Alprostadil Iloprost PAD: Systematic Review with ☸SAIMSARA.

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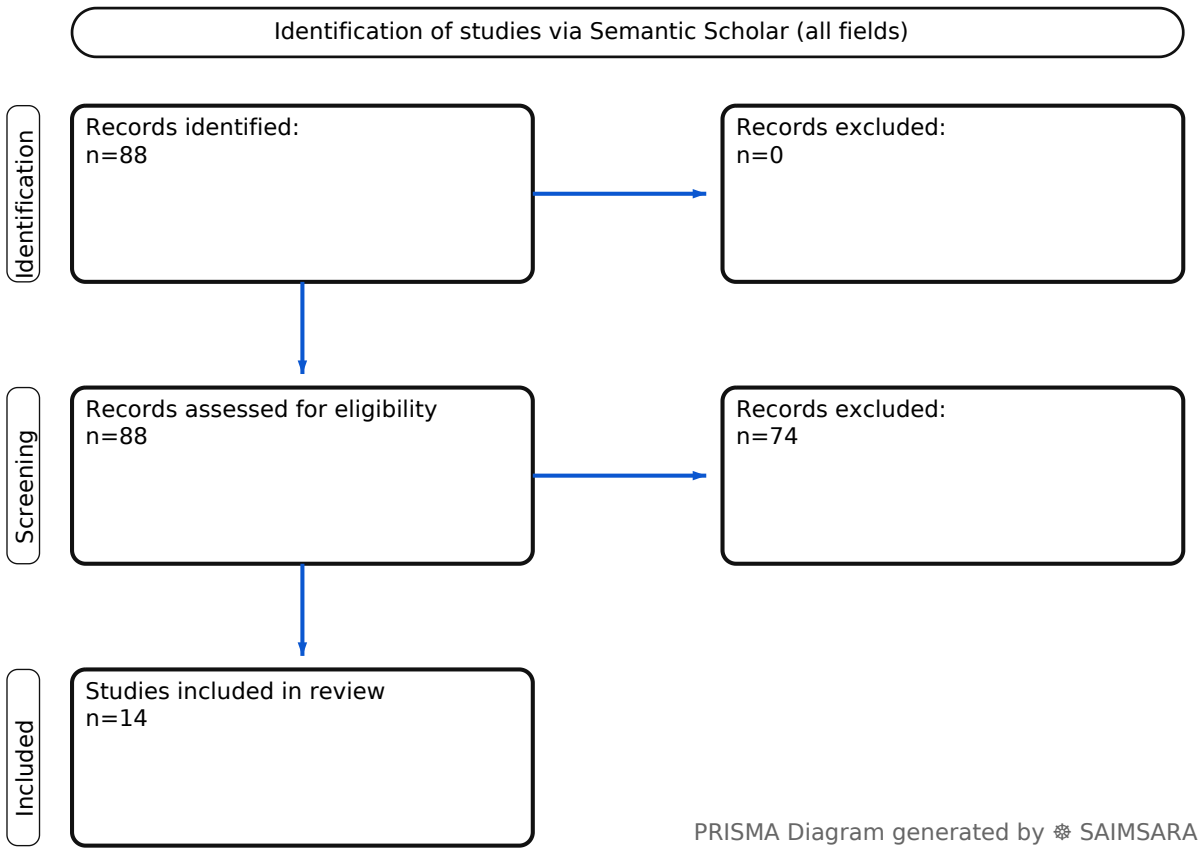
Abstract: Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details). The review utilises 14 studies with 1400 total participants (naïve ΣN). For ulcer healing and pain relief in conditions like Buerger's disease, comparisons between iloprost and alprostadil showed no clear difference, though iloprost infusion therapy in Peripheral Arterial Disease (PAD) patients was associated with a 41.86% incidence of acute kidney injury (AKI). Both drugs demonstrate efficacy in improving outcomes for patients with microvascular conditions like systemic sclerosis-related Raynaud's phenomenon and digital ulcers, as well as in PAD. The heterogeneity of study designs and small sample sizes represent the most significant limitations affecting the certainty and generalizability of findings. Future research should prioritize large-scale, head-to-head comparative efficacy randomized controlled trials for alprostadil and iloprost in Peripheral Arterial Disease.

