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Review Article

Targeted muscle reinnervation and regenerative peripheral nerve interface for the prevention and management of post-amputation pain: A systematic review.

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Abstract

Background

Post-amputation pain, including phantom limb pain, residual limb pain, and neuroma-related pain, remains a persistent clinical problem despite advances in surgical care. Physiologic nerve reconstruction techniques such as targeted muscle reinnervation (TMR) and regenerative peripheral nerve interface (RPNI) have been introduced to improve nerve regeneration and reduce neuropathic pain following limb loss.

Objective: To evaluate the clinical effectiveness of TMR and RPNI in preventing and treating post-amputation pain.

Methods

A systematic review was conducted according to PRISMA 2020 guidelines. PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar were searched through January 2026. Eligible studies included peer-reviewed clinical investigations evaluating TMR and/or RPNI in upper- or lower-limb amputees reporting pain-related outcomes. Risk of bias was assessed using ROB-2 and ROBINS-I tools.

Results

Six studies were included: one randomized clinical trial and five prospective or retrospective studies. In the randomized trial, TMR produced significantly greater reduction in phantom limb pain compared with standard neuroma excision (mean change −3.2 vs −0.2 on a 0–10 scale; $p < 0.05$). Prophylactic TMR reduced symptomatic phantom limb pain incidence (19% vs 47%; $p < 0.05$). TMR was also associated with significant improvements in residual limb pain and PROMIS pain interference scores at 12 months ($p < 0.05$). Prophylactic RPNI reduced symptomatic neuroma formation (0% vs 13%; $p < 0.05$). Complications were infrequent and predominantly minor.

Conclusion

TMR and RPNI reduce post-amputation pain, particularly when performed prophylactically.

Further research

Large multicenter randomized trials with standardized outcome measures are needed to define optimal timing and long-term effectiveness.

Keywords: *Amputation, Neuroma, Phantom limb pain, Post-amputation pain, Regenerative peripheral nerve interface, Residual limb pain, Targeted muscle reinnervation*
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Introduction

Limb amputation is a life-altering procedure that is frequently complicated by chronic pain syndromes, which substantially impair quality of life, psychological well-being, and functional recovery[1,2]. Despite advances in surgical technique, perioperative care, and rehabilitation, post-amputation pain remains a prevalent and challenging clinical problem[3-5]. It is estimated that a significant proportion of amputees experience persistent pain, which may persist for years following surgery and negatively affect prosthetic tolerance and long-term rehabilitation outcomes[6-8].

Post-amputation pain encompasses a spectrum of neuropathic conditions, most commonly phantom limb pain, residual limb pain, and pain arising from symptomatic neuroma formation[3,9]. Phantom limb pain is characterized by painful sensations perceived in the absent limb, while residual limb pain originates from the amputation stump and may be associated with mechanical irritation, ischemia, or nerve injury[4,10-13]. Symptomatic neuromas develop as a result of aberrant axonal regeneration following nerve transection and are a major contributor to chronic residual limb pain[14,15]. These pain syndromes are often refractory to conventional medical management, including pharmacologic therapy and neuromodulation, and can significantly limit prosthetic use, mobility, and overall functional independence[10,16].

Traditional nerve management techniques employed during amputation, such as traction neurectomy, nerve ligation, or burying nerve ends within surrounding soft tissues, aim to reduce neuroma formation by physically isolating transected nerves. However, these approaches do not provide a physiologic target for regenerating axons[17,18]. Consequently, regenerating nerve fibers often undergo disorganized growth, leading to ectopic neural firing, hypersensitivity, and persistent neuropathic pain. The limitations of these conventional techniques have prompted the development of alternative strategies focused on restoring more physiologic nerve regeneration[19,20].

Targeted muscle reinnervation (TMR) was initially introduced as a method to improve myoelectric prosthetic control by transferring transected peripheral nerves to redundant motor nerve branches innervating nearby muscles. By reestablishing nerve–muscle continuity, TMR allows regenerating axons to innervate functional motor end plates, thereby generating meaningful electromyographic signals for prosthetic control. Subsequent clinical observations demonstrated that this physiologic redirection of nerve regeneration also markedly reduces neuroma formation and phantom limb pain, positioning TMR as a promising strategy for both functional restoration and pain prevention[21-23].

Regenerative peripheral nerve interface (RPNI) was later developed as an alternative nerve reconstruction technique aimed at achieving similar goals through a different surgical approach. RPNI involves implantation of transected peripheral nerves into free, denervated muscle grafts, which serve as biologic scaffolds for axonal ingrowth and reinnervation. By providing a stable and receptive end organ for regenerating axons, RPNI facilitates organized nerve regeneration, reduces neuroma formation, and enhances signal transduction[24-26]. Compared with TMR, RPNI may offer technical advantages in certain clinical scenarios, particularly when suitable motor nerve targets are limited[27].

With growing clinical adoption of both TMR and RPNI in primary and revision amputation surgery, there is increasing interest in their role as preventive and therapeutic strategies for post-amputation pain. However, existing evidence is derived from studies with varying designs, patient populations, and outcome measures. A systematic evaluation of the available clinical literature is therefore necessary to critically assess the effectiveness of TMR and RPNI in managing post-amputation pain and to guide evidence-based clinical decision-making.

Materials and methods

Study design

This study was designed as a systematic review evaluating the clinical effectiveness of targeted muscle reinnervation (TMR) and regenerative peripheral nerve interface (RPNI) in the prevention and treatment of post-amputation pain. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines[28].

Review question

What is the effectiveness of targeted muscle reinnervation and regenerative peripheral nerve interface in reducing post-amputation pain, including phantom limb pain, residual limb pain, and neuroma-related pain?

Search strategy

A comprehensive electronic search was performed in the following databases: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The final search was conducted on 15 January 2026. The databases were searched from inception to 15 January 2026. No date restrictions were applied.

The following search terms and Boolean combinations were used:

"targeted muscle reinnervation," "regenerative peripheral nerve interface," "TMR," "RPNI," "amputation," "post-amputation pain," "phantom limb pain," "residual limb pain," and "neuroma."

