

# PAD Bypass: Systematic Review with SAIMSARA.

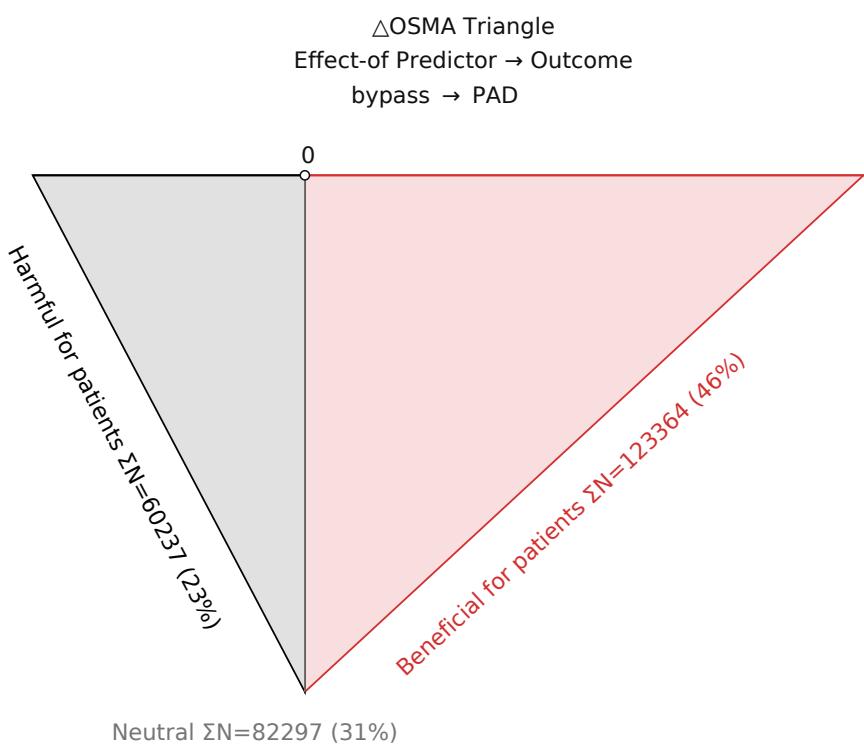
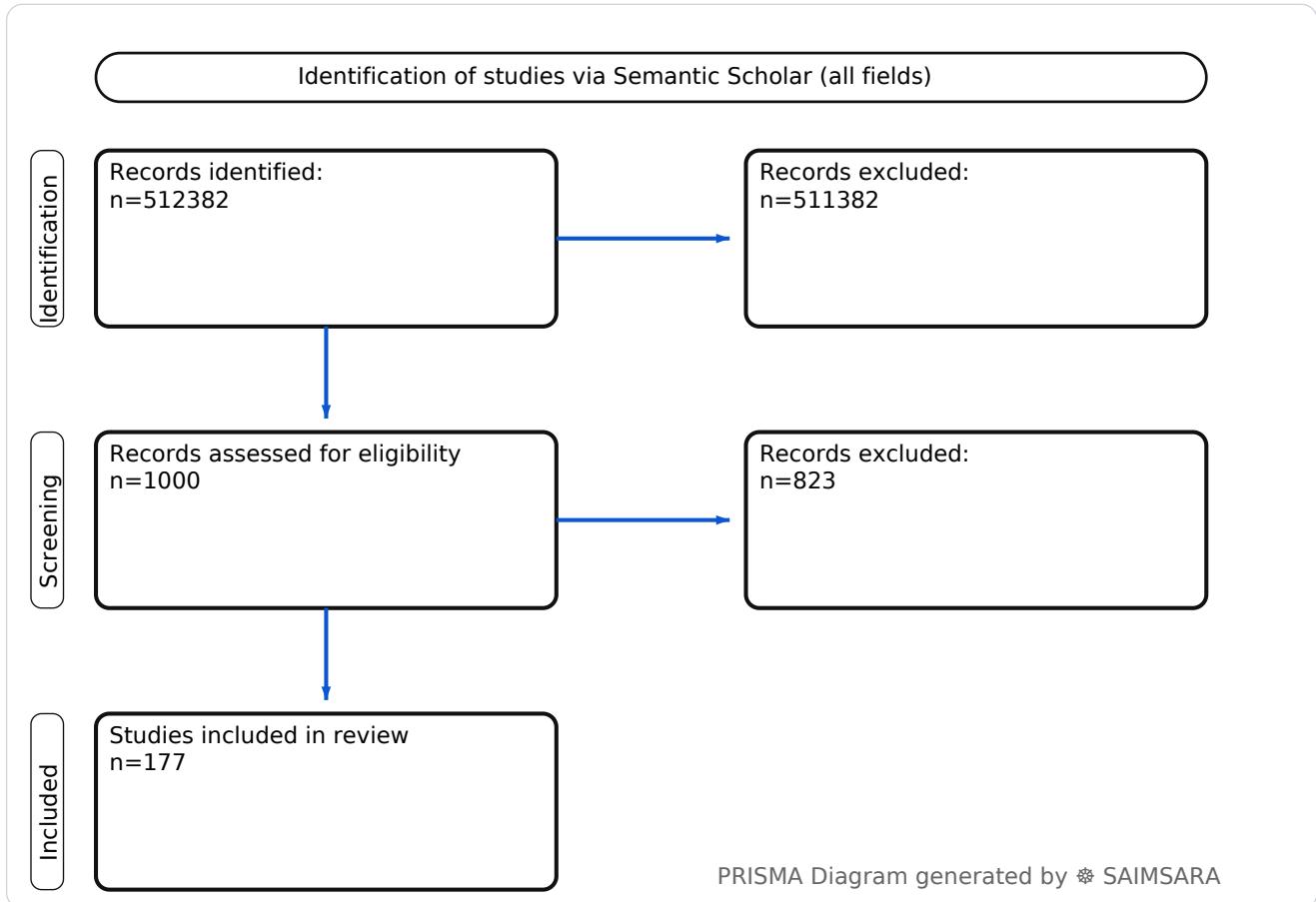
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**Abstract:** This paper aims to systematically review the current evidence on PAD bypass surgery, synthesizing findings related to its efficacy, safety, patient-specific outcomes, and comparative performance against alternative revascularization strategies, as well as identifying key biological insights and areas for future research. The review utilises 177 studies with 265898 total participants (naïve ΣN). Amputation-free survival was significantly better in the bypass surgery group (43.4 months) compared to the angioplasty and stenting group (39.8 months) for patients with ulcers or toe gangrenes. This suggests that for specific presentations of peripheral arterial disease, bypass surgery offers superior limb salvage outcomes. However, the heterogeneity of studies, particularly the prevalence of retrospective designs, represents the single limitation that most affects the certainty of these findings. Clinicians should consider bypass surgery as a primary revascularization strategy for critical limb ischemia, especially when a usable saphenous vein is available, while actively managing patient-specific risk factors like glycemic control and pre-operative cardiac status.