Keywords: Alprostadil; Iloprost; Peripheral Arterial Disease

Review Stats

- Generated: 2026-02-02 23:16:20 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: 88
- Downloaded Abstracts/Papers: 88
- Included original Abstracts/Papers: 14
- Total study participants (naïve ΣN): 1400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Identification
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n=88
Records excluded:
n=0
Screening
Records assessed for eligibility
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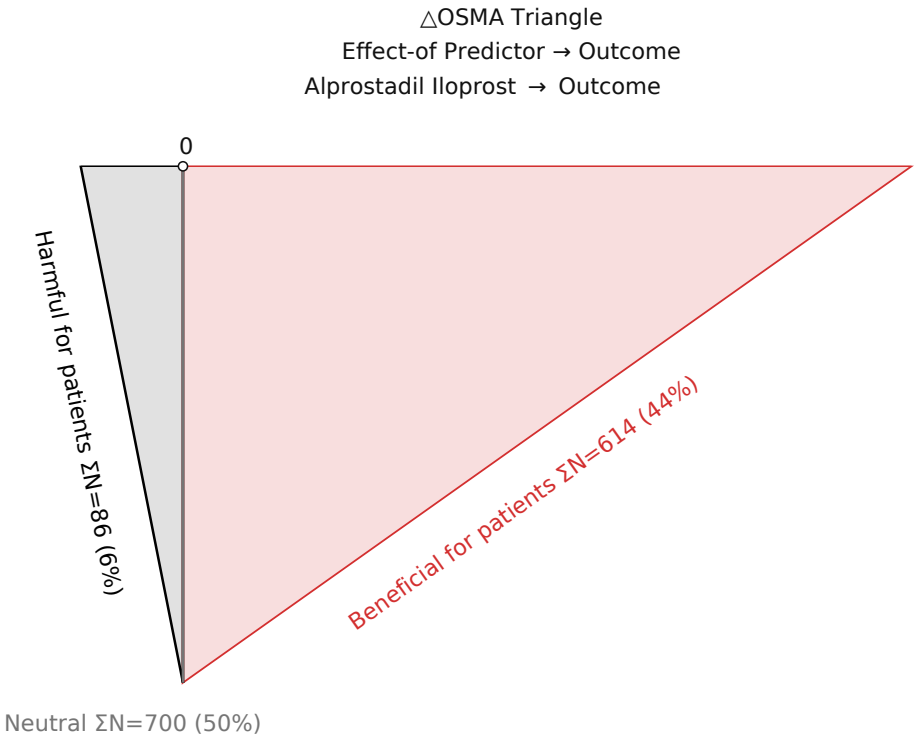
Records excluded:
n=74
Included
Studies included in review
n=14
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
Alprostadil Iloprost → Outcome
0
Harmful for patients ΣN=86 (6%)
Beneficial for patients ΣN=614 (44%)
Neutral ΣN=700 (50%)
△OSMA Triangle generated by ☸SAIMSARA

Outcome-Sentiment Meta-Analysis (OSMA): *(LLM-only)*
Frame: Effect-of Predictor → Outcome • *Source*: Semantic Scholar
Outcome: Outcome Reported metrics: %, CI, p.
Common endpoints: Common endpoints: healing, complications.
Predictor: Alprostadil Iloprost — exposure/predictor. Routes seen: intravenous, oral. Typical comparator: alprostadil, ilomedin, control, aspirin in buerger….

- **1) Beneficial for patients** — Outcome with Alprostadil Iloprost — [4], [6], [8], [9], [11], [12], [13] — ΣN=614
- **2) Harmful for patients** — Outcome with Alprostadil Iloprost — [7] — ΣN=86
- **3) No clear effect** — Outcome with Alprostadil Iloprost — [1], [2], [3], [5], [10], [14] — ΣN=700

1) Introduction
Peripheral Arterial Disease (PAD) and related microvascular conditions, such as Raynaud's phenomenon (RP) and digital ulcers (DUs) associated with systemic sclerosis (SSc), represent significant clinical challenges. Prostaglandin I2 (PGI2) analogs, including iloprost and alprostadil, are established therapeutic agents used for their vasodilatory and anti-platelet properties. These agents aim to improve blood flow, facilitate ulcer healing, and alleviate pain in patients suffering from ischemic conditions. This paper synthesizes current evidence on the comparative efficacy, safety, and mechanisms of alprostadil and iloprost in the context of PAD and related vascular disorders.