Reference lists of eligible articles were manually screened to identify additional relevant studies.

Eligibility criteria

Inclusion criteria

Studies were included if they met all of the following criteria:

- Original peer-reviewed clinical studies
- Human subjects undergoing upper- or lower-limb amputation
- Evaluation of TMR and/or RPNI
- Reporting outcomes related to post-amputation pain
- Published in the English language

Exclusion criteria

Studies were excluded if they met any of the following criteria:

- Animal, cadaveric, or laboratory-based studies
- Technical descriptions without clinical outcome data
- Review articles, editorials, or expert opinion papers
- Conference abstracts without full-text availability

Study selection

Titles and abstracts of all retrieved records were screened to exclude irrelevant studies. Full-text articles were subsequently assessed for eligibility based on the predefined inclusion and exclusion criteria. Study selection was performed independently by two reviewers. Disagreements were resolved through discussion and consensus. Several studies that initially appeared relevant were excluded after full-text review. For example, Fulton et al. (2022) were excluded because it was a systematic review rather than a primary clinical study. Chappell et al. (2025) was excluded as it provided a narrative review of TMR techniques without original outcome data. Hespe and Brown (2024) described dermal sensory RPNI but did not report standardized post-amputation pain outcomes. Vu et al. (2020) was excluded because its primary outcome was prosthetic control performance rather than pain-related outcomes. These studies were excluded in accordance with predefined eligibility criteria requiring original clinical pain outcome data.

Data extraction

Data extraction was carried out using a standardized data collection form. The following information was extracted from each included study:

- Author and year of publication
- Study design
- Patient population and amputation level
- Intervention type (TMR or RPNI)
- Timing of intervention (primary or secondary)
- Duration of follow-up
- Pain-related outcomes and assessment methods

Data synthesis

Given the heterogeneity in study designs, patient populations, outcome measures, and follow-up durations, a quantitative meta-analysis was not performed. Instead, the results were synthesized using a qualitative narrative approach.

Effect measures

For continuous pain-related outcomes, including phantom limb pain and residual limb pain assessed using numeric rating scales (NRS), visual analog scales (VAS), or PROMIS pain interference scores, results were extracted as mean differences with corresponding measures of variance (standard deviation or confidence intervals) when reported.

For dichotomous outcomes, including incidence of symptomatic neuroma formation or presence of chronic phantom limb pain, data were extracted as proportions or risk differences between intervention and comparator groups.

Due to clinical and methodological heterogeneity across included studies, pooled effect estimates were not calculated. Effect measures were therefore presented descriptively in the qualitative synthesis.

Certainty of evidence

The certainty of evidence for key outcomes, including phantom limb pain reduction, residual limb pain reduction, and neuroma prevention, was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Certainty was assessed across the domains of risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Given the predominance of non-randomized study designs, small sample sizes, and heterogeneity in outcome measurement tools, the overall certainty of evidence was judged to range from low to moderate across outcomes.

Results

Study selection

The electronic database search identified 312 records across PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. After the removal of 96 duplicate records, 216 unique records remained for title and abstract screening. Of these, 183 records were excluded due to irrelevance to the review topic, non-clinical study design, or absence of outcomes related to post-amputation pain.

The full texts of 33 articles were assessed for eligibility. Following full-text review, 27 studies were excluded for the following reasons: animal or cadaveric studies (n = 8), technical or descriptive reports without clinical outcomes (n = 8), review articles or expert opinions (n = 6), and studies not specifically evaluating targeted muscle reinnervation or regenerative peripheral nerve interface for post-amputation pain (n = 5).

Ultimately, 6 studies met all inclusion criteria and were included in the final qualitative synthesis. The study selection process is summarized in the PRISMA flow diagram. (Figure 1)

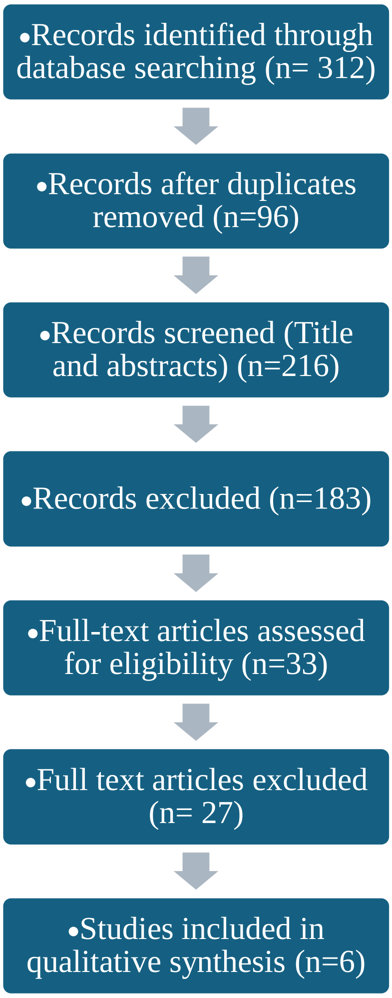

Figure 1: PRISMA flowchart

Study characteristics

The included studies comprised one randomized clinical trial, prospective cohort studies, and retrospective comparative or case-series studies evaluating targeted muscle reinnervation and regenerative peripheral nerve interface in amputee populations. Both upper and lower limb amputations were represented. Interventions were performed either prophylactically at the time of primary amputation or as secondary procedures for the management of established post-amputation pain. The key characteristics of the included studies are summarized in Table 1.