**Keywords:** Peripheral Arterial Disease; Bypass Surgery; Lower Extremity Revascularization; Graft Patency; Infrainguinal

## Review Stats

- Generated: 2026-02-03 11:33:19 CET
- Plan: Pro (expanded craft tokens; source: Semantic Scholar)
- Source: Semantic Scholar
- Scope: All fields
- Keyword Gate: Fuzzy ( $\geq 60\%$  of required terms, minimum 2 terms matched in title/abstract)
- Total Abstracts/Papers: 512382
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 177
- Total study participants (naïve ΣN): 265898



△OSMA Triangle generated by ♻ SAIMSARA

## Outcome-Sentiment Meta-Analysis (OSMA): (LLM-only)

Frame: Effect-of Predictor → Outcome • Source: Semantic Scholar

Outcome: PAD Typical timepoints: peri/post-op, 1-y. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: mortality, complications, patency.

Predictor: bypass — procedure/intervention. Routes seen: oral, topical. Typical comparator: saphenous vein grafts in both, non-diabetic patients, single antiplatelet therapy, best medical treatment....

- **1) Beneficial for patients** — PAD with bypass — [1], [9], [10], [12], [14], [15], [18], [24], [25], [27], [29], [31], [38], [39], [42], [44], [46], [47], [49], [51], [52], [60], [62], [67], [119], [122], [151], [164], [166], [172], [173], [175] —  $\Sigma N=123364$
- **2) Harmful for patients** — PAD with bypass — [2], [3], [4], [7], [8], [16], [20], [21], [23], [28], [30], [32], [41], [48], [55], [61], [69], [118], [120], [125], [153], [157], [165], [176] —  $\Sigma N=60237$
- **3) No clear effect** — PAD with bypass — [5], [6], [11], [13], [17], [19], [22], [26], [33], [34], [35], [36], [37], [40], [43], [45], [50], [53], [54], [56], [57], [58], [59], [63], [64], [65], [66], [68], [70], [71], [72], [73], [74], [75], [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], [121], [123], [124], [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], [154], [155], [156], [158], [159], [160], [161], [162], [163], [167], [168], [169], [170], [171], [174], [177] —  $\Sigma N=82297$

## Introduction

Peripheral arterial disease (PAD) represents a significant global health burden, characterized by stenoses or occlusions in arteries supplying the limbs, most commonly the lower extremities. Surgical bypass remains a cornerstone of revascularization strategies for PAD, particularly in cases of critical limb ischemia (CLTI) where limb salvage is paramount. This procedure aims to restore blood flow to ischemic tissues, thereby alleviating symptoms, promoting wound healing, and preventing amputation. Beyond the immediate technical success, the long-term efficacy, patient-specific outcomes, and comparative effectiveness against evolving endovascular therapies are subjects of ongoing research. Understanding the multifaceted aspects of PAD bypass, including its biological benefits, patient risk factors, and the influence of systemic conditions, is crucial for optimizing patient

management and improving clinical outcomes.

## Aim

This paper aims to systematically review the current evidence on PAD bypass surgery, synthesizing findings related to its efficacy, safety, patient-specific outcomes, and comparative performance against alternative revascularization strategies, as well as identifying key biological insights and areas for future research.

## Methods

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

- **Bias:** The included studies predominantly consist of retrospective cohort studies and mixed designs, with fewer prospective randomized controlled trials (RCTs). This introduces a potential for selection bias and confounding, particularly in observational comparisons between different treatment modalities or patient subgroups. Case reports, while offering unique insights, have limited generalizability. Variability in study populations, surgical techniques, and follow-up durations across studies further contributes to heterogeneity and potential bias in synthesizing results.

## Results

### 4.1 Study characteristics:

The extracted literature comprises a diverse range of study designs, including numerous retrospective cohort studies, mixed-design investigations, and several prospective randomized controlled trials or cohort studies. Populations frequently include patients with peripheral arterial disease (PAD) undergoing various bypass procedures (e.g., infra-inguinal, femoropopliteal, aortoiliac), as well as those undergoing coronary artery bypass grafting (CABG) with concomitant PAD. Typical follow-up periods range from 30 days to 10 years, with several studies reporting 1-year, 3-year, or 5-year outcomes.

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

Amputation-free survival (AFS) was reported to be significantly better in the bypass surgery group (median 43.4 months, range 43.4 to 39.8 months) compared to the angioplasty and stenting group (median 39.8 months, range 43.4 to 39.8 months) for patients with ulcers or toe gangrenes [119].

