# Abdominal Aortic Aneurysm and Medication: Systematic Review with ☸SAIMSARA.

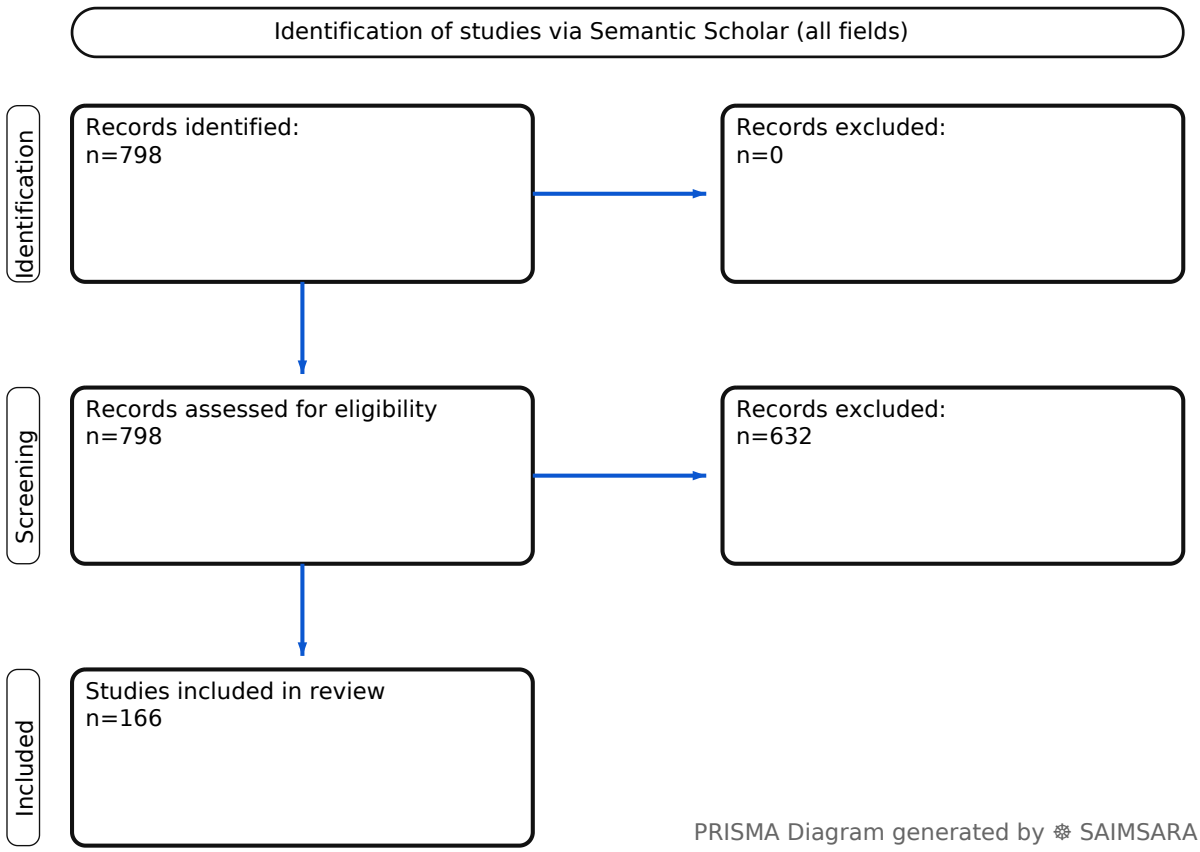
saimsara.com • Download PDF • URL

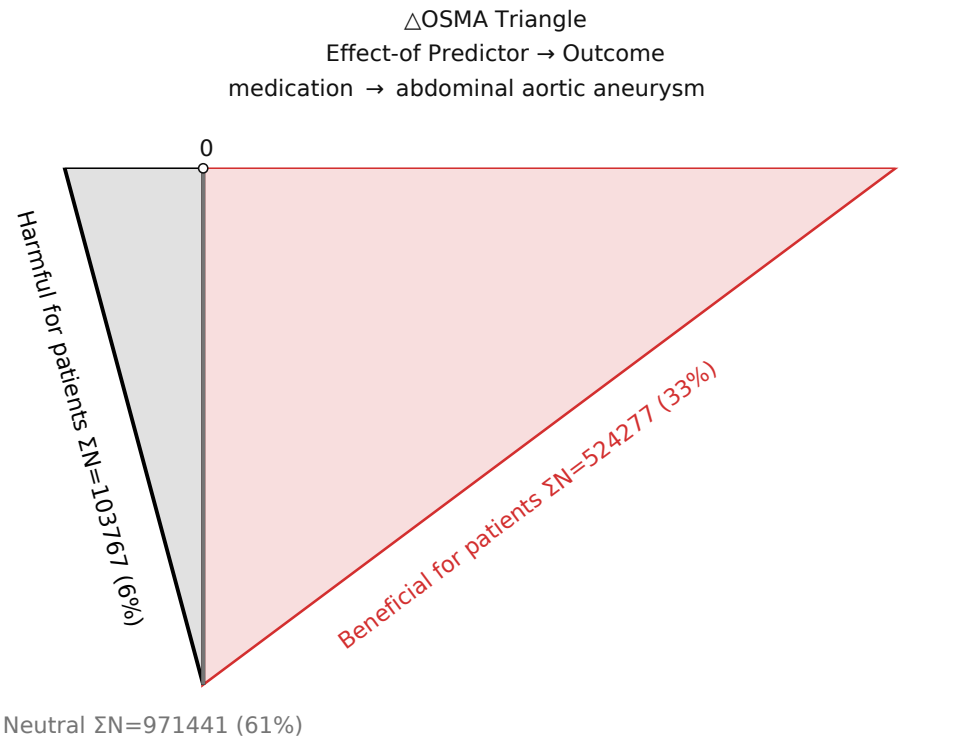
**Abstract:** Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details). The review utilises 166 studies with 1599485 total participants (naïve ΣN). Metformin was associated with a reduction in abdominal aortic aneurysm growth rate, with a median reduction of -0.38 mm/year and a reported range from -0.30 mm/year to -1.30 mm/year. These findings, alongside evidence for other medications like statins and RAASIs, suggest a promising role for pharmacological interventions in modulating AAA progression and improving patient outcomes, particularly in the context of small aneurysms and perioperative care. However, the prevalence of retrospective designs and heterogeneous study populations represents the most significant limitation to the certainty and generalizability of these findings. Therefore, a concrete next step is to conduct large-scale, high-quality randomized controlled trials to definitively validate the efficacy of metformin and other promising medications in limiting AAA progression and reducing rupture risk.

