Risk Factors of Aortic Aneurysm: Systematic Review with ☸SAIMSARA.

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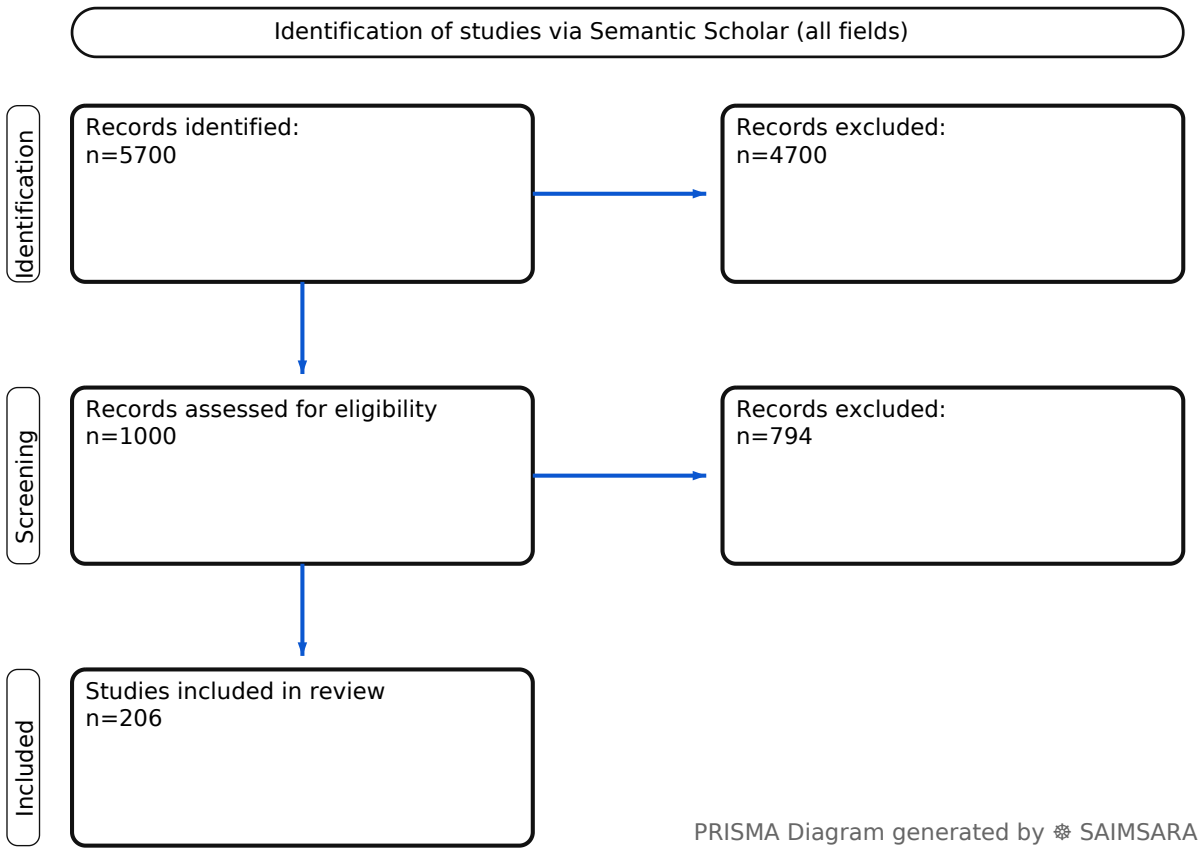
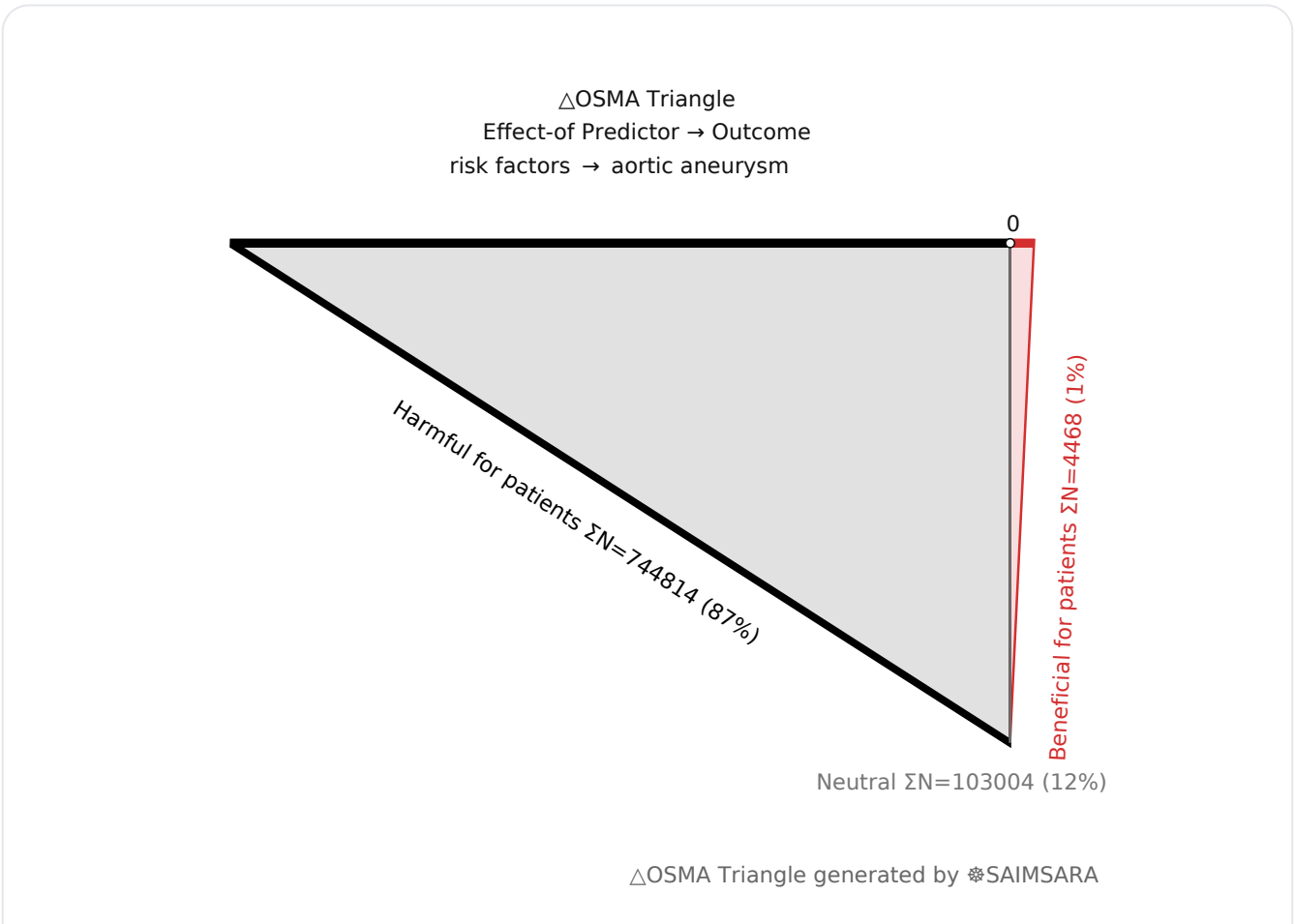
Abstract: The aim of this paper is to systematically identify and synthesize the risk factors associated with aortic aneurysm and dissection based on a structured extraction summary of scientific literature. The review utilises 206 studies with 852286 total participants (naïve ΣN). The prevalence of abdominal aortic aneurysm (AAA) ranges from 0.33% to 9.0%, with a median prevalence of 2.3% across diverse populations and screening contexts. This highlights the significant, albeit variable, burden of aortic aneurysm disease. The generalizability of these findings is somewhat limited by the heterogeneity of study designs and populations included in the synthesis. The inconsistent outcome metrics across studies most affects certainty in drawing universal conclusions. Clinicians should prioritize aggressive management of modifiable risk factors, particularly smoking and hypertension, and consider targeted screening for high-risk individuals.

