Peripheral Artery Disease Outcome: Systematic Review with ☸SAIMSARA.

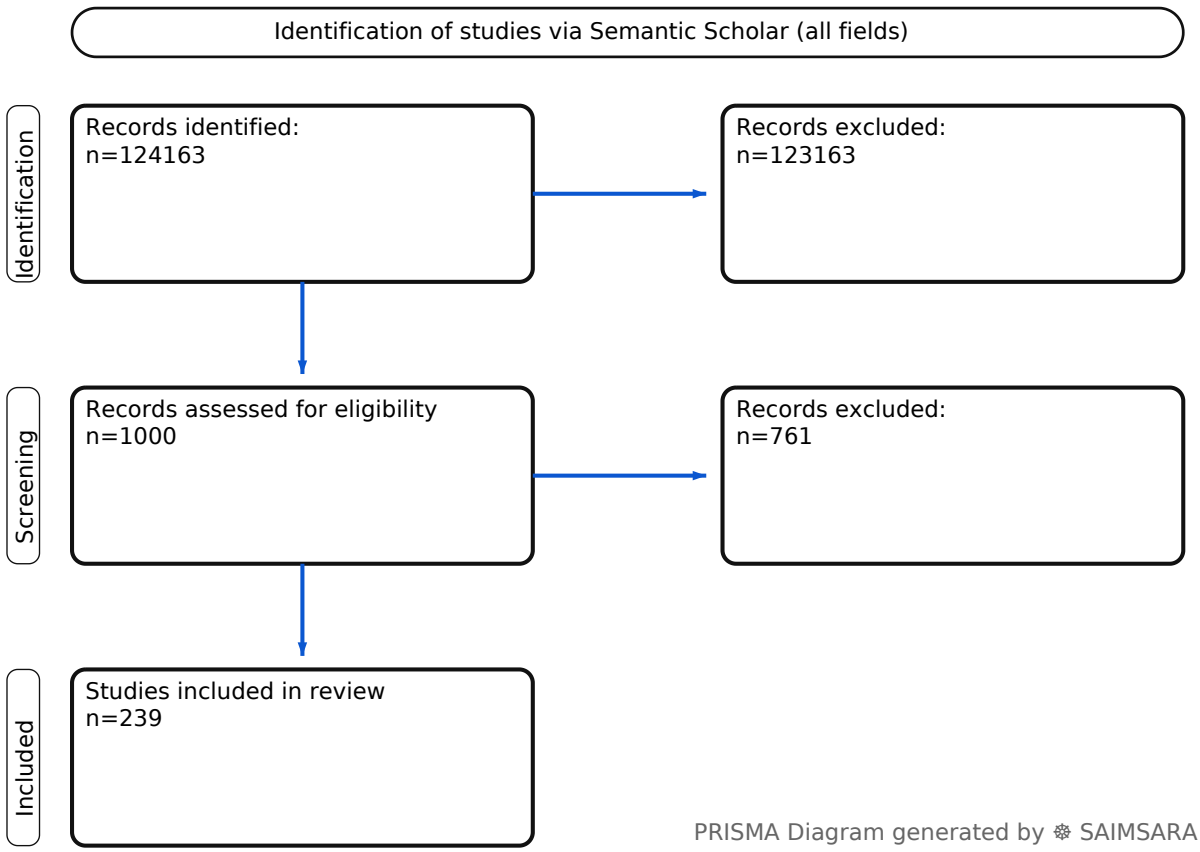
saimsara.com • Download PDF • URL

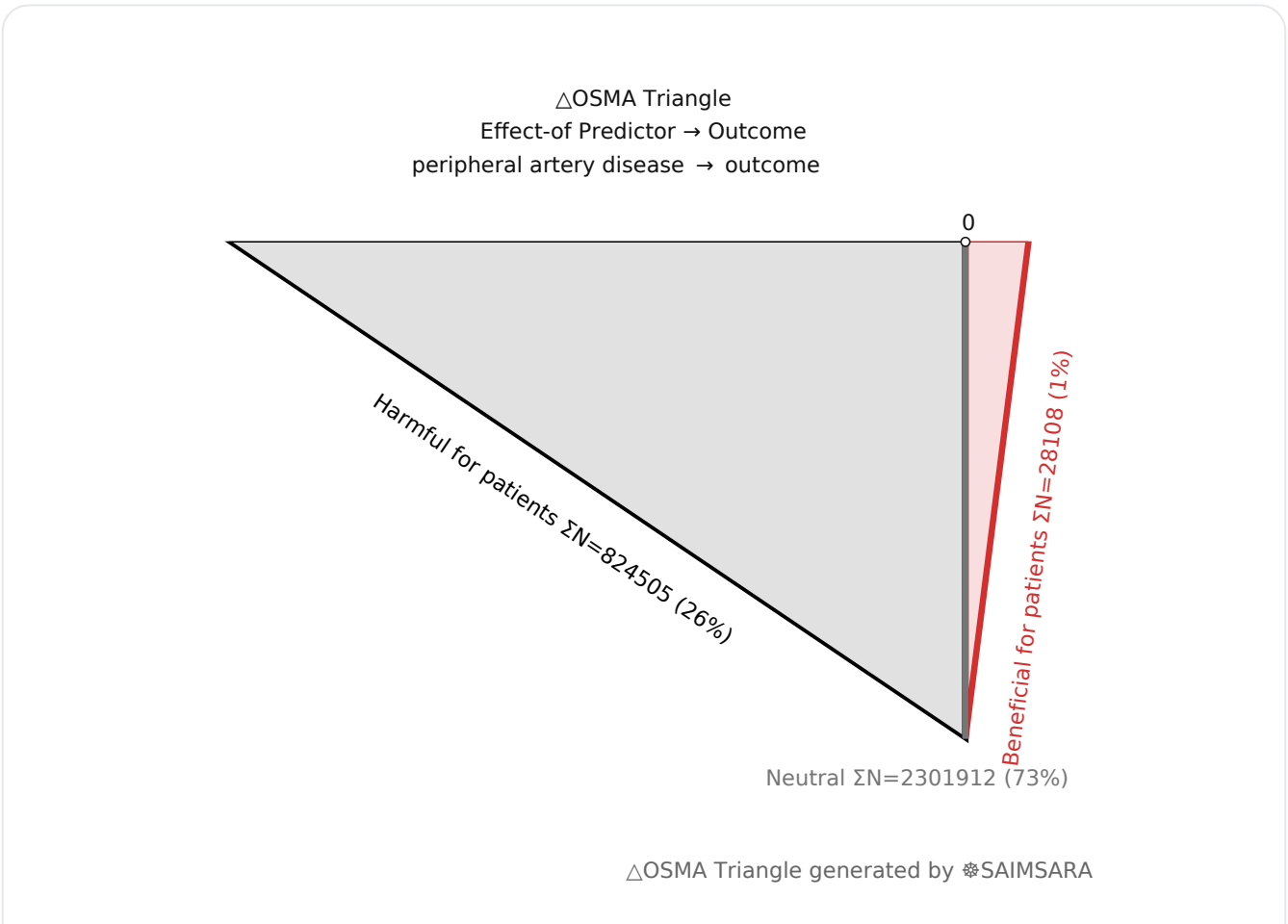
Abstract: This paper aims to systematically synthesize the current evidence on peripheral artery disease outcomes, identifying key prognostic indicators, the efficacy of various therapeutic strategies, and the influence of patient characteristics and comorbidities on disease progression and event rates. The review utilises 239 studies with 3154525 total participants (naïve ΣN). Outcomes in peripheral artery disease (PAD) patients demonstrate significant variability depending on disease severity, comorbidities, and treatment strategies. For instance, the annual death rate for symptomatic PAD patients admitted for endovascular repair was reported at 7.1%. This review highlights the complex interplay of prognostic factors, the efficacy of various pharmacological and interventional strategies, and the pervasive impact of health disparities on PAD outcomes. The heterogeneity of outcome reporting and the prevalence of observational study designs represent the most significant limitations to drawing definitive conclusions. Moving forward, a concrete next study should focus on implementing and evaluating targeted interventions to reduce the observed socioeconomic and racial disparities in PAD care and outcomes.

Keywords: Peripheral Artery Disease; Mortality; Limb Amputation; Major Adverse Limb Events; Major Adverse Cardiovascular Events; Revascularization

Review Stats

- Generated: 2026-01-30 17:39:46 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: 124163
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 239
- Total study participants (naïve ΣN): 3154525


Identification of studies via Semantic Scholar (all fields)
Identification
Records identified:
n=124163
Records excluded:
n=123163
Screening
Records assessed for eligibility
n=1000
Records excluded:
n=761
Included
Studies included in review
n=239
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
peripheral artery disease → outcome
0
Harmful for patients ΣN=824505 (26%)
Beneficial for patients ΣN=28108 (1%)
Neutral ΣN=2301912 (73%)
△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, admission.