**Keywords:** Abdominal aortic aneurysm; Medication therapy; Metformin; AAA growth rate; ACE inhibitors; Angiotensin receptor blockers; Medication adherence; Perianeurysmal fibrosis; Endovascular aneurysm repair; Antihypertensive drugs

**Review Stats**

- Generated: 2026-02-13 15:08:23 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: 798
- Downloaded Abstracts/Papers: 798
- Included original Abstracts/Papers: 166
- Total study participants (naïve ΣN): 1599485


Identification of studies via Semantic Scholar (all fields)
Identification
Records identified:
n=798
Records excluded:
n=0
Screening
Records assessed for eligibility
n=798
Records excluded:
n=632
Included
Studies included in review
n=166
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
medication → abdominal aortic aneurysm
0
Harmful for patients ΣN=103767 (6%)
Beneficial for patients ΣN=524277 (33%)
Neutral ΣN=971441 (61%)
△OSMA Triangle generated by ☸SAIMSARA

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

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

*Outcome*: abdominal aortic aneurysm Typical timepoints: peri/post-op, 1-y. Reported metrics: %, CI, p.

*Common endpoints*: Common endpoints: mortality, complications, los.

*Predictor*: medication — exposure/predictor. Routes seen: intravenous. Typical comparator: usual care, single antiplatelet therapy, placebo, control….