Keywords: Smoking; Hypertension; Obesity; Dyslipidemia; Alcohol consumption; Physical inactivity; Genetic factors; High systolic blood pressure; Dietary sodium intake; Lead exposure

Review Stats

- Generated: 2026-02-12 23:07:51 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: 5700
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 206
- Total study participants (naïve ΣN): 852286


Identification of studies via Semantic Scholar (all fields)
Identification
Records identified:
n=5700
Records excluded:
n=4700
Screening
Records assessed for eligibility
n=1000
Records excluded:
n=794
Included
Studies included in review
n=206
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
risk factors → aortic aneurysm
0
Harmful for patients ΣN=744814 (87%)
Beneficial for patients ΣN=4468 (1%)
Neutral ΣN=103004 (12%)
△OSMA Triangle generated by ☸SAIMSARA

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

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

Outcome: aortic aneurysm Typical timepoints: peri/post-op, 10-y. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: mortality, complications, survival.

Predictor: risk factors — exposure/predictor. Doses/units seen: 25 kg, 455g. Routes seen: oral, iv. Typical comparator: thoracic aortic aneurysms, noncarriers, controls, patients operated on for….

- **1) Beneficial for patients** — aortic aneurysm with risk factors — [125] — ΣN=4468
- **2) Harmful for patients** — aortic aneurysm with risk factors — [1], [2], [3], [4], [5], [7], [8], [9], [10], [12], [13], [14], [16], [18], [19], [21], [23], [24], [26], [27], [29], [31], [33], [37], [38], [41], [42], [45], [46], [48], [50], [64], [69], [70], [75], [76], [80], [81], [85], [86], [87], [89], [90], [91], [92], [94], [95], [97], [99], [106], [107], [109], [110], [111], [118], [119], [121], [123], [126], [128], [129], [130], [132], [133], [134], [136], [137], [138], [140], [141], [142], [143], [144], [145], [147], [148], [149], [150], [165], [176], [177], [180], [181], [182], [183], [184], [186], [190], [191], [192], [194], [195], [196], [197], [198], [199], [200], [201], [202], [204], [205] — ΣN=744814
- **3) No clear effect** — aortic aneurysm with risk factors — [6], [11], [15], [17], [20], [22], [25], [28], [30], [32], [34], [35], [36], [39], [40], [43], [44], [47], [49], [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63], [65], [66], [67], [68], [71], [72], [73], [74], [77], [78], [79], [82], [83], [84], [88], [93], [96], [98], [100], [101], [102], [103], [104], [105], [108], [112], [113], [114], [115], [116], [117], [120], [122], [124], [127], [131], [135], [139], [146], [151], [152], [153], [154], [155], [156], [157], [158], [159], [160], [161], [162], [163], [164], [166], [167], [168], [169], [170], [171], [172], [173], [174], [175], [178], [179], [185], [187], [188], [189], [193], [203], [206] — ΣN=103004

1) Introduction

Aortic aneurysms (AA) and aortic dissections (AD) represent significant cardiovascular pathologies with increasing global burden, particularly early-onset forms [2]. While age-standardized mortality rates have shown some decline in certain regions and globally over past decades [8, 10, 35], recent projections indicate a potential rebound and increase in the global death burden of AA [9]. Identifying and understanding the diverse risk factors contributing to the development, progression, and rupture of aortic aneurysms is crucial for effective prevention, early diagnosis, and improved patient outcomes. This paper synthesizes current research on established and emerging risk factors,

encompassing demographic, lifestyle, metabolic, genetic, and hemodynamic influences.

2) Aim

The aim of this paper is to systematically identify and synthesize the risk factors associated with aortic aneurysm and dissection based on a structured extraction summary of scientific literature.

3) 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 exhibit a range of designs, predominantly cohort and mixed-design Mendelian randomization studies, with some case-control, cross-sectional, and randomized controlled trials (RCTs). The qualitative assessment suggests potential for selection bias in retrospective studies and those focusing on specific populations (e.g., single ethnicity, specific comorbidities, or post-operative cohorts). Mendelian randomization studies aim to infer causality, but their generalizability can be limited by the genetic variants studied. Heterogeneity in study populations, definitions of outcomes, and follow-up durations across studies also introduces variability.

4) Results

4.1 Study characteristics:

The structured summary includes studies with diverse designs, primarily cohort (n=30), mixed (n=30), and case-control (n=7), along with cross-sectional (n=3) and one RCT. Populations ranged from global cohorts across 204 countries and regions [2, 8] to specific demographics such as 65-year-old men in Oslo [21], community-based Japanese cohorts [5], and patients of European ancestry [3]. Follow-up periods varied significantly, from short-term (e.g., 90-day incidence [119]) to long-term durations up to 34 years [26].

4.2 Main numerical result aligned to the query:

The prevalence of abdominal aortic aneurysm (AAA) varied considerably across different populations and screening contexts, with a median prevalence of 2.3% and a range from 0.33% in Middle China (aged 40 years or older) [25] to 9.0% in patients with intermittent claudication [80]. Specifically, the overall prevalence of aortic aneurysms was reported as 2.1% in the general population [118], 4.8% in Europe [201], and 0.92% globally among persons aged 30 to 79 years [180].