### 4.3 Topic synthesis:

- **Biological Benefits of Revascularization:** Surgical bypass attenuates AIM2 inflammasome expression and pyroptotic caspase activity in PAD muscle, demonstrating a unique biological benefit of muscle revascularization [1]. Impaired angiogenesis was identified in ischemic adipose tissue from PAD patients undergoing infrainguinal bypass, linked to novel microRNA pathways [56].
- **Patient-Specific Risk Factors and Outcomes:** Female gender is independently associated with significantly longer hospital stays following infra-inguinal bypass for PAD [2, 23]. Elevated pre-operative NTProBNP is independently associated with medium-term mortality following infra-inguinal bypass [8]. Glycaemic variability (GV) and mean HbA1c are associated with adverse outcomes, including lower primary and secondary patency, and GV is an independent predictor of graft failure following infra-inguinal bypass [3, 4]. Hemodialysis (HD) patients undergoing bypass surgery for PAD have significantly lower long-term survival rates from major adverse cardiovascular events (MACE) and higher mortality compared to non-HD patients [48, 61]. Frailty is associated with higher mortality and unplanned amputations in lower extremity bypass patients [138]. Lower preoperative ABI is associated with postoperative intensive care unit delirium [85]. Myeloproliferative neoplasms (MPN) increase the risk of major adverse limb events (MALE) and readmissions in PAD patients [137]. Anemia in diabetic patients is linked to more frequent bypass surgeries and higher mortality [140].
- **Comparative Efficacy of Revascularization Strategies:** Vein bypass (VBP) retains advantages over endovascular therapy (ET) for infrainguinal PAD in terms of efficacy and safety, showing lower risks of reintervention and major reintervention [9]. Saphenous vein (SV) grafts showed higher primary patency rates compared to polytetrafluoroethylene (PTFE) grafts in femoro-above-the-knee (AK) bypasses [51], and are considered the best graft for above-the-knee femoropopliteal bypass [17]. For complex femoro-popliteal lesions, endovascular procedures show better outcomes at 24 months than prosthetic bypasses [27]. Endoluminal bypass using heparin-bonded self-expanding covered stents provided comparable clinical and health-related outcomes to surgical bypass for extensive femoropopliteal disease through 5 years, though with a higher reintervention rate [20]. Endovascular intervention and surgical bypass demonstrated comparable long-term outcomes in patients with aortoiliac PAD [11]. Surgical bypass was associated with a significantly lower incidence of major adverse limb events or death compared to endovascular intervention in patients with a usable great saphenous vein for bypass [122]. Amputation-free survival was significantly better in the bypass surgery group (43.4 months) compared to the angioplasty and stenting group (39.8 months) [119].
- **Complications and Graft Management:** Chronic obstructive pulmonary disease (COPD) patients had higher sepsis, wound complications, and 30-day readmission rates after infrainguinal bypass surgery [16]. Post-operative transfusion is associated with infrainguinal

bypass graft failure [30]. Poor adherence to ultrasound surveillance is significantly associated with infrainguinal bypass graft failure [21]. Open bypass grafting was associated with increased FVIII activity and bypass graft thrombosis [81]. A concomitant femoropopliteal (FEM-POP) bypass significantly worsened long-term femorofemoral (FEM-FEM) bypass patency and limb salvage rate [41].

- **Adjunctive Therapies and Monitoring:** Optimal medical therapy, including statins, smoking cessation, and management of hypertension and diabetes, is essential for maximizing the benefits of lower extremity bypass and reducing long-term risks in PAD patients [18]. Direct oral anticoagulants (DOACs) appear to be a viable alternative to warfarin in maintaining graft patency in below-the-knee autologous vein bypasses [12]. Continuous aspirin use in hemodialysis patients with PAD was associated with a reduced risk of surgical bypass [60]. An individualized exercise program significantly improved health-related quality of life (HRQOL) and walking distance in patients recovering from bypass surgery [44, 86]. Calibrated Automated Thrombography (CAT) may serve as a complementary tool for predicting thrombosis risk in PAD patients post-revascularization [55]. An electronic vascular conduit was developed for *in situ*, real-time, and long-term monitoring of hemadostenosis and thrombosis following bypass surgery [50].
- **Surgical Techniques and Training:** There is high variability in surgical experience, techniques, and training exposure for tibial and pedal bypass surgery in Germany [6]. *In situ* saphenous vein bypass is effective and safe, with a high technical success rate [29]. The posterior approach provides excellent exposure for distal surgical revascularization, such as popliteal to peroneal bypass [31]. Axillofemoral bypass is a viable bailout procedure for severe aortoiliac disease when standard reconstruction is complicated [13]. Thoracofemoral extra-anatomic bypass is an easy and safe alternative for patients with high laparotomy risks [22].
- **Systemic and Socioeconomic Influences:** Adverse social determinants of health, such as government/self-pay insurance and low income, are associated with an increased risk of incident PAD, including bypass [7]. Medicaid Expansion was associated with a significant increase in infrainguinal bypass for non-severe and elective cases, along with improved in-hospital mortality and major adverse limb events (MALE) at 1 year [39]. Racial disparities exist in CLTI treatment, with Black patients less likely to receive open bypass surgery [72].