- **1) Beneficial for patients** — abdominal aortic aneurysm with medication — [5], [7], [10], [31], [35], [39], [40], [41], [42], [44], [47], [53], [54], [56], [59], [66], [69], [71], [72], [80], [84], [98], [112], [119], [120], [141], [161] — ΣN=524277
- **2) Harmful for patients** — abdominal aortic aneurysm with medication — [3], [20], [32], [60], [97], [110], [162] — ΣN=103767
- **3) No clear effect** — abdominal aortic aneurysm with medication — [1], [2], [4], [6], [8], [9], [11], [12], [13], [14], [15], [16], [17], [18], [19], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [33], [34], [36], [37], [38], [43], [45], [46], [48], [49], [50], [51], [52], [55], [57], [58], [61], [62], [63], [64], [65], [67], [68], [70], [73], [74], [75], [76], [77], [78], [79], [81], [82], [83], [85], [86], [87], [88], [89], [90], [91], [92], [93], [94], [95], [96], [99], [100], [101], [102], [103], [104], [105], [106], [107], [108], [109], [111], [113], [114], [115], [116], [117], [118], [121], [122], [123], [124], [125], [126], [127], [128], [129], [130], [131], [132], [133], [134], [135], [136], [137], [138], [139], [140], [142], [143], [144], [145], [146], [147], [148], [149], [150], [151], [152], [153], [154], [155], [156], [157], [158], [159], [160], [163], [164], [165], [166] — ΣN=971441

**1) Introduction**

Abdominal aortic aneurysm (AAA) represents a significant cardiovascular pathology characterized by localized dilatation of the abdominal aorta, carrying substantial risks of rupture and associated mortality. The management of AAA encompasses surveillance, surgical intervention (open repair or endovascular aneurysm repair (EVAR)), and increasingly, pharmacological strategies aimed at mitigating disease progression and associated complications. The intricate interplay between various medications and AAA development, growth, and perioperative outcomes is a critical area of research. This paper synthesizes current evidence on the role of medication in the context of AAA, from its incidence and growth suppression to perioperative management and long-term survival.

**2) Aim**

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

**3) Methods**

- **Bias:** The qualitative assessment of bias indicates a prevalence of retrospective cohort studies, mixed-design studies, and case reports, which inherently carry a higher risk of selection and confounding biases. While prospective cohort studies and randomized controlled trials (RCTs) offer stronger evidence, they are less frequent, particularly for definitive medication efficacy in AAA growth. Many studies lacked specified directionality or detailed statistical reporting, further limiting the certainty of findings. Experimental studies in animal models or cell lines also limit direct generalizability to human clinical outcomes.

**4) Results**

**4.1 Study characteristics:**

The reviewed literature comprises a diverse range of study designs, predominantly cohort studies (retrospective and prospective), mixed-design studies, and randomized controlled trials. Populations frequently include patients undergoing elective EVAR for infrarenal AAA, individuals with small AAAs under surveillance, and broader cohorts from screening programs. Follow-up periods vary significantly, ranging from a few months (e.g., 4 months [2]) to several years (e.g., 5.99 years [141], median 16 years [126], 24.3 years [50]), with some studies not specifying follow-up duration.

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

Metformin was associated with a reduction in abdominal aortic aneurysm growth rate, with a median reduction of -0.38 mm/year [5] and a reported range from -0.30 mm/year to -1.30 mm/year [10]. This suggests a potential therapeutic effect of metformin in slowing AAA expansion.

**4.3 Topic synthesis:**

- **Metformin and AAA Growth/Risk:** Metformin is associated with slower AAA growth (-0.38 mm/year [5], -0.30 to -1.30 mm/year [10]), reduced AAA occurrence (28% reduction [10]), and improved quality of life (QoL) in AAA patients (superior QoL score, $p = 0.038$ [120], superior health status [142]). It is being investigated in RCTs for growth suppression and complication risk reduction [8, 9, 37].
- **Renin-Angiotensin-Aldosterone System Inhibitors (RAASIs) and AAA:** Angiotensin-converting enzyme (ACE) inhibitors (-0.243(0.07) mm/year [5]) and angiotensin receptor blockers (ARBs) (-0.253(0.08) mm/year [5]) are associated with slower AAA growth. RAASIs were linked to lower postoperative mortality (OR, 0.3 [95% CI, 0.1–0.6]) and 1-year mortality

(HR, 0.4 [95% CI, 0.4–0.5]) after AAA repair compared to beta-blockers [80]. However, ACEIs/ARBs were identified as an independent risk factor for postoperative acute kidney injury (AKI) after elective EVAR (OR, 2.60; 95% CI: 1.17–5.76; P = 0.019) [60].