4.3 Topic synthesis:

- **Lifestyle and Metabolic Risk Factors:** Smoking is consistently identified as a primary and strong risk factor for AA and AD, significantly increasing risk (e.g., OR 3.6 [64], 7-15 times higher risk [13]) and mortality [2, 4, 5, 8, 13, 18, 19, 21, 27, 51, 64, 77, 83, 94, 96, 111, 114, 118, 159, 180, 201, 205]. Alcohol consumption also increases AA risk [1, 8]. Obesity traits, including high body mass index (BMI) and waist circumference, are associated with higher AA risk (BMI OR 1.58 [3], HR 1.43 [18], HR 1.69 for BMI ≥ 30 kg/m2 [24]) [1, 3, 8, 13, 16, 18, 21, 22, 24, 75, 96, 118, 180]. Dyslipidemia, characterized by high LDL-C and triglycerides and low HDL-C, increases AA risk (e.g., LDL-C OR 1.66, triglycerides OR 1.69, HDL-C OR 0.67 [46]) [1, 5, 8, 13, 19, 46, 69, 75, 96, 118, 153, 180, 193]. A diet high in sodium and lead exposure are also linked to increased AA mortality [4].
- **Hemodynamic and Blood Pressure Factors:** Hypertension is a significant causal risk factor for AA and AD (pooled OR 4.30 [3], HR 1.61-2.95 [5]), with high systolic blood pressure (SBP) being a particularly important attributable risk factor for mortality, projected to surpass smoking [4, 5, 8, 9, 10, 12, 13, 16, 20, 21, 27, 33, 44, 74, 80, 81, 83, 84, 86, 90, 91, 96, 116, 118, 132, 153, 172, 180, 181, 200, 201, 202]. Aortic size (e.g., ≥6.0 cm HR 1.78 [26]), maximum diameter (OR 1.095 [7]), curvature [7, 91, 148], and abnormal wall shear stress (WSS) and relative residence time (RRT) [7, 122, 147, 152] are also critical factors influencing aneurysm formation, expansion, and rupture.
- **Demographic and Clinical Characteristics:** Advanced age is a consistent risk factor for AA incidence and mortality (e.g., incidence increases with age [94], age >65 years associated with AAA [31]) [2, 4, 5, 8, 9, 11, 13, 17, 21, 25, 26, 27, 31, 33, 35, 44, 47, 50, 53, 71, 74, 75, 80, 82, 83, 85, 87, 90, 92, 94, 96, 106, 107, 111, 114, 116, 118, 120, 121, 123, 134, 145, 153, 160, 172, 174, 178, 180, 182, 186, 199, 200, 201, 203]. Male sex is frequently associated with a higher prevalence and risk of AA (e.g., 0.55% vs 0.14% prevalence [25], HR 4.8 [18]) [18, 25, 27, 38, 44, 74, 75, 77, 83, 87, 90, 94, 96, 111, 118, 122, 134, 136, 138, 145, 160, 176, 180, 186, 196, 199, 201].
- **Genetic and Heritable Predispositions:** Family history of AA is an independent risk factor (e.g., HR 6.70 for first-degree relatives [177]) [75, 96, 130, 145, 177, 180, 194]. Specific genetic polymorphisms (e.g., IL-6 rs1800796 [12], SEPP1 [16], TLR4 and MMP2 [29], KIF6 719Arg [76], fibrinogen β chain −455 G/A [175], HLA-DR2(15) [149], Chromosome 16p13.1 duplications [194]) and genome-wide association studies have identified numerous risk loci [15, 171]. Connective tissue diseases like Marfan syndrome [84, 127, 138, 185, 190, 199] and bicuspid aortic valve (BAV) [27, 67, 93, 184] are significant predisposing factors.
- **Inflammation and Molecular Pathways:** Inflammation is a key factor in AA development and progression [15, 20, 28, 156]. Elevated levels of inflammatory markers such as matrix metalloproteinase-9 (MMP9) [165], plasma inflammatory cytokines [156], neutrophil counts [14, 38, 80], eosinophil counts [38, 137], and myeloperoxidase [141] are associated with increased risk and growth. Oxidative stress [79, 141, 166], dysregulated endocytosis [36],

and specific cellular pathways (e.g., HIF-1α signaling [167], IL18 [140], Malat1+ VSMCs [32], Nrf2 activity [139]) contribute to pathogenesis.