Predictor: peripheral artery disease — exposure/predictor. Doses/units seen: 1.94 mg, 1.35 mg, 30 mg. Routes seen: oral. Typical comparator: patients without bb, bare metal stents, usual care, control….

- **1) Beneficial for patients** — outcome with peripheral artery disease — [8], [9], [15], [16], [17], [19], [25], [28], [29], [32], [45], [72], [74], [75], [165], [175], [201], [204], [228], [229], [233] — ΣN=28108
- **2) Harmful for patients** — outcome with peripheral artery disease — [1], [2], [6], [7], [10], [12], [13], [18], [20], [21], [24], [26], [27], [31], [33], [34], [35], [36], [38], [40], [42], [48], [49], [50], [55], [59], [62], [63], [64], [66], [67], [68], [69], [151], [159], [163], [164], [166], [169], [172], [202], [203], [205], [206], [207], [208], [209], [210], [211], [212], [213], [215], [216], [218], [220], [221], [222], [223], [224], [226], [231], [232], [235], [237], [238], [239] — ΣN=824505
- **3) No clear effect** — outcome with peripheral artery disease — [3], [4], [5], [11], [14], [22], [23], [30], [37], [39], [41], [43], [44], [46], [47], [51], [52], [53], [54], [56], [57], [58], [60], [61], [65], [70], [71], [73], [76], [77], [78], [79], [80], [81], [82], [83], [84], [85], [86], [87], [88], [89], [90], [91], [92], [93], [94], [95], [96], [97], [98], [99], [100], [101], [102], [103], [104], [105], [106], [107], [108], [109], [110], [111], [112], [113], [114], [115], [116], [117], [118], [119], [120], [121], [122], [123], [124], [125], [126], [127], [128], [129], [130], [131], [132], [133], [134], [135], [136], [137], [138], [139], [140], [141], [142], [143], [144], [145], [146], [147], [148], [149], [150], [152], [153], [154], [155], [156], [157], [158], [160], [161], [162], [167], [168], [170], [171], [173], [174], [176], [177], [178], [179], [180], [181], [182], [183], [184], [185], [186], [187], [188], [189], [190], [191], [192], [193], [194], [195], [196], [197], [198], [199], [200], [214], [217], [219], [225], [227], [230], [234], [236] — ΣN=2301912

1) **Introduction**

Peripheral artery disease (PAD) is a chronic, progressive atherosclerotic condition affecting arteries outside of the heart and brain, predominantly in the lower extremities. It manifests with symptoms ranging from intermittent claudication (IC) to critical limb ischemia (CLI), significantly impacting patients' quality of life and functional capacity. PAD is associated with a high burden of

cardiovascular morbidity and mortality, including major adverse cardiovascular events (MACE) and major adverse limb events (MALE), as well as an increased risk of amputation. Understanding the diverse outcomes in PAD, including prognostic factors, effective interventions, and existing disparities, is crucial for improving patient management and long-term prognosis.

2) **Aim**

This paper aims to systematically synthesize the current evidence on peripheral artery disease outcomes, identifying key prognostic indicators, the efficacy of various therapeutic strategies, and the influence of patient characteristics and comorbidities on disease progression and event rates.

3) **Methods**

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

- **Bias:** The evidence base comprises a mix of study designs, including numerous cohort studies (both retrospective and prospective) and mixed-design studies, alongside randomized controlled trials (RCTs). The prevalence of observational and retrospective designs introduces potential for selection bias, confounding, and information bias, which may affect the certainty and generalizability of some findings, particularly regarding associations and less direct causal inferences. RCTs, while providing stronger evidence for interventions, are fewer in number for some specific outcome areas.

4) **Results**

4.1 **Study characteristics:** The included studies predominantly consist of cohort designs (e.g., [1, 3, 4, 7]), mixed-design studies (e.g., [2, 5, 6]), and randomized controlled trials (RCTs) (e.g., [8, 9, 11]). Populations generally comprise patients with symptomatic PAD, often undergoing endovascular repair or revascularization, or those with specific comorbidities like diabetes. Sample sizes vary widely, from small experimental studies (e.g., N=15 [25]) to large registry analyses (e.g., N=41,702 [2], N=59,784 [5]). Follow-up periods range from short-term (e.g., 8 weeks [19]) to long-term (e.g., 10 years [32, 88]) or even decades (e.g., 21 years [64]).