- **Statins and AAA Outcomes:** Postoperative statin treatment markedly improved long-term survival after AAA repair (HR 1.43, 95% c.i. 1.34 to 1.54) [40]. Discharge with statins improved survival after EVAR (HR 1.26, P < .001) [141]. Statin use increased over time in AAA patients, alongside a decrease in cardiovascular comorbidity and all-cause mortality [98]. Preoperative statin use did not reduce 90-day perioperative mortality [40]. Statin therapy is also being studied for its association with body composition in AAA patients [33].
- **Antiplatelet Therapy and AAA:** Antiplatelet drugs suppress AAA growth in patients [112]. Discharge with aspirin improved survival after EVAR (HR 1.26, P < .001) [141]. Dual antiplatelet therapy (DAPT) was not associated with improved cardiovascular or procedural outcomes but was linked to increased bleeding risk (HR: 1.20 [95% CI, 1.02–1.41]) compared to single antiplatelet therapy in EVAR patients without established atherosclerotic cardiovascular disease [20]. Ticagrelor did not significantly reduce small AAA growth [103].
- **Antihypertensive Medication and Hypertension Control:** Medication was identified as a risk factor associated with AAA (p=0.0018) [3]. Patients with hypertension and AAA showed insufficient medication adherence (31% high adherence) [4]. The number of antihypertensive drugs prescribed was a negative predictor of hypertension control one year after EVAR [65]. Hypertension is a major risk factor for AAA (HR 2.64 [95% CI 1.33 to 5.25]) [126].
- **Sex-Specific Differences in Medication Use:** Sex-specific differences in perioperative medication use were observed, with women less likely to receive secondary prevention for cardiac disease (34.9% vs 39.6%, P=0.015) [6]. Women were more likely to meet overall cardiovascular risk prevention standards (52.1% vs 47.3%, P<0.001) [6].
- **Novel Therapeutic Targets:** PCSK9 inhibitors show promise in curtailing AAA formation and progression by mediating macrophage inflammation and elastin degradation [41, 42], and PCSK9 is a potential therapeutic target for repurposing [31]. Pepducin inhibition of protease-activated receptor 2 (PAR2) attenuated AAA in a mouse model [69]. Drugs inhibiting IL-6R may be useful in AAA management [84]. Apicidin, an HDAC4 inhibitor, is a potential candidate drug for AAA treatment [44]. Inhibition of microbiome-derived TMAO may serve as a novel therapeutic approach [47]. Formoterol attenuates AAA via β2AR/cAMP/SIRT1 pathways [39].
- **Medication Adherence and Screening:** Nurse-led telephone follow-up did not significantly improve medication adherence (anti-platelets or lipid-lowering) in patients with screen-detected AAA [19]. Screening programs can identify AAA patients needing pharmacotherapy (17.0% [164]). Lipid-lowering medication was associated with a lower risk of major ECG abnormalities and coexisting AAA [119].

- **Perioperative Medication and Complications:** Coumarin derivatives were associated with fewer complications following EVAR (OR 0.21, 95%CI 0.05-0.90), while anti-emetic drugs (OR 4.37, 95%CI 1.10-17.3) and analgesics (OR 3.81, 95%CI 1.32-11.0) were associated with more complications [14]. NSAID use within 24 hours after EVAR was a significant risk factor for Type II endoleak (OR: 21.2; 95% CI: 1.5–308.4; P = 0.026) [97]. Intravenous ketorolac was associated with lower in-hospital mortality after open AAA repair (adjusted odds 0.58 (0.36–0.93)) [66].
- **Other Medications and Factors:** Gliclazide was associated with lower AAA growth rates [7]. Anticoagulants were associated with a reduced risk of AAA-related events (adjusted HR 0.61; 95% CI 0.42, 0.90, p = 0.013) [59]. Glucocorticoid use was associated with an increased risk of AAA (HR = 1.93 (95% CI 1.47–2.53)) [162]. Fenofibrate therapy did not significantly reduce AAA growth [11]. Beta-adrenergic blockade was investigated for its effect on AAA growth [24, 27].
- **Lifestyle and Medication:** Pharmacological treatment is most effective when initiated during the small diameter stage and should be accompanied by lifestyle changes [13]. Smoking cessation significantly reduces AAA risk [145].

## 5) Discussion

### 5.1 Principal finding:

The principal finding indicates that metformin is associated with a reduction in abdominal aortic aneurysm growth rate, with a median reduction of -0.38 mm/year [5] and a reported range from -0.30 mm/year to -1.30 mm/year [10].

