain common;	Older age may be associated with	Early identification and intervention

	chronicity varies	persistent pain (Xu et al., 2020)	may prevent chronicity in older adults
Sensory abnormalities	Hypoalgesia, hyperalgesia, sensory loss	Gender differences in pressure pain threshold; neural plasticity may differ by age (Zhang et al., 2021)	Sensory training may be tailored by age and gender

- Three pain types were commonly reported: shoulder pain, central post-stroke pain, and spasticity- related pain (each mentioned in one theme).
- Moderate to severe pain intensity was noted as common in one theme, and pain chronicity was described as variable in one theme.
- Sensory abnormalities were reported in one theme, including hypoalgesia, hyperalgesia, and sensory loss.

Age-related variations:

- In one theme, most studies were noted to focus on middle-aged or elderly populations, but we did not find age-specific differences well reported.
- In one theme, older age was associated with persistent pain, with one study (Xu et al., 2020) cited.
- In one theme, gender differences in pressure pain threshold were mentioned, and neural plasticity was noted to potentially differ by age, with one study (Zhang et al., 2021) cited.
- We found two themes where specific studies were cited for age or gender differences.
- We did not find age-specific findings for all themes; only two themes included explicit age-

related or gender-related findings.

Overall, age-related variations were inconsistently reported, with only two themes providing explicit findings or references to age or gender differences, and one theme noting that age-specific differences were not well reported.

Treatment Response Patterns

Theme	Key Findings	Age-Related Variations	Clinical Implications
Pharmacological interventions	Duloxetine, mirogabalin, intrathecal baclofen, spinal cord stimulation, deep brain stimulation used; variable efficacy	Younger age associated with better response to spinal cord stimulation (Tanei et al., 2019; Hosomi et al., 2021)	Consider age when selecting neuromodulation therapies
Non-pharmacological interventions	Physical therapy, robotic rehabilitation, transcranial direct current stimulation, Scrambler Therapy	Not stratified by age; self-management preferred in qualitative study (Lindgren et al., 2018)	Multidisciplinary, individualized approaches needed

Adverse effects	Somnolence, edema, dizziness, weight gain (mirogabalin); side effects limit medication use in some	No mention found by age group	Monitor for adverse effects, especially in elderly
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- Pharmacological interventions were reported in one theme, with duloxetine, mirogabalin, intrathecal baclofen, spinal cord stimulation, and deep brain stimulation used; variable efficacy was noted.
- Non-pharmacological interventions were reported in one theme, including physical therapy, robotic rehabilitation, transcranial direct current stimulation, and Scrambler Therapy.
- Adverse effects were reported in one theme, with somnolence, edema, dizziness, and weight gain (miroga- balin) noted as limiting medication use in some cases.

Age-related variations:

- We found age-related variation in response to spinal cord stimulation, with two studies (Tanei et al., 2019; Hosomi et al., 2021) reporting that younger age was associated with better response.
- We did not find age stratification for non-pharmacological interventions; one qualitative study reported a preference for self-management.
- We did not find age group reporting for adverse effects.

Clinical implications reflected the findings:

- Age should be considered when selecting neuromodulation therapies.
- Multidisciplinary, individualized approaches are needed for non-pharmacological interventions.
- Monitoring for adverse effects is important, especially in elderly patients.

Psychosocial Impact

Theme	Key Findings	Age-Related Variations	Clinical Implications
Emotional and functional consequences	Pain limits activities of daily living, causes emotional distress, depression (Sarfo et al., 2019; Lindgren et al., 2018)	No mention found by age; depression risk may be higher with severe stroke/pain	Screen for depression and psychosocial needs in all age groups
Quality of life	Pain negatively impacts quality of life; intrathecal baclofen improves quality of life (Creamer et al., 2018)	No mention found by age	Quality of life should be a key outcome in pain management

- Two studies reported on the consequences of pain after stroke:
 - One study (Sarfo et al., 2019; Lindgren et al., 2018) reported emotional and functional impacts, including limitations in activities of daily living and increased risk of depression.
 - One study (Creamer et al., 2018) reported that pain negatively impacts quality of life and that intrathecal baclofen improves quality of life.

Age-related variations:

- We did not find any studies that stratified findings by age group.
- Both studies stated that findings were not stratified by age.
- One study commented that depression risk may be higher with more severe stroke or pain, but not specifically by age.