4.2 **Main numerical result aligned to the query:**

Outcomes in peripheral artery disease (PAD) patients demonstrate significant variability depending on disease severity, comorbidities, and treatment strategies. For instance, the annual death rate for symptomatic PAD patients admitted for endovascular repair was reported at 7.1% [1]. One-year major amputation rates ranged from 0.7% in patients with claudication (Rutherford categories 2-3) to 18.3% in those with significant tissue loss (Rutherford category 6) following peripheral endovascular

intervention [175]. Similarly, 1-year major adverse cardiovascular events (MACE) ranged from 8.2% in non-chronic limb-threatening ischemia (CLTI) patients to 29.5% in CLTI patients undergoing peripheral vascular intervention [197].

4.3 **Topic synthesis:**

- **Prognostic Factors and Biomarkers:** Elevated NT-proBNP levels (HR 1.71 for all-cause mortality [1]), psoas muscle CT value [3], elevated C-reactive protein (CRP) (HR 1.89 for MACE [7]), and impaired renal function (HR 1.68 for MACE [7]) are independently associated with adverse outcomes. Higher urinary Cystatin C to creatinine ratio (uCystatinC/uCr) predicts worsening PAD status (HR 1.78 [13]). Low leg muscle density (rate ratio 1.60 for cardiovascular events [26]), high lipoprotein(a) (Lp(a)) levels (HR 1.41 for PAD progression, HR 22.75 for limb amputation [80]), and high growth differentiation factor 15 (GDF15) levels (HR 4.01 for major amputation [126]) are also significant predictors.
- **Comorbidities and Systemic Associations:** Diabetes mellitus (DM) is a critical comorbidity, with Type 1 DM patients having a 44.6% limb amputation rate at 4 years [2], and DM independently predicting increased in-hospital mortality (OR 1.077 [91]) and major limb amputation (aOR 1.22 [110]). Chronic kidney disease (CKD) significantly increases risks of mortality, cardiovascular events, and lower-limb complications, with 10- to 12-fold higher risks in advanced CKD with PAD [100]. Polyvascular disease (involvement of multiple arterial beds) substantially increases the risk of MACE (aHR 1.99 for PAD + CAD + CVD [114]) and lower-extremity revascularization (aHR 1.34 for PAD + CAD + CVD [114]).
- **Therapeutic Interventions: Pharmacological and Revascularization:** Combination therapy of low-dose rivaroxaban plus aspirin significantly reduces major adverse cardiovascular and limb events (HR 0.85 [6]) and acute limb ischemia (ALI) (HR 0.67 [15]), but increases major bleeding (HR 1.42 [6]). High-intensity statin therapy is associated with improved survival (HR 0.52 [123]). Drug-eluting stents (DES) demonstrate significantly greater 12-month primary patency (83.2% vs 74.3%) and clinical improvement compared to bare metal stents (BMS) [8]. Drug-coated balloons (DCBs) show superiority over percutaneous transluminal angioplasty (PTA) with 12-month primary patency rates of 83.9% vs 60.6% [119].
- **Lifestyle and Rehabilitative Strategies:** Home-based walking exercise interventions improve walking distance (16.7 m difference at 3 months [9]) and health-related quality of life. Supervised exercise therapy (SET) can be successfully integrated into rehabilitation programs [23] and significantly improves claudication onset time (COT) and peak walking time (PWT) [28]. Ankle-foot orthoses (AFO) significantly improve peak walking time (PWT) and claudication onset time (COT) (e.g., PWT from 7.8 to 9.3 min [25]).

- **Health Disparities and Socioeconomic Determinants:** Women with PAD experience worse clinical outcomes [63, 66], including higher rates of death, myocardial infarction, or major amputation after endovascular treatment (adjusted HR 1.350 [20]), and stronger thrombotic propensity on aspirin [59]. Black and Hispanic patients undergoing revascularization have worse limb outcomes, including higher rates of major adverse limb events (MALEs) (HR 1.17 for Black patients, HR 1.22 for Hispanic patients) and amputations (HR 1.52 for Black patients, HR 1.45 for Hispanic patients) compared to White patients [89]. Socioeconomic deprivation is associated with a higher incidence of PAD [34] and increased amputation rates (4.4% higher per $10,000 lower median household income [194]).
- **Advanced Prediction and Risk Stratification:** Machine learning models can accurately predict outcomes after infrainguinal bypass (AUROC 0.94 [5]), detect PAD risk (AUC 0.96 [82]), and predict in-hospital mortality [83]. The Rutherford category (RC) system effectively stratifies outcomes, with 12-month freedom from major amputation ranging from 99.3% in RC2,3 to 81.7% in RC6 [175]. Ankle-brachial indices (ABI) are associated with limb outcomes, with ABI ≥1.4 linked to amputation and ABI <0.5 to revascularization [125].
- **Pathophysiological Mechanisms and Disease Progression:** Medial artery calcification (MAC) independently correlates with major amputation and mortality rates [62]. Critical limb ischemia (CLI) is associated with elevated levels of numerous circulating cytokines, suggesting a systemic inflammatory condition [54]. Microvascular disease (MVD) in PAD patients is associated with an augmented risk for major and minor amputations, MACE, in-hospital mortality, and readmission (OR 1.30 for major amputation [68]).