### 5.2 Clinical implications:

- **Early Pharmacological Intervention:** Given that pharmacological treatment for AAA is most effective when initiated during the small diameter stage, and considering the potential of metformin, clinicians should consider its role in patients with small AAAs, especially those with diabetes or at risk [13, 5, 10].
- **Optimizing Post-Operative Care:** Ensuring patients without contraindications are discharged with aspirin and statin medications significantly improves survival after EVAR [141]. This highlights the importance of adherence to secondary prevention guidelines in the perioperative period.
- **Hypertension Management:** Insufficient medication adherence to antihypertensive therapy is prevalent in AAA patients [4]. Improved strategies for blood pressure control and medication adherence are crucial, as uncontrolled hypertension is a risk factor for recurrent vascular events and death [147].

- **Sex-Specific Considerations:** Clinicians should be aware of observed sex-specific differences in perioperative medication use, particularly the lower likelihood of women receiving secondary prevention for cardiac disease, and address these disparities to optimize patient care [6].
- **Caution with Certain Medications:** The use of NSAIDs within 24 hours after EVAR is a significant risk factor for Type II endoleak [97], and ACEIs/ARBs may increase the risk of postoperative AKI after EVAR [60], necessitating careful risk-benefit assessment.

**5.3 Research implications / key gaps:**

- **Metformin Efficacy Validation:** Conduct large-scale, high-quality randomized controlled trials (RCTs) to definitively validate the efficacy of metformin in limiting AAA progression and reducing rupture risk in diverse AAA populations, including non-diabetic individuals [8, 9, 37, 53].
- **Novel Therapeutic Target Evaluation:** Further experimental and clinical research is needed to evaluate the therapeutic potential of emerging targets such as PCSK9 inhibitors [31, 41, 42], PAR2 pepducin inhibition [69], IL-6R inhibitors [84], and HDAC4 inhibitors like Apicidin [44] for AAA treatment.
- **Optimal Medication Regimens:** Investigate optimal dosing, timing, and combination therapies for medications showing promise in AAA management (e.g., statins, RAASIs, antiplatelets) across different stages of AAA progression and in various patient subgroups [13, 5, 10].
- **Mechanistic Understanding:** Elucidate the precise molecular and cellular mechanisms by which medications like metformin, RAASIs, and statins exert their protective or detrimental effects on AAA pathogenesis and progression [5, 41, 47].
- **AI Model Integration:** Develop and validate multimodal artificial intelligence (AI) models that integrate medication use data with clinical, imaging, and biological parameters to predict AAA shrinkage post-EVAR and identify patients at higher risk for adverse outcomes [1, 100].

**5.4 Limitations:**

- **Retrospective Design** — Many studies are retrospective, introducing potential for selection bias and confounding that may limit the certainty of observed associations [1, 2, 4, 5, 6, 7, 10, 14, 19, 20, 40, 49, 50, 51, 59, 60, 62, 64, 66, 72, 80, 85, 91, 95, 96, 97, 98, 105, 110, 113, 141, 144, 147].

- **Heterogeneous Populations** — Studies often include diverse patient populations (e.g., small AAA, post-EVAR, hypertensive, diabetic), making it challenging to generalize findings across the entire spectrum of AAA disease [2, 4, 7, 11, 13, 16, 19, 29, 49, 51, 52, 56, 57, 61, 63, 65, 71, 73, 75, 76, 77, 78, 87, 96, 98, 102, 103, 110, 111, 117, 118, 119, 120, 126, 128, 132, 138, 140, 142, 143, 144, 147, 160, 162, 164].
- **Short Follow-up** — Several studies have relatively short follow-up periods, which may not capture long-term effects of medications on AAA progression or rupture risk [2, 11, 16, 19, 75, 77, 102].
- **Limited RCTs** — While some RCTs exist, there is a scarcity of large-scale, definitive randomized controlled trials specifically evaluating the impact of various medications on AAA growth and clinical outcomes, leading to reliance on observational data [8, 9, 11, 19, 37, 56, 76, 77, 102, 103, 120].
- **Small Sample Sizes** — Many studies, particularly case reports, mixed designs, and experimental studies, involve small sample sizes or animal models, which limits the statistical power and generalizability of their findings to broader human populations [2, 4, 7, 12, 14, 16, 22, 23, 26, 30, 32, 34, 35, 39, 41, 42, 44, 45, 46, 47, 55, 69, 70, 72, 78, 79, 82, 83, 84, 86, 88, 89, 90, 91, 93, 94, 96, 97, 100, 101, 103, 108, 109, 110, 111, 112, 113, 115, 118, 120, 123, 124, 125, 129, 130, 131, 133, 134, 135, 137, 138, 139, 143, 146, 148, 149, 150, 151, 152, 153, 154, 156, 158, 159, 165].

