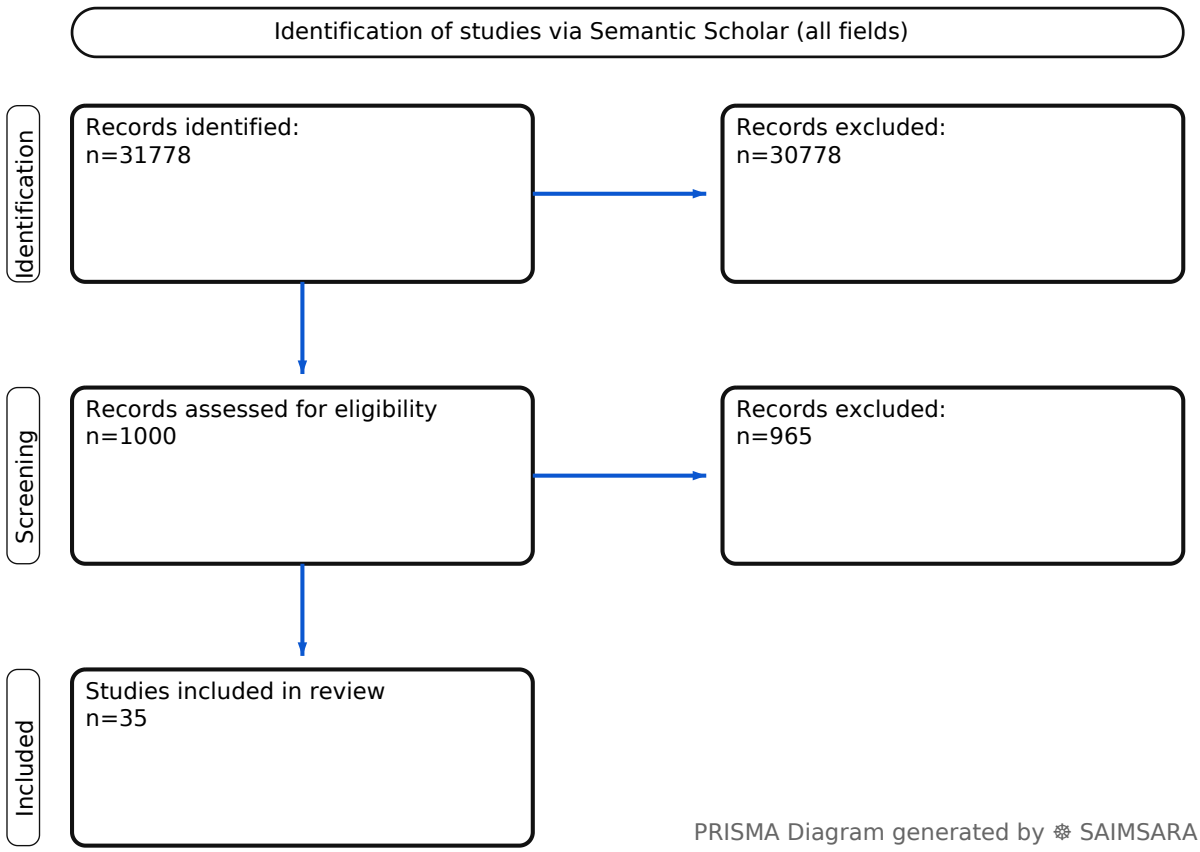
Spinal Cord Stimulation PAD CLI CLTI: Systematic Review with ☸SAIMSARA.

Abstract: To systematically review the efficacy and impact of spinal cord stimulation in patients with chronic limb-threatening ischemia (CLTI) and critical limb ischemia (CLI), as well as to contextualize findings with related applications of spinal cord stimulation and functional electrical stimulation. The review utilises 35 studies with 664 total participants (naïve ΣN). For patients with chronic limb-threatening ischemia (CLTI) or end-stage peripheral artery disease (PAD) unsuitable for revascularization, spinal cord stimulation (SCS) demonstrated a median limb salvage rate of 94.65% (range: 92.3% to 97%) at 1-year follow-up. These findings, primarily from cohort studies, suggest that SCS is a promising intervention for preserving limbs and improving quality of life in this challenging patient group. However, the reliance on retrospective and mixed study designs with relatively small sample sizes represents the most significant limitation, impacting the certainty and generalizability of the results. Future randomized controlled trials are critically needed to establish the definitive efficacy and optimal application of SCS in CLTI.