5) **Discussion**

5.1 **Principal finding:** The annual death rate for symptomatic peripheral artery disease patients admitted for endovascular repair was reported at 7.1% [1], highlighting the significant mortality burden associated with this condition.

5.2 **Clinical implications:**

- **Risk Stratification:** Clinicians should utilize prognostic markers such as NT-proBNP [1], CRP [7], and uCystatinC/uCr [13] to identify PAD patients at higher risk for adverse cardiovascular and limb events, enabling more aggressive management.
- **Comorbidity Management:** Intensive management of diabetes mellitus [91, 110] and chronic kidney disease [100] is critical, as these comorbidities significantly worsen PAD outcomes, including mortality and amputation risk.
- **Personalized Therapy:** Consideration of combination antithrombotic therapy with low-dose rivaroxaban and aspirin should be prioritized for PAD patients after revascularization to

reduce MACE and MALE [6, 15], balancing efficacy with bleeding risk.

- **Rehabilitation Emphasis:** Integrating supervised exercise therapy and home-based walking programs into standard care is essential to improve functional capacity and quality of life for patients with claudication [9, 23, 28].
- **Addressing Disparities:** Awareness and proactive strategies are needed to mitigate sex-based (e.g., worse outcomes in women [20, 63]) and socioeconomic/racial disparities (e.g., higher amputation rates in disadvantaged populations [89, 194]) in PAD care and outcomes.

5.3 **Research implications / key gaps:**

- **Long-term Outcomes of Novel Interventions:** Further randomized controlled trials are needed to compare the long-term efficacy and safety of newer revascularization techniques (e.g., atherectomy vs. stenting [220]) across diverse patient populations and lesion characteristics.
- **Biomarker Validation:** Prospective studies are required to validate emerging biomarkers (e.g., sortilin [102], GDF15 [126], MFAP4 [127]) as routine prognostic tools and to determine their utility in guiding personalized treatment strategies.
- **Disparity Interventions:** Research protocols should be developed to test targeted interventions aimed at reducing health disparities in PAD outcomes, particularly focusing on socioeconomic and racial factors [89, 194].
- **Machine Learning Integration:** Prospective studies are needed to evaluate the clinical impact and cost-effectiveness of integrating machine learning models for risk prediction [5, 82] into routine PAD patient management workflows.
- **Microvascular Disease Impact:** Further investigation into the specific mechanisms and optimal management strategies for comorbid microvascular disease in PAD patients is warranted, given its synergistic effect on amputation risk [68, 94].

5.4 **Limitations:**

- **Heterogeneity of Outcomes** — Varied definitions, timepoints, and reporting of outcomes across studies limit direct comparisons and comprehensive quantitative synthesis.
- **Observational Study Bias** — A significant proportion of the evidence comes from cohort studies, which are susceptible to confounding and selection bias, potentially affecting the generalizability of associations.
- **Lack of Standardized Metrics** — Inconsistent use of functional and quality of life metrics across studies makes it challenging to draw definitive conclusions on patient-reported

outcomes.

- **Geographic and Population Specificity** — Many studies are limited to specific geographic regions or patient subgroups, which may affect the applicability of findings to broader, diverse PAD populations.
- **Limited Causal Inference** — While associations are identified, the non-randomized nature of many studies precludes definitive conclusions about causality for many risk factors and interventions.

5.5 **Future directions:**

- **Standardized Outcome Reporting** — Develop and implement core outcome sets for PAD research to facilitate comparability and meta-analysis.
- **Comparative Effectiveness Trials** — Conduct large-scale RCTs comparing different revascularization strategies and medical therapies in specific PAD subgroups.
- **Biomarker-Guided Therapies** — Design trials to assess the efficacy of personalized treatment approaches based on novel prognostic biomarkers.
- **Health Equity Interventions** — Implement and evaluate community-based programs to address socioeconomic and racial disparities in PAD care.
- **AI-Driven Decision Support** — Develop and prospectively validate AI models for real-time risk stratification and treatment guidance in clinical settings.