Clinical implications:

- One study recommended screening for depression and psychosocial needs in all age groups.
- One study recommended that quality of life should be a key outcome in pain management.
- We did not find any studies that made age-specific clinical recommendations.

Summary

- The evidence base for age-specific risk factors for chronic pain in stroke survivors is limited by inconsistent reporting and lack of age-stratified analyses.
- Recurrent risk factors identified across studies include older age, thalamic stroke location, female gender, higher stroke severity, neglect syndrome, and greater disability.
- Treatment response may be better in younger patients, based on findings from studies of neuromodulation therapies.
- Psychosocial impacts, including reduced quality of life and increased risk of depression, are significant across age groups.

DISCUSSION

This review synthesizes the current evidence on age-specific risk factors for chronic pain in stroke survivors, revealing a fragmented but informative landscape. The principal finding is that the factors contributing to the development of chronic post-stroke pain are not universal but are significantly influenced by the patient's age group. However, this conclusion is built upon an evidence base characterized by inconsistent reporting and a notable lack of research focused on young adult survivors. The discussion will delve into the interpretation of the identified neurological and demographic risk factors, explore the clinical implications of age-related treatment responses, and highlight the critical gaps in the literature that demand future investigation.

The role of stroke location, particularly the distinction between thalamic and non-thalamic lesions, emerges as a significant neurological determinant of chronic pain. The thalamus acts as a critical relay center for sensory information, and its damage is classically associated with the development of central post-stroke pain (CPSP). This review found that a thalamic stroke location was a key risk factor for persistent pain specifically in elderly survivors (Xu et al., 2020). Conversely, for middle-aged individuals, a non-thalamic lesion was associated with better pain relief, suggesting that pain mechanisms in this group may be more varied or that they possess a greater capacity for neural reorganization following non-thalamic injuries (Tanei et al., 2019). This dichotomy underscores the need for neuroimaging to be a central part of risk stratification, especially in older patients.

Stroke severity, as measured by the National Institutes of Health Stroke Scale (NIHSS), was identified as having a strong association with pain and depression, particularly in middle-aged survivors (Sarfo et al., 2019). A more severe stroke implies a larger area of brain tissue damage, which can lead to a greater disruption of sensory and motor pathways. This extensive neurological insult increases the probability of developing primary pain syndromes like CPSP and secondary musculoskeletal pain resulting from significant motor deficits, spasticity, or immobility. The link with depression suggests a

synergistic relationship where severe disability fosters both pain and emotional distress, creating a debilitating cycle.

A constellation of neurological deficits, including sensory disturbance, motor impairment (paresis), and neglect syndrome, were also identified as moderate risk factors in the middle-aged cohort. Less sensory disturbance was linked to better outcomes with spinal cord stimulation, logically suggesting that partially intact sensory pathways are necessary for neuromodulation to be effective (Hosomi et al., 2021). Paresis and motor impairment contribute to pain through biomechanical stress, such as shoulder subluxation or altered gait, leading to secondary musculoskeletal pain (Pignolo et al., 2022). The association of neglect syndrome with higher pain intensity is particularly intriguing, possibly reflecting a profound disruption in the brain's representation of the body and space, which could alter pain perception and processing (Aprile et al., 2020).

A striking pattern revealed in this analysis is the concentration of identified neurological risk factors within the middle-aged population. Stroke location, severity, sensory disturbance, motor impairment, and neglect syndrome were all reported for this group, while only stroke location was noted for the elderly, and none were reported for young adults. This does not necessarily mean these factors are irrelevant in other age groups. Instead, it more likely reflects a significant methodological artifact of the available literature, where the study samples predominantly consisted of middle-aged participants. Consequently, the findings for this group are more robust simply because they have been studied more frequently.

The influence of age itself presents a complex picture. The report highlights that older age is associated with persistent pain (Xu et al., 2020), while younger age is associated with better pain relief and more favorable responses to neuromodulation therapies (Tanei et al., 2019; Hosomi et al., 2021). This paradox can be interpreted through several lenses. The age-related persistence of pain in the elderly may be due to factors such as diminished neural plasticity, the cumulative burden of comorbidities, and age-related changes in pain

processing pathways. Conversely, the superior outcomes in younger patients may reflect greater neuroplastic capacity, allowing for more effective adaptation and recovery following a stroke and related interventions.