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

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. Studies varied in design from prospective mixed studies and randomized controlled trials (RCTs) to retrospective analyses and cohort studies, introducing potential for selection and reporting biases. Small sample sizes in several studies [1, 3, 4, 6, 8, 9, 10, 11, 12] limit generalizability, and a lack of specified study type or directionality in some reports [2, 4, 5, 10, 11, 12, 14] suggests

potential for unstated biases.

4) Results

4.1 Study characteristics (1–2 sentences):

The included studies comprised a mix of prospective, retrospective, and cohort designs, including randomized controlled trials and mixed methodologies. Populations primarily consisted of patients with systemic sclerosis, Raynaud's phenomenon, digital ulcers, or Peripheral Arterial Disease, alongside animal models (rats, rabbits) and human smooth muscle cells, with follow-up periods ranging from 30 minutes to 3 years.

4.2 Main numerical result aligned to the query (2–4 sentences):

For ulcer healing and pain relief in conditions like Buerger's disease, comparisons between iloprost and alprostadil showed no clear difference [14]. However, iloprost infusion therapy in Peripheral Arterial Disease (PAD) patients was associated with a 41.86% incidence of acute kidney injury (AKI) [7]. No comparable numerical outcomes for direct head-to-head efficacy between alprostadil and iloprost across the same metric, unit, and timepoint were consistently reported.

4.3 Topic synthesis (5–7 topics):

- **Efficacy in Systemic Sclerosis (SSc) and Raynaud's Phenomenon (RP):** Both alprostadil and iloprost improve digital ulcers (DUs) and RP in SSc patients [4, 6, 8, 9, 11, 12, 13]. Alprostadil (Vasoprostan) showed a significant reduction in pain compared to iloprost (Ilomedin) in SSc digital ulcers [4]. Alprostadil 60 microgram infusions demonstrated significant immediate and intermediate efficacy in symptomatic SSc-RP [6]. Iloprost is indicated for medium and high RP expression levels, while alprostadil is indicated for medium and low levels [11].
- **Differential Tissue Protection in Ischemia/Reperfusion (I/R) Injury:** Alprostadil and iloprost significantly reduced lung I/R injury [5]. Iloprost provided significantly higher renal protection compared to alprostadil in a rat model, while alprostadil was more effective in protecting lung tissue [3]. Conversely, alprostadil showed more prominent protective effects against renal I/R injury, while iloprost was superior in protecting skeletal muscle tissue in Wistar albino rats [5].
- **Peripheral Arterial Disease (PAD) Management:** In PAD patients, an increase in post-occlusive reactive hyperemia (PORH) after an alprostadil challenge test provides information on endothelial function and could reflect the presence of collaterals [10]. Intravenous iloprost showed moderate-certainty evidence of improved ulcer healing and rest pain compared to aspirin in Buerger's disease [14].

- **Safety and Administration:** Long peripheral catheters (LPCs) for intravenous infusions of iloprost or alprostadil in rheumatologic outpatients registered no procedural or late complications [1]. However, a retrospective analysis showed that 41.86% of PAD patients developed acute kidney injury (AKI) after iloprost infusion therapy, with smoking and not using acetylsalicylic acid identified as primary predictors [7].
- **Novel Drug Development:** Prostanit, a novel anti-PAD NO-donating alprostadil-based drug, was investigated for its pharmacokinetics and nitric oxide (NO) generation in rabbit plasma, isolated rat aorta, and human smooth muscle cells [2].
- **Treatment Patterns and Patient Outcomes:** A survey among German centers found that 56% of patients with systemic sclerosis and symptoms of Raynaud's phenomenon and digital ulcers were treated with prostacyclin derivatives (iloprost/alprostadil), reporting improvements [13]. After seven days of either iloprost or alprostadil therapy, Fluorescence Optical Imaging (FOI) showed a significant reduction in indocyanine green (ICG) enhancement in SSc patients, with iloprost showing slightly stronger anti-inflammatory effects [9].