Table 1. Characteristics of included studies

Study	Design	Sample Size	Outcome	Intervention Group Result	Comparator Result	Effect Estimate	Precision	p-value
Dumanian 2019	RCT	TMR (n=28) vs Control (n=25)	PLP (NRS 0–10)	−3.2 mean change	−0.2 mean change	MD −3.0	95% CI reported in the study	<0.05
Valerio 2019	Retrospective cohort	TMR (n=51) vs Control (n=51)	Chronic PLP incidence	19%	47%	Risk difference −28%	CI not reported	<0.05
Mioton 2020	Prospective cohort	n=33	PROMIS Pain Interference	Significant reduction at 12 mo	—	Mean change reported	SD reported	<0.05
Kubiak 2019	Retrospective comparative	RPNI (n=45) vs Control (n=45)	Symptomatic neuroma	0%	13%	Risk difference −13%	CI not reported	<0.05
Woo 2016	Case series	n=16	Neuroma pain	Marked reduction	—	Descriptive	—	—
Cheesborough 2014	Case report	n=1	PLP	None reported	—	Descriptive	—	—

Pain outcomes

Across studies evaluating targeted muscle reinnervation, consistent reductions in phantom limb pain and residual limb pain were reported. The randomized clinical trial demonstrated significantly lower pain scores in patients undergoing TMR compared with conventional neuroma management techniques. Prophylactic application of TMR at the time of amputation was associated with a lower incidence and severity of chronic post-amputation pain during follow-up.

Studies evaluating regenerative peripheral nerve interface similarly demonstrated meaningful reductions in neuroma-related pain and phantom limb pain. Patients undergoing prophylactic RPNI exhibited lower rates of symptomatic neuroma formation and chronic neuropathic pain compared with standard nerve management approaches.

Complications

Reported complications across the included studies were infrequent and generally minor, consisting primarily of wound-related issues. No study reported a significant increase in surgical morbidity attributable to either targeted muscle reinnervation or regenerative peripheral nerve interface.

Risk of bias

Risk-of-bias assessment demonstrated a low overall risk for the randomized clinical trial, while non-randomized studies were judged to have a moderate risk of bias, primarily related to confounding and study design. No study demonstrated a high risk of bias in outcome measurement or reporting. The results of the risk-of-bias assessment are presented in Table 2.

Table 2. Risk-of-bias assessment of included studies: Randomized study (ROB-2 Tool)

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Outcome Measurement	Overall Risk
Dumanian et al. (2019)[35]	Low	Low	Low	Low	Low risk

Table 3: Non-randomized studies (ROBINS-I Tool)

Study	Confounding	Selection Bias	Classification of Intervention	Outcome Measurement	Reporting Bias	Overall Risk
Cheesborough et al. (2014)[31]	Moderate	Moderate	Low	Low	Low	Moderate
Woo et al. (2016)[32]	Moderate	Moderate	Low	Low	Low	Moderate
Kubiak et al. (2019)[33]	Moderate	Low	Low	Low	Low	Moderate
Valerio et al. (2019)[34]	Moderate	Low	Low	Low	Low	Moderate
Mioton et al. (2020)[36]	Moderate	Low	Low	Low	Low	Moderate

Investigation of heterogeneity

Clinical heterogeneity was assessed qualitatively based on amputation level, timing of intervention (primary vs secondary), study design, and outcome measurement tool. Greater analgesic benefit was observed in studies implementing prophylactic TMR or RPNI at the time of amputation compared with delayed intervention. Variability in pain assessment instruments (NRS, VAS, PROMIS) limited direct quantitative comparison. Due to substantial clinical and methodological heterogeneity, statistical heterogeneity (I^2) was not calculated.

Sensitivity analysis

Formal sensitivity analyses were not performed due to the absence of quantitative meta-analysis. However, exclusion of case reports and small case-series studies did not alter the overall direction of findings, as the randomized clinical trial and comparative cohort studies consistently demonstrated a reduction in post-amputation pain following TMR or RPNI.

Assessment of reporting bias

Given the limited number of included studies (n=6), formal assessment of publication bias using funnel plots was not feasible. Selective reporting within studies was assessed during ROB-2 and ROBINS-I evaluation. No evidence of high risk of selective outcome reporting was identified; however, small sample sizes and single-center designs increase the possibility of publication bias.

Certainty of evidence

Using the GRADE framework, certainty of evidence was rated separately for key outcomes:
Phantom limb pain reduction: Moderate certainty (downgraded for imprecision)
Residual limb pain reduction: Low to moderate certainty (downgraded for study design limitations)
Neuroma prevention: Low certainty (downgraded for non-randomized design and imprecision)
Overall certainty was limited by small sample sizes and predominance of observational studies.

Discussion

This systematic review demonstrated that targeted muscle reinnervation (TMR) and regenerative peripheral nerve interface (RPNI) were effective surgical strategies for reducing post-amputation pain, including phantom limb pain, residual limb pain, and neuroma-related pain by addressing the biological mechanisms underlying disordered nerve regeneration. The analgesic effects observed across the included studies supported the long-standing surgical principle that providing a physiologic end-organ target for regenerating axons reduced painful neuroma formation and aberrant neuropathic signaling. Earlier work by Dellon and Mackinnon (1986)[37] showed that implantation of nerve ends into muscle following neuroma excision produced clinical benefit, while Sunderland (1990)[38] described how injured nerves predictably attempted regeneration and could form symptomatic neuromas in the absence of appropriate distal targets. Mechanistic evidence further strengthened this rationale, as Devor et al. (1993)[39] demonstrated injury-related changes in sodium channel expression and distribution during neuroma formation that contributed to neural hyperexcitability and pain. Collectively, these foundational studies supported the premise that modern physiologic nerve reconstruction techniques, such as TMR and RPNI, reduced neuropathic pain by creating stable and biologically appropriate targets for nerve ingrowth.

The included clinical studies[31-36] consistently suggested that post-amputation pain was influenced by both peripheral and central mechanisms and that modifying peripheral nerve biology could influence clinically meaningful pain outcomes. Vaso et al. (2014)[40] provided evidence supporting a peripheral nervous system origin for phantom limb pain in a subset of patients, which aligned with the clinical improvements reported following peripheral nerve reconstruction. Concurrently, phantom limb pain had been conceptualized as a manifestation of maladaptive central nervous system plasticity, with Flor (2002)[41] and Flor et al. (2006)[42] describing mechanisms of altered sensory processing and cortical reorganization following limb loss. Neuroimaging studies further demonstrated associations between phantom movements and pain (Lotze et al., 2001)[43], while Raffin et al. (2016)[44] showed that changes in the primary motor cortex correlated with phantom limb pain and the ability to move the phantom limb, reinforcing the role of abnormal sensorimotor integration in pain persistence. Giummarra and Moseley (2011)[45] additionally emphasized the contribution of bodily awareness and multisensory integration to phantom limb pain, suggesting that effective peripheral nerve stabilization could plausibly reduce abnormal afferent input that fueled central amplification. When considered together, these mechanistic and neurobiological findings supported the observed clinical pattern in which early, biologically informed peripheral nerve reconstruction was associated with improved pain outcomes.

