Carotid Disease and Stroke: Systematic Review with ☸SAIMSARA.

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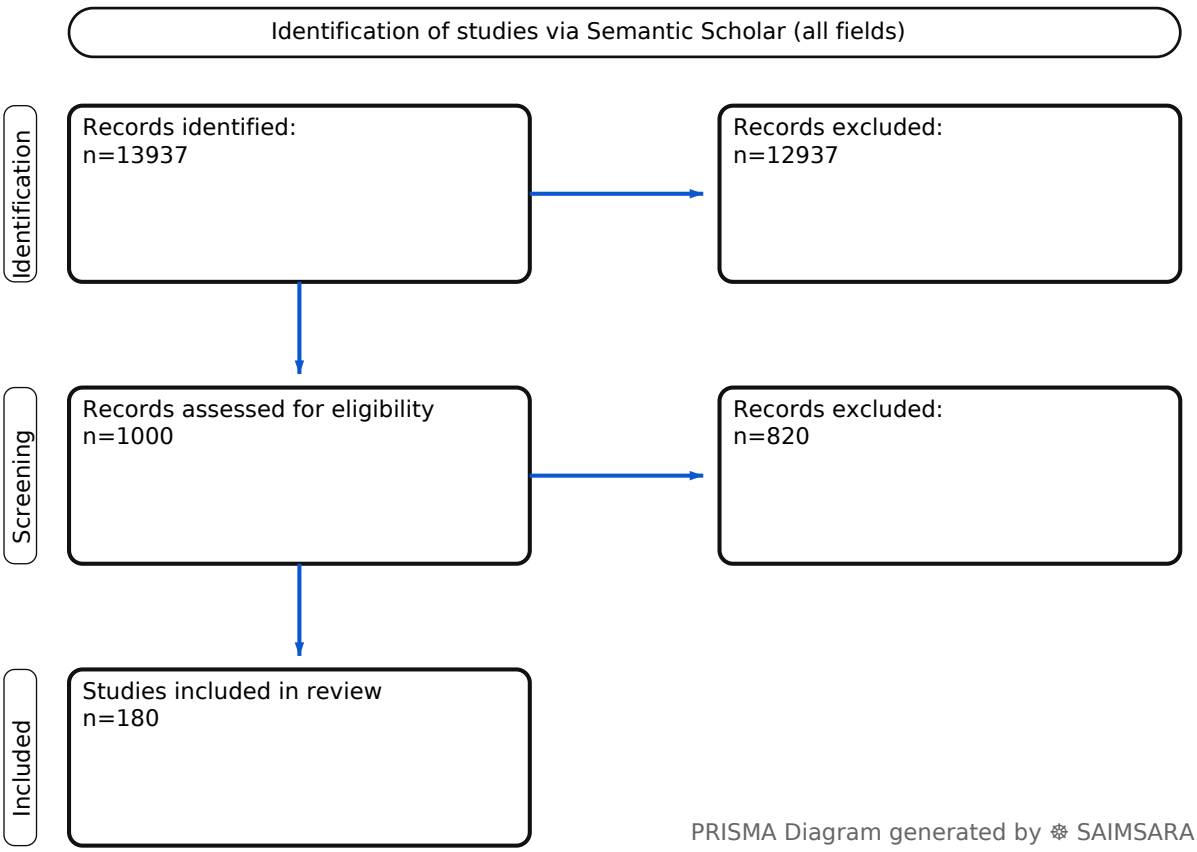
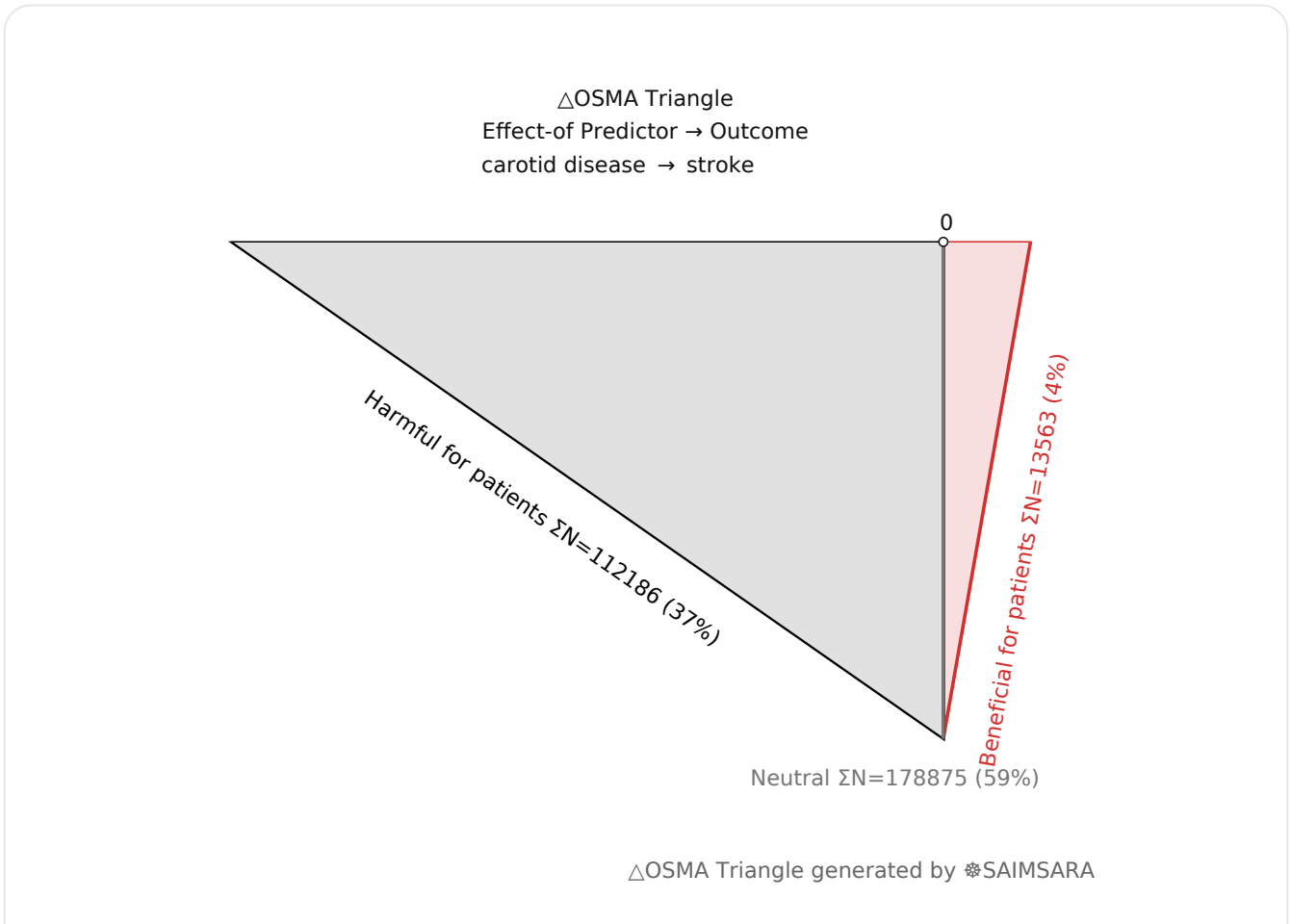
Abstract: Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details). The review utilises 180 studies with 304624 total participants (naïve ΣN). The median perioperative or 30-day stroke or death rate associated with carotid interventions or cardiac procedures where carotid disease is a factor was 2.1%, with a range of 0.6% to 4.3%. These findings are drawn from a wide array of study designs and patient populations, limiting the overall generalizability of the aggregated evidence. The most significant limitation affecting certainty is the variability in patient populations, which makes it difficult to draw universal conclusions. Clinicians should prioritize comprehensive carotid plaque characterization beyond stenosis alone to identify vulnerable plaques and individualize stroke prevention strategies.