6) **Conclusion**

Outcomes in peripheral artery disease (PAD) patients demonstrate significant variability depending on disease severity, comorbidities, and treatment strategies. For instance, the annual death rate for symptomatic PAD patients admitted for endovascular repair was reported at 7.1% [1]. This review highlights the complex interplay of prognostic factors, the efficacy of various pharmacological and interventional strategies, and the pervasive impact of health disparities on PAD outcomes. The heterogeneity of outcome reporting and the prevalence of observational study designs represent the most significant limitations to drawing definitive conclusions. Moving forward, a concrete next study should focus on implementing and evaluating targeted interventions to reduce the observed socioeconomic and racial disparities in PAD care and outcomes.

References

SAIMSARA Session Index — session.json

Figure 1. Publication-year distribution of included originals

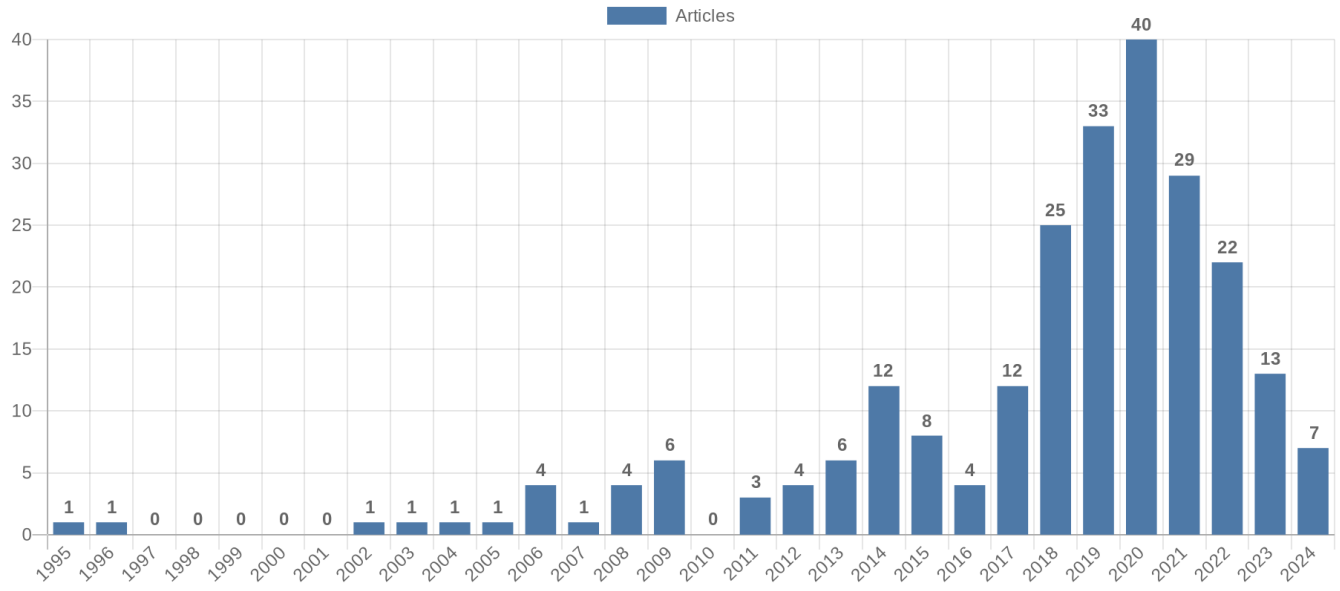


Figure 2. Study-design distribution of included originals

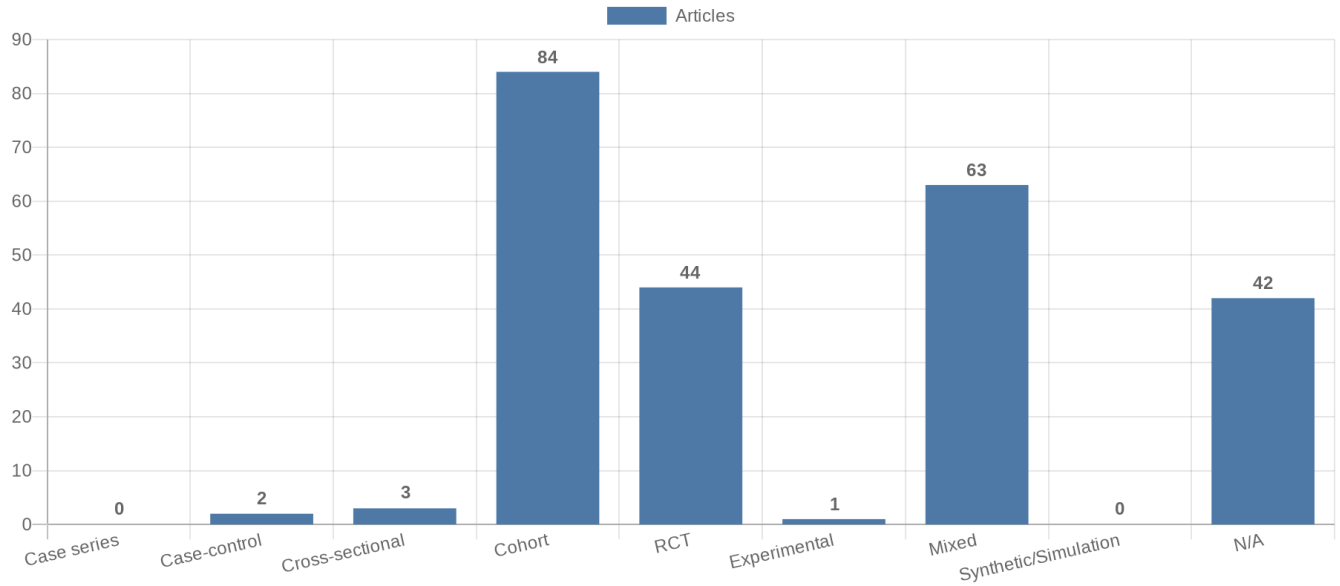