Among the included TMR studies, the strongest evidence for efficacy was provided by the randomized clinical trial conducted by Dumanian et al. (2019)[35], which demonstrated that TMR significantly reduced neuroma pain and phantom limb pain compared with standard neuroma excision and conventional nerve management.

This randomized evidence strengthened causal inference and helped distinguish the effect of physiologic nerve reconstruction from the nonspecific benefit of surgical revision alone. The preventive effect of TMR was particularly evident when correlated with the findings of Valerio et al. (2019)[34], who reported reduced phantom limb pain and residual limb pain when TMR was performed preemptively at the time of major limb amputation. This observation suggested that prophylactic intervention may have limited the establishment of persistent neuropathic pain pathways, consistent with neuroplasticity frameworks described by Flor (2002)[41] and Flor et al. (2006)[42]. The prospective study by Mioton et al. (2020)[36] further complemented these findings by demonstrating that TMR improved phantom limb pain, residual limb pain, and limb function in a cohort of major limb amputees, supporting both analgesic and functional relevance, indicating that pain reduction was accompanied by measurable improvements in patient-centered outcomes. Taken together, the concordance among Dumanian et al. (2019)[35], Valerio et al. (2019)[34], and Mioton et al. (2020)[36] suggested a coherent evidence pattern in which TMR conferred benefit across both therapeutic and prophylactic settings and across pain and functional domains, with outcomes appearing more favorable when nerve reconstruction was integrated early. The remaining included TMR studies strengthened the generalizability and feasibility of these findings. Bowen et al. (2019)[46] described a targeted muscle reinnervation technique specifically for below-knee amputation, supporting the applicability of TMR to a common amputation level and suggesting that procedural standardization could facilitate broader clinical adoption. Cheesborough et al. (2014)[31] reported the feasibility of TMR in the initial management of traumatic upper-extremity amputation, reinforcing that TMR could be implemented in acute trauma settings and supporting the practicality of an early-intervention approach outside elective circumstances. Together, these studies complemented higher-level evidence by demonstrating that TMR could be adapted across different anatomical contexts and clinical pathways, thereby supporting the external validity of the primary clinical conclusions.

The RPNI studies included in this review provided convergent evidence that a biologic muscle target could reduce neuroma-related pain through a distinct technical approach, reinforcing the principle that target-based nerve regeneration rather than the specific coaptation strategywas a central driver of analgesic benefit. Woo et al. (2016)[32] reported that RPNI reduced post-amputation neuroma pain in a pilot clinical study, supporting its role as a therapeutic intervention for established neuroma-related pain. Kubiak et al. (2019)[33] extended this approach into prevention by demonstrating that prophylactic RPNI reduced post-amputation pain, paralleling the prophylactic benefit observed with TMR in Valerio et al. (2019)[34]. When the prophylactic TMR and prophylactic RPNI evidence were considered together, both approaches supported the concept that early provision of a physiologic target for nerve regeneration reduced the later development of chronic neuropathic pain. The translational relevance of RPNI as a stable biologic interface was further supported by Vu et al. (2020)[47], who demonstrated that RPNI enabled real-time control of an artificial hand, indicating that reinnervated muscle grafts could support reliable neural signal generation. This functional signal evidence aligned conceptually with the foundational objective of TMR to create useful myoelectric signals through reinnervated muscles (Kuiken et al., 2007[48]; Kuiken et al., 2009[49]) and suggested that both techniques facilitated organized nerve–muscle integration that plausibly reduced disordered pain signaling.

The dual functional role of TMR was further supported by prior prosthetic control literature, which provided indirect mechanistic reinforcement for its analgesic potential. Kuiken et al. (2007)[48] demonstrated enhanced prosthetic function following targeted reinnervation in a proximal amputee, while Kuiken et al. (2009)[49] showed real-time myoelectric control of multifunction artificial arms after TMR, supporting the concept that transferred nerves achieved stable reinnervation and meaningful physiologic continuity. Hargrove et al. (2013)[50] similarly demonstrated robotic leg control with EMG decoding in an amputee who underwent nerve transfers, reinforcing the principle that nerve transfer–based approaches could support robust bioelectric interfaces. Although these studies primarily focused on function rather than pain outcomes, they strengthened the biological plausibility that reinnervated muscle targets acted as effective end organs for regenerating axons, aligning with the analgesic benefits observed in clinical pain-focused TMR studies. Johnson et al. (2021)[51] subsequently framed TMR as a paradigm shift in neuroma management and prosthesis control, supporting the broader interpretation that TMR operated at the intersection of pain prevention and functional restoration.