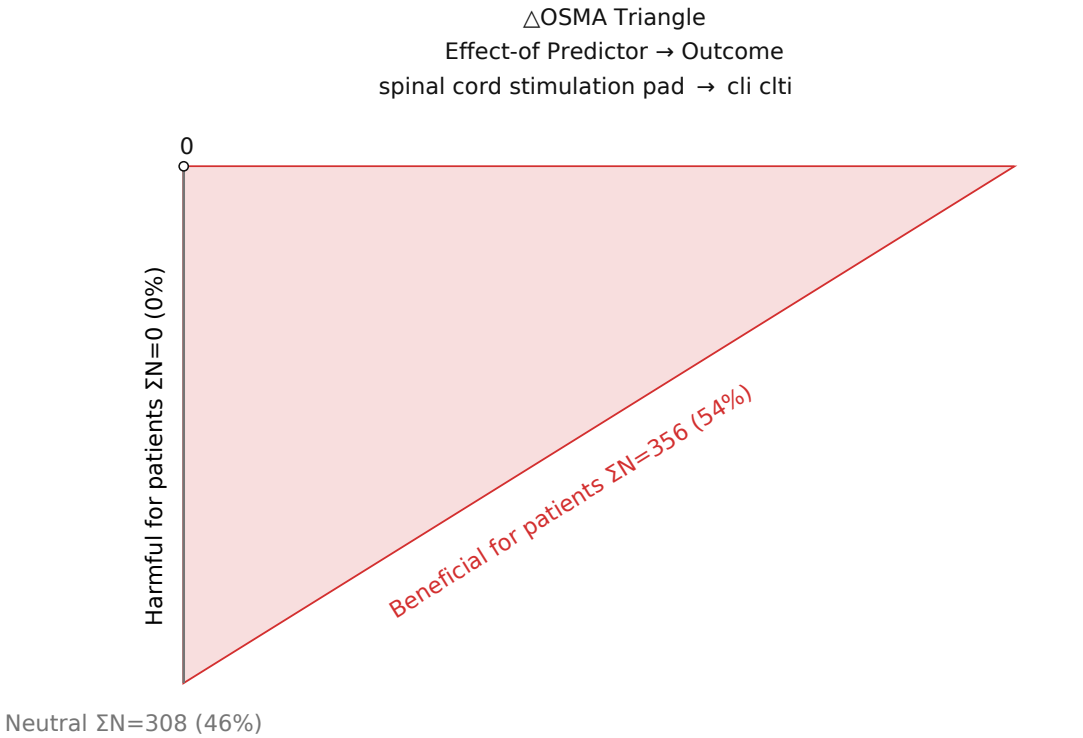
Keywords: Spinal Cord Stimulation; Chronic Limb-Threatening Ischemia; Critical Limb Ischemia

Review Stats

- Generated: 2026-02-02 23:26:30 CET
- Plan: Pro (expanded craft tokens; source: Semantic Scholar)
- Source: Semantic Scholar
- Scope: All fields
- Keyword Gate: Fuzzy (≥60% of required terms, minimum 2 terms matched in title/abstract)
- Total Abstracts/Papers: 31778
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 35
- Total study participants (naïve ΣN): 664



PRISMA Diagram generated by ☸ SAIMSARA



△OSMA Triangle generated by ☸SAIMSARA

Outcome-Sentiment Meta-Analysis (OSMA): *(LLM-only)*
Frame: Effect-of Predictor → Outcome • *Source*: Semantic Scholar
Outcome: cli clti Typical timepoints: 24-mo, 1-y. Reported metrics: %, CI, p.
Common endpoints: Common endpoints: functional, qol, healing.
Predictor: spinal cord stimulation pad — exposure/predictor. Routes seen: sc. Typical comparator: cylindrical leads for, trt alone on untrained muscles, trt alone, the nutritional counseling….