Keywords: Carotid Disease; Stroke; Carotid Artery Stenosis; Carotid Plaque; Intima-Media Thickness; Ischemic Stroke; Stroke Risk Factors; Carotid Revascularization; Plaque Imaging; Transient Ischemic Attack

Review Stats

- Generated: 2026-02-04 11:33:04 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: 13937
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 180
- Total study participants (naïve ΣN): 304624


Identification of studies via Semantic Scholar (all fields)
Identification
Records identified:
n=13937
Records excluded:
n=12937
Screening
Records assessed for eligibility
n=1000
Records excluded:
n=820
Included
Studies included in review
n=180
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
carotid disease → stroke
0
Harmful for patients ΣN=112186 (37%)
Beneficial for patients ΣN=13563 (4%)
Neutral ΣN=178875 (59%)
△OSMA Triangle generated by ☸SAIMSARA

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

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

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

Common endpoints: Common endpoints: complications, mortality, functional.

Predictor: carotid disease — exposure/predictor. Routes seen: oral, iv. Typical comparator: cea, tf-cas, women, a population-based cohort….

- **1) Beneficial for patients** — stroke with carotid disease — [29], [32], [34], [44], [97], [99], [141], [145], [148] — ΣN=13563
- **2) Harmful for patients** — stroke with carotid disease — [2], [3], [4], [6], [10], [13], [14], [16], [17], [18], [19], [24], [25], [26], [27], [28], [35], [36], [38], [42], [47], [48], [49], [50], [77], [80], [83], [85], [88], [89], [93], [96], [103], [104], [105], [112], [121], [131], [132], [135], [137], [139], [143], [147], [151], [152], [153], [154], [158], [159], [160], [161], [164], [169], [174], [175], [176], [178] — ΣN=112186
- **3) No clear effect** — stroke with carotid disease — [1], [5], [7], [8], [9], [11], [12], [15], [20], [21], [22], [23], [30], [31], [33], [37], [39], [40], [41], [43], [45], [46], [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63], [64], [65], [66], [67], [68], [69], [70], [71], [72], [73], [74], [75], [76], [78], [79], [81], [82], [84], [86], [87], [90], [91], [92], [94], [95], [98], [100], [101], [102], [106], [107], [108], [109], [110], [111], [113], [114], [115], [116], [117], [118], [119], [120], [122], [123], [124], [125], [126], [127], [128], [129], [130], [133], [134], [136], [138], [140], [142], [144], [146], [149], [150], [155], [156], [157], [162], [163], [165], [166], [167], [168], [170], [171], [172], [173], [177], [179], [180] — ΣN=178875

1) Introduction

Carotid artery disease, primarily atherosclerosis, is a major contributor to ischemic stroke, a leading cause of morbidity and mortality worldwide. The pathogenesis involves the development of plaques within the carotid arteries, which can lead to stroke through luminal stenosis, plaque rupture with subsequent embolization, or hemodynamic compromise. Understanding the intricate relationship between carotid disease characteristics—such as intima-media thickness (IMT), plaque burden, composition, and inflammation—and the risk of stroke is crucial for effective prevention, diagnosis, and management. This paper synthesizes current research on this critical association, exploring risk factors, diagnostic advancements, therapeutic interventions, and areas requiring further investigation.

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, including prospective and retrospective cohorts, cross-sectional analyses, randomized controlled trials (RCTs), and case series. The qualitative inference suggests a range of potential biases, with observational studies being more susceptible to confounding, while RCTs generally offer higher certainty.

4) Results

4.1 Study characteristics:

The included studies primarily comprised cohort (prospective and retrospective), cross-sectional, and mixed designs, with a smaller number of randomized controlled trials and case series. Populations ranged from general middle-aged and elderly adults to specific patient groups undergoing transcatheter aortic valve replacement (TAVR), coronary artery bypass grafting (CABG), or presenting with transient ischemic attack (TIA) and acute ischemic stroke. Follow-up periods varied widely, from immediate perioperative outcomes to long-term observations spanning up to 28 years.

