Peripheral Artery Disease and Gender: Systematic Review with ☸SAIMSARA.

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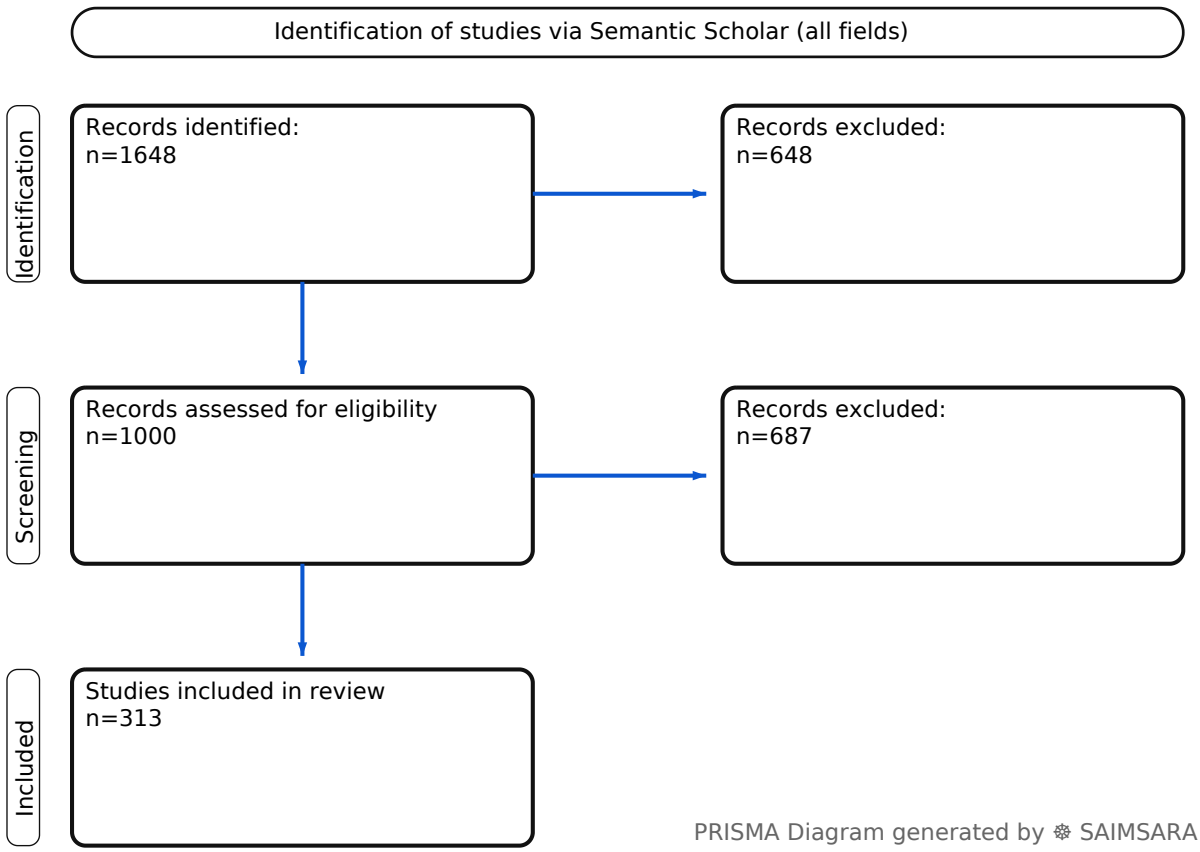
Abstract: The aim of this paper is to systematically review and synthesize the current evidence regarding peripheral artery disease and gender, identifying specific differences in epidemiology, pathophysiology, clinical characteristics, treatment, and outcomes. The review utilises 313 studies with 2050605 total participants (naïve ΣN). The relationship between gender and peripheral artery disease (PAD) burden and outcomes is complex and often contradictory across studies, preventing a single, directly comparable numerical central value. For instance, age-adjusted multiple cause-of-death (MCOD) rates for PAD were higher in males (25.6) than females (19.4) in the US from 1999-2017. The generalizability of findings is limited by the diverse study populations and varying definitions of PAD and its outcomes. The most significant limitation affecting certainty is the Inconsistent Outcome Definitions, which hinders direct comparison and synthesis of numerical results. A practical takeaway for clinicians is to be aware of the nuanced and often conflicting evidence regarding gender differences in PAD, and to consider individualized risk assessment and management strategies that account for these disparities.