**5.5 Future directions:**

- **Large-scale RCTs** — Conduct large-scale, multicenter, randomized controlled trials to evaluate the long-term efficacy and safety of promising medications, such as metformin and PCSK9 inhibitors, on AAA growth, rupture, and mortality [8, 9, 37, 41, 42, 53].
- **Mechanism Elucidation** — Further investigate the molecular and cellular mechanisms by which identified medications and novel therapeutic targets (e.g., PCSK9, PAR2, IL-6R, HDAC4, TMAO) influence AAA pathogenesis, inflammation, and vascular remodeling [31, 32, 34, 35, 39, 41, 44, 47, 58, 69, 70, 79, 84, 86, 88, 89, 92, 99, 112, 154, 156].
- **Personalized Medicine** — Develop strategies for personalized medicine in AAA management by identifying patient subgroups that would most benefit from specific pharmacological interventions, potentially leveraging genetic profiles and biomarker analysis [31, 43, 46, 48, 50, 52, 55, 57, 61, 63, 67, 79, 81, 84, 87, 88, 93, 100, 106, 107, 111, 117, 118, 119, 126, 128, 131, 134, 135, 137, 138].
- **Longitudinal Observational Studies** — Establish and utilize large, prospective, longitudinal observational cohorts with comprehensive data on medication use, adherence, AAA characteristics, and long-term outcomes to better understand real-world effectiveness

and identify emerging trends [5, 10, 19, 29, 40, 49, 50, 51, 59, 61, 63, 95, 98, 106, 111, 119, 126, 136, 138, 141, 144, 147].

- **AI Model Development** — Advance multimodal artificial intelligence (AI) models that integrate diverse data types, including medication history, imaging features, and genetic information, to predict AAA growth, rupture risk, and optimal treatment strategies, and to assess post-EVAR outcomes [1, 100, 111, 118].

## 6) Conclusion

Metformin was associated with a reduction in abdominal aortic aneurysm growth rate, with a median reduction of -0.38 mm/year [5] and a reported range from -0.30 mm/year to -1.30 mm/year [10]. These findings, alongside evidence for other medications like statins and RAASIs, suggest a promising role for pharmacological interventions in modulating AAA progression and improving patient outcomes, particularly in the context of small aneurysms and perioperative care. However, the prevalence of retrospective designs and heterogeneous study populations represents the most significant limitation to the certainty and generalizability of these findings. Therefore, a concrete next step is to conduct large-scale, high-quality randomized controlled trials to definitively validate the efficacy of metformin and other promising medications in limiting AAA progression and reducing rupture risk.

