Aortic Aneurysm and Diameter: Systematic Review with ☸SAIMSARA.

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Abstract: To comprehensively synthesize current research on the relationship between aortic aneurysm and diameter, including its role in disease progression, rupture risk, diagnostic methods, and therapeutic interventions. The review utilises 289 studies with 148337 total participants (naïve ΣN). The median maximum diameter reported for ruptured abdominal aortic aneurysms was 72.0 mm, with a range of 60.0 mm to 86.0 mm. This finding highlights the critical role of diameter in assessing rupture risk for abdominal aortic aneurysms, though its generalizability is impacted by the diverse populations and methodologies across studies. The heterogeneous study designs, particularly the reliance on animal models and retrospective human cohorts, most affects certainty. A concrete next step is to develop and validate integrated risk assessment models that combine diameter with biomechanical parameters, genetic markers, and inflammatory biomarkers for improved prediction of aneurysm events.

Keywords: Aortic aneurysm; Aneurysm diameter; Abdominal aortic aneurysm; Thoracic aortic aneurysm; Aneurysm rupture; Aneurysm growth; Aortic dimensions; Endovascular repair; Aortic stiffness; Ascending aorta

Review Stats

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- Scope: All fields
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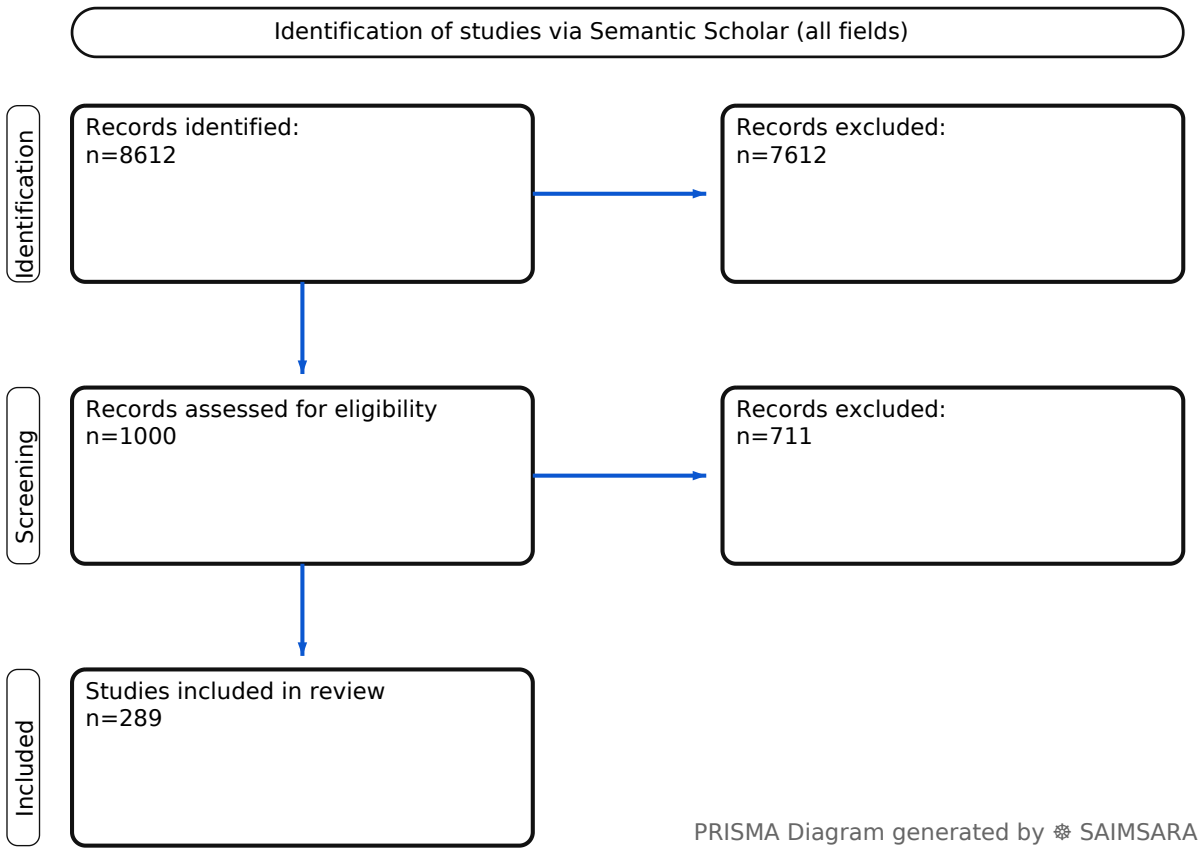
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 289
- Total study participants (naïve ΣN): 148337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Records excluded:
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Screening
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Included
Studies included in review
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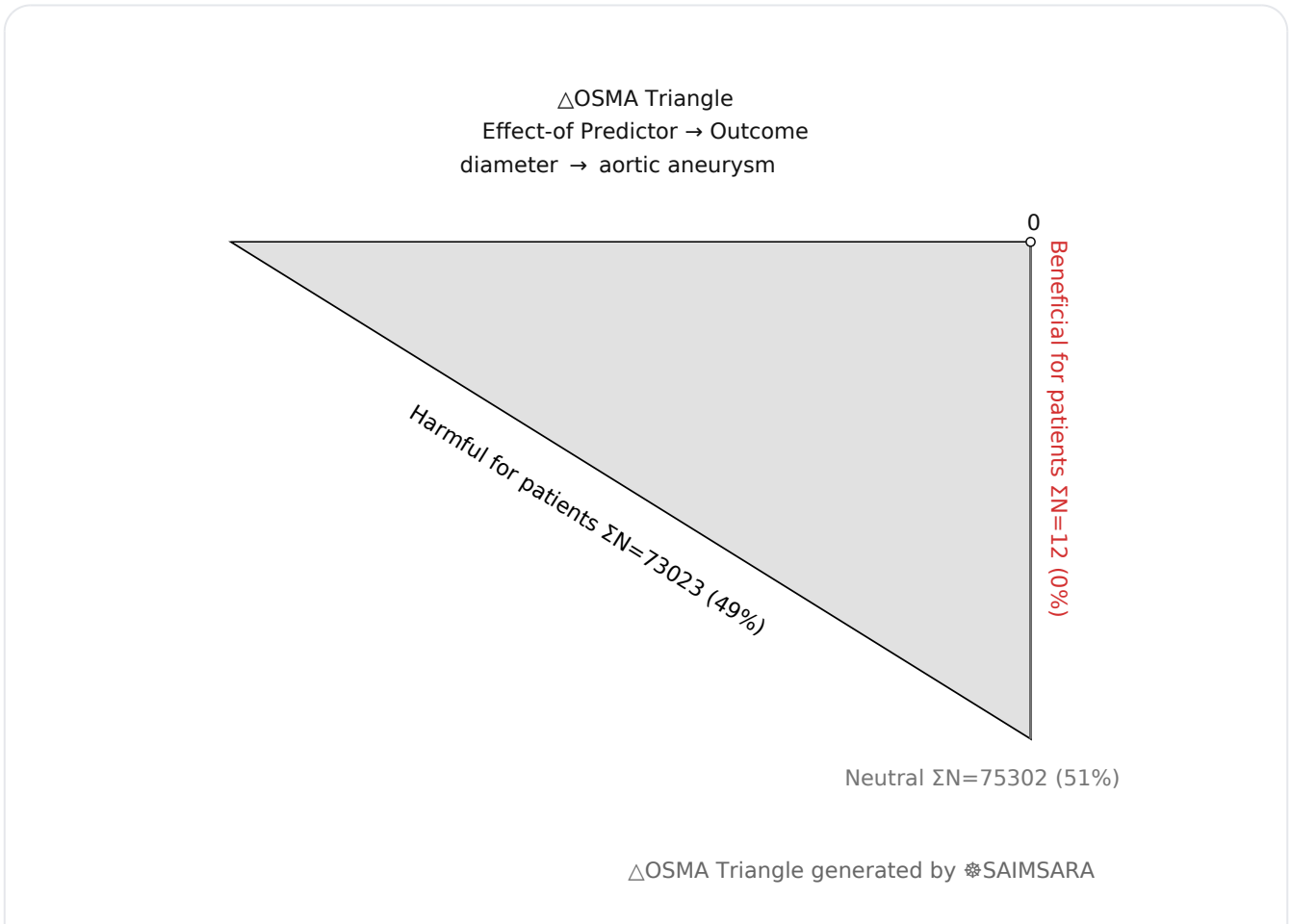
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
diameter → aortic aneurysm
0
Beneficial for patients ΣN=12 (0%)
Harmful for patients ΣN=73023 (49%)
Neutral ΣN=75302 (51%)
△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: 28-day, 2-y. Reported metrics: %, CI, p.