## Discussion

### 5.1 Principal finding:

For patients presenting with ulcers or toe gangrenes, bypass surgery was associated with a significantly better amputation-free survival of 43.4 months compared to 39.8 months for angioplasty and stenting [119].

## 5.2 Clinical implications:

- Surgical bypass should be prioritized over endovascular intervention for CLTI patients with a usable great saphenous vein, given its association with lower major adverse limb events or death [122].
- Aggressive management of glycemic variability and mean HbA1c is critical in PAD patients undergoing infra-inguinal bypass to improve graft patency and reduce adverse outcomes [3, 4].
- Pre-operative screening for elevated NTProBNP should be considered in infra-inguinal bypass candidates to identify patients at higher risk of medium-term mortality [8].
- Continuous aspirin use should be encouraged in hemodialysis patients with PAD to reduce the risk of surgical bypass and improve cardiovascular outcomes [60].
- Individualized exercise programs and optimal medical therapy are essential adjunctive treatments post-bypass to improve quality of life and reduce long-term risks [18, 44, 86].

## 5.3 Research implications / key gaps:

- **Long-Term Graft Patency:** Future prospective studies are needed to compare long-term primary and secondary patency rates of various graft materials (e.g., saphenous vein vs. prosthetic) in different anatomical locations (e.g., femoropopliteal above-knee vs. below-knee) beyond 5 years [51].
- **Biomarkers for Thrombosis:** Research should focus on validating calibrated automated thrombography (CAT) and other novel biomarkers for predicting thrombosis risk in PAD patients post-revascularization in larger cohorts [55].
- **Impact of Social Determinants:** Further investigation is warranted into how adverse social determinants of health influence access to and outcomes of bypass surgery for PAD, and how to mitigate these disparities [7, 72].
- **Inflammation and Graft Failure:** Prospective studies could explore the role of persistent inflammation and specific inflammatory markers (e.g., AIM2 inflammasome, FVIII activity) in predicting bypass graft failure and informing targeted anti-inflammatory therapies [1, 77, 81].
- **Surgical Training Standardization:** A multi-center study could evaluate the impact of standardized training programs for tibial and pedal bypass surgery on surgical outcomes and patency rates across different centers [6].

## 5.4 Limitations:

- **Heterogeneity of Studies** — The varied study designs, populations, and outcome metrics limit direct comparisons and generalizability.
- **Retrospective Design Dominance** — Many studies are retrospective, introducing potential for selection bias and confounding factors.
- **Limited Long-Term Data** — While some studies report long-term outcomes, comprehensive, consistent long-term data across all bypass types and patient subgroups are scarce.
- **Inconsistent Outcome Reporting** — Diverse reporting of patency rates, complications, and patient-reported outcomes hinders meta-analysis.
- **Small Sample Sizes** — Several studies, particularly those on biological mechanisms or specific techniques, have very small sample sizes, limiting statistical power.

## 5.5 Future directions:

- **Prospective Comparative Trials** — Conduct large-scale RCTs comparing bypass techniques.
- **Standardized Outcome Reporting** — Implement uniform reporting guidelines for bypass outcomes.
- **Novel Graft Material Assessment** — Evaluate new graft materials in long-term studies.
- **Personalized Risk Stratification** — Develop tools for individualized risk prediction.
- **Remote Graft Surveillance** — Investigate electronic conduits for real-time monitoring.