In contrast, traditional approaches to neuroma prevention and treatment demonstrated variable outcomes, reinforcing the rationale for adopting physiologic reconstruction methods. Pet et al. (2015)[52] reported outcomes of traction neurectomy for painful residual limb neuroma, illustrating the persistent clinical challenge of managing neuroma pain using conventional strategies. Domeshek et al. (2017)[53] demonstrated that surgical treatment of neuromas improved not only patient-reported pain but also depression and quality of life, highlighting the broader impact of effective nerve management and supporting the clinical significance of reducing neuroma-related pain beyond symptom scores alone. Scott et al. (2022)[54] reviewed surgical approaches for neuroma prevention at the time of peripheral nerve injury and emphasized the growing interest in proactive strategies, which aligned with the prophylactic emphasis observed in Valerio et al. (2019)[34] and Kubiak et al. (2019)[33]. Fulton et al. (2022)[55] synthesized evidence supporting the role of TMR in trauma-related amputees, providing additional context that reinforced the feasibility and clinical momentum of integrating TMR into acute injury pathways, as suggested by Cheesborough et al. (2014)[31]. Despite these encouraging findings, the evidence base remained limited by small sample sizes, heterogeneous outcome measures, variable follow-up durations, and the predominance of non-randomized study designs in several included studies. Pain assessment tools varied considerably, limiting direct comparisons of effect size, and patient populations differed by amputation level, etiology, and timing of intervention, contributing to clinical heterogeneity. Nevertheless, the consistency in outcome direction across included studies particularly the randomized trial evidence from Dumanian et al. (2019)[35], the prophylactic cohort evidence from Valerio et al. (2019)[34] and Kubiak et al. (2019)[33], the prospective outcome data from Mioton et al. (2020)[36] and the therapeutic RPNI signal from Woo et al. (2016)[32] supported the conclusion that physiologic nerve reconstruction reduced post-amputation pain and represented a meaningful advancement over traditional nerve management approaches. When interpreted alongside mechanistic and neurobiological evidence describing peripheral nerve hyperexcitability and maladaptive central plasticity[38-44], these findings suggested that integrating TMR or RPNI into primary or revision amputation care could reduce neuroma formation, decrease chronic neuropathic pain, improve patient-reported outcomes and potentially enhance functional rehabilitation, while underscoring the need for additional multicenter randomized trials with standardized endpoints to clarify optimal timing, technique selection and long-term durability.

The findings of this review must be interpreted in light of important limitations within both the included evidence and the review process. The available literature is dominated by small, predominantly single-center observational studies, with only one randomized clinical trial, limiting causal inference and increasing susceptibility to selection bias, confounding, and imprecision. Sample sizes were modest, confidence intervals were inconsistently reported, and outcome assessment tools varied widely, including numeric rating scales, visual analog scales, PROMIS instruments, and incidence-based reporting, precluding quantitative pooling and limiting direct comparability. Follow-up durations were generally short to intermediate, restricting conclusions regarding the long-term durability of analgesic benefit. Most studies originated from specialized centers in the United States, which may limit generalizability across healthcare systems. Within the review process, exclusion of non-English and unpublished studies may have introduced publication bias, and formal meta-analysis, funnel plot assessment, and extensive sensitivity analyses were not feasible due to heterogeneity and the small number of studies. Despite these constraints, the consistency in direction of effect across randomized and comparative cohorts supports the clinical relevance of physiologic nerve reconstruction. For practice, integration of targeted muscle reinnervation or regenerative peripheral nerve interface at the time of amputation may reduce chronic phantom limb pain and symptomatic neuroma formation and potentially decrease long-term opioid reliance and revision procedures. At the policy level, these findings support consideration of incorporating physiologic nerve reconstruction into standardized amputation care pathways, while emphasizing the need for multicenter randomized trials with standardized outcome reporting to inform definitive clinical guidelines.

Conclusion

This systematic review demonstrated that targeted muscle reinnervation and regenerative peripheral nerve interface were effective surgical strategies for reducing post-amputation pain, including phantom limb pain, residual limb pain, and neuroma-related pain, by providing regenerating peripheral nerves with a physiologic muscle target. Early or prophylactic application at the time of amputation was consistently associated with superior pain outcomes compared with conventional nerve management, while secondary application also resulted in meaningful symptom reduction. Although targeted muscle reinnervation offered additional benefits related to prosthetic signal generation, the regenerative peripheral nerve interface provided a technically versatile alternative with comparable analgesic effects. Despite encouraging findings, heterogeneity in study design and outcome measures highlighted the need for further high-quality randomized trials to establish standardized, evidence-based clinical guidelines.

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List of abbreviations

TMR – Targeted Muscle Reinnervation
RPNI – Regenerative Peripheral Nerve Interface
PLP – Phantom Limb Pain
NRS – Numeric Rating Scale
VAS – Visual Analog Scale
PROMIS – Patient-Reported Outcomes Measurement Information System
ROB-2 – Risk of Bias 2 Tool
ROBINS-I – Risk Of Bias In Non-randomized Studies of Interventions
GRADE – Grading of Recommendations Assessment, Development and Evaluation

Author contributions

Dr. Karthik Shunmugavelu conceptualized the study, developed the review protocol, performed literature screening and data extraction, conducted risk-of-bias assessment, and drafted the manuscript.

Dr. Evangeline Cynthia Dhinakaran contributed to data extraction, methodological appraisal, interpretation of findings, and critical revision of the manuscript for intellectual content.

Dr. Manigandan Dhatchnamoorthy contributed to study selection, data verification, interpretation of clinical implications, and final manuscript approval.

All authors reviewed and approved the final version of the manuscript.

Author biography

Dr. Karthik Shunmugavelu is an academic clinician with advanced training in oral and maxillofacial pathology and translational research, with scholarly interests in neuropathic pain mechanisms, regenerative biology, and surgical innovation.

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Dr. Manigandan Dhatchnamoorthy is an orthopedic surgeon with clinical experience in limb trauma, amputation surgery, and musculoskeletal rehabilitation.

Registration and protocol

This systematic review was conducted in accordance with PRISMA 2020 guidelines. The review protocol was not prospectively registered in PROSPERO or any other international systematic review registry.

Support

No external financial funding was received for this review. The study was conducted using institutional academic resources. No sponsor or funding body had any role in study design, literature search, data extraction, analysis, interpretation of findings, manuscript preparation, or decision to submit for publication.

Competing interests

The authors declare that they have no competing financial or non-financial interests related to this work.

Availability of data, code, and other materials

The data extraction form used in this review is available from the corresponding author upon reasonable request. Extracted study data and risk-of-bias assessments are available upon request. No analytic code was generated, as quantitative meta-analysis was not performed. All included studies are publicly available through the respective indexed databases cited in the manuscript.