- **1) Beneficial for patients** — cli clti with spinal cord stimulation pad — [1], [2], [4], [10], [12] — ΣN=356
- **2) Harmful for patients** — cli clti with spinal cord stimulation pad — — — ΣN=0
- **3) No clear effect** — cli clti with spinal cord stimulation pad — [3], [5], [6], [7], [8], [9], [11], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35] — ΣN=308

1) Introduction

Chronic limb-threatening ischemia (CLTI), often a severe manifestation of peripheral artery disease (PAD), presents a significant challenge in vascular medicine, frequently leading to amputation and reduced quality of life, particularly in patients for whom revascularization is not an option. Spinal cord stimulation (SCS) has emerged as a neuromodulatory intervention, offering a potential therapeutic avenue by influencing pain pathways and improving microcirculation. This paper synthesizes current evidence on SCS, specifically its application in CLTI and critical limb ischemia (CLI), alongside broader insights into SCS technologies and mechanisms gleaned from related applications in chronic pain and spinal cord injury (SCI).

2) Aim

To systematically review the efficacy and impact of spinal cord stimulation in patients with chronic limb-threatening ischemia (CLTI) and critical limb ischemia (CLI), as well as to contextualize findings with related applications of spinal cord stimulation and functional electrical stimulation.

3) Methods

Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details).

- **Bias:** Qualitatively inferred from study design fields. The included studies predominantly consist of retrospective cohort designs and mixed study types, with a limited number of prospective cohorts and randomized controlled trials (RCTs), suggesting a moderate to high risk of selection and reporting bias, particularly in the absence of detailed methodology for many entries. Narrative reviews and studies not specifying directionality further contribute to potential bias.

4) Results

4.1 Study characteristics:

The included studies comprise retrospective and prospective cohort studies, mixed designs, and randomized controlled trials, alongside narrative reviews and case series. Populations primarily include diabetic patients with CLTI or end-stage PAD unsuitable for revascularization [1, 2, 4], as well as patients with chronic low back and leg pain [10, 12] and individuals with spinal cord injury [8, 9, 16, 17, 19, 20, 28]. Follow-up periods range from 6 months to 30 months, with some studies focusing on immediate outcomes or lacking specified follow-up.

4.2 Main numerical result aligned to the query:

For patients with chronic limb-threatening ischemia (CLTI) or end-stage peripheral artery disease (PAD) unsuitable for revascularization, spinal cord stimulation (SCS) demonstrated a median limb salvage rate of 94.65% (range: 92.3% to 97%) at 1-year follow-up [1, 2]. One study reported an 88% limb salvage rate at 2-year follow-up [4]. Additionally, SCS significantly improved pain intensity and quality of life in these populations, with pain reduction from a median VAS of 7.5 to 0 at 2 years in one cohort [4].

4.3 Topic synthesis:

- **CLTI/PAD Limb Salvage:** SCS achieved a median limb salvage rate of 94.65% (range: 92.3% to 97%) at 1 year for patients with CLTI/PAD not amenable to revascularization [1, 2], with one study showing 88% at 2 years [4].
- **Pain and Quality of Life Improvement:** Significant reduction in pain intensity (e.g., median VAS from 7.5 to 0, $p < 0.001$) and improved quality of life were consistently observed in CLTI/PAD patients receiving SCS [1, 2, 4].
- **Functional Improvements in CLTI/PAD:** SCS led to improved walking distance in end-stage PAD patients (median 50m to 150m, $p < 0.001$) [4].
- **SCS Lead Technologies:** High-frequency spinal cord stimulation (HF10 therapy) demonstrated superior long-term back and leg pain reduction (e.g., 66.9% vs 41.1% back pain reduction, $p < 0.001$) compared to traditional SCS [10, 12], and paddle leads were

effective for intractable low back pain [15] and complex regional pain syndrome [14].

- **Spinal Cord Injury (SCI) Applications:** Functional electrical stimulation (FES) cycling improved body composition, metabolic, and neural factors in SCI patients [21], reduced pain [8], and promoted muscle hypertrophy [19, 20]. Noninvasive transcutaneous electrical spinal cord stimulation normalized blood pressure and cerebral blood flow during orthostatic challenge in SCI [9].
- **Mechanistic Insights:** Studies explored spinal reflex mechanisms [32], the role of astrocytes in primary afferent depolarization (PADs) [34], and the impact of peripheral injury on spinal excitability [29], offering insights into how SCS might modulate neural activity.
- **SCS as an Alternative Therapy:** SCS is considered an alternative for diabetic foot patients with CLTI lacking revascularization options [3], and as an additional therapy for refractory cases of CLTI [5], though some reviews note insufficient evidence for broad recommendation [3, 6, 33].