4.2 Main numerical result aligned to the query:

The median perioperative or 30-day stroke or death rate associated with carotid interventions or cardiac procedures where carotid disease is a factor was 2.1%, with a range of 0.6% [21] to 4.3% [158].

4.3 Topic synthesis:

- **Carotid Plaque as a Stroke Predictor:** Carotid artery intima-media thickness (IMT) and carotid plaque are significantly associated with an increased risk of stroke [3, 6, 131]. The carotid plaque score is a strong predictor of ischemic stroke, with a hazard ratio (HR) of 1.25 (95% CI, 1.15–1.36) [4]. Common carotid artery (CCA) diameter is also associated with incident stroke, with an HR of 1.5 (95% CI, 1.1–2.0) for the highest tertile [89].
- **Plaque Vulnerability and Composition:** Bilateral carotid disease is a significant risk factor for perioperative strokes following transcatheter aortic valve implantation (TAVI), with an odds ratio (OR) of 4.46 (95% CI = 2.03–9.82) [2]. Plaque inflammation-related 18F-FDG

uptake independently predicted future recurrent stroke (HR 2.2; 95% CI, 1.1–4.5) [17]. Intraluminal thrombus, maximum soft plaque thickness, and the rim sign provide superior discrimination of ipsilateral carotid sources of stroke compared to stenosis alone (AUC 78.3% vs 67.4%) [13].

- **Risk Factors for Carotid Disease and Stroke:** Chronic kidney disease (CKD) is associated with carotid atherosclerosis and symptomatic ischemic stroke (OR 0.868; 95% CI, 0.769–0.979 for eGFR) [10]. Cadmium was associated with ischemic stroke, both independently and synergistically with carotid plaques (HR 2.88; 95% CI, 1.79–4.63 for plaque and high cadmium) [24]. Microplastics and nanoplastics (MNPs) in carotid artery plaque were associated with a significantly higher risk of myocardial infarction, stroke, or death (HR 4.53; 95% CI, 2.00 to 10.27) [103].
- **Interventional Outcomes:** Transcarotid artery revascularization (TCAR) showed excellent early outcomes with a 30-day stroke rate of 1.9% and a composite stroke/death rate of 2.3% [21]. Perioperative stroke or death was greater following TCAR compared with carotid endarterectomy (CEA) (OR 0.74; 95% CI, 0.55–0.99 for CEA vs TCAR), but at 1 year there was no significant difference [9]. A short time interval (up to 7 days) between neurologic index event and carotid artery stenting (CAS) was associated with an increased risk for stroke or death [26].
- **Advanced Diagnostics and Risk Stratification:** An attention-based UNet deep learning model shows high accuracy in segmenting carotid plaques (AUC 0.97), potentially aiding in stroke risk stratification [8]. High-resolution magnetic resonance imaging (HR-MRI) can distinguish and quantify different components of carotid plaque, with a higher proportion of vulnerable plaque in symptomatic patients ($P<0.05$) [102]. Plaque echolucency on ultrasound can identify asymptomatic carotid artery stenosis patients who benefit from CEA [99].
- **Non-Stenosing Carotid Plaque as a Stroke Mechanism:** Total plaque thickness was greater on the infarcted side than the contralateral side among embolic stroke of undetermined source (ESUS) cases ($P=0.006$), suggesting nonstenosing plaques as a mechanism [23]. Intraplaque high-intensity signal (IHIS) in nonstenosing carotid plaque ipsilateral to ischemic stroke was significantly higher than on the contralateral side ($P=0.01$) [34].
- **Systemic Atherosclerosis and Cognitive Impact:** Coronary artery calcium (CAC) score was a stronger predictor of cardiovascular disease (CVD) than carotid plaque score, with similar predictive values for stroke/TIA [27]. Patients with severe carotid stenosis showed significantly below-expected cognitive performance, particularly in memory ($P<0.0001$ for Word List Recall and Learning) [46].
- **Under-investigation and Under-treatment:** Elderly patients with transient ischemic attack and stroke are underinvestigated and undertreated for carotid disease [5]. Lower

rates of intervention for symptomatic carotid stenosis in women compared to men reflect differences in disease incidence [106].