## References

SAIMSARA Session Index — session.json

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

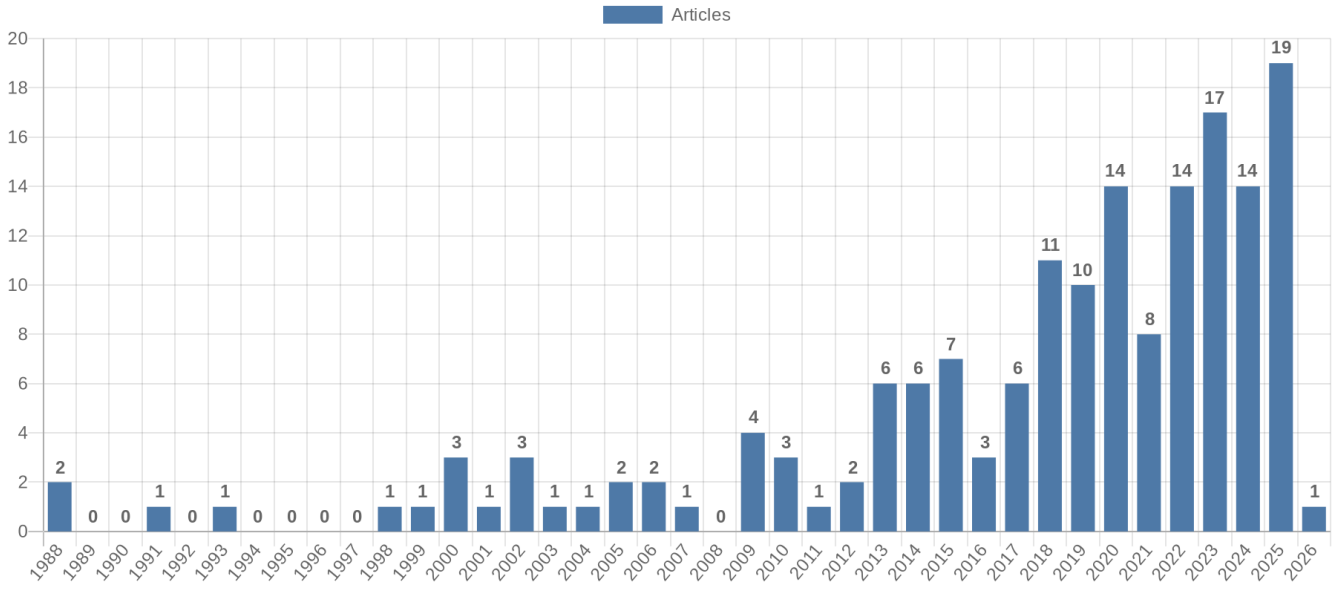



**Figure 2. Study-design distribution of included originals**

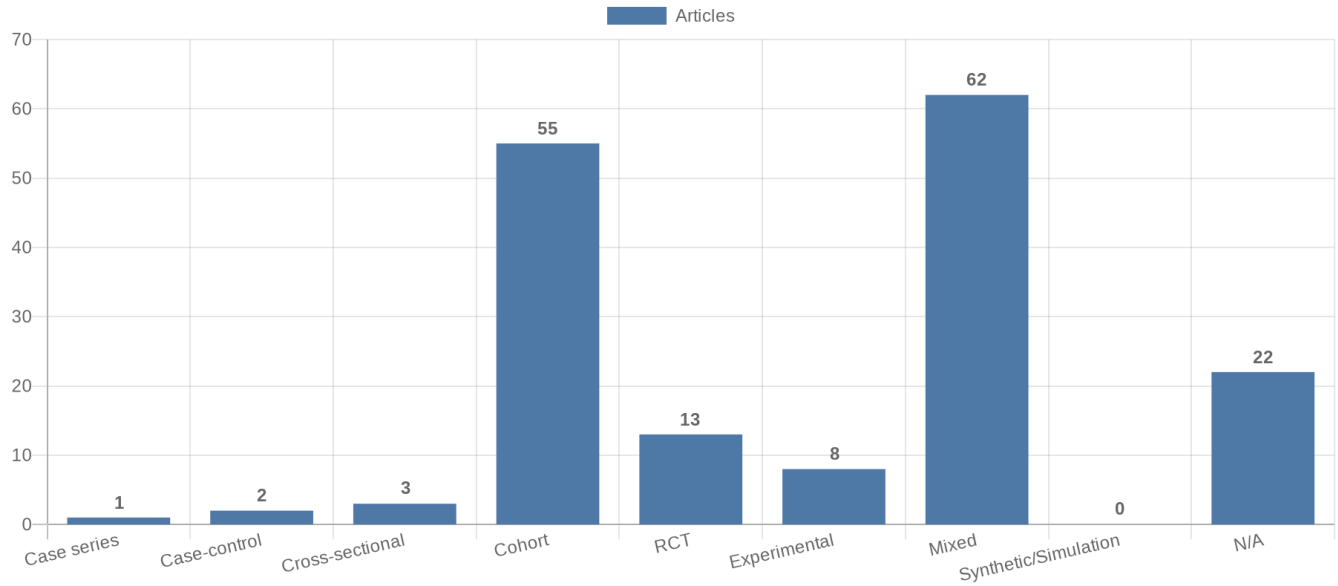