5) Discussion

5.1 Principal finding:

The principal finding is that spinal cord stimulation (SCS) achieved a median limb salvage rate of 94.65% (range: 92.3% to 97%) at 1-year follow-up in patients with chronic limb-threatening ischemia (CLTI) or end-stage peripheral artery disease (PAD) who were not candidates for revascularization [1, 2]. This suggests a significant potential for SCS in preserving limbs in a highly vulnerable patient population.

5.2 Clinical implications:

- **Refractory CLTI/PAD Treatment:** SCS should be considered for patients with CLTI or end-stage PAD who have exhausted revascularization options, as it offers high limb salvage rates and significant improvements in pain and quality of life [1, 2, 4].
- **Pain Management and Functional Improvement:** Beyond limb salvage, SCS provides substantial pain relief and improved walking distance for CLTI/PAD patients, directly addressing critical symptoms and enhancing daily function [4].
- **Technology Considerations:** High-frequency SCS (HF10 therapy) has shown superior long-term pain relief for chronic back and leg pain compared to traditional SCS [10, 12], suggesting its potential relevance for pain components in CLTI.
- **Patient Selection:** SCS appears particularly beneficial for diabetic patients with CLTI [1] and those with end-stage PAD [4], highlighting specific patient subgroups that may benefit most.

- **Multimodal Approach:** While effective, SCS is often mentioned as an alternative or additional therapy in refractory cases [3, 5], implying it may integrate into a broader conservative management strategy for CLTI.

5.3 Research implications / key gaps:

- **Comparative Effectiveness Trials:** Conduct randomized controlled trials comparing SCS to best medical therapy or other conservative interventions in CLTI/PAD patients not eligible for revascularization, with limb salvage and long-term functional outcomes as primary endpoints [3, 33].
- **Optimal Stimulation Parameters:** Investigate the optimal SCS parameters (e.g., frequency, pulse width, amplitude, lead placement, paddle vs. cylindrical leads) for improving microcirculation and promoting wound healing in CLTI, potentially through prospective cohort studies [10, 11].
- **Mechanisms of Action in CLTI:** Elucidate the precise neurovascular mechanisms by which SCS improves limb perfusion and pain in CLTI, potentially using advanced imaging and physiological markers in experimental or clinical studies [32, 34].
- **Long-term Outcomes and Durability:** Establish the long-term efficacy and durability of SCS for limb salvage, pain relief, and quality of life beyond 2 years, particularly in diverse CLTI/PAD populations [1, 2, 4].
- **Non-invasive SCS for CLTI:** Explore the feasibility and efficacy of transcutaneous spinal cord stimulation (tSCS) or other non-invasive neuromodulation techniques as an alternative or adjunct to implanted SCS for CLTI, drawing lessons from SCI applications [7, 9].

5.4 Limitations:

- **Retrospective Study Designs** — Many studies were retrospective or mixed designs [1, 2, 8, 12, 22], limiting the ability to establish causality and control for confounding variables.
- **Small Sample Sizes** — The sample sizes in several key studies on CLTI/PAD were small (e.g., N=13, N=29, N=34) [1, 2, 4], which restricts the generalizability of findings.
- **Heterogeneous Populations** — The included literature covered diverse populations, from CLTI/PAD to chronic pain and spinal cord injury, making direct comparisons and synthesis challenging for specific indications.
- **Lack of Control Groups** — Many studies on CLTI/PAD lacked a concurrent control group, making it difficult to definitively attribute observed improvements solely to SCS rather than natural disease progression or concomitant therapies.

- **Limited Mechanistic Understanding** — While some studies touched on spinal reflexes and pain pathways [29, 31, 32, 34], a comprehensive understanding of SCS mechanisms in CLTI is still emerging.

5.5 Future directions:

- **Randomized Controlled Trials** — Conduct RCTs for SCS in CLTI.
- **Standardized Outcome Metrics** — Develop and use consistent outcome measures.
- **Biomarker Identification** — Discover biomarkers for SCS response.
- **Long-Term Follow-up** — Extend follow-up beyond 2 years.
- **Cost-Effectiveness Analysis** — Evaluate economic impact of SCS.