Figure 3. Study-type (directionality) distribution of included originals

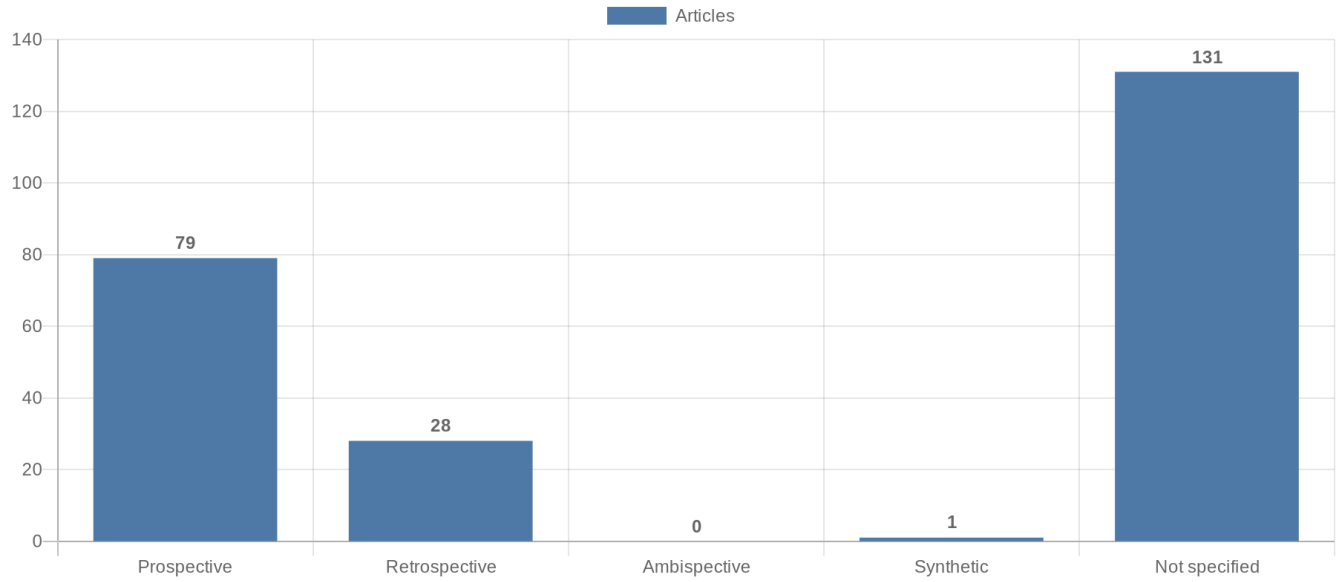


Figure 4. Main extracted research topics

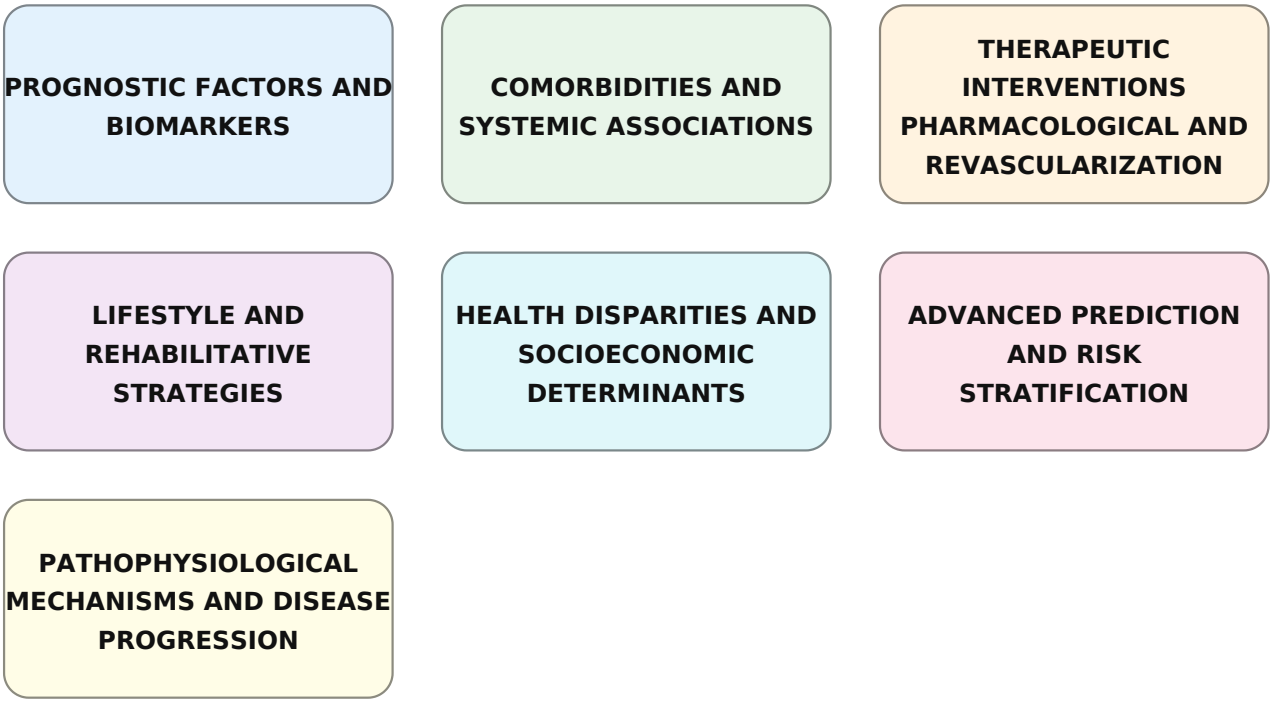


Figure 5. Limitations of current studies (topics)

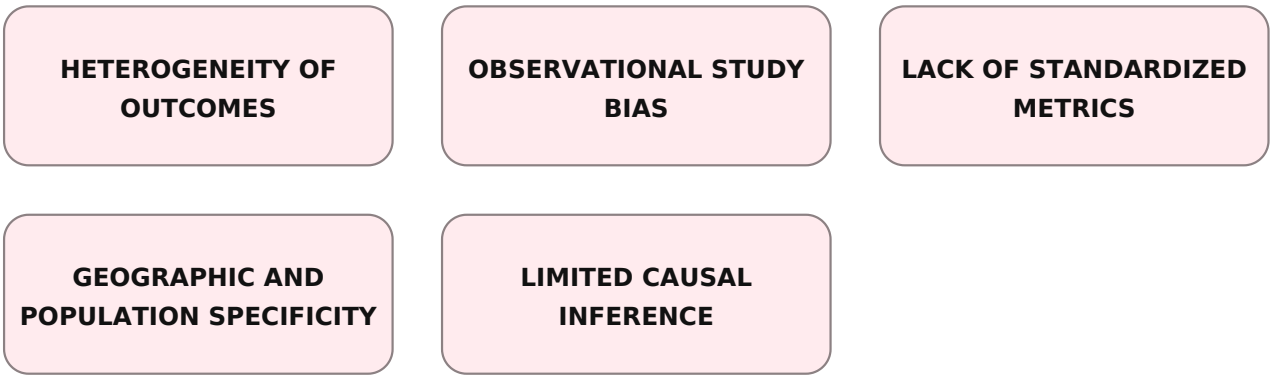


Figure 6. Future research directions (topics)

LONG-TERM OUTCOMES OF NOVEL INTERVENTIONS

BIOMARKER VALIDATION

DISPARITY INTERVENTIONS

MACHINE LEARNING INTEGRATION

MICROVASCULAR DISEASE IMPACT

STANDARDIZED OUTCOME REPORTING

COMPARATIVE EFFECTIVENESS TRIALS