**Figure 3. Study-type (directionality) distribution of included originals**

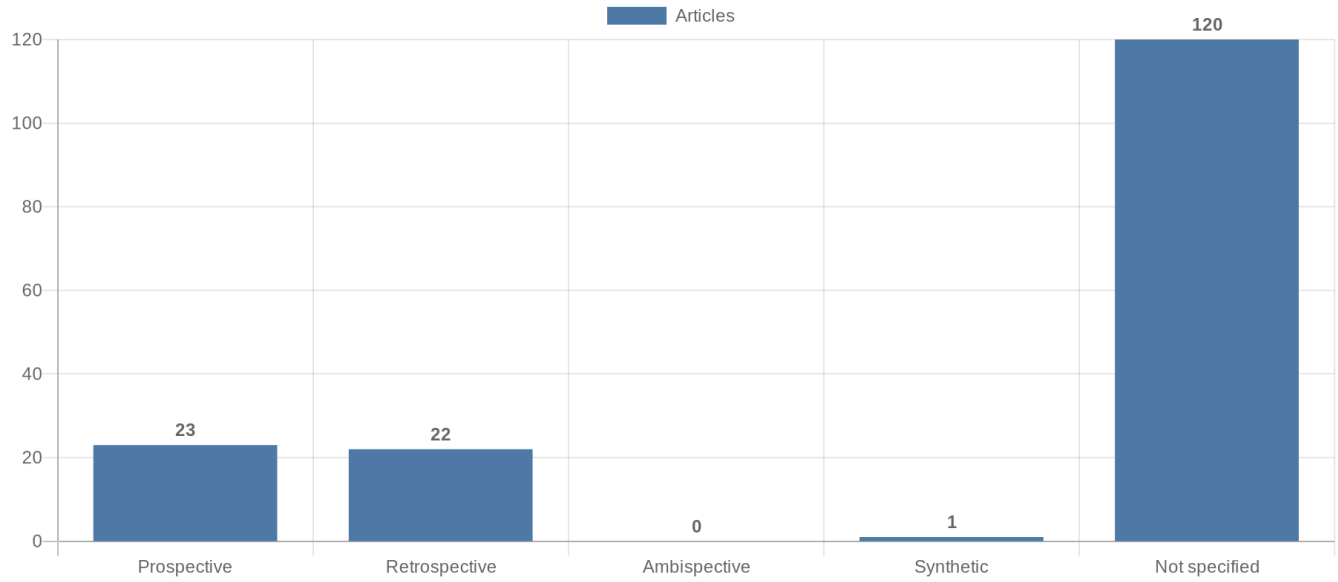



**Figure 4. Main extracted research topics**

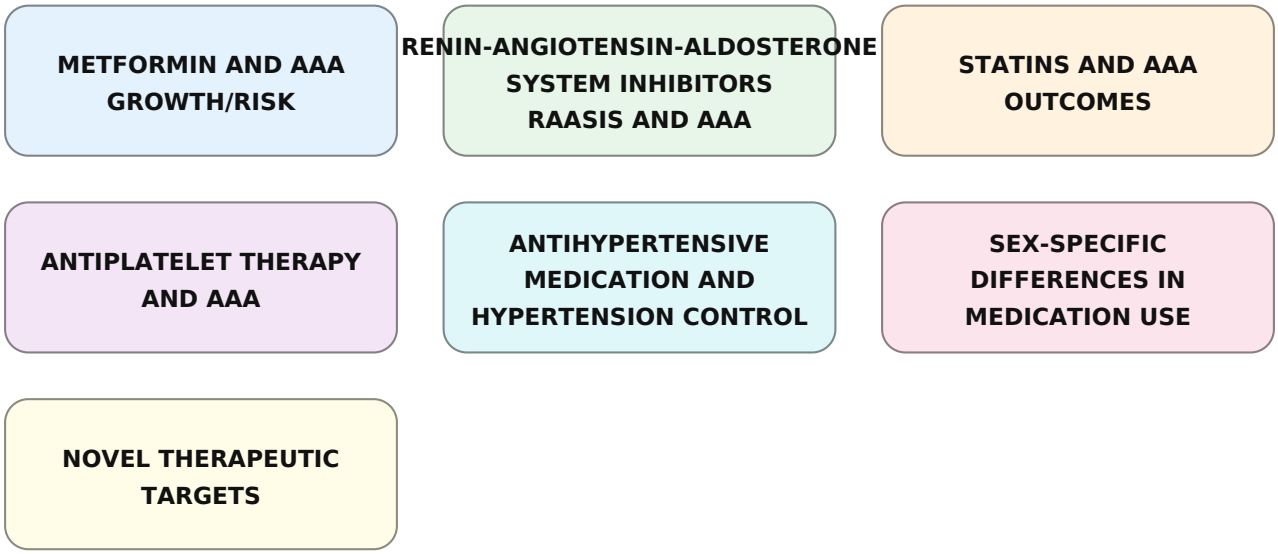



**Figure 5. Limitations of current studies (topics)**


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