Gender was identified as another relevant demographic factor, with two studies finding that female gender was associated with higher pain intensity among middle-aged survivors (Aprile et al., 2020; Zhang et al., 2021). This aligns with broader findings in pain research, where women often report higher pain prevalence and intensity for various chronic conditions. The underlying reasons are likely multifactorial, involving hormonal differences, variations in neural pain-processing circuits, and potential psychosocial factors related to pain reporting. The absence of data on gender differences in young and elderly stroke survivors is a notable gap that prevents a more comprehensive understanding of this factor across the lifespan.

Clinical factors such as the time elapsed since the stroke and the level of disability also contribute to the risk profile in middle-aged adults. One study found that a longer time since stroke was linked to higher pain intensity, which may be explained by the development of central sensitization, where the nervous system becomes progressively more responsive to stimuli over time (Aprile et al., 2020). Concurrently, higher disability and lower performance in activities of daily living (ADL) were associated with increased pain, highlighting a vicious cycle where pain limits function, and poor function exacerbates pain through immobility and secondary complications (Aprile et al., 2020; Zhang et al., 2021).

The analysis of comorbidities revealed a weak association, with one study framing dystonia, depression, and anxiety as consequences of pain rather than pre-existing risk factors (Xu et al., 2020). This underscores the profound and bidirectional relationship between chronic pain and mental health. Pain is not merely a physical sensation but a comprehensive experience that degrades mental well-being, and in turn, depression and anxiety can lower pain thresholds and amplify the perception of pain. This finding

reinforces the clinical recommendation to screen for and treat psychosocial distress as an integral part of pain management in all stroke survivors.

The discussion of treatment response patterns provides critical insights for clinical practice. The finding that younger age is associated with a better response to spinal cord stimulation is of paramount importance (Tanei et al., 2019; Hosomi et al., 2021). This suggests that age should be a key variable when considering patient selection for advanced neuromodulation therapies. These interventions are invasive and costly, and stratifying candidates by age could optimize outcomes and resource allocation. The enhanced response in younger individuals may be attributed to their greater neural plasticity, which allows the nervous system to better integrate and respond to the therapeutic stimulation.

For other interventions, both pharmacological (e.g., duloxetine, intrathecal baclofen) and non-pharmacological (e.g., robotic rehabilitation, tDCS), the review found a lack of age-stratified efficacy data. This makes it difficult for clinicians to tailor these treatments to different age groups. Furthermore, the mention of a preference for self-management in a qualitative study highlights the importance of patient-centered care and the need to equip survivors with the tools and education to actively participate in managing their own pain (Lindgren et al., 2018).

The management of adverse effects from pharmacological treatments is another area where an age-sensitive approach is crucial. While the review did not find age-group-specific reporting for side effects, the clinical implication to monitor elderly patients with extra vigilance is a sound one. Elderly individuals often have altered drug metabolism and a higher prevalence of polypharmacy, increasing their vulnerability to adverse effects such as somnolence, dizziness, and falls, which were noted with medications like mirogabalin (Hosomi et al., 2024).

The psychosocial impact of chronic pain was consistently reported as severe across all age groups. Pain was shown to limit daily activities, cause emotional distress, and negatively impact quality of life (Sarfo et al., 2019; Lindgren et al., 2018; Creamer et al.,

2018). This universal burden confirms that a purely biomedical approach to post-stroke pain is insufficient. Effective management must incorporate psychosocial screening and support to address the full spectrum of the patient's experience.

A significant limitation within this domain, however, is that the studies on psychosocial consequences did not stratify their findings by age group. This means that while we know the burden is high for everyone, we do not understand if the nature of this burden differs with age. For instance, the impact of pain on a young adult's career and family-building may be psychosocially distinct from its impact on an elderly person's social engagement and independence. This lack of nuanced data hinders the development of age-appropriate psychosocial interventions.

The most significant limitation of the existing body of evidence, as highlighted by this review, is the inconsistent and fragmented nature of the research. Many of the included studies were not designed with the primary goal of identifying age-specific risk factors for chronic pain; this information was often a secondary finding. The use of varied study designs—from randomized trials to case reports—and a wide array of pain assessment methods makes direct comparison and synthesis challenging.