- **Comorbidities:** Coronary artery disease (CAD) [14, 31, 48, 75, 92, 110, 115, 153, 160, 192], peripheral arterial disease (PAD) [16, 33, 75, 92, 111, 129, 153, 180, 202, 204], chronic kidney disease (CKD) [11, 17, 34, 82, 96, 106, 121, 153, 160, 180, 182], cerebrovascular disease [92, 106, 153, 180, 182, 192], and respiratory disorders (e.g., COPD) [74, 75, 92, 117, 143, 180, 182] are frequently identified as comorbidities and independent risk factors. Depression is also associated with a higher risk of AAA [123, 192].
- **Diabetes Paradox:** Type 2 diabetes mellitus (T2DM) appears to be protective against AA development in several studies (e.g., protective against AA [1], lower HR 0.50 [5], inverse association OR 0.52 [21], lower risk with Metformin use [125]) [1, 5, 21, 24, 85, 125, 145, 196]. However, diabetes is also identified as a risk factor for postoperative complications like incisional hernias after AAA repair [6], postoperative myocardial infarction [110], and is associated with concurrent intracranial aneurysms [44] and diabetic kidney disease [153].
- **Emerging and Specific Risk Factors:** Fluoroquinolone use is associated with an increased incidence of AA [119]. Oral steroid usage is an important risk factor for AAA expansion [50]. Low socioeconomic position (SEP) is linked to higher rates of ruptured AAA and increased mortality [158, 164]. Hyperuricemia is an independent risk factor for aortic dissection-related death [181]. HIV infection is independently associated with aortic aneurysms, with obesity and hepatitis B co-infection being additional risk factors in this population [176]. Autoimmune conditions like Takayasu arteritis [69] and Giant Cell Arteritis (GCA) [89] can lead to aneurysm formation, as can cardiovascular syphilis [206]. Pregnancy in Marfan syndrome patients significantly increases the risk of aortic dissection [190].

5) Discussion

5.1 Principal finding:

The prevalence of abdominal aortic aneurysm (AAA) ranges from 0.33% to 9.0%, with a median prevalence of 2.3% across diverse populations and screening contexts [25, 48, 64, 75, 80, 118, 176, 180, 201]. This highlights the significant, albeit variable, burden of aortic aneurysm disease.

5.2 Clinical implications:

- **Targeted Screening:** Given the strong association of male sex, advanced age, and smoking with AAA, targeted screening programs for these high-risk individuals are critical for early detection and intervention [21, 27, 94, 111, 118, 145, 180].
- **Aggressive Risk Factor Modification:** Intensive management of modifiable risk factors such as hypertension, dyslipidemia, and obesity is paramount for preventing AA

development and progression [1, 3, 4, 5, 8, 13, 18, 21, 96, 118, 180].

- **Diabetes Management Nuance:** While diabetes often shows a protective association with AA development, its role in post-operative complications and co-morbidities necessitates careful management [1, 5, 6, 21, 24, 44, 85, 92, 110, 116, 125, 145, 153, 160, 196].
- **Genetic Counseling:** Patients with a family history of AA or known genetic syndromes like Marfan syndrome should receive appropriate genetic counseling and tailored surveillance strategies [75, 84, 96, 130, 145, 177, 180, 190].
- **Post-operative Vigilance:** Patients undergoing aortic aneurysm repair are at risk for various complications, including acute kidney injury, incisional hernias, delirium, and myocardial infarction, requiring vigilant post-operative care and long-term monitoring for reintervention [6, 11, 17, 34, 108, 110, 112, 120, 129, 142, 182].

5.3 Research implications / key gaps:

- **Diabetes Pathophysiology:** Further research is needed to elucidate the mechanisms underlying the dual, sometimes conflicting, role of diabetes in AA development versus post-operative outcomes [1, 5, 6, 21, 24, 44, 85, 92, 110, 116, 125, 145, 153, 160, 196].
- **Sex-Specific Differences:** More studies are required to understand the biological and clinical reasons for sex-specific differences in AA prevalence, growth rates, rupture risk, and post-operative outcomes [13, 25, 74, 87, 134, 136, 138, 160, 186, 196, 199].
- **Inflammatory Biomarkers:** Prospective studies are needed to validate the predictive value of emerging inflammatory and molecular biomarkers for AA progression and rupture in diverse populations [15, 20, 28, 79, 137, 141, 156, 165, 166, 167].
- **Environmental and Lifestyle Interactions:** Research should explore complex interactions between environmental factors (e.g., lead exposure, diet, socioeconomic status) and genetic predispositions in AA pathogenesis [4, 15, 16, 29, 119, 158, 164, 171, 175, 176].
- **Longitudinal Hemodynamic Studies:** Longitudinal studies using advanced imaging are needed to track changes in aortic diameter, curvature, and wall shear stress over time and correlate them with clinical outcomes [7, 58, 91, 113, 122, 147, 148, 152, 155, 162, 174].