Review Stats

- Generated: 2026-01-27 19:40:20 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: 1648
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 313
- Total study participants (naïve ΣN): 2050605


Identification of studies via Semantic Scholar (all fields)
Identification
Records identified:
n=1648
Records excluded:
n=648
Screening
Records assessed for eligibility
n=1000
Records excluded:
n=687
Included
Studies included in review
n=313
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
gender → peripheral artery disease
0
Harmful for patients ΣN=676924 (33%)
Beneficial for patients ΣN=13384 (1%)
Neutral ΣN=1360297 (66%)
△OSMA Triangle generated by ☸SAIMSARA

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

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

Outcome: peripheral artery disease Typical timepoints: peri/post-op, 5-y. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: mortality, complications, admission.

Predictor: gender — exposure/predictor. Doses/units seen: 25.04 mg, 52.73 mg, 0.22 mg, 0.23 mg. Routes seen: iv. Typical comparator: men, women over a 13-year period, males, 54....

- **1) Beneficial for patients** — peripheral artery disease with gender — [18], [20], [53], [136], [158], [164], [168], [172], [189], [193], [196], [199] — ΣN=13384
- **2) Harmful for patients** — peripheral artery disease with gender — [1], [4], [11], [13], [14], [16], [23], [27], [30], [33], [34], [41], [44], [50], [55], [62], [68], [71], [74], [75], [76], [77], [79], [81], [88], [97], [98], [99], [103], [105], [114], [119], [123], [130], [131], [135], [138], [139], [140], [142], [143], [145], [148], [150], [152], [155], [156], [157], [159], [161], [167], [170], [174], [188], [190], [194], [195], [197], [226], [231], [247], [250], [260], [264], [269], [275], [282], [283], [286], [302], [303], [309] — ΣN=676924
- **3) No clear effect** — peripheral artery disease with gender — [2], [3], [5], [6], [7], [8], [9], [10], [12], [15], [17], [19], [21], [22], [24], [25], [26], [28], [29], [31], [32], [35], [36], [37], [38], [39], [40], [42], [43], [45], [46], [47], [48], [49], [51], [52], [54], [56], [57], [58], [59], [60], [61], [63], [64], [65], [66], [67], [69], [70], [72], [73], [78], [80], [82], [83], [84], [85], [86], [87], [89], [90], [91], [92], [93], [94], [95], [96], [100], [101], [102], [104], [106], [107], [108], [109], [110], [111], [112], [113], [115], [116], [117], [118], [120], [121], [122], [124], [125], [126], [127], [128], [129], [132], [133], [134], [137], [141], [144], [146], [147], [149], [151], [153], [154], [160], [162], [163], [165], [166], [169], [171], [173], [175], [176], [177], [178], [179], [180], [181], [182], [183], [184], [185], [186], [187], [191], [192], [198], [200], [201], [202], [203], [204], [205], [206], [207], [208], [209], [210], [211], [212], [213], [214], [215], [216], [217], [218], [219], [220], [221], [222], [223], [224], [225], [227], [228], [229], [230], [232], [233], [234], [235], [236], [237], [238], [239], [240], [241], [242], [243], [244], [245], [246], [248], [249], [251], [252], [253], [254], [255], [256], [257], [258], [259], [261], [262], [263], [265], [266], [267], [268], [270], [271], [272], [273], [274], [276], [277], [278], [279], [280], [281], [284], [285], [287], [288], [289], [290], [291], [292], [293], [294], [295], [296], [297], [298], [299], [300], [301], [304], [305], [306], [307], [308], [310], [311], [312], [313] — ΣN=1360297