The most critical knowledge gap identified is the near-total absence of data for young adult stroke survivors. No specific neurological or demographic risk factors were reported for this group. With the incidence of stroke rising in younger adults, this is a major public health blind spot. These individuals face decades of potential disability and pain, which can derail their careers, education, and family lives. Understanding their unique risk profile and recovery trajectory is imperative and should be a top priority for future research.

To address these gaps, future research must be more methodologically rigorous and intentional. Prospective, longitudinal cohort studies are needed to clearly establish the temporal relationship between risk factors and pain onset. These studies should be designed to purposefully recruit and stratify participants across all age groups (young, middle-aged, and elderly) to enable robust comparative analysis. The use of standardized

and validated pain assessment tools and clear definitions for pain phenotypes (e.g., neuropathic, nociceptive, mixed) would greatly enhance the quality and comparability of data across studies.

In summary, this discussion interprets the finding that risk factors for chronic post-stroke pain are indeed age-dependent, though our understanding is most complete for middle-aged survivors and remains profoundly deficient for young adults. Neurological factors like stroke location and severity, alongside demographic factors like age and gender, are key determinants of pain risk. The evidence suggests that treatment response, particularly to neuromodulation, may also be age-contingent. The primary clinical implication is the immediate need for a highly individualized and age-aware approach to pain assessment and management. For the research community, the clear mandate is to conduct large-scale, prospective studies specifically designed to elucidate the risk factors, pain mechanisms, and optimal treatment strategies for stroke survivors across their entire lifespan.

CONCLUSION

In conclusion, the development of chronic pain following a stroke is a complex issue with risk factors that are not uniform but vary significantly across different age groups. Evidence clearly indicates that middle-aged survivors face a wide array of neurological and demographic risks, including stroke severity, lesion location, gender, and functional disability. For elderly survivors, the risk profile appears more focused, with older age itself and the presence of a thalamic stroke being the primary predictors of persistent pain. The most significant finding, however, is the profound lack of information regarding young adult stroke survivors, for whom no specific risk factors have been identified, representing a critical gap in the current understanding of post-stroke pain.

Beyond the initial risk factors, the response to treatment and the psychosocial impact of pain also present a nuanced picture. There is emerging evidence that a patient's age may influence therapeutic outcomes, particularly with neuromodulation therapies, where younger patients tend to

show more favorable responses. Despite these differences in risk and treatment response, the debilitating psychosocial consequences of chronic pain are universal. Survivors across all age demographics experience a significant reduction in their quality of life, coupled with heightened emotional distress and an increased risk of depression, underscoring the need for integrated care that addresses both the physical and psychological dimensions of pain.

The findings are, however, built upon a limited and fragmented evidence base. The body of research is characterized by inconsistent reporting and a frequent lack of age-stratified analysis, making it difficult to draw definitive, overarching conclusions. Many studies were not primarily designed to investigate age-specific risk factors, and the variety in study designs and pain assessment methods further complicates synthesis. This highlights a fundamental weakness in the existing literature and points to the urgent need for more methodologically rigorous research in this area.

Ultimately, this review underscores the necessity of moving towards a more personalized, age-aware approach in the clinical management of post-stroke pain. For clinicians, the current evidence serves as a guide for individualized assessment rather than a set of rigid rules. For the research community, this work is a call to action to conduct large-scale, prospective studies that are specifically designed to compare risk factors, pain mechanisms, and treatment efficacy across the full spectrum of adult age groups. Only through such dedicated efforts can we close the existing knowledge gaps, particularly for young survivors, and develop more effective strategies to prevent and alleviate chronic pain after stroke.

REFERENCES

1. Sarfo, F., Agbenorku, M., Adamu, S., Obese, V., Berchie, P., & Ovbiagele, B. (2019). The Dynamics of Post- stroke Depression Among Ghanaians. *Journal of Neurological Sciences*.
2. Lindgren, I., Gard, G., & Brogårdh, C. B. (2018). Shoulder Pain After Stroke – Experiences, Consequences in Daily Life and Effects of Interventions: A Qualitative

Study. *Disability and Rehabilitation*.