5.4 Limitations:

- **Heterogeneous Study Designs** — The synthesis draws from various study designs, limiting the ability to perform robust meta-analysis or direct comparisons across all reported metrics.

- **Population Specificity** — Many studies focus on specific populations (e.g., Chinese, Japanese, men, older adults, or those with comorbidities), which may limit the generalizability of findings to broader demographics.
- **Inconsistent Outcome Metrics** — Variability in how risk factors are measured and how outcomes (e.g., prevalence, incidence, rupture, mortality, expansion rate) are reported makes direct quantitative comparison challenging.
- **Lack of Causal Inference** — While Mendelian randomization studies infer causality, many cohort and case-control studies identify associations, and definitive causal links for all factors cannot be established from the summary alone.
- **Limited Data on Rare Factors** — Data on less common or emerging risk factors (e.g., specific genetic mutations, drug exposures, certain infections) are often from smaller studies, requiring further validation.

5.5 Future directions:

- **Standardize Outcome Reporting** — Future studies should standardize reporting of AA prevalence, incidence, and risk factor effect sizes to enable more robust meta-analyses.
- **Longitudinal Multi-Ethnic Cohorts** — Conduct large-scale, prospective, multi-ethnic cohort studies to better understand the interplay of genetic and environmental factors.
- **Integrate Multi-Omics Data** — Utilize multi-omics approaches (genomics, proteomics, metabolomics) to identify novel biomarkers and therapeutic targets.
- **Advanced Imaging Biomarkers** — Develop and validate advanced imaging biomarkers for early detection of aneurysm progression and rupture risk.
- **Clinical Guideline Updates** — Regularly update clinical guidelines based on emerging evidence for risk factors, screening recommendations, and personalized management strategies.

6) Conclusion

The prevalence of abdominal aortic aneurysm (AAA) ranges from 0.33% to 9.0%, with a median prevalence of 2.3% across diverse populations and screening contexts [25, 48, 64, 75, 80, 118, 176, 180, 201]. This highlights the significant, albeit variable, burden of aortic aneurysm disease. The generalizability of these findings is somewhat limited by the heterogeneity of study designs and populations included in the synthesis. The inconsistent outcome metrics across studies most affects certainty in drawing universal conclusions. Clinicians should prioritize aggressive management of modifiable risk factors, particularly smoking and hypertension, and consider targeted screening for high-risk individuals.

References

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Figure 1. Publication-year distribution of included originals