5) Discussion

5.1 Principal finding:

The median perioperative or 30-day stroke or death rate associated with carotid interventions or cardiac procedures where carotid disease is a factor was 2.1%, with a range of 0.6% [21] to 4.3% [158], highlighting the persistent risk of cerebrovascular events despite advancements in care.

5.2 Clinical implications:

- **Enhanced Risk Stratification:** Incorporate advanced imaging (e.g., HR-MRI, PET-FDG) and plaque characteristics (e.g., intraluminal thrombus, inflammation, IHIS) beyond stenosis alone for more precise stroke risk assessment [13, 17, 34, 102].
- **Personalized Intervention Timing:** Consider delaying carotid revascularization for symptomatic patients beyond the immediate 0-2 day window to reduce perioperative stroke/death risk, as early intervention is associated with higher complication rates [26, 176].
- **Proactive Screening in High-Risk Groups:** Implement routine screening for carotid disease in elderly patients with TIA/stroke, patients undergoing CABG, and those with multiple atherosclerosis risk factors to identify undertreated populations [5, 164].
- **Optimized Surgical Approach:** Favor local anesthesia for carotid endarterectomy (CEA) when feasible, as it is associated with a lower risk of stroke or death [158]. Transcarotid artery revascularization (TCAR) shows favorable outcomes compared to transfemoral carotid artery stenting (TF-CAS) [9].
- **Long-term Medical Management:** Emphasize continuous statin therapy in patients with significant carotid disease, as it is associated with a 25% lower risk of long-term adverse cardiovascular events [97].

5.3 Research implications / key gaps:

- **Non-Stenosing Plaque Mechanisms:** Further investigate the precise mechanisms by which non-stenosing carotid plaques, including carotid web, cause stroke, especially in younger patients and ESUS cases [15, 23, 34, 157].
- **Novel Biomarker Utility:** Conduct prospective studies to validate the clinical utility of emerging biomarkers such as perivascular adipose tissue (PCAT) attenuation, soluble LOX-1,

and circR-284:miR-221 ratio for predicting plaque vulnerability and stroke risk [16, 18, 63].

- **Impact of Environmental Factors:** Explore the long-term effects of environmental exposures like cadmium and microplastics/nanoplastics on carotid plaque development, vulnerability, and subsequent stroke risk in diverse populations [24, 103].
- **Genetic Predisposition and Stroke:** Conduct larger genetic association studies to identify novel susceptibility loci for carotid intima-media thickness (IMT) and plaque, and their specific genetic correlations with different stroke subtypes [53].
- **AI-Enhanced Predictive Models:** Develop and rigorously validate deep learning models that integrate multimodal imaging data (ultrasound, CTA, MRI) with clinical risk factors and genetic information for superior, personalized stroke risk prediction [8, 70].

5.4 Limitations:

- **Heterogeneous Study Designs** — The included studies span various designs (cohort, cross-sectional, RCT, case series, mixed), which limits direct comparability and the strength of aggregated evidence.
- **Variability in Patient Populations** — Studies involve diverse populations, from general adults to specific surgical cohorts (TAVR, CABG) and ethnic groups, affecting generalizability of findings.
- **Inconsistent Outcome Definitions** — "Stroke" and "carotid disease" are defined and measured differently across studies (e.g., IMT vs. plaque vs. stenosis, perioperative vs. long-term stroke), complicating synthesis.
- **Lack of Standardized Follow-up** — Follow-up periods vary significantly (N/A to 28 years), making it challenging to assess long-term effects or compare outcomes consistently.
- **Qualitative Bias Assessment** — Bias was inferred qualitatively from study design, lacking a formal quantitative assessment tool, potentially over- or underestimating study quality.