6) Conclusion

For patients with chronic limb-threatening ischemia (CLTI) or end-stage peripheral artery disease (PAD) unsuitable for revascularization, spinal cord stimulation (SCS) demonstrated a median limb salvage rate of 94.65% (range: 92.3% to 97%) at 1-year follow-up [1, 2]. These findings, primarily from cohort studies, suggest that SCS is a promising intervention for preserving limbs and improving quality of life in this challenging patient group. However, the reliance on retrospective and mixed study designs with relatively small sample sizes represents the most significant limitation, impacting the certainty and generalizability of the results. Future randomized controlled trials are critically needed to establish the definitive efficacy and optimal application of SCS in CLTI.

References

SAIMSARA Session Index — session.json

Figure 1. Publication-year distribution of included originals

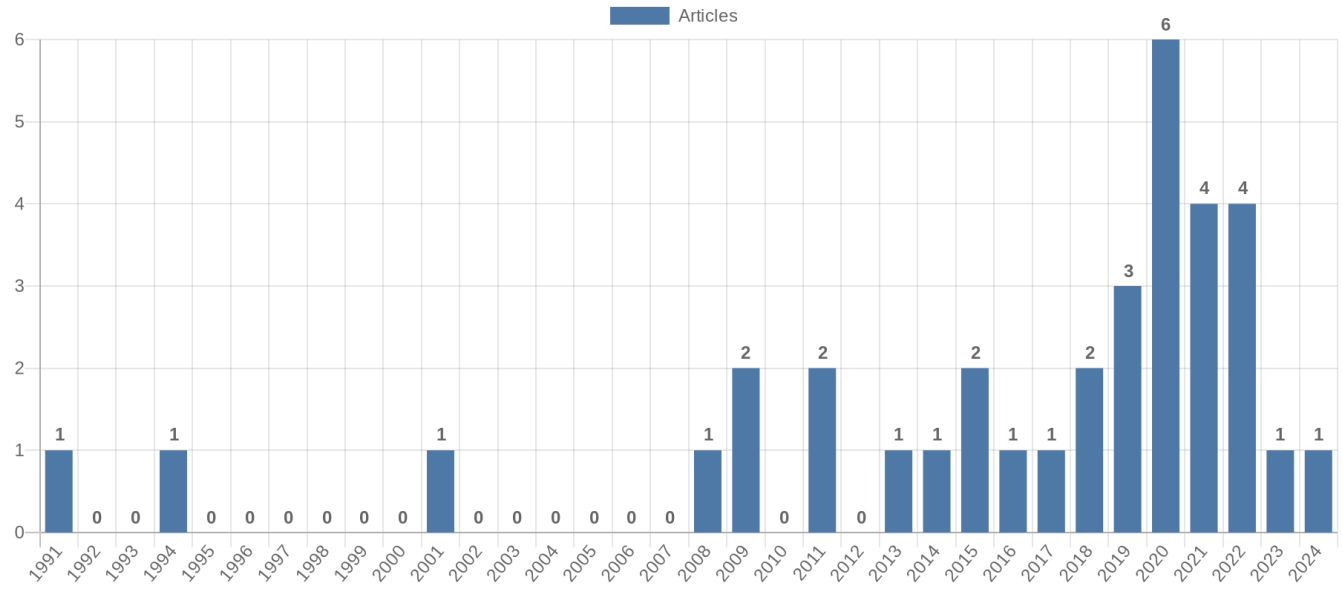


Figure 2. Study-design distribution of included originals

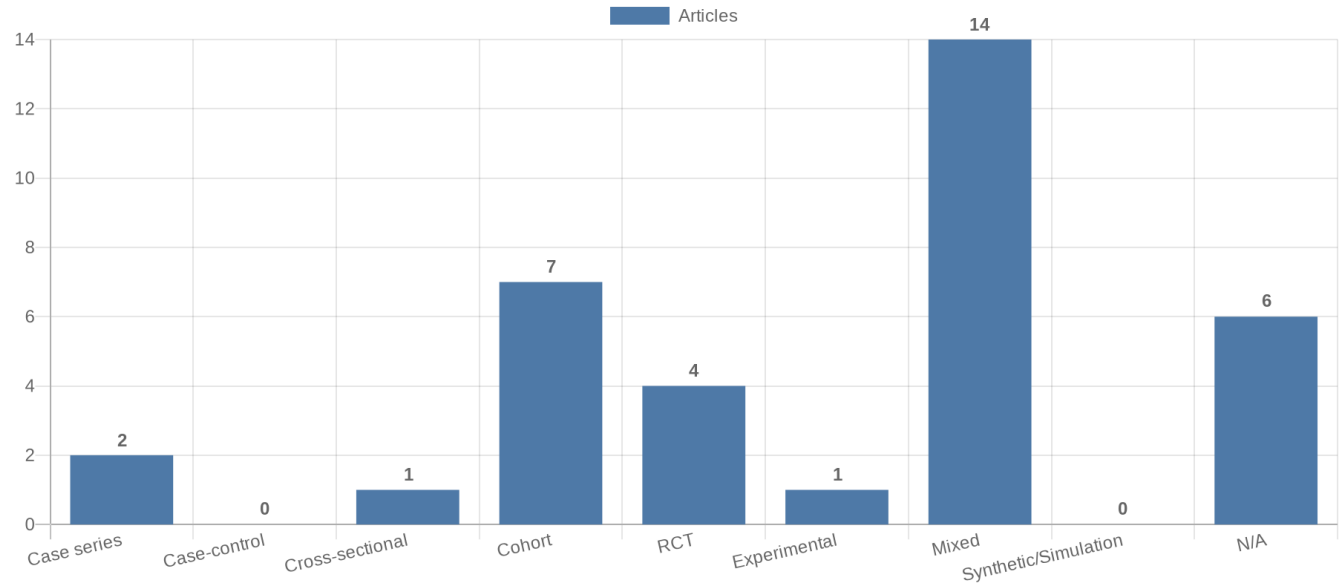


Figure 3. Study-type (directionality) distribution of included originals

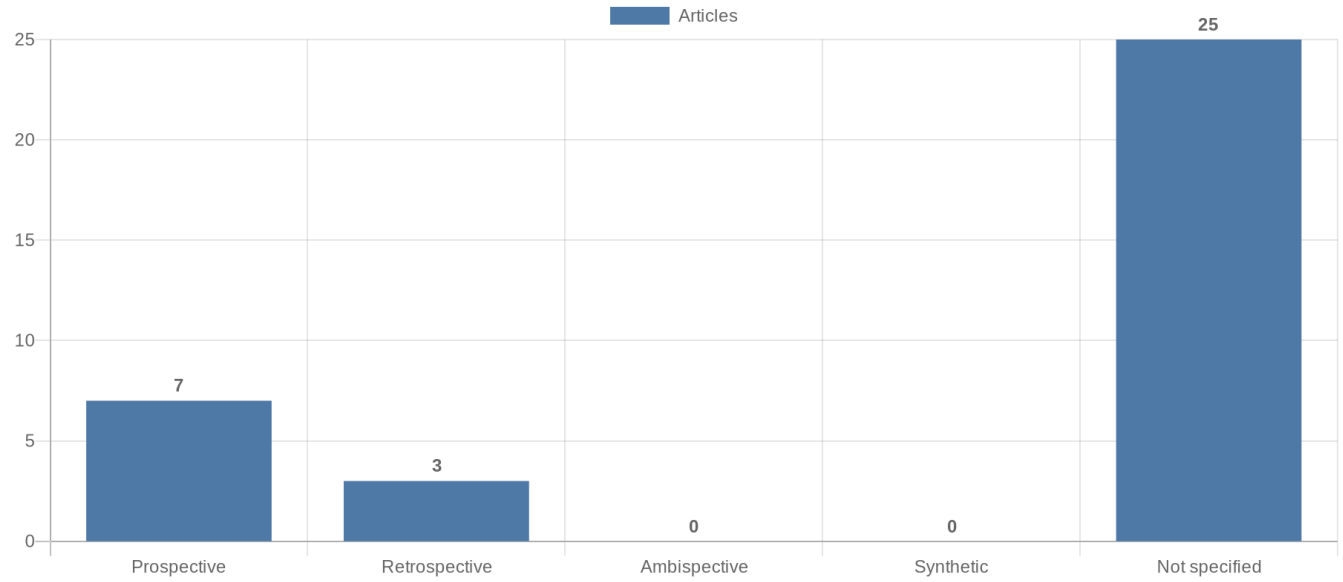


Figure 4. Main extracted research topics

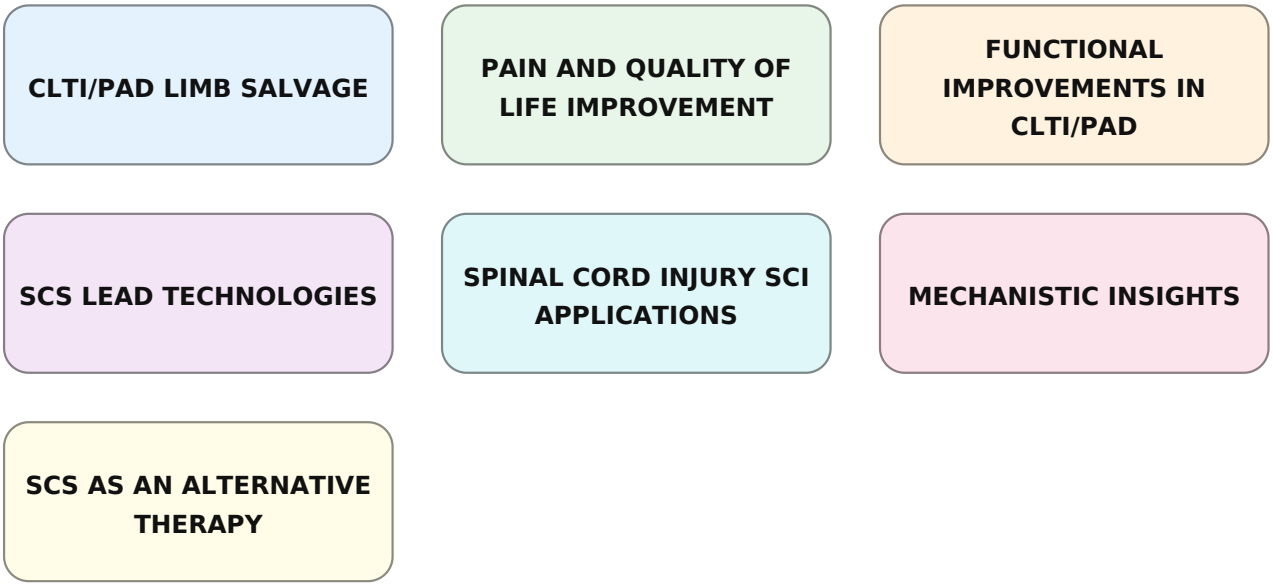


Figure 5. Limitations of current studies (topics)

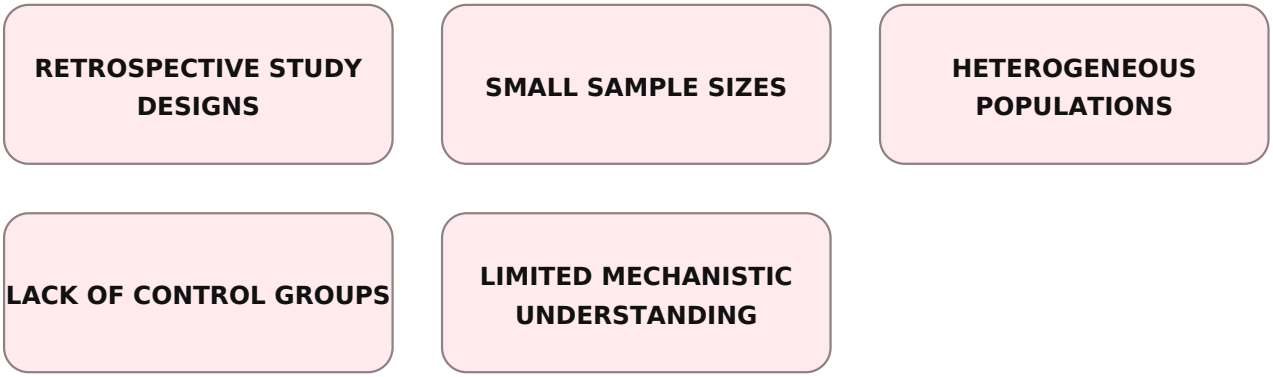


Figure 6. Future research directions (topics)