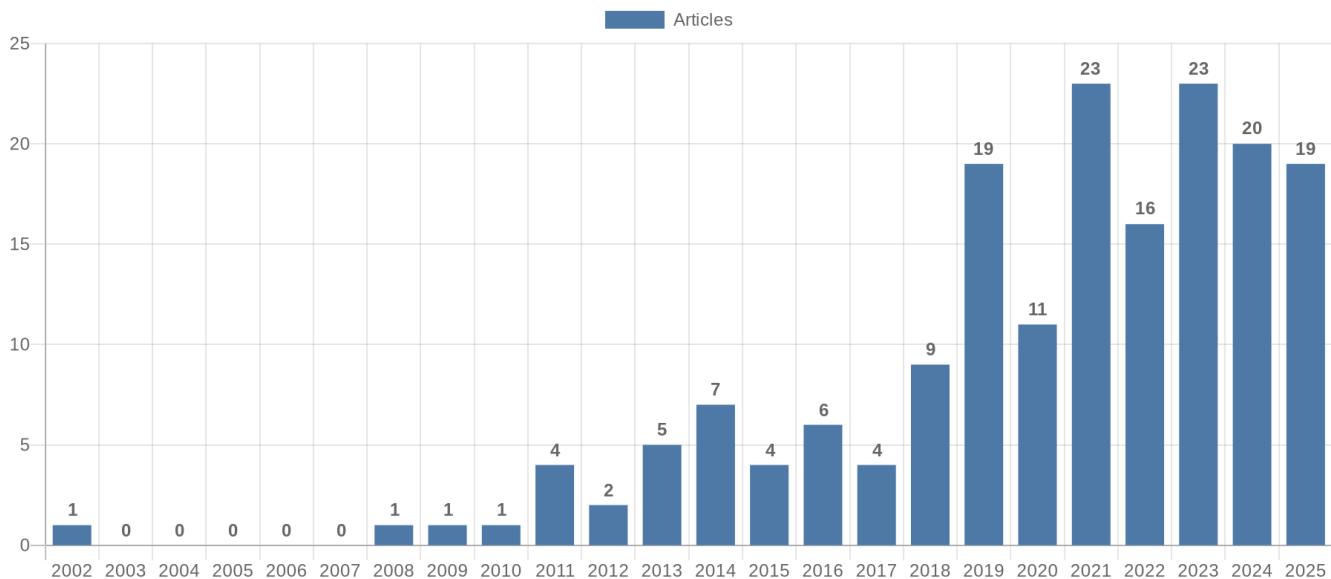
## Conclusion

Amputation-free survival was significantly better in the bypass surgery group (43.4 months) compared to the angioplasty and stenting group (39.8 months) for patients with ulcers or toe gangrenes [119]. This suggests that for specific presentations of peripheral arterial disease, bypass surgery offers superior limb salvage outcomes. However, the heterogeneity of studies, particularly the prevalence of retrospective designs, represents the single limitation that most affects the certainty of these findings. Clinicians should consider bypass surgery as a primary revascularization strategy for critical limb ischemia, especially when a usable saphenous vein is available, while actively managing patient-specific risk factors like glycemic control and pre-operative cardiac status.