1) Introduction

Peripheral artery disease (PAD) is a significant global public health concern, characterized by the narrowing of arteries that supply blood to the limbs, most commonly the legs. Its burden and temporal trends vary considerably by location, age, socioeconomic status, and notably, gender [7, 14, 152]. Understanding these gender-specific differences in PAD prevalence, risk factors, clinical presentation, treatment responses, and outcomes is crucial for optimizing diagnosis, management, and prognosis [3, 16]. While some studies suggest a heavier absolute burden in males, others indicate elevated age-standardized rates or worse clinical outcomes in females, highlighting complex and interacting factors contributing to gender-related inequities in PAD [14, 16, 152]. This paper synthesizes current research on the interplay between PAD and gender, identifying key themes and research gaps.

2) Aim

The aim of this paper is to systematically review and synthesize the current evidence regarding peripheral artery disease and gender, identifying specific differences in epidemiology, pathophysiology, clinical characteristics, treatment, and outcomes.

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. Retrospective cohort and cross-sectional studies are prevalent, introducing potential for selection and recall bias. Many studies did not specify directionality or follow-up, limiting causal inference. Small sample sizes in some studies and reliance on specific populations (e.g., diabetic patients, surgical inpatients) may limit generalizability.

4) Results

4.1 Study characteristics

The included studies predominantly employed cohort (e.g., [1, 5, 10]) and cross-sectional designs (e.g., [2, 9, 18]), often retrospective, with some mixed-design studies [3, 4, 11]. Populations ranged from large national registries [8, 14, 15] and multi-ethnic cohorts [10] to specific patient groups such as those with type 2 diabetes mellitus (T2DM) [1, 29, 33], vascular surgery inpatients [2], or individuals undergoing specific interventions [4, 11, 30]. Follow-up periods varied widely, from 30-day post-operative [4] to 13 years [15], or were not specified for cross-sectional designs.

4.2 Main numerical result aligned to the query

The relationship between gender and peripheral artery disease (PAD) burden and outcomes is complex and often contradictory across studies, preventing a single, directly comparable numerical central value. For instance, age-adjusted multiple cause-of-death (MCOD) rates for PAD were higher in males (25.6) than females (19.4) in the US from 1999-2017 [8]. Conversely, in a Thai population, the age-standardized prevalence of PAD was 9.00% in women compared to 3.88% in men, with female gender being a statistically significant risk factor (OR = 1.9) [174]. In another cohort, the risk of PAD was positively correlated with metabolic syndrome (MetS) components, with a significantly stronger association observed in female patients [1]. Similarly, females exhibited elevated age-standardized rates of PAD from 1990-2019 in the United States, despite males bearing a heavier absolute burden [14]. In contrast, male gender was identified as an independent predictor of PAD (OR = 0.441, 95% CI: 0.249-0.782) in one cohort [18] and was associated with a 1.77-fold higher odds of PAD in T2DM patients in another [135].

4.3 Topic synthesis

- **Prevalence and Burden:** While males may bear a heavier absolute PAD burden, females often exhibit elevated age-standardized rates globally and in specific populations [14, 152, 167, 174]. Age-adjusted PAD mortality rates were higher in males (25.6 vs 19.4) but the gap is decreasing [8, 130].
- **Risk Factors and Associations:** The association between metabolic syndrome components and PAD is stronger in females [1]. TyG Index (TyGI) shows a linear correlation with PAD in males, but a non-linear relationship with a threshold in females [2]. Baseline coronary artery calcium score (CACs) is associated with incident PAD in males (1.11-fold higher odds per unit increase), but not in females [10]. Male gender is a significant contributor to PAD risk factors like age, smoking, and hyperlipidemia [12, 150].
- **Clinical Presentation and Disease Severity:** Women with PAD are often older, have a higher mean BMI, and more frequently present with hypercholesterolemia, obesity, cerebrovascular disease, and chronic kidney disease, while men are more frequent smokers and have more coronary artery disease [3, 144]. Women undergoing endovascular interventions for PAD present with more severe disease [11]. Male gender is associated with increased PAD severity (OR: 6.0, 95% CI: 1.1–32.2) [123].
- **Treatment and Management Disparities:** Optimal medical treatment (OMT) for PAD, including statins and renin-angiotensin-aldosterone system inhibitors, is insufficiently prescribed, particularly in women [6]. Female patients undergoing endovascular lower extremity (LE) interventions for PAD have higher rates of clinically driven target lesion revascularization (TLR) [50, 231] and are less likely to be taking statins (73% vs 78%) [11]. Female gender is also associated with lower initiation rates of cardioprotective glucose-lowering drugs in T2DM patients with CVD [43].

