Peripheral Artery Disease Treatment: Systematic Review with ☸SAIMSARA.

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Abstract: The aim of this systematic review is to synthesize findings from recent research on peripheral artery disease treatments to identify current best practices, emerging therapies, patient-specific considerations, and existing gaps in knowledge. The review utilises 157 studies with 533650 total participants (naïve ΣN). For femoropopliteal peripheral artery disease, drug-coated balloons demonstrated superior primary patency compared to percutaneous transluminal angioplasty at approximately 1 year, with a median patency of 85.6% for DCBs versus 58.7% for PTA. This advantage suggests a shift towards drug-eluting technologies for improved vessel patency in symptomatic PAD patients. The heterogeneity of reported outcomes across studies, particularly in terms of metrics and follow-up durations, represents the most significant limitation to synthesizing a comprehensive understanding of treatment efficacy. Clinicians should prioritize evidence-based endovascular interventions and aggressive medical management, while future research should focus on standardized outcome reporting and large-scale comparative effectiveness trials to refine treatment guidelines.

Keywords: ["Peripheral Artery Disease"; "PAD Treatment"; "Intermittent Claudication"; "Critical Limb Ischemia"; "Endovascular Procedures"; "

Review Stats

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- Scope: All fields
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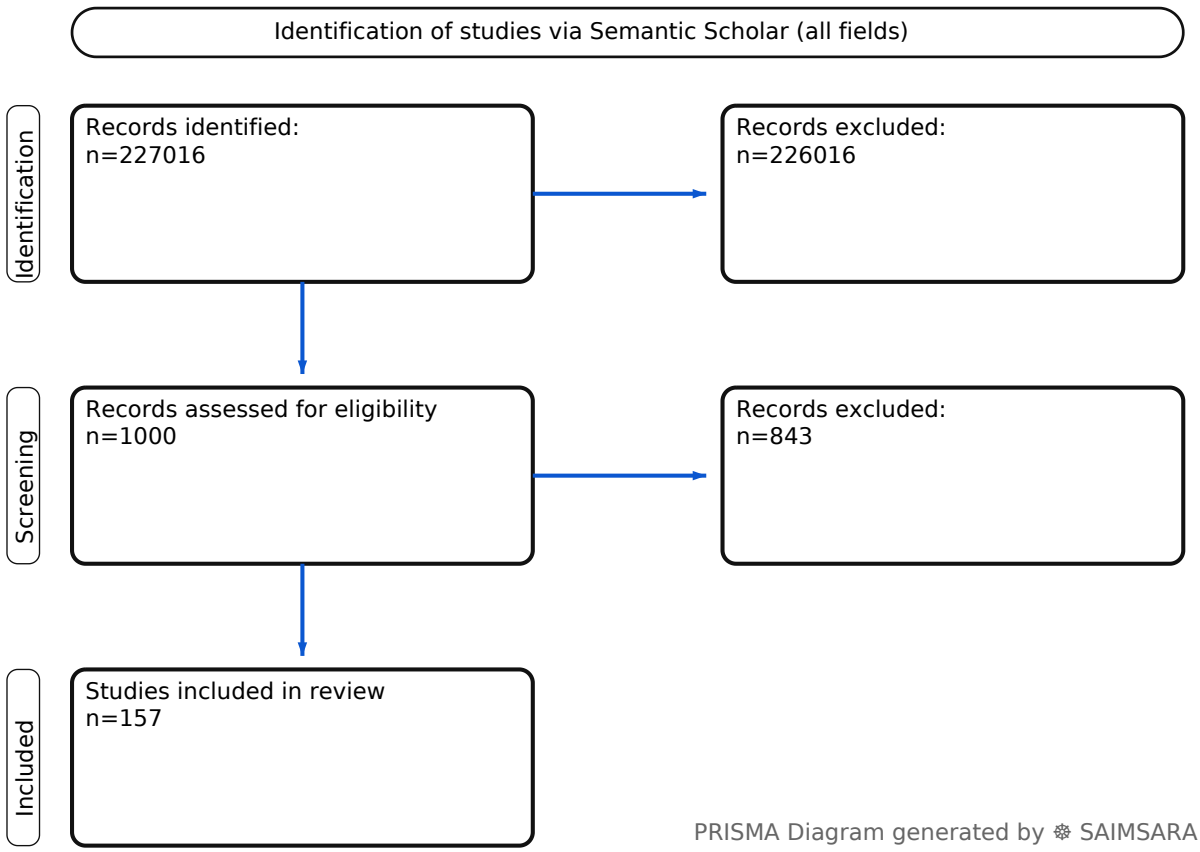
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 157
- Total study participants (naïve ΣN): 533650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Identification
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Records excluded:
n=226016
Screening
Records assessed for eligibility
n=1000
Records excluded:
n=843
Included
Studies included in review
n=157
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
peripheral artery disease treatment → Outcome
0
Harmful for patients ΣN=363391 (68%)
Beneficial for patients ΣN=54973 (10%)
Neutral ΣN=115286 (22%)
△OSMA Triangle generated by ☸SAIMSARA