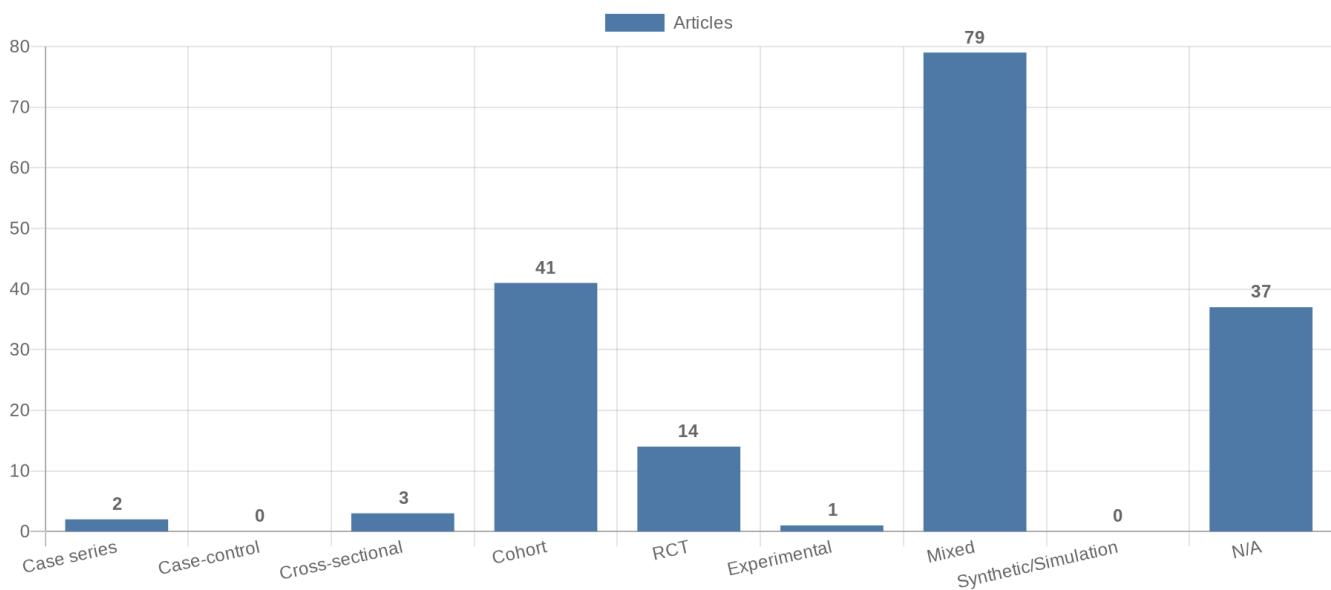
## References

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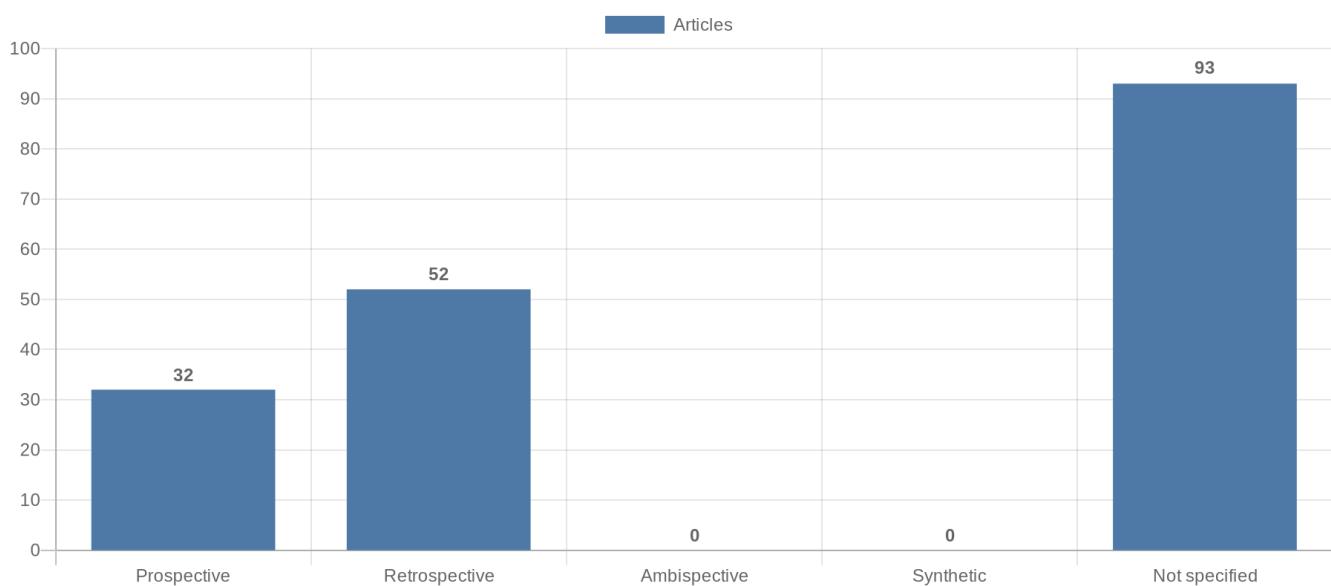
## Figure 1. Publication-year distribution of included originals