5) Discussion

5.1 Principal finding (1–2 sentences):

For ulcer healing and pain relief in conditions like Buerger's disease, comparisons between iloprost and alprostadil showed no clear difference [14], though both demonstrated efficacy in various vascular disorders. Notably, iloprost infusion therapy in Peripheral Arterial Disease (PAD) patients was associated with a 41.86% incidence of acute kidney injury (AKI) [7].

5.2 Clinical implications (3–5 bullets):

- Patients with systemic sclerosis experiencing Raynaud's phenomenon and digital ulcers can benefit from both iloprost and alprostadil for symptom relief and ulcer healing [4, 8, 11, 12].
- Choice between iloprost and alprostadil for Raynaud's phenomenon may depend on severity, with iloprost indicated for medium/high expression levels and alprostadil for medium/low levels [11].
- Clinicians should be vigilant for acute kidney injury (AKI) when administering iloprost to PAD patients, particularly in smokers or those not on acetylsalicylic acid [7].
- The use of long peripheral catheters (LPCs) is a safe and effective method for the intravenous administration of iloprost or alprostadil in rheumatologic outpatients [1].
- Alprostadil challenge tests could serve as a valuable diagnostic tool in PAD to assess endothelial function and collateral development [10].

5.3 Research implications / key gaps (3–5 bullets):

- **Comparative Efficacy in PAD:** Further randomized controlled trials are needed to directly compare the efficacy of alprostadil versus iloprost for specific outcomes in Peripheral Arterial Disease, beyond Buerger's disease [14].
- **Organ-Specific Protection Mechanisms:** Research should elucidate the precise mechanisms underlying the differential organ-protective effects of alprostadil and iloprost in ischemia/reperfusion injury [3, 5].
- **Long-term Safety of Novel Drugs:** Prospective studies are required to evaluate the long-term safety profile and clinical efficacy of novel alprostadil-based drugs, such as Prostanit, in human populations [2].
- **Predictors of AKI with Iloprost:** Investigations into genetic or biochemical markers that predict acute kidney injury development in PAD patients receiving iloprost could optimize patient selection and monitoring [7].
- **Optimal Dosing and Administration Protocols:** Standardized protocols for intravenous prostaglandin I2 analog (IV-PGI2A) therapy, including optimal dosing and administration frequency, are needed for various rheumatic diseases [1, 13].

5.4 Limitations (up to 5; parse-friendly):

- **Heterogeneity of Study Designs** — The diverse study designs, ranging from animal models to retrospective human cohorts and small RCTs, limit the ability to draw definitive comparative conclusions across all outcomes.
- **Small Sample Sizes** — Many studies involved small patient cohorts (e.g., N=26 [1], N=23 [3], N=42 [4]), which reduces the statistical power and generalizability of their findings.
- **Conflicting Tissue Protection** — The reported differential tissue-protective effects of alprostadil and iloprost in ischemia/reperfusion injury are inconsistent across studies, making it difficult to establish clear guidelines for organ-specific therapy [3, 5].
- **Lack of Direct PAD Comparison** — A significant gap exists in direct comparative efficacy data between alprostadil and iloprost specifically for Peripheral Arterial Disease outcomes, beyond limited findings in Buerger's disease [7, 10, 14].
- **Limited Follow-up Duration** — Several studies had relatively short follow-up periods (e.g., 120 min [3], 7 days [9]), which may not capture long-term efficacy or safety outcomes.

5.5 Future directions (up to 5; parse-friendly):

- **Comparative Efficacy RCTs** — Conduct large-scale, multicenter randomized controlled trials directly comparing alprostadil and iloprost in diverse PAD populations.
- **Long-term Safety Studies** — Investigate the long-term safety profile of iloprost, particularly the incidence and predictors of acute kidney injury in PAD patients.
- **Tissue-Specific Efficacy Trials** — Design studies to determine the optimal prostaglandin analog for specific organ protection in various ischemia/reperfusion injury scenarios.
- **Biomarker-Guided Therapy** — Develop and validate biomarkers to predict individual patient response and risk of adverse events to alprostadil or iloprost therapy.
- **Novel Drug Evaluation** — Evaluate the clinical efficacy and long-term safety of novel alprostadil-based compounds, like Prostanit, in human trials for PAD.