5.5 Future directions:

- **Standardized Plaque Imaging** — Develop and validate standardized imaging protocols for carotid plaque characterization (e.g., HR-MRI, PET) to improve stroke risk stratification.
- **Longitudinal Cohort Studies** — Conduct large, prospective cohort studies with consistent definitions of carotid disease and stroke outcomes across diverse populations.
- **Biomarker Validation Trials** — Validate novel biomarkers (e.g., sLOX-1, circR-284:miR-221 ratio, PCAT attenuation, MNPs) for vulnerable plaque detection and stroke prediction in clinical trials.

- **Comparative Effectiveness Research** — Perform head-to-head comparative effectiveness research on different carotid revascularization strategies (CEA, CAS, TCAR) in specific patient subgroups.
- **AI-Driven Risk Prediction** — Integrate advanced deep learning models with multimodal imaging and clinical data to enhance personalized stroke risk prediction and guide intervention.

6) Conclusion

The median perioperative or 30-day stroke or death rate associated with carotid interventions or cardiac procedures where carotid disease is a factor was 2.1%, with a range of 0.6% [21] to 4.3% [158]. These findings are drawn from a wide array of study designs and patient populations, limiting the overall generalizability of the aggregated evidence. The most significant limitation affecting certainty is the variability in patient populations, which makes it difficult to draw universal conclusions. Clinicians should prioritize comprehensive carotid plaque characterization beyond stenosis alone to identify vulnerable plaques and individualize stroke prevention strategies.

References

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Figure 1. Publication-year distribution of included originals