- **Post-operative Outcomes and Complications:** Females exhibit a significantly higher risk of post-operative stroke ($p < 0.001$), all-cause morbidity ($p = 0.004$), mortality ($p < 0.001$), and major adverse cardiovascular events ($p < 0.001$) in PAD surgery [4]. Women undergoing LE endovascular interventions also have higher adjusted rates of in-hospital mortality (OR 1.25, 95% CI 1.09-1.44) [11]. Conversely, male gender is an independent predictor of re-PTA [30], amputation [3, 41, 88, 97, 119, 159, 158], and death after amputation [140], and is associated with higher in-hospital mortality in acute myocardial infarction (AMI) patients with PAD [35]. Female gender was associated with significantly worse amputation-free survival in acute limb ischemia (ALI) patients treated with aspiration mechanical thrombectomy (OR 2.71, 1.03–7.17) [226].
- **Functional Status and Quality of Life:** Women with PAD report poorer physical (PCS: 37±10 vs 40±10, P=0.004) and mental (MCS: 47±12 vs 49±11, P=0.005) health status at diagnosis and follow-up compared to men [34, 44]. However, female gender was a protective factor for high quality of life in patients with in-stent restenosis after interventional therapy [20].
- **Biological Markers and Pathophysiology:** Gender differences exist in Elabela expression, with males generally showing higher levels [22]. Lp(a) levels are higher in women than in men [56, 209]. Male gender is associated with higher coronary artery calcium score (CACS) values [145] and greater total plaque burden in non-calcified plaque groups [271]. Atherosclerosis is higher in males, while thrombosis is more prevalent in females with T2DM and PAD [48].

5) Discussion

5.1 Principal finding

The relationship between gender and peripheral artery disease (PAD) burden and outcomes is complex and often contradictory across studies, preventing a single, directly comparable numerical central value. For instance, age-adjusted multiple cause-of-death (MCOD) rates for PAD were higher in males (25.6) than females (19.4) in the US from 1999-2017 [8].

5.2 Clinical implications

- **Tailored Risk Assessment:** Clinicians should recognize that risk factor associations (e.g., MetS, TyGI, CACs) and their predictive power for PAD can differ significantly by gender, necessitating gender-specific risk stratification [1, 2, 10].
- **Enhanced Monitoring for Women:** Given the higher risk of post-operative stroke, overall morbidity, and mortality in females undergoing PAD surgery [4], and higher rates of reintervention post-endovascular therapy [50, 231], women may require more intensive

post-procedural monitoring and follow-up.

- **Addressing Treatment Disparities:** The under-prescription of optimal medical treatment (OMT), including statins and cardioprotective glucose-lowering drugs, in women with PAD [6, 11, 43] highlights a critical need for interventions to ensure equitable care.
- **Focus on Amputation Risk in Men:** The consistent identification of male gender as a predictor for amputation and reamputation in PAD patients, particularly those with diabetes [3, 41, 88, 97, 119, 159], suggests a need for targeted amputation prevention strategies in men.
- **Holistic Patient Support:** Poorer physical and mental health status observed in women with PAD [34, 44] indicates a need for comprehensive support systems that address both physical and psychological well-being.