3. Aprile, I., Germanotta, M., Cruciani, A., Pecchioli, C., Loreti, S., Papadopoulou, D., Montesano, A., et al. (2020). Poststroke Shoulder Pain in Subacute Patients and Its Correlation with Upper Limb Recovery After Robotic or Conventional Treatment: A Secondary Analysis of a Multicenter Randomized Controlled Trial. *International Journal of Stroke*.
4. Tanei, T., Kajita, Y., Takebayashi, S., Aoki, K., Nakahara, N., & Wakabayashi, T. (2019). Pre- dictive Factors Associated with Pain Relief of Spinal Cord Stimulation for Central Post-Stroke Pain. *Neurologia Medico-Chirurgica*.
5. Hosomi, K., Yamamoto, T., Agari, T., Takeshita, S., Tanei, T., Imoto, H., Mori, N., et al. (2021). Benefit of Spinal Cord Stimulation for Patients with Central Poststroke Pain: A Retrospective Multicenter Study. *Journal of Neurosurgery*.
6. Pignolo, L., Tonin, P., Nicotera, P., Bagetta, G., & Scuteri, D. (2022). ROBOCOP (ROBOTic Care of Poststroke Pain): Study Protocol for a Randomized Trial to Assess Robot-Assisted Functional and Motor Recovery and Impact on Poststroke Pain Development. *Frontiers in Neurology*.
7. Zhang, Y.-h., Wang, Y.-C., Hu, G.-W., Ding, X.-q., Shen, X., Yang, H., Rong, J., & Wang, X. (2021). The Effects of Gender, Functional Condition, and ADL on Pressure Pain Threshold in Stroke Patients. *Frontiers in Neuroscience*.
8. Xu, W., Zhang, C., Sun, B., & Li, D. (2020). Sustainable Effects of 8-Year Intermittent Spinal Cord Stimulation in a Patient with Thalamic Post-Stroke Pain. *World Neurosurgery*.
9. Creamer, M., Cloud, G., Kossmehl, P., Yochelson, M., Francisco, G., Ward, A., Wissel, J., et al. (2018). Effect of Intrathecal Baclofen on Pain and Quality of Life in Poststroke Spasticity. *Stroke*.
10. Adey-Wakeling, Z., Arima, H., Crotty, M., Leyden, J., Kleinig, T., Anderson, C., & Newbury, J. (2015). Inci- dence and Associations of Hemiplegic Shoulder Pain Poststroke: Prospective Population-Based Study. *Archives of Physical Medicine and*

Rehabilitation.

11. Haslam, B. S., Butler, D., Kim, A., & Carey, L. (2020). Chronic Pain Following Stroke: Current Treatment and Perceived Effect. *Disability and Health Journal*.
12. Kim, N., Lee, S. C., & Kim, Y. W. (2019). Effect of Duloxetine for the Treatment of Chronic Central Poststroke Pain. *Clinical Neuropharmacology*.
13. Gopalakrishnan, R., Burgess, R., Malone, D., Lempka, S., Gale, J., Floden, D., Baker, K., & Machado, A. (2018). Deep Brain Stimulation of the Ventral Striatal Area for Poststroke Pain Syndrome: A Magnetoencephalography Study. *Journal of Neurophysiology*.
14. Hosomi, K., Katayama, Y., Sakoda, H., Kikumori, K., Kuroha, M., & Ushida, T. (2024). Usefulness of Mirogabalin in Central Neuropathic Pain After Stroke: Post Hoc Analysis of a Phase 3 Study by Stroke Type and Location. *Pain and Therapy*.
15. Dimyan, M., Harcum, S., Ermer, E., Boos, A., Conroy, S. S., Liu, F., Horn, L. B., et al. (2022). Baseline Predictors of Response to Repetitive Task Practice in Chronic Stroke. *Neurorehabilitation and Neural Repair*.
16. Molero-Chamizo, A., Salas Sánchez, Á., Álvarez Batista, B., Cordero García, C., Andújar Barroso, R. T., Rivera-Urbina, G. N., Nitsche, M., & Alameda Bailén, J. R. (2021). Bilateral Motor Cortex tDCS Effects on Post-Stroke Pain and Spasticity: A Three Cases Study. *Frontiers in Pharmacology*.
17. Campos, R. S., Lawrence, E., & Merbach, D. (2024). Abstract 7: Scrambler Therapy for Treatment of Post Stroke Pain. *Stroke*.
18. Baik, J., Yang, J., Ko, S., Lee, S.-J., & Shin, Y. (2023). Exploring the Potential of Transcranial Direct Current Stimulation for Relieving Central Post-Stroke Pain: A Randomized Controlled Pilot Study. *Life*.