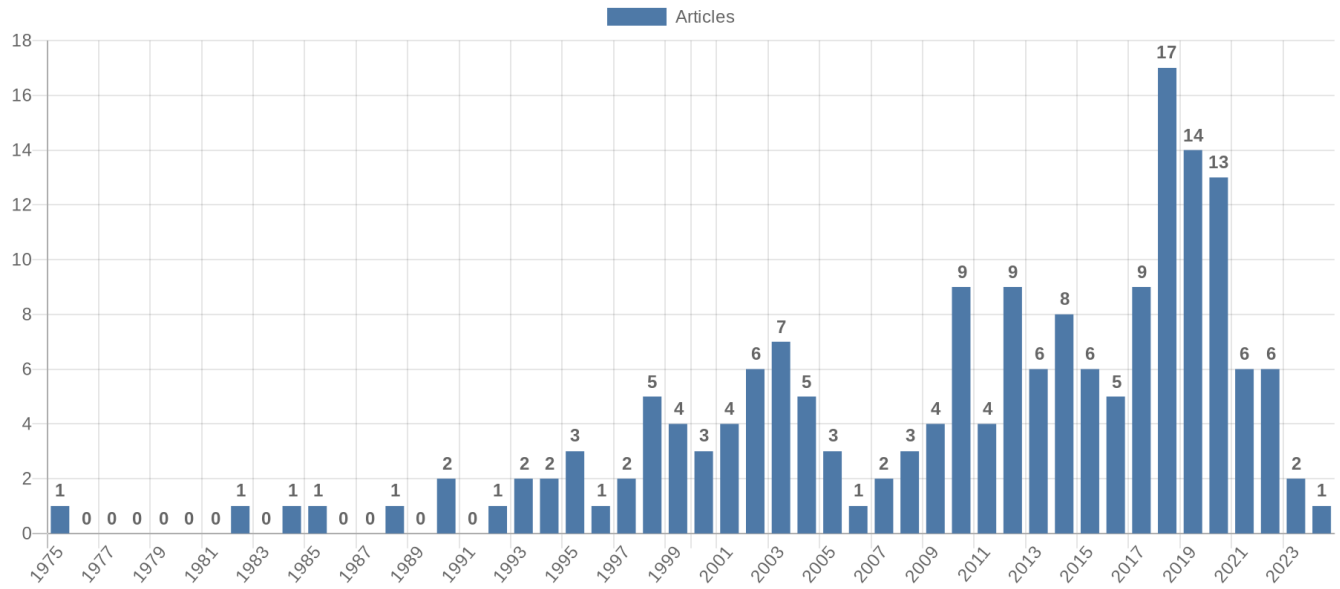

Figure 2. Study-design distribution of included originals

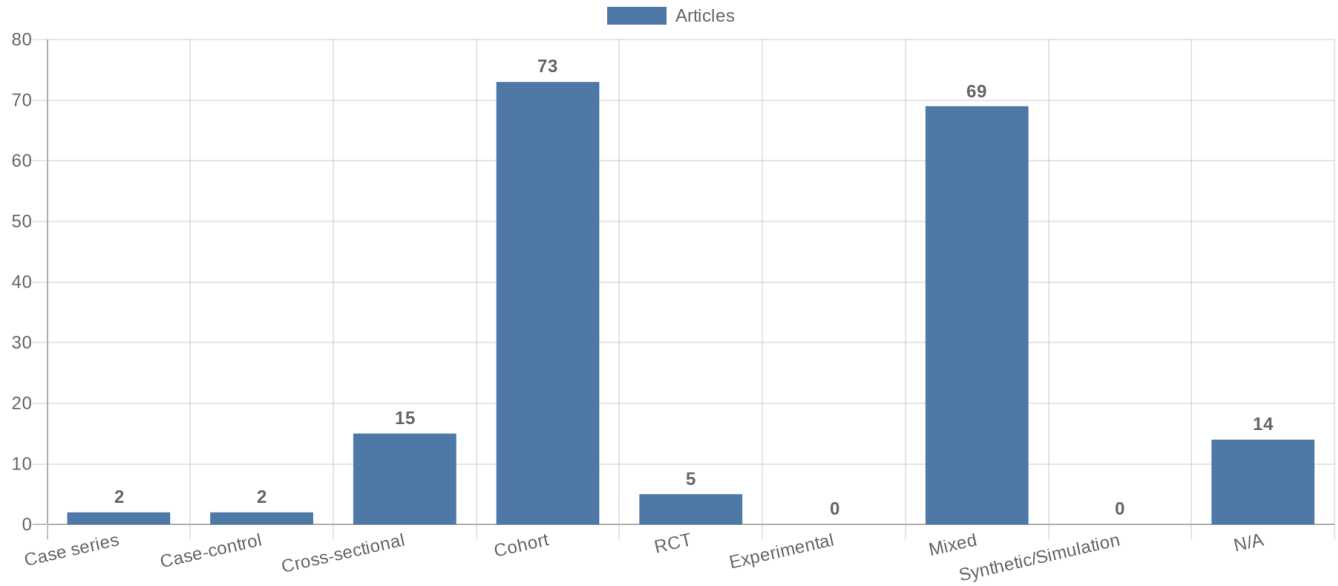

Figure 3. Study-type (directionality) distribution of included originals