5.3 Research implications / key gaps

- **Standardized Gender-Stratified Outcomes:** Future studies need to standardize outcome definitions (e.g., PAD prevalence, amputation, mortality) and consistently report gender-stratified analyses to allow for more robust comparisons and meta-analyses [8, 174].
- **Mechanistic Studies on Biological Markers:** Research is needed to elucidate the underlying biological mechanisms driving gender differences in markers like Elabela [22], Lp(a) [56], and CACs [10, 145], and how these contribute to PAD pathogenesis and progression.
- **Prospective Studies on Treatment Efficacy:** There is a gap in prospective studies evaluating the gender-specific efficacy and safety of various PAD interventions (e.g., exercise programs, endovascular therapies, surgical revascularization) to inform tailored treatment guidelines [5, 50, 69].
- **Impact of Socioeconomic and Psychosocial Factors:** Further research should explore how socioeconomic status, access to care, and psychosocial factors (e.g., depression, health literacy) interact with gender to influence PAD burden and outcomes [39, 19, 24].
- **Longitudinal Quality of Life Assessment:** Longitudinal studies are needed to understand the long-term trajectory of physical and mental quality of life in PAD patients, with detailed gender stratification and identification of modifiable factors [34, 44].

5.4 Limitations

- **Heterogeneous Study Designs** — The diverse range of study designs (cohort, cross-sectional, mixed, retrospective) limits the ability to draw definitive causal conclusions or

directly compare outcomes across all studies.

- **Varying Population Samples** — Studies were conducted in diverse populations (e.g., T2DM patients, surgical inpatients, general population, specific ethnicities), making it challenging to generalize findings broadly.
- **Inconsistent Outcome Definitions** — Different studies used varying definitions for PAD, its severity, and associated complications, which can lead to discrepancies in reported prevalence and risk factors.
- **Lack of Standardized Metrics** — The absence of a single, consistently reported quantitative metric for gender-specific PAD burden or outcomes prevented a direct numerical synthesis across all studies.
- **Qualitative Bias Inference** — Bias was inferred qualitatively from study designs, and a formal quantitative assessment of bias was not performed, which could affect the interpretation of the strength of evidence.

5.5 Future directions

- **Standardize Reporting Guidelines** — Implement standardized reporting guidelines for gender-specific PAD outcomes and risk factors in all cardiovascular research.
- **Large-scale Prospective Cohorts** — Conduct large-scale, prospective cohort studies with balanced gender representation and long-term follow-up across diverse populations.
- **Investigate Biological Pathways** — Explore specific biological and hormonal pathways that contribute to observed gender differences in PAD susceptibility and progression.
- **Develop Gender-specific Guidelines** — Create and test gender-specific clinical guidelines for PAD screening, diagnosis, and management based on robust evidence.
- **Assess Healthcare Access Disparities** — Research the impact of healthcare access, health literacy, and socioeconomic factors on gender disparities in PAD care and outcomes.

6) Conclusion

The relationship between gender and peripheral artery disease (PAD) burden and outcomes is complex and often contradictory across studies, preventing a single, directly comparable numerical central value. For instance, age-adjusted multiple cause-of-death (MCOD) rates for PAD were higher in males (25.6) than females (19.4) in the US from 1999-2017 [8]. The generalizability of findings is limited by the diverse study populations and varying definitions of PAD and its outcomes. The most significant limitation affecting certainty is the **Inconsistent Outcome Definitions**, which hinders direct comparison and synthesis of numerical results. A practical takeaway for clinicians is to be aware of the nuanced and often conflicting evidence regarding gender differences in PAD, and to

consider individualized risk assessment and management strategies that account for these disparities.