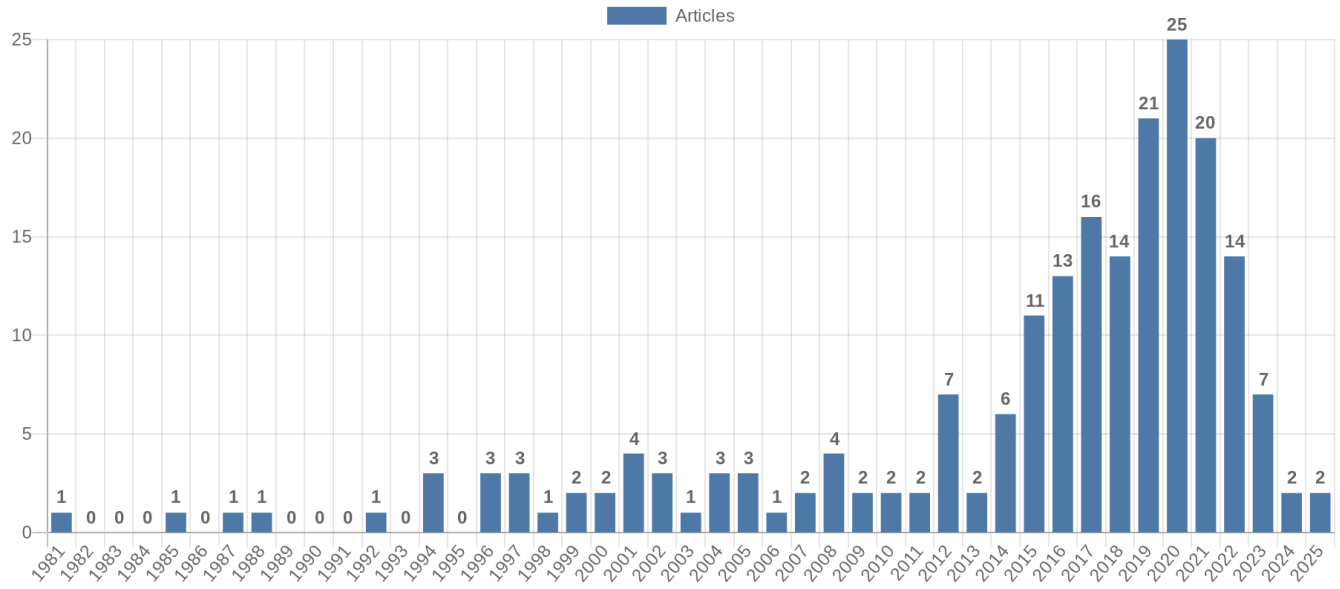

Figure 2. Study-design distribution of included originals

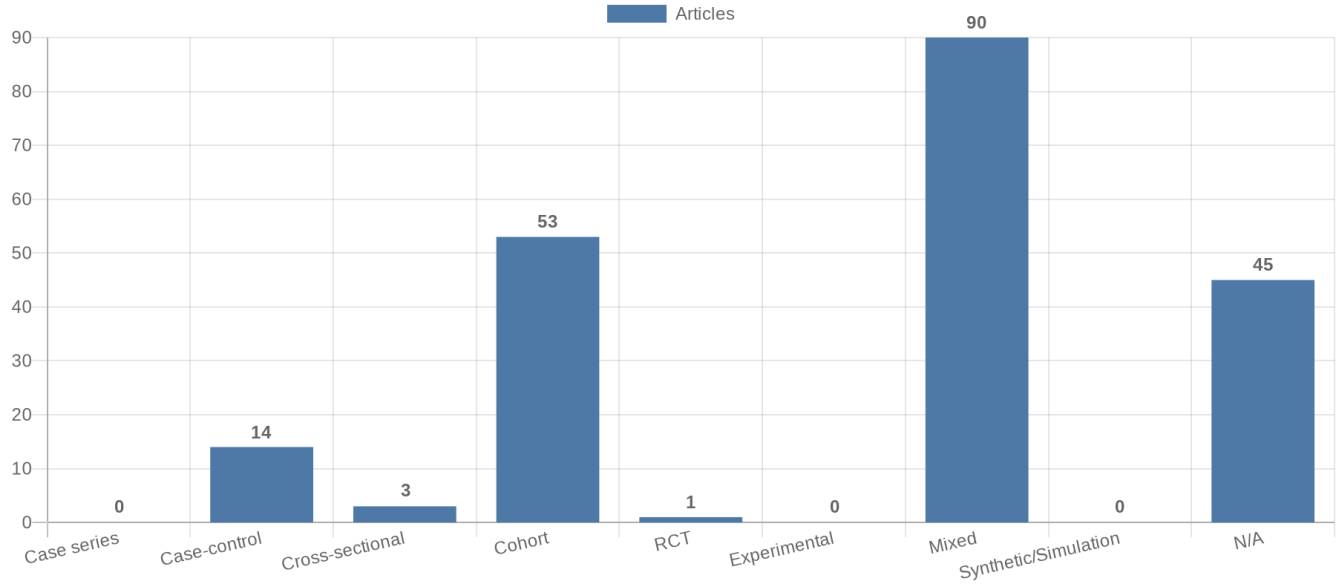

Figure 3. Study-type (directionality) distribution of included originals

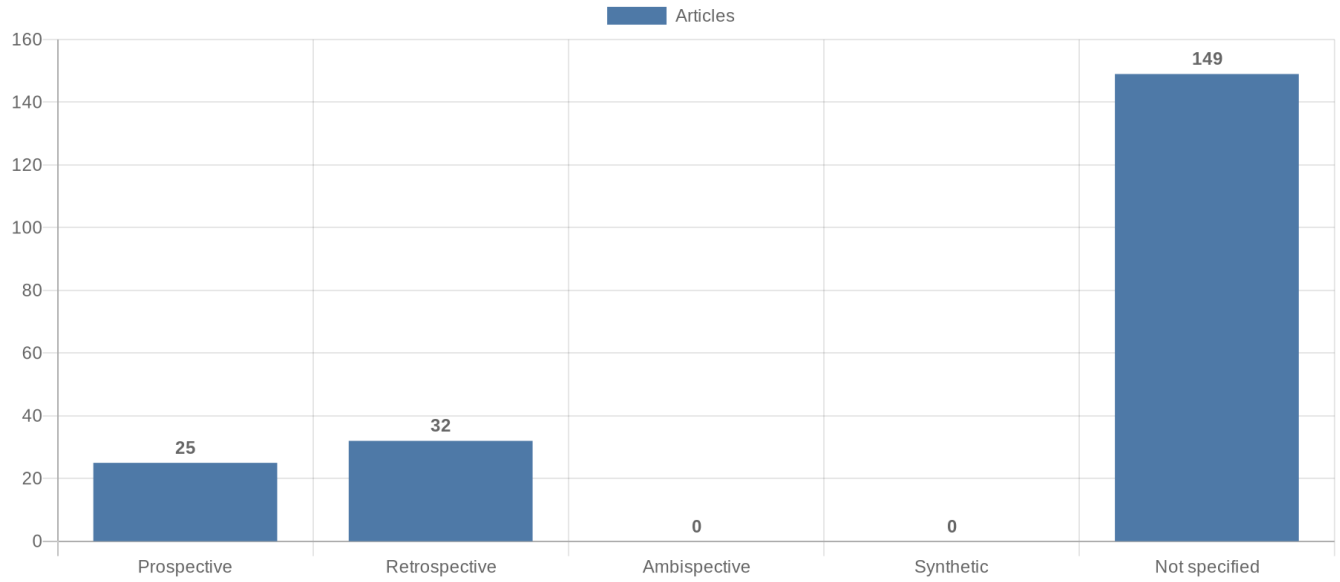

Figure 4. Main extracted research topics

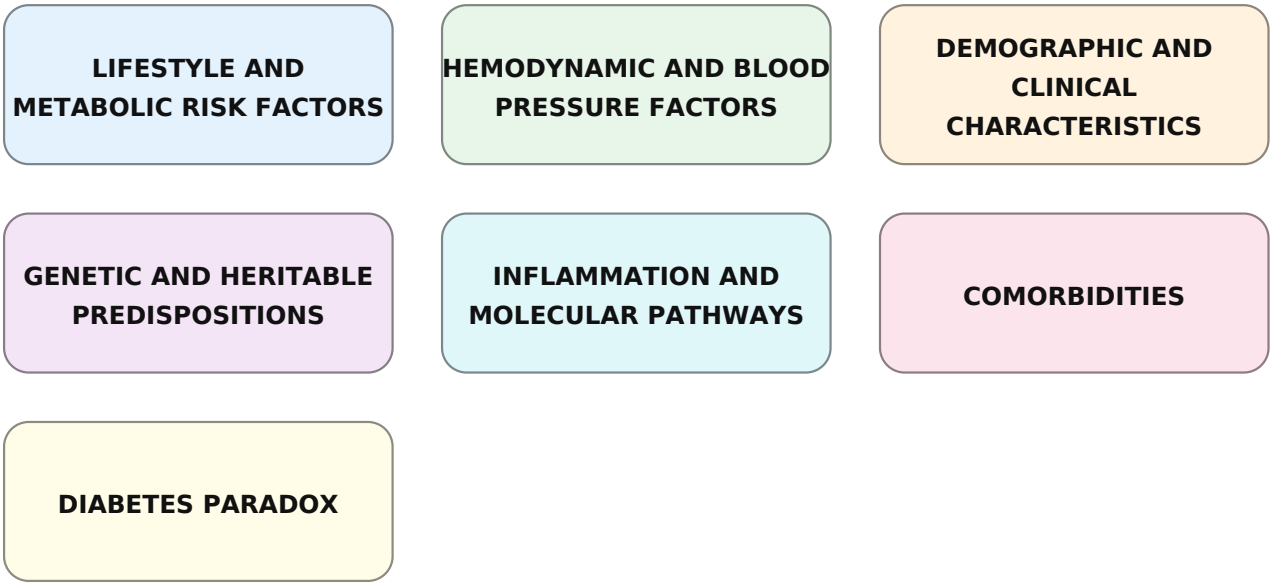

Figure 5. Limitations of current studies (topics)

Figure 6. Future research directions (topics)

DIABETES PATHOPHYSIOLOGY

SEX-SPECIFIC DIFFERENCES

INFLAMMATORY BIOMARKERS

ENVIRONMENTAL AND LIFESTYLE INTERACTIONS

LONGITUDINAL HEMODYNAMIC STUDIES

STANDARDIZE OUTCOME REPORTING

LONGITUDINAL MULTI-ETHNIC COHORTS