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

Predictor: diameter — exposure/predictor. Routes seen: intravenous, oral. Typical comparator: 3d, lower levels, placebo did not significantly, placebo….

- **1) Beneficial for patients** — aortic aneurysm with diameter — [76] — ΣN=12
- **2) Harmful for patients** — aortic aneurysm with diameter — [2], [4], [9], [22], [23], [26], [27], [39], [41], [51], [64], [65], [79], [81], [82], [84], [85], [145], [157], [179], [180], [182], [208], [210], [214], [226], [228], [233], [234], [235], [236], [240], [242], [243], [244], [251] — ΣN=73023
- **3) No clear effect** — aortic aneurysm with diameter — [1], [3], [5], [6], [7], [8], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [24], [25], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [40], [42], [43], [44], [45], [46], [47], [48], [49], [50], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63], [66], [67], [68], [69], [70], [71], [72], [73], [74], [75], [77], [78], [80], [83], [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], [118], [119], [120], [121], [122], [123], [124], [125], [126], [127], [128], [129], [130], [131], [132], [133], [134], [135], [136], [137], [138], [139], [140], [141], [142], [143], [144], [146], [147], [148], [149], [150], [151], [152], [153], [154], [155], [156], [158], [159], [160], [161], [162], [163], [164], [165], [166], [167], [168], [169], [170], [171], [172], [173], [174], [175], [176], [177], [178], [181], [183], [184], [185], [186], [187], [188], [189], [190], [191], [192], [193], [194], [195], [196], [197], [198], [199], [200], [201], [202], [203], [204], [205], [206], [207], [209], [211], [212], [213], [215], [216], [217], [218], [219], [220], [221], [222], [223], [224], [225], [227], [229], [230], [231], [232], [237], [238], [239], [241], [245], [246], [247], [248], [249], [250], [252], [253], [254], [255], [256], [257], [258], [259], [260], [261], [262], [263], [264], [265], [266], [267], [268], [269], [270], [271], [272], [273], [274], [275], [276], [277], [278], [279], [280], [281], [282], [283], [284], [285], [286], [287], [288], [289] — ΣN=75302

Introduction

Aortic aneurysms represent a critical cardiovascular pathology characterized by localized dilation of the aorta, posing significant risks of rupture and dissection. The diameter of an aortic aneurysm is

widely recognized as a primary indicator for disease progression, rupture risk, and the necessity for intervention. Understanding the multifaceted relationship between aortic diameter and various pathophysiological, genetic, and environmental factors is crucial for effective diagnosis, surveillance, and therapeutic management. This paper synthesizes current research on aortic aneurysm and diameter, exploring its role in risk stratification, disease mechanisms, and treatment outcomes across different aortic segments and patient populations.

Aim

To comprehensively synthesize current research on the relationship between aortic aneurysm and diameter, including its role in disease progression, rupture risk, diagnostic methods, and therapeutic interventions.

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 studies and animal models are prevalent, introducing potential for selection bias and limited generalizability to human clinical settings, respectively. Many studies lack specified directionality or statistical reporting, limiting definitive conclusions.

Results

4.1 Study characteristics

The included studies comprise a diverse range of designs, predominantly cohort studies, mixed methods, and experimental animal models. Retrospective analyses are common for human patient data, while animal models frequently investigate mechanistic pathways and therapeutic interventions. Follow-up periods vary significantly, from short-term (e.g., 7 days in animal models [62, 229]) to long-term (e.g., 10 years for post-EVAR reintervention [214] or mortality follow-up [157]). Patient populations include those with abdominal aortic aneurysms (AAAs), thoracic aortic aneurysms (TAAs), ascending aortic aneurysms (AsAAs), and specific genetic conditions like Marfan syndrome, as well as healthy controls and various rodent models.

4.2 Main numerical result aligned to the query

The median maximum diameter reported for ruptured abdominal aortic aneurysms (AAAs) was 72.0 mm, with a range of 60.0 mm to 86.0 mm [4, 9, 65, 73].

4.3 Topic synthesis

- **Diameter as a Primary Rupture Risk Predictor:** Maximum aortic diameter is a well-established predictor of aneurysm rupture, with ruptured abdominal aortic aneurysms (AAAs) typically exhibiting larger diameters (e.g., median 70 mm [73], mean 8.6 cm [65]) compared to unruptured ones [9, 19, 4]. Thoracic aortic aneurysms (TAAs) also show increased risk of dissection or rupture as diameter approaches 6 cm [145]. However, Type A