References

SAIMSARA Session Index — session.json

Figure 1. Publication-year distribution of included originals

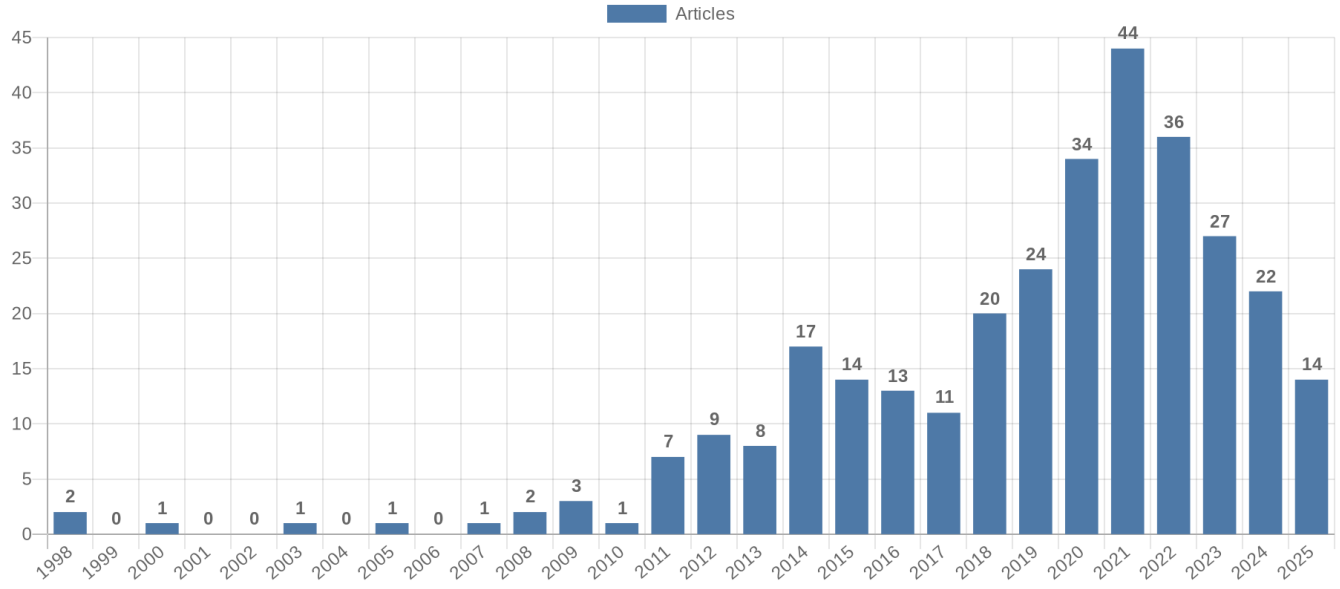


Figure 2. Study-design distribution of included originals

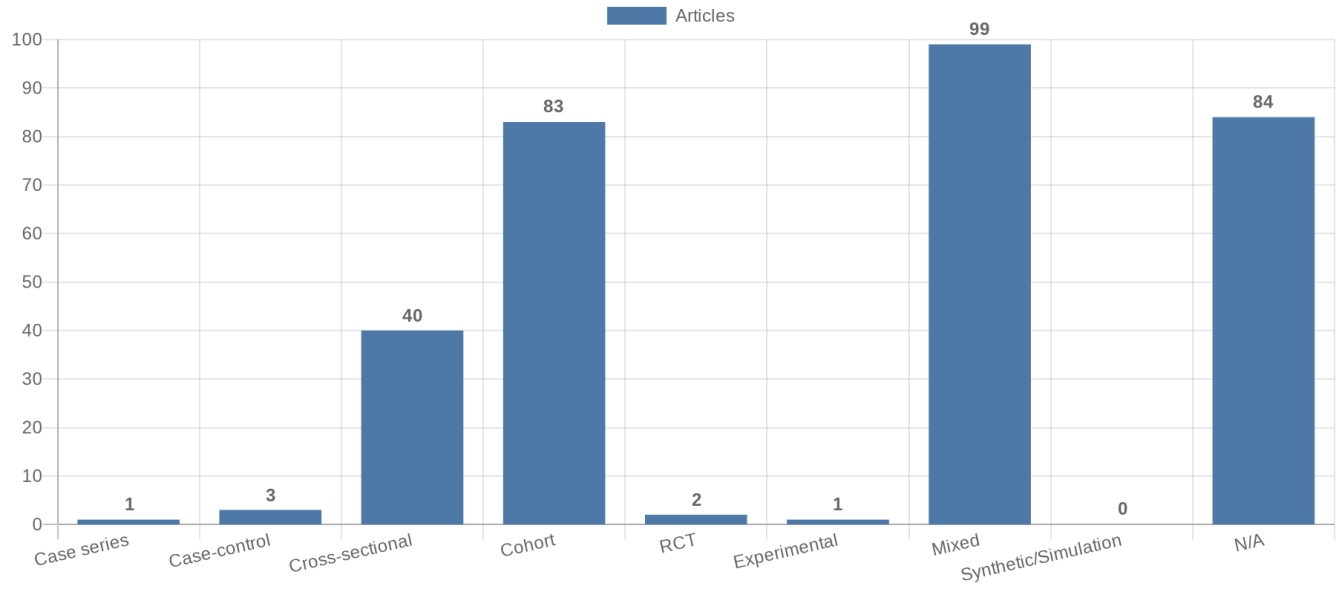