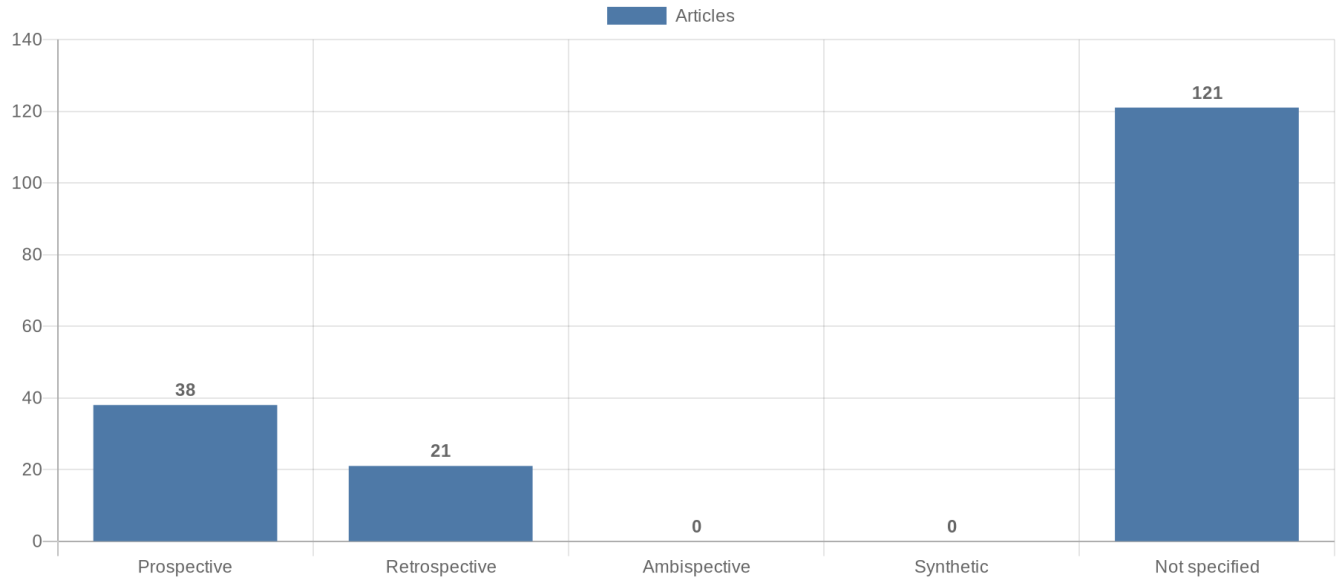

Figure 4. Main extracted research topics

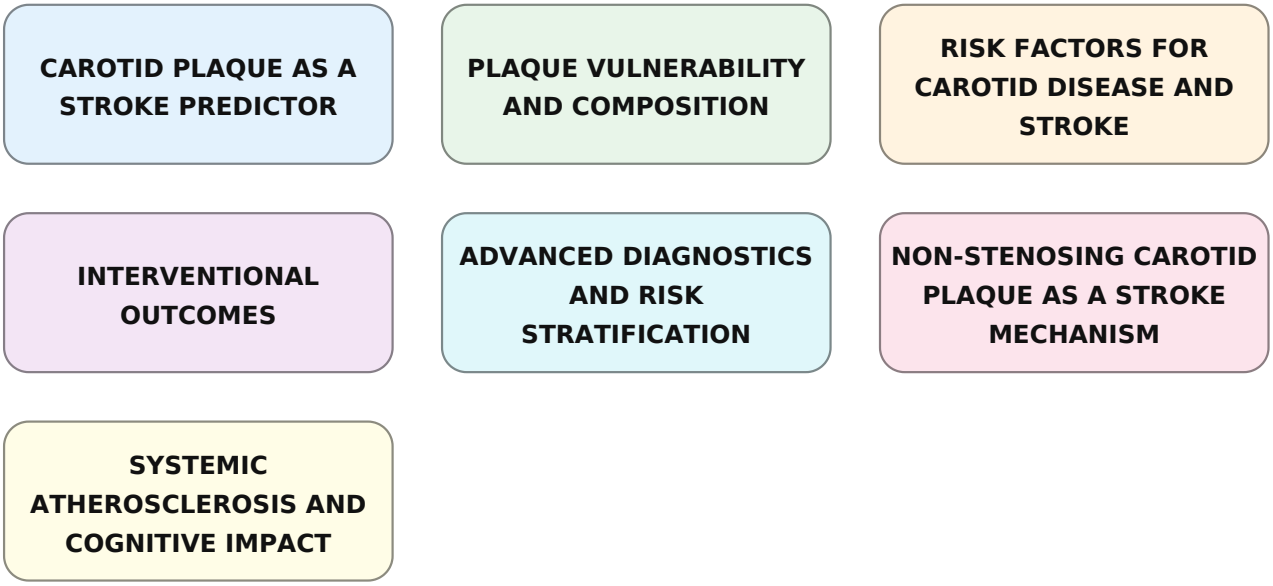

Figure 5. Limitations of current studies (topics)

Figure 6. Future research directions (topics)