Outcome-Sentiment Meta-Analysis (OSMA): *(LLM-only)*
Frame: Effect-of Predictor → Outcome • *Source*: Semantic Scholar
Outcome: Outcome Typical timepoints: 1-y, 12-mo. Reported metrics: %, CI, p.
Common endpoints: Common endpoints: mortality, complications, patency.
Predictor: peripheral artery disease treatment — exposure/predictor. Routes seen: oral. Typical comparator: those without anxiety. among, those managed noninvasively, conventional treatment of, clopidogrel and aspirin….

- **1) Beneficial for patients** — Outcome with peripheral artery disease treatment — [1], [3], [4], [7], [8], [11], [13], [16], [17], [20], [24], [25], [34], [55], [57], [78], [79], [95], [100], [101], [102], [104], [119], [121], [125], [146], [155] — ΣN=54973
- **2) Harmful for patients** — Outcome with peripheral artery disease treatment — [10], [12], [14], [21], [22], [27], [54], [75], [77], [88], [94], [99], [105], [113], [116], [117], [120], [122], [124], [133], [137], [138], [145], [152], [156] — ΣN=363391
- **3) No clear effect** — Outcome with peripheral artery disease treatment — [2], [5], [6], [9], [15], [18], [19], [23], [26], [28], [29], [30], [31], [32], [33], [35], [36], [37], [38], [39], [40], [41], [42], [43], [44], [45], [46], [47], [48], [49], [50], [51], [52], [53], [56], [58], [59], [60], [61], [62], [63], [64], [65], [66], [67], [68], [69], [70], [71], [72], [73], [74], [76], [80], [81], [82], [83], [84], [85], [86], [87], [89], [90], [91], [92], [93], [96], [97], [98], [103], [106], [107], [108], [109], [110], [111], [112], [114], [115], [118], [123], [126], [127], [128], [129], [130], [131], [132], [134], [135], [136], [139], [140], [141], [142], [143], [144], [147], [148], [149], [150], [151], [153], [154], [157] — ΣN=115286

1) Introduction

Peripheral artery disease (PAD) is a prevalent circulatory condition characterized by narrowed arteries that reduce blood flow to the limbs, most commonly the legs. This can lead to symptoms such as claudication, critical limb-threatening ischemia (CLTI), and an increased risk of major adverse cardiovascular events (MACE) and major adverse limb events (MALE), including amputation. Effective treatment strategies for PAD are crucial for improving patient outcomes, alleviating symptoms, and preventing severe complications. This paper synthesizes current research on various therapeutic approaches for PAD, encompassing medical, endovascular, surgical, and novel experimental interventions, while also addressing patient-centered care and disparities in treatment.

2) Aim

The aim of this systematic review is to synthesize findings from recent research on peripheral artery disease treatments to identify current best practices, emerging therapies, patient-specific considerations, and existing gaps in knowledge.

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. Cohort studies and mixed designs, especially those that are retrospective or lack specified directionality, inherently carry a higher risk of selection bias and confounding compared to prospective randomized controlled trials (RCTs). The presence of multiple review articles and studies without specified populations or sample sizes further limits the ability to assess generalizability and potential biases.

4) Results

4.1 Study characteristics

The included studies predominantly comprised prospective cohort studies and randomized controlled trials (RCTs), alongside numerous mixed-design and retrospective analyses. Populations typically involved patients experiencing new-onset or worsening claudication, symptomatic PAD of various severities, or specific subgroups such as those with diabetes or undergoing endovascular procedures. Follow-up periods ranged from 6 months to 5 years, with many studies reporting 12-month outcomes.