6) Conclusion

For ulcer healing and pain relief in conditions like Buerger's disease, comparisons between iloprost and alprostadil showed no clear difference [14], though iloprost infusion therapy in Peripheral Arterial Disease (PAD) patients was associated with a 41.86% incidence of acute kidney injury (AKI) [7]. Both drugs demonstrate efficacy in improving outcomes for patients with microvascular conditions like systemic sclerosis-related Raynaud's phenomenon and digital ulcers, as well as in PAD. The heterogeneity of study designs and small sample sizes represent the most significant limitations affecting the certainty and generalizability of findings. Future research should prioritize large-scale, head-to-head comparative efficacy randomized controlled trials for alprostadil and iloprost in Peripheral Arterial Disease.

References

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Figure 1. Publication-year distribution of included originals

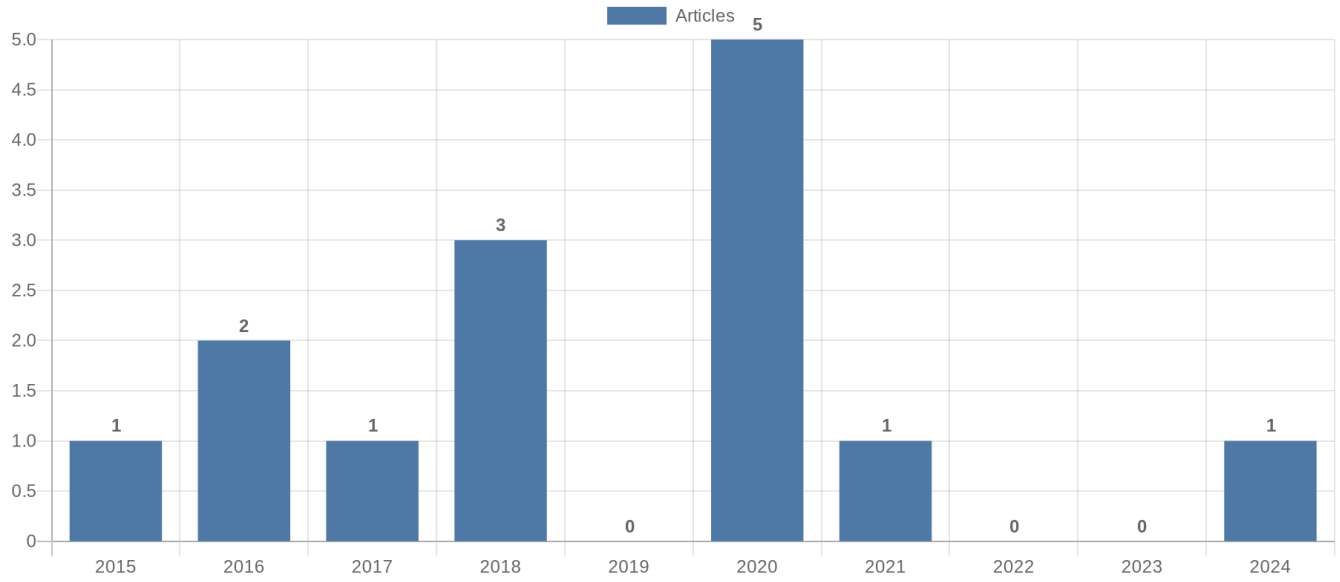

Figure 2. Study-design distribution of included originals

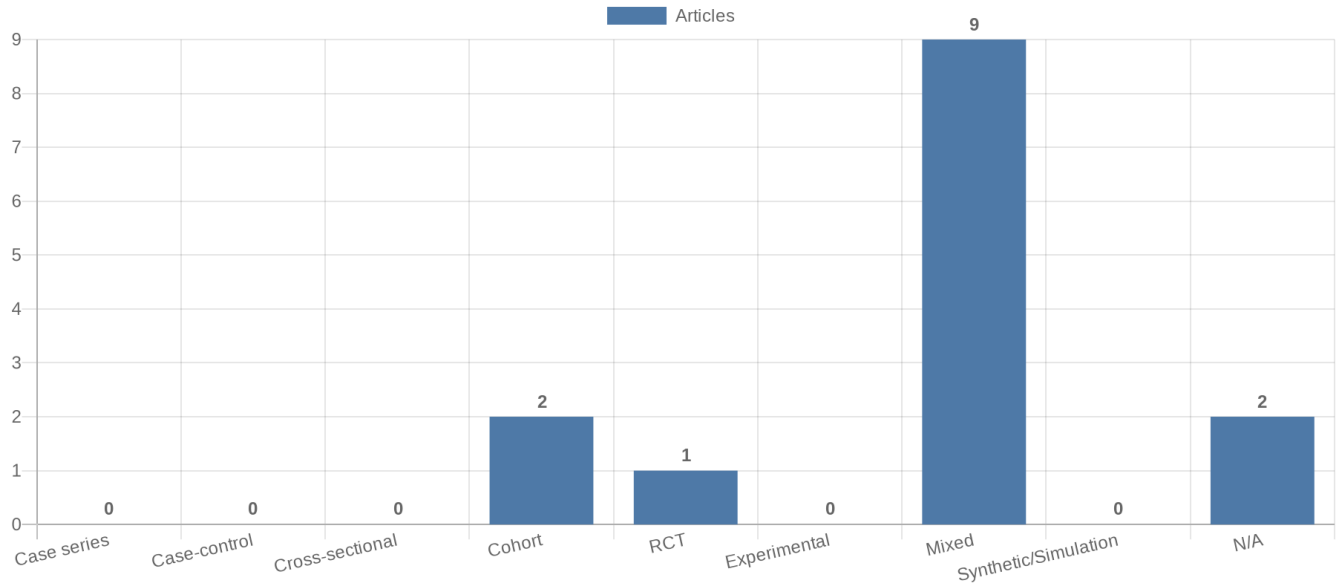

Figure 3. Study-type (directionality) distribution of included originals

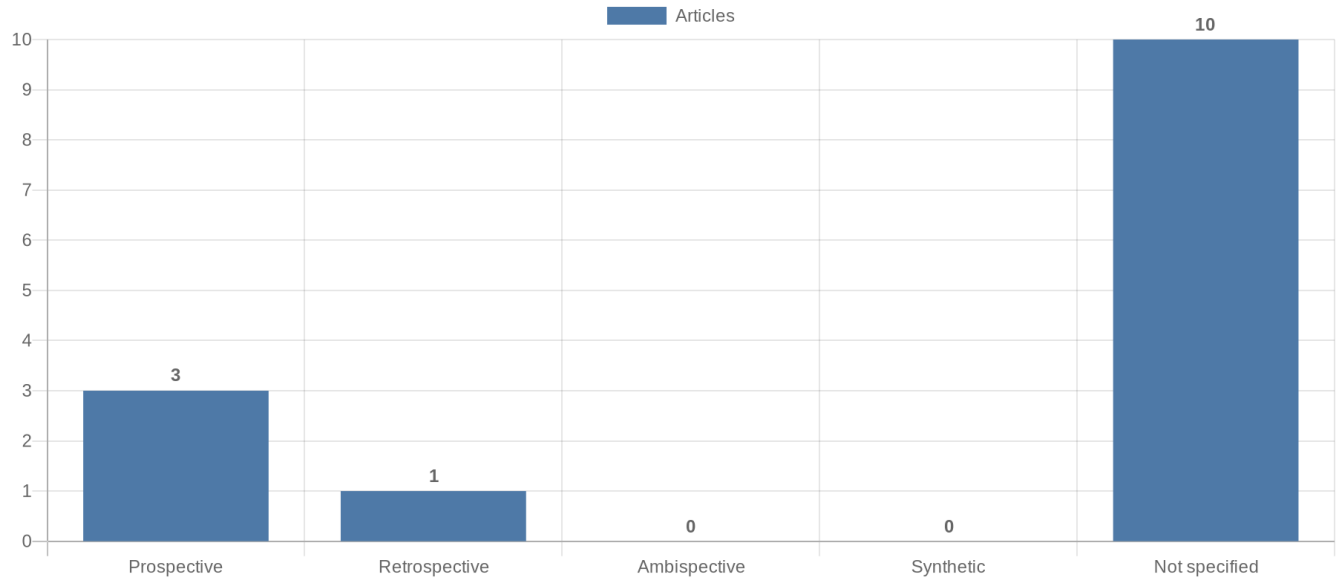

Figure 4. Main extracted research topics

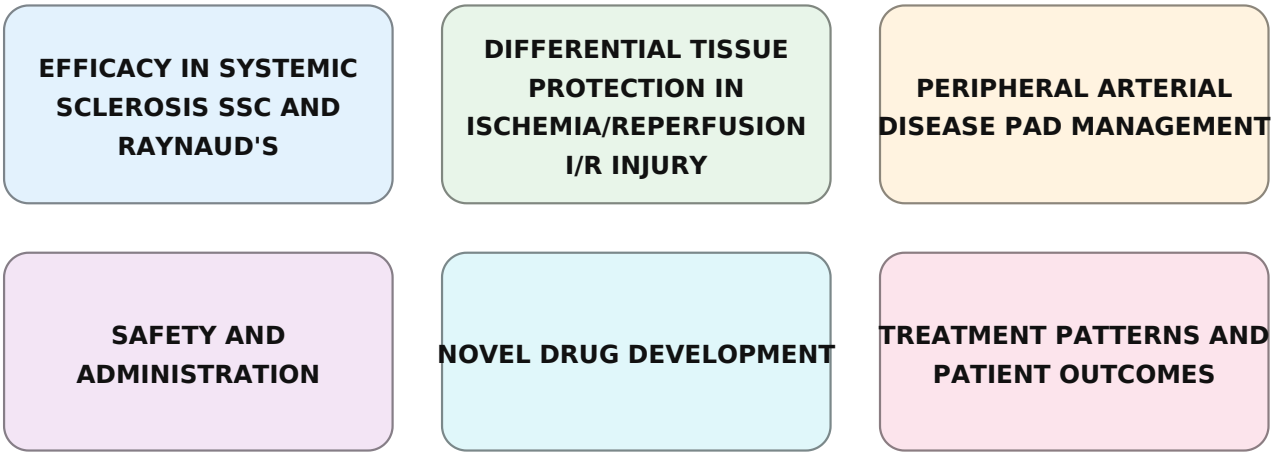

Figure 5. Limitations of current studies (topics)

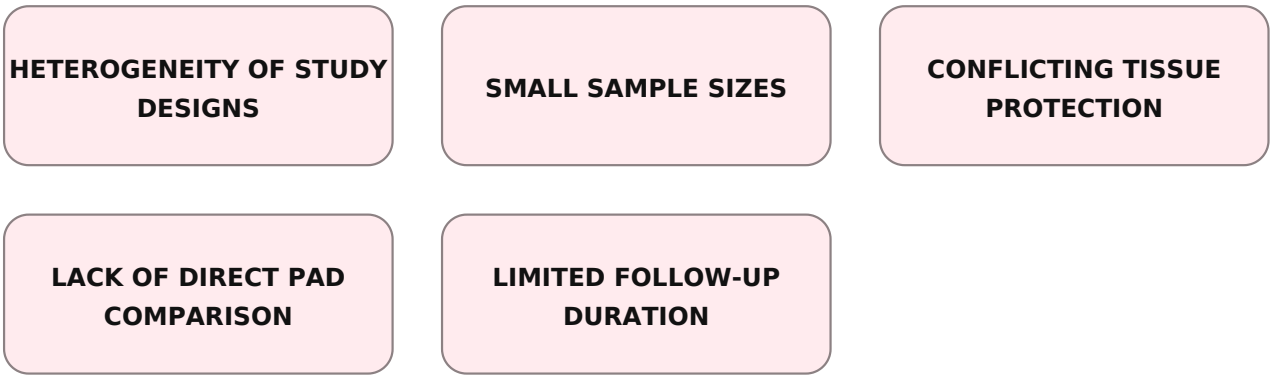

Figure 6. Future research directions (topics)