References

1. Grzebień A, Chabowski M, Malinowski M et al. Analysis of selected factors determining quality of life in patients after lower limb amputation- a review article. Pol Przegl Chir 2017; 89(2): 57-61. https://doi.org/10.5604/01.3001.0009.8980. PMid:28537564
2. Loyal, S., & Hanna, E. (2024). The Psychological Preparation of Patients for Amputation Surgery: A Narrative Review of the Literature. Sage Open, 14(4). https://doi.org/10.1177/21582440241295940
3. Hsu E, Cohen SP. Postamputation pain: epidemiology, mechanisms and treatment. J Pain Res. 2013;6:121-36. doi: 10.2147/JPR.S32299. Epub 2013 Feb 13. PMID: 23426608; PMCID: PMC3576040.
4. Doshi TL, Dolomisiewicz E, Caterina MJ, Belzberg A, Kastl AJ, Cohen SP. Postamputation pain: a multidisciplinary review of epidemiology, mechanisms, prevention and treatment. Reg Anesth Pain Med. 2025 Feb 5;50(2):175-183. https://doi.org/10.1136/rapm-2024-105817 PMid:39909547
5. Srivastava D. Chronic post-amputation pain: peri-operative management - Review. Br J Pain. 2017 Nov;11(4):192-202. https://doi.org/10.1177/2049463717736492 PMid:29123664 PMCid:PMC5661696
6. Jo SH, Kang SH, Seo WS, Koo BH, Kim HG, Yun SH. Psychiatric understanding and treatment of patients with amputations. Yeungnam Univ J Med. 2021 Jul;38(3):194-201. https://doi.org/10.12701/yujm.2021.00990 PMid:33971697 PMCid:PMC8225497
7. Erlenwein, Joachima,*; Diers, Martinb; Ernst, Jenniferc; Schulz, Friederiked; Petzke, Franka. Clinical updates on phantom limb pain. PAIN Reports 6(1):p e888, | https://doi.org/10.1097/PR9.0000000000000888 PMid:33490849 PMCid:PMC7813551
8. Z B Perkins, H D De'Ath, G Sharp, N R M Tai, Factors affecting outcome after traumatic limb amputation, British Journal of Surgery, Volume 99, Issue Supplement_1, January 2012, Pages 75-86, https://doi.org/10.1002/bjs.7766 PMid:22441859
9. Nees TA, Matt C, Deisenhofer J, Block J, Wolf SI, Renkawitz T, Lehner B, Alimusaj M. Pain After Lower Limb Amputations: Insights from the Heidelberg Amputation Registry. Medicina. 2024; 60(11):1887. https://doi.org/10.3390/medicina60111887 PMid:39597072 PMCid:PMC11597051
10. Hanyu-Deutmeyer AA, Cascella M, Varacallo MA. Phantom Limb Pain. [Updated 2023 Aug 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448188/
11. Tian S, Nick S, Wu H. Phantom limb pain: A review of evidence-based treatment options. World J Anesthesiol 2014; 3(2): 146-153 [DOI: 10.5313/wja.v3.i2.146] https://doi.org/10.5313/wja.v3.i2.146
12. Ahmed A, Bhatnagar S, Mishra S, Khurana D, Joshi S, Ahmad SM. Prevalence of Phantom Limb Pain, Stump Pain, and Phantom Limb Sensation among the Amputated Cancer Patients in India: A Prospective, Observational Study. Indian J Palliat Care. 2017 Jan-Mar;23(1):24-35.