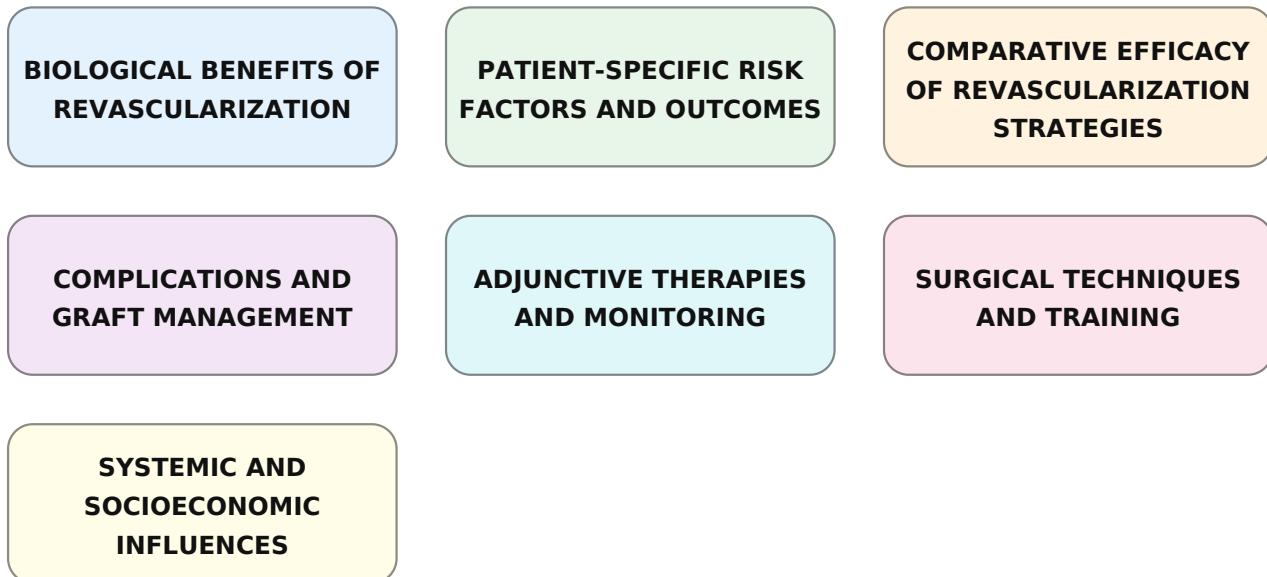
**Figure 2. Study-design distribution of included originals**



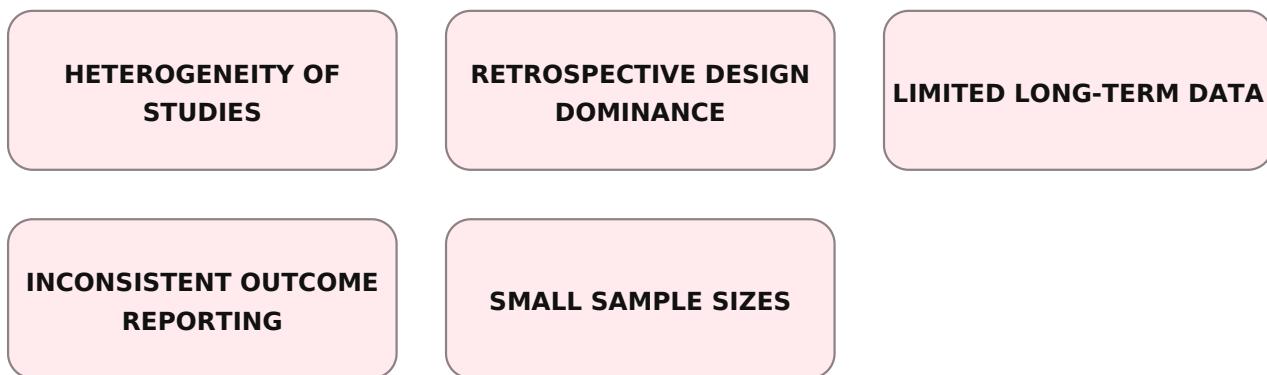
**Figure 3. Study-type (directionality) distribution of included originals**



**Figure 4. Main extracted research topics**



**Figure 5. Limitations of current studies (topics)**



**Figure 6. Future research directions (topics)**