4.2 Main numerical result aligned to the query

For femoropopliteal peripheral artery disease, drug-coated balloons (DCBs) demonstrated superior primary patency compared to percutaneous transluminal angioplasty (PTA) at approximately 1 year. The median primary patency for DCBs was 85.6% (range: 82.2%–89.0%) versus 58.7% (range: 52.4%–65.0%) for PTA [11, 25]. This superiority was also observed at 36 months, with DCBs achieving 69.5% primary patency compared to 45.1% for PTA [100].

4.3 Topic synthesis

- **Endovascular Intervention Efficacy:** Drug-coated balloons (DCBs) consistently show superior primary patency (median 85.6% at 1 year [11, 25]) and lower clinically driven target lesion revascularization (5.9% vs 16.7% [25]) compared to plain balloon angioplasty (PTA) for femoropopliteal lesions. Drug-eluting stents (DES) also demonstrated superior 1-year primary patency (83.2% vs 74.3%) and greater sustained clinical improvement compared to bare metal stents (BMS) [13]. Phoenix atherectomy was safely performed with

low bail-out stenting rates (4% for common femoral artery, 16% for femoropopliteal, 3% for BTK lesions) and acceptable target lesion revascularization (TLR) rates (87.5% for claudication, 82.3% for CLTI) [14]. However, atherectomy may be associated with higher risks of major amputation and MALE compared to stenting and PTA alone [152].

- **Pharmacological Management:** Dual antiplatelet therapy with rivaroxaban and aspirin significantly reduced MACE or MALE (4.2% absolute risk reduction) in high-risk symptomatic lower extremity PAD patients compared to aspirin alone [17]. Low-dose rivaroxaban also reduced ischemic events independently of risk factors [20]. The PCSK9 inhibitor alirocumab reduced PAD events (HR 0.69, 95% CI 0.54–0.89) in statin-treated patients with acute coronary syndrome [16]. Liraglutide increased transcutaneous oxygen pressure (TcPo2) and may prevent clinical progression of PAD in type 2 diabetes patients [7]. Rosuvastatin and atorvastatin show comparable efficacy for composite cardiovascular outcomes, but rosuvastatin was associated with higher new-onset diabetes risk [12]. Edoxaban and aspirin showed similar bleeding risks but lower restenosis/reocclusion rates compared to clopidogrel and aspirin after femoropopliteal endovascular therapy (EVT) [8]. Optimal medical treatment is often insufficiently prescribed, especially in women [5, 23].
- **Lifestyle and Behavioral Interventions:** Supervised exercise therapy (SET) referral rates are low, particularly in the US [18]. Home-based walking exercise programs improved self-efficacy, physical functioning, pain acceptance, and social functioning [78]. Smoking cessation is critical, with a high relapse rate (36% probability) and 72% of baseline smokers still smoking at 12 months [31]. Community walking programs are also reviewed [43, 58].
- **Novel and Regenerative Therapies:** A hyaluronic acid hydrogel system shows potential for treating ischemic legs by reducing lipid oxidation, enhancing local blood flow, and improving running capacity [4]. Therapeutic angiogenesis via gene therapy (pl-VEGF165) demonstrated persistent effects, achieving 95% limb salvage compared to 67% in controls and a 288% increase in pain-free walking distance over 5 years [34, 86, 89]. Stem cell therapies, including peripheral blood-derived autologous stem cells, are being evaluated for late-stage PAD and critical limb ischemia, though practical and scientific issues limit widespread use [30, 42, 153]. Autologous bone marrow-derived aldehyde dehydrogenase bright (ALDHbr) cells did not improve exercise performance or limb perfusion, but a post hoc analysis suggested increased collateral arteries in a subgroup [28].
- **Psychological and Social Factors:** Patients with anxiety showed significantly lower health status (PAQ Summary scores) at 3, 6, and 12 months [1]. Among anxious patients, early invasive treatment led to higher PAQ scores, indicating greater benefit [1]. Women with PAD have a high burden of depressive symptoms, which are associated with worse health status recovery [21]. Gaps exist in shared decision-making frameworks for symptomatic PAD [2].
- **Risk Factors and Comorbidities:** Non-medicated diabetes is common and associated with poor outcomes, including increased mortality and need for intervention [77]. Type 1

diabetes patients have the highest risk for limb amputation, while type 2 diabetes patients have higher mortality [10]. Both high and low systolic blood pressure (SBP) and low diastolic blood pressure (DBP) were associated with increased PAD events [27]. Elevated remnant cholesterol (HR 1.6, 95% CI 1.1–2.3) increases PAD risk in diabetes [133]. Patients with PAD and heart failure have a high risk for MACE and death [120].