https://doi.org/10.4103/0973-1075.197944 PMid:28216859 PMCid:PMC5294433

13. Stover, Gary & Prahlow, Nathan. (2020). Residual limb pain: An evidence-based review. NeuroRehabilitation. 47. 10.3233/NRE-208005.https://doi.org/10.3233/NRE-208005 PMid:32986622
14. List EB, Krijgh DD, Martin E, Coert JH. Prevalence of residual limb pain and symptomatic neuromas after lower extremity amputation: a systematic review and meta-analysis. Pain. 2021 Jul 1;162(7):1906-1913. https://doi.org/10.1097/j.pain.0000000000002202 PMid:33470746
15. Ducic I, Yoon J, Eberlin KR. Treatment of Neuroma-induced Chronic Pain and Management of Nerve Defects with Processed Nerve Allografts. Plast Reconstr Surg Glob Open. 2019 Dec 19;7(12):e2467. https://doi.org/10.1097/GOX.0000000000002467 PMid:32537284 PMCid:PMC7288900
16. David Parvizi, Sugeeth Kandikattu, Ramtin Sahafi, Artin Allahverdian, Blake Han, Marcel P Fraix, Devendra K Agrawal. Multimodal Approaches for Pain Management and Improving Functional Outcomes Following Amputation. Journal of Orthopedics and Sports Medicine. 7 (2025): 449-463. https://doi.org/10.26502/josm.511500227
17. Hespe GE, Brown DL. Management of Neuropathic Pain with Neurectomy Combined with Dermal Sensory Regenerative Peripheral Nerve Interface (DS-RPNI). Semin Plast Surg. 2024 Jan 19;38(1):48-52. https://doi.org/10.1055/s-0043-1778041 PMid:38495065 PMCid:PMC10942836
18. Sisti andrea & Uygur, Safak & Lopez-Schultz, Samson & Konofaos, Petros. (2023). Nerve Capping Techniques for Neuroma Management: A Comprehensive Literature Review. Annals of Plastic Surgery. 92. https://doi.org/10.1097/SAP.0000000000003714 PMid:37962245
19. Foy CA, Kuffler DP. Limitations to clinically restoring meaningful peripheral nerve function across gaps and overcoming them. Exp Biol Med (Maywood). 2025 May 27;250:10566. https://doi.org/10.3389/ebm.2025.10566 PMid:40495880 PMCid:PMC12150083
20. Wan T, Li Q-C, Qin M-Y, Wang Y-L, Zhang F-S, Zhang X-M, Zhang Y-C, Zhang P-X. Strategies for Treating Traumatic Neuromas with Tissue-Engineered Materials. Biomolecules. 2024; 14(4):484. https://doi.org/10.3390/biom14040484 PMid:38672500 PMCid:PMC11048257
21. Chappell AG, Ramsey MD, Park S, Dumanian GA, Ko JH. Targeted Muscle Reinnervation-an Up-to-Date Review: Evidence, Indications and Technique. Arch Plast Surg. 2025 Apr 1;52(3):153-168. https://doi.org/10.1055/a-2521-2199 PMid:40386007 PMCid:PMC12081100
22. Pettersen E, Sassu P, Pedrini FA, Granberg H, Reinholdt C, Breyer JM, Roche A, Hart A, Ladak A, Power HA, Leung M, Lo M, Valerio I, Eberlin KR, Kung TA, Cederna P, Souza JM, Aszmann O, Ko J, Dumanian GA, Ortiz-Catalan M. Targeted Muscle Reinnervation: Surgical Protocol for a Randomized Controlled Trial in Postamputation Pain. J Vis Exp. 2024 Mar 8;(205). https://doi.org/10.3791/66379
23. Vadalà G, Di Pino G, Ambrosio L, Diaz Balzani L, Denaro V. Targeted muscle reinnervation for improved control of myoelectric upper limb prostheses. J Biol Regul Homeost Agents. 2017 Oct-Dec;31(4 suppl 1):183-189. PMID: 29188681.
24. Lee JC, Kemp SWP, Kung TA. Regenerative Peripheral Nerve Interface Surgery for the Management of Chronic Posttraumatic Neuropathic Pain. Semin Plast Surg. 2024 Jan 19;38(1):19-24. https://doi.org/10.1055/s-0043-1778078 PMid:38495062 PMCid:PMC10942837
25. Leach GA, Dean RA, Kumar NG, Tsai C, Chiarappa FE, Cederna PS, Kung TA, Reid CM. Regenerative Peripheral Nerve Interface Surgery: Anatomic and Technical Guide. Plast Reconstr Surg Glob Open. 2023 Jul 17;11(7):e5127. https://doi.org/10.1097/GOX.0000000000005127 PMid:37465283 PMCid:PMC10351954
26. González-Prieto J, Cristóbal L, Arenillas M, Giannetti R, Muñoz Frías JD, Alonso Rivas E, Sanz Barbero E, Gutiérrez-Pecharromán A, Díaz Montero F, Maldonado AA. Regenerative Peripheral Nerve Interfaces (RPNIs) in Animal Models and Their Applications: A Systematic Review. International Journal of Molecular Sciences. 2024; 25(2):1141. https://doi.org/10.3390/ijms25021141 PMid:38256216 PMCid:PMC10816042
27. Zimbulis AJ, An VVG, Symes M, et al. Targeted Muscle Reinnervation Compared to Standard Peripheral Nerve Management Following

Amputation: A Systematic Review and Meta-Analysis. HAND. 2024;20(8):1197-1206. https://doi.org/10.1177/15589447241284811 PMid:39469890 PMCid:PMC11559798

28. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. https://doi.org/10.1136/bmj.n71 PMid:33782057 PMCid:PMC8005924
29. Sterne J A C, SavoviÄ‡ J, Page M J, Elbers R G, Blencowe N S, Boutron I et al. RoB 2: a revised tool for assessing risk of bias in randomised trials BMJ 2019; 366:l4898 https://doi.org/10.1136/bmj.l4898 PMid:31462531
30. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016 Oct 12;355:i4919. https://doi.org/10.1136/bmj.i4919 PMid:27733354 PMCid:PMC5062054
31. Cheesborough JE, Souza JM, Dumanian GA, Bueno RA Jr. Targeted muscle reinnervation in the initial management of traumatic upper extremity amputation injury. Hand (N Y). 2014 Jun;9(2):253-7. https://doi.org/10.1007/s11552-014-9602-5 PMid:24839430 PMCid:PMC4022965
32. Woo SL, Kung TA, Brown DL, Leonard JA, Kelly BM, Cederna PS. Regenerative Peripheral Nerve Interfaces for the Treatment of Postamputation Neuroma Pain: A Pilot Study. Plast Reconstr Surg Glob Open. 2016 Dec 27;4(12):e1038. https://doi.org/10.1097/GOX.0000000000001038 PMid:28293490 PMCid:PMC5222635
33. Kubiak CA, Kemp SWP, Cederna PS, Kung TA. Prophylactic Regenerative Peripheral Nerve Interfaces to Prevent Postamputation Pain. Plast Reconstr Surg. 2019 Sep;144(3):421e-430e. https://doi.org/10.1097/PRS.0000000000005922 PMid:31461024
34. Valerio IL, Dumanian GA, Jordan SW, Mioton LM, Bowen JB, West JM, Porter K, Ko JH, Souza JM, Potter BK. Preemptive Treatment of Phantom and Residual Limb Pain with Targeted Muscle Reinnervation at the Time of Major Limb Amputation. J Am Coll Surg. 2019 Mar;228(3):217-226. https://doi.org/10.1016/j.jamcollsurg.2018.12.015 PMid:30634038
35. Dumanian GA, Potter BK, Mioton LM, Ko JH, Cheesborough JE, Souza JM, Ertl WJ, Tintle SM, Nanos GP, Valerio IL, Kuiken TA, Apkarian AV, Porter K, Jordan SW. Targeted Muscle Reinnervation Treats Neuroma and Phantom Pain in Major Limb Amputees: A Randomized Clinical Trial. Ann Surg. 2019 Aug;270(2):238-246. https://doi.org/10.1097/SLA.0000000000003088 PMid:30371518
36. Mioton LM, Dumanian GA, Shah N, Qiu CS, Ertl WJ, Potter BK, Souza JM, Valerio IL, Ko JH, Jordan SW. Targeted Muscle Reinnervation Improves Residual Limb Pain, Phantom Limb Pain, and Limb Function: A Prospective Study of 33 Major Limb Amputees. Clin Orthop Relat Res. 2020 Sep;478(9):2161-2167. https://doi.org/10.1097/CORR.0000000000001323 PMid:32452928 PMCid:PMC7431223
37. Dellon AL, Mackinnon SE. Treatment of the painful neuroma by neuroma resection and muscle implantation. Plast Reconstr Surg. 1986 Mar;77(3):427-38. https://doi.org/10.1097/00006534-198603000-00016 PMid:2937074
38. Sunderland S. The anatomy and physiology of nerve injury. Muscle Nerve. 1990 Sep;13(9):771-84. https://doi.org/10.1002/mus.880130903 PMid:2233864
39. Devor M, Govrin-Lippmann R, Angelides K. Na+ channel immunolocalization in peripheral mammalian axons and changes following nerve injury and neuroma formation. J Neurosci. 1993 May;13(5):1976-92. https://doi.org/10.1523/JNEUROSCI.13-05-01976.1993 PMid:7683047 PMCid:PMC6576562
40. Vaso A, Adahan HM, Gjika A, Zahaj S, Zhurda T, Vyshka G, Devor M. Peripheral nervous