Figure 3. Study-type (directionality) distribution of included originals

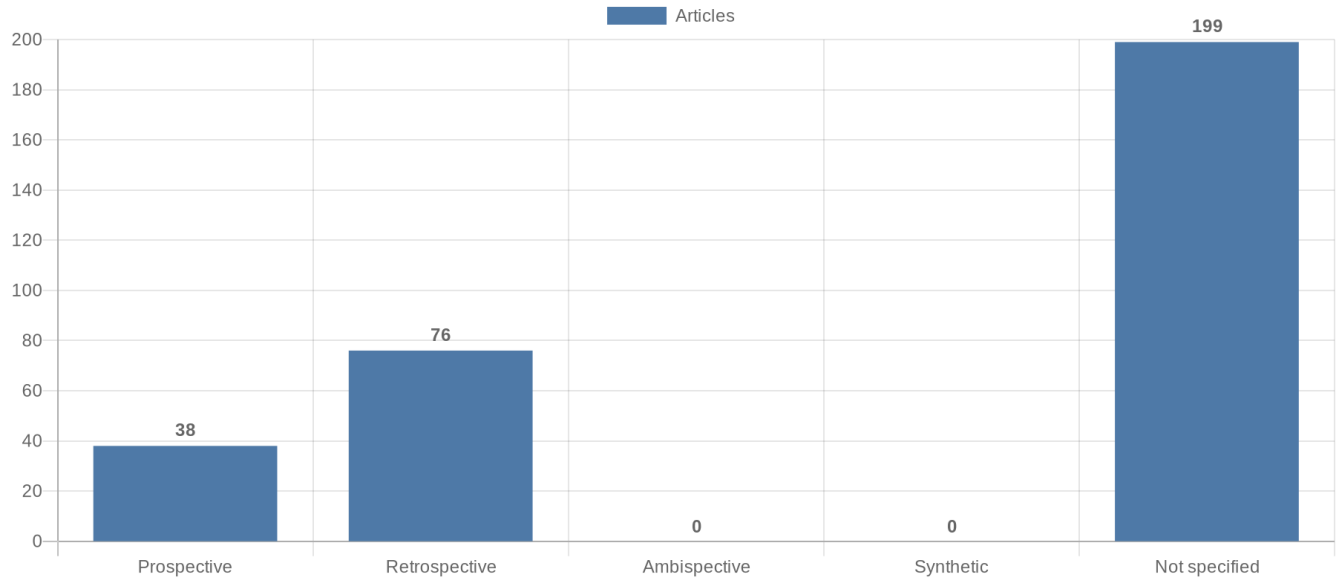


Figure 4. Main extracted research topics

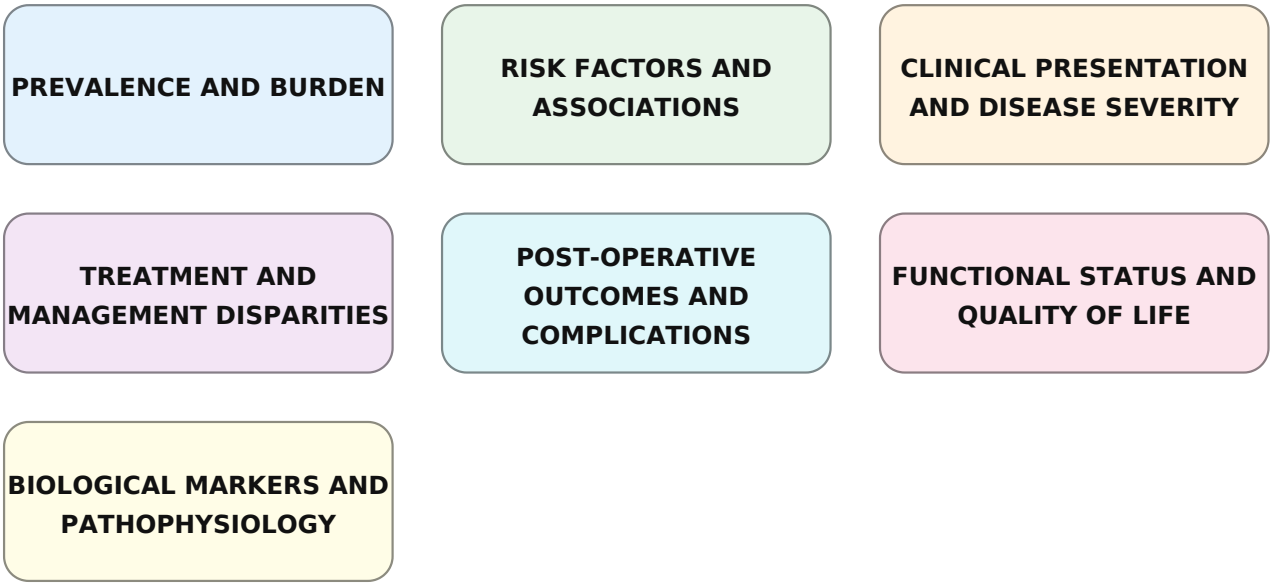


Figure 5. Limitations of current studies (topics)

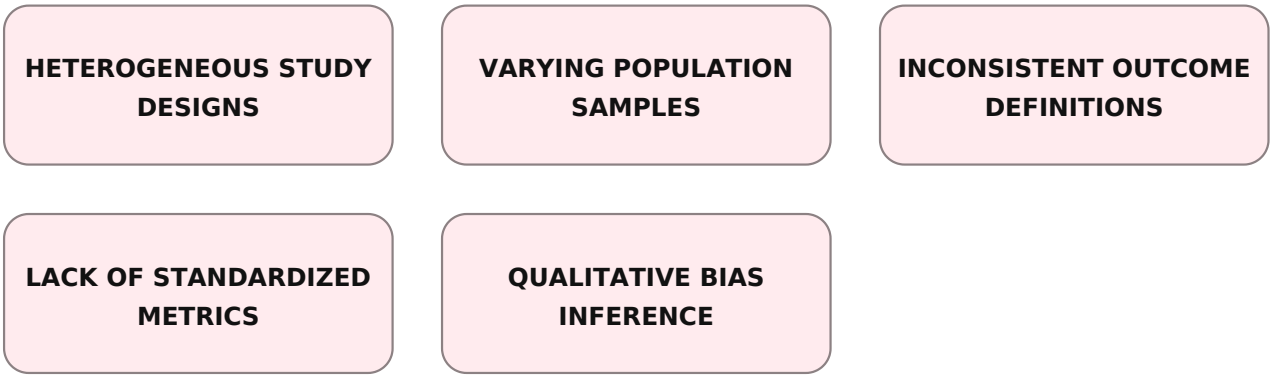


Figure 6. Future research directions (topics)

STANDARDIZED GENDER-STRATIFIED OUTCOMES

MECHANISTIC STUDIES ON BIOLOGICAL MARKERS

PROSPECTIVE STUDIES ON TREATMENT EFFICACY

IMPACT OF SOCIOECONOMIC AND PSYCHOSOCIAL FACTORS

LONGITUDINAL QUALITY OF LIFE ASSESSMENT

STANDARDIZE REPORTING GUIDELINES

LARGE-SCALE PROSPECTIVE COHORTS