- **Disparities and Adherence:** Racial and ethnic disparities in amputation rates are substantial [9]. Hispanic/Latino individuals with PAD underuse guideline-recommended cardiovascular medications [23]. Optimal medical treatment is insufficiently prescribed, especially in women [5]. Adherence to guideline-recommended therapies varies significantly across sites [18].

5) Discussion

5.1 Principal finding

For femoropopliteal peripheral artery disease, drug-coated balloons demonstrated superior primary patency compared to percutaneous transluminal angioplasty at approximately 1 year, with a median patency of 85.6% for DCBs versus 58.7% for PTA [11, 25]. This highlights the sustained advantage of drug-eluting technologies in maintaining vessel patency.

5.2 Clinical implications

- **Enhanced Revascularization Strategies:** Drug-coated balloons (DCBs) and drug-eluting stents (DES) should be prioritized over plain balloon angioplasty (PTA) and bare metal stents (BMS) for femoropopliteal lesions due to superior patency and reduced reintervention rates [11, 13, 25, 100].
- **Optimized Pharmacotherapy:** Combined rivaroxaban and aspirin therapy offers significant benefits in reducing major adverse cardiovascular and limb events in high-risk PAD patients [17, 20]. Liraglutide may prevent PAD progression in type 2 diabetes [7].
- **Holistic Patient Care:** Early invasive treatment may offer greater benefit for PAD patients with anxiety, suggesting the importance of addressing psychological comorbidities [1]. Shared decision-making frameworks need improvement to better support symptomatic PAD patients [2].
- **Addressing Treatment Gaps:** There is a critical need to improve the prescription and adherence to optimal medical treatment, particularly for women and Hispanic/Latino populations, and to enhance referral to supervised exercise therapy [5, 18, 23].
- **Smoking Cessation Urgency:** Given the high rates of active smoking and relapse, intensive, evidence-based smoking cessation interventions are paramount, especially early in the treatment course [31].

5.3 Research implications / key gaps

- **Long-Term Comparative Effectiveness:** Future studies should focus on long-term (beyond 3-5 years) comparative effectiveness of newer endovascular devices (e.g., atherectomy vs. DCBs vs. DES) on limb salvage and mortality [15, 152].
- **Personalized Pharmacotherapy:** Research is needed to identify specific patient subgroups who will benefit most from novel oral anticoagulants in combination with aspirin, as well as the optimal duration of dual antiplatelet therapy in various PAD scenarios [29, 142].
- **Psychosocial Intervention Impact:** Prospective studies are warranted to evaluate the direct impact of integrated psychological interventions (e.g., for anxiety and depression) on PAD-specific health status and treatment outcomes [1, 21].
- **Novel Angiogenesis Mechanisms:** Further investigation into the involvement of NOX isoforms in promoting therapeutic angiogenesis is needed to develop new treatment options to slow or reverse PAD [37].
- **Stem Cell Therapy Optimization:** Future research should address the practical and scientific issues limiting widespread use of stem cell treatments for critical limb ischemia, focusing on efficacy, safety, and patient selection [153].

5.4 Limitations

- **Heterogeneity of Outcomes** — Varied metrics, units, and follow-up durations across studies limited the ability to pool numerical results for a single central value for many interventions.
- **Lack of Direct Comparisons** — Many studies focused on single interventions or comparisons between two, making it difficult to establish a comprehensive hierarchy of all treatment options.
- **Generalizability of Findings** — A significant number of studies were cohort or mixed designs without specified directionality, potentially limiting the generalizability of their findings due to inherent biases.
- **Underreported Patient Characteristics** — Some studies lacked detailed demographic or clinical characteristics for their populations, hindering a full understanding of treatment applicability.
- **Focus on Specific Lesions** — Many endovascular studies concentrated on femoropopliteal lesions, potentially overlooking distinct treatment considerations for other arterial beds.

5.5 Future directions

- **Standardize Outcome Reporting** — Future studies should adopt standardized metrics for patency, revascularization, and limb salvage.
- **Comparative Effectiveness Trials** — Conduct large-scale RCTs comparing multiple endovascular and medical therapies.
- **Integrate Psychosocial Care** — Develop and test multidisciplinary care models that integrate mental health support for PAD patients.
- **Biomarker-Guided Therapy** — Investigate biomarkers (e.g., GDF15) to guide personalized treatment decisions for PAD [124].
- **Home-Based Exercise Implementation** — Implement and evaluate scalable home-based exercise programs with technology support [78].