system origin of phantom limb pain. Pain. 2014 Jul;155(7):1384-1391. https://doi.org/10.1016/j.pain.2014.04.018 PMid:24769187

41. Flor H. Phantom-limb pain: characteristics, causes and treatment. Lancet Neurol. 2002 Jul;1(3):182-9. https://doi.org/10.1016/S1474-4422(02)00074-1 PMid:12849487
42. Flor H, Nikolajsen L, Staehelin Jensen T. Phantom limb pain: a case of maladaptive CNS plasticity? Nat Rev Neurosci. 2006 Nov;7(11):873-81. https://doi.org/10.1038/nrn1991 PMid:17053811
43. Lotze M, Flor H, Grodd W, Larbig W, Birbaumer N. Phantom movements and pain. An fMRI study in upper limb amputees. Brain. 2001 Nov;124(Pt 11):2268-77. https://doi.org/10.1093/brain/124.11.2268 PMid:11673327
44. Raffin E, Richard N, Giraux P, Reilly KT. Primary motor cortex changes after amputation correlate with phantom limb pain and the ability to move the phantom limb. Neuroimage. 2016 Apr 15;130:134-144. https://doi.org/10.1016/j.neuroimage.2016.01.063 PMid:26854561
45. Giummarra MJ, Moseley GL. Phantom limb pain and bodily awareness: current concepts and future directions. Curr Opin Anaesthesiol. 2011 Oct;24(5):524-31. https://doi.org/10.1097/ACO.0b013e32834a105f PMid:21772144
46. Bowen JB, Ruter D, Wee C, West J, Valerio IL. Targeted Muscle Reinnervation Technique in Below-Knee Amputation. Plast Reconstr Surg. 2019 Jan;143(1):309-312. https://doi.org/10.1097/PRS.0000000000005133 PMid:30589808
47. Vu PP, Vaskov AK, Irwin ZT, Henning PT, Lueders DR, Laidlaw AT, Davis AJ, Nu CS, Gates DH, Gillespie RB, Kemp SWP, Kung TA, Chestek CA, Cederna PS. A regenerative peripheral nerve interface allows real-time control of an artificial hand in upper limb amputees. Sci Transl Med. 2020 Mar 4;12(533):eaay2857. https://doi.org/10.1126/scitranslmed.aay2857 PMid:32132217 PMCid:PMC8082695
48. Kuiken TA, Miller LA, Lipschutz RD, Lock BA, Stubblefield K, Marasco PD, Zhou P, Dumanian GA. Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study. Lancet. 2007 Feb 3;369(9559):371-80. https://doi.org/10.1016/S0140-6736(07)60193-7 PMid:17276777
49. Kuiken TA, Li G, Lock BA, Lipschutz RD, Miller LA, Stubblefield KA, Englehart KB. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. JAMA. 2009 Feb 11;301(6):619-28 https://doi.org/10.1001/jama.2009.116 PMid:19211469 PMCid:PMC3036162
50. Hargrove LJ, Simon AM, Young AJ, Lipschutz RD, Finucane SB, Smith DG, Kuiken TA. Robotic leg control with EMG decoding in an amputee with nerve transfers. N Engl J Med. 2013 Sep 26;369(13):1237-42. doi: 10.1056/NEJMoa1300126. Erratum in: N Engl J Med. 2013 Dec 12;369(24):2364. PMID: 24066744. https://doi.org/10.1056/NEJMoa1300126 PMid:24066744
51. Johnson CC, Loeffler BJ, Gaston RG. Targeted Muscle Reinnervation: A Paradigm Shift for Neuroma Management and Improved Prosthesis Control in Major Limb Amputees. J Am Acad Orthop Surg. 2021 Apr 1;29(7):288-296. https://doi.org/10.5435/JAAOS-D-20-00044 PMid:33405489
52. Pet MA, Ko JH, Friedly JL, Smith DG. Traction Neurectomy for Treatment of Painful Residual Limb Neuroma in Lower Extremity Amputees. J Orthop Trauma. 2015 Sep;29(9):e321-5. https://doi.org/10.1097/BOT.0000000000000337 PMid:25875175
53. Domeshek LF, Krauss EM, Snyder-Warwick AK, Laurido-Soto O, Hasak JM, Skolnick GB, Novak CB, Moore AM, Mackinnon SE. Surgical Treatment of Neuromas Improves Patient-Reported Pain, Depression, and Quality of Life. Plast Reconstr Surg. 2017 Feb;139(2):407-418. https://doi.org/10.1097/PRS.0000000000003018 PMid:28125533
54. Scott BB, Winograd JM, Redmond RW. Surgical Approaches for Prevention of Neuroma at the Time of Peripheral Nerve Injury. Front Surg. 2022 Jun 27;9:819608. https://doi.org/10.3389/fsurg.2022.819608 PMid:35832494 PMCid:PMC9271873
55. Fulton ZW, Boothby BC, Phillips SA. Targeted Muscle Reinnervation for Trauma-Related Amputees: A Systematic Review. Cureus. 2022 Aug 27;14(8):e28474. doi: 10.7759/cureus.28474. PMID: 36176851;

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