6) Conclusion

For femoropopliteal peripheral artery disease, drug-coated balloons demonstrated superior primary patency compared to percutaneous transluminal angioplasty at approximately 1 year, with a median patency of 85.6% for DCBs versus 58.7% for PTA [11, 25]. This advantage suggests a shift towards drug-eluting technologies for improved vessel patency in symptomatic PAD patients. The heterogeneity of reported outcomes across studies, particularly in terms of metrics and follow-up durations, represents the most significant limitation to synthesizing a comprehensive understanding of treatment efficacy. Clinicians should prioritize evidence-based endovascular interventions and aggressive medical management, while future research should focus on standardized outcome reporting and large-scale comparative effectiveness trials to refine treatment guidelines.

References

SAIMSARA Session Index — session.json

Figure 1. Publication-year distribution of included originals

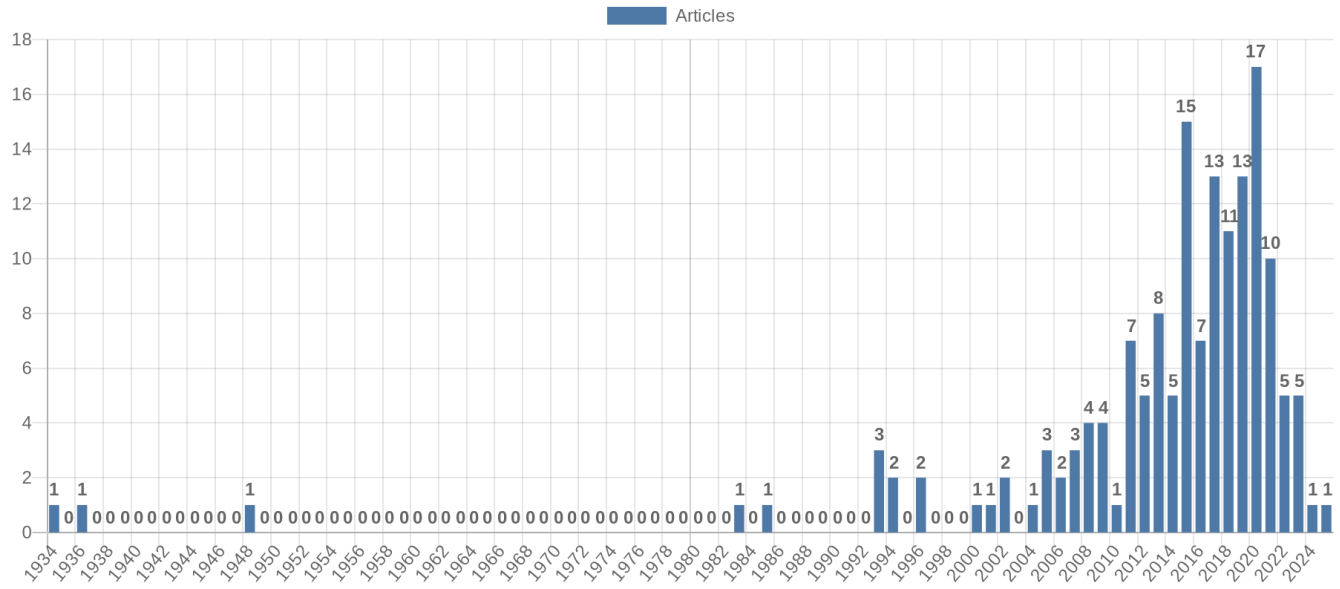

Figure 2. Study-design distribution of included originals

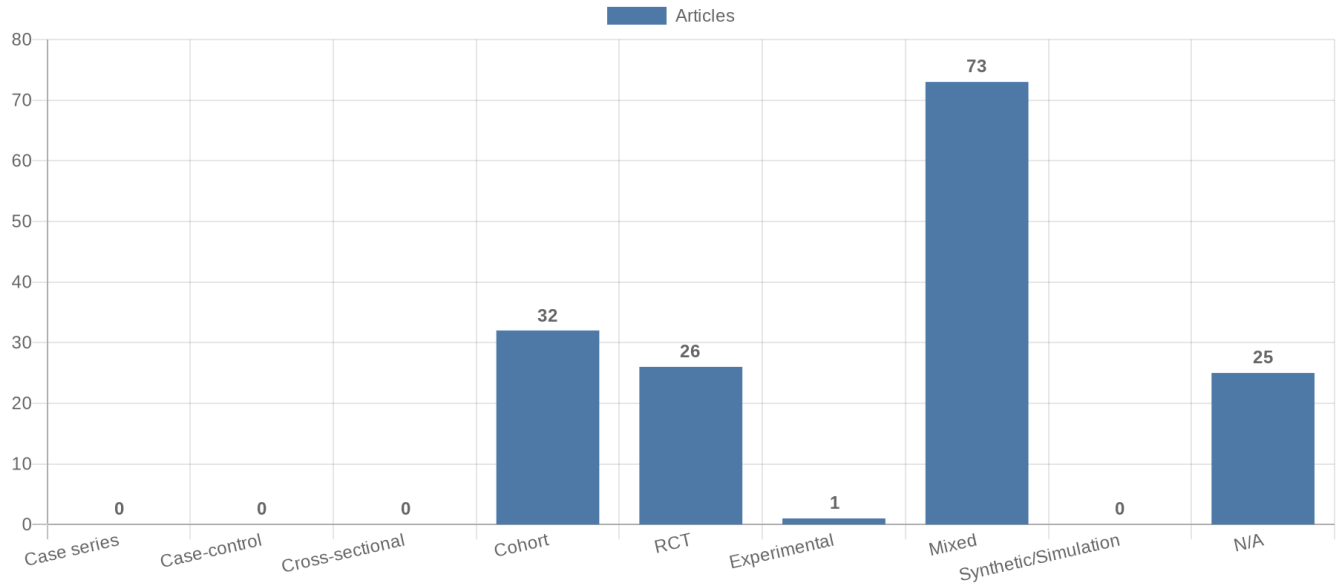

Figure 3. Study-type (directionality) distribution of included originals

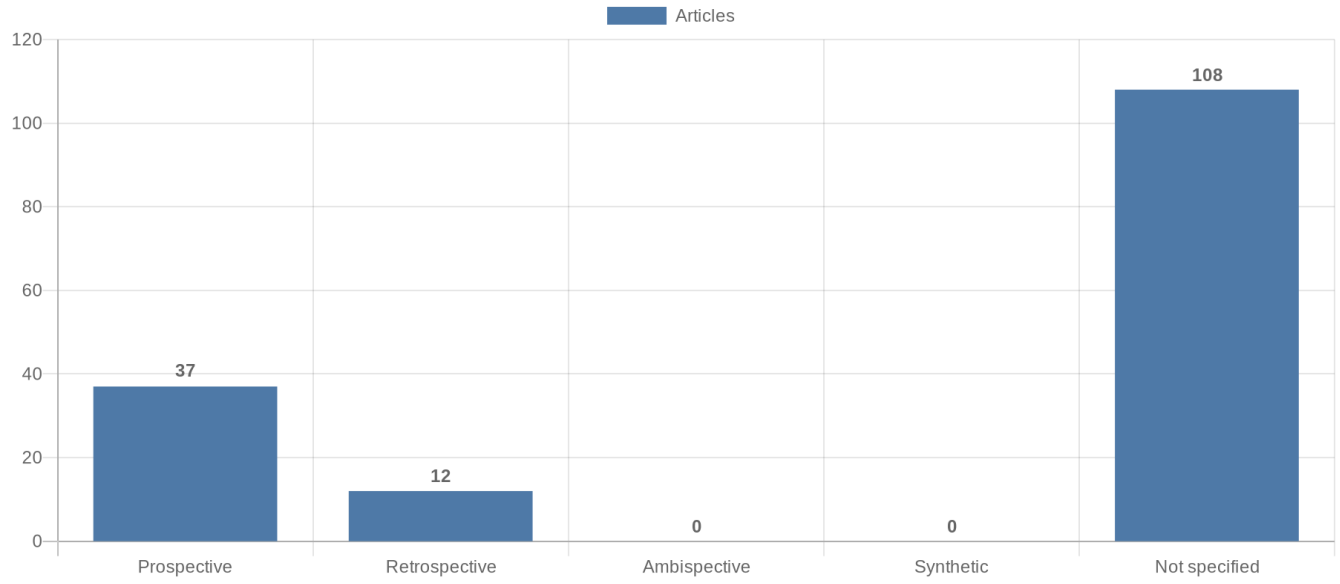

Figure 4. Main extracted research topics

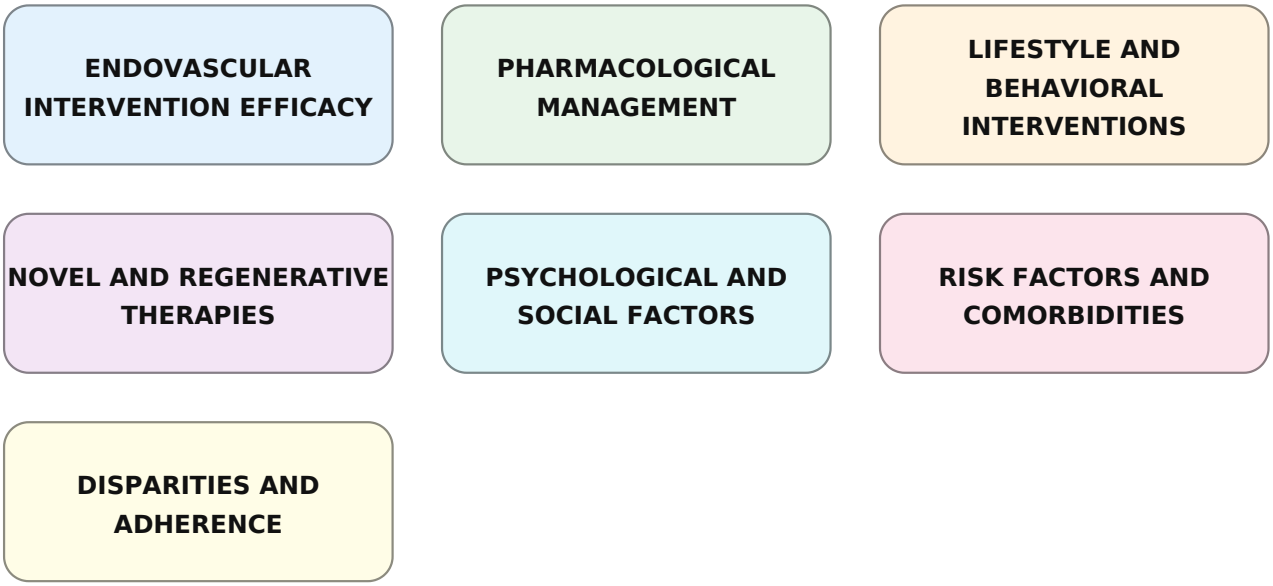

Figure 5. Limitations of current studies (topics)

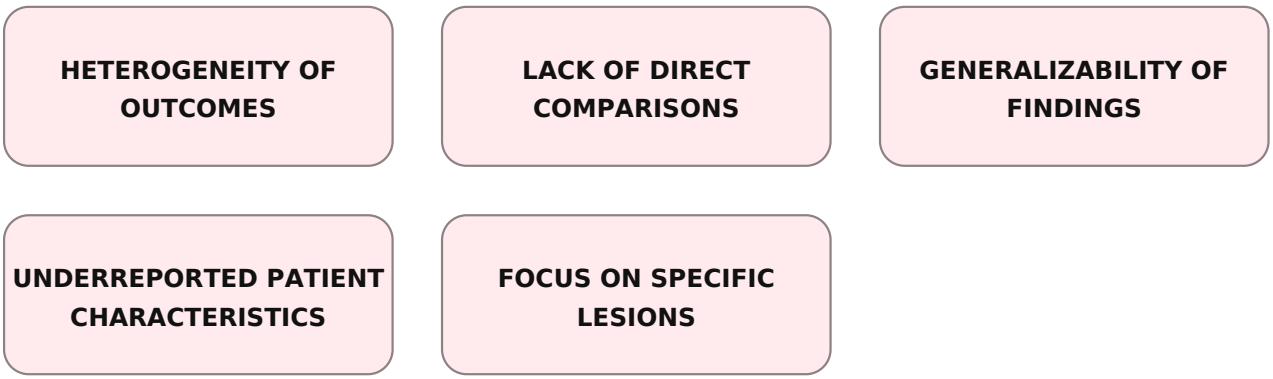

Figure 6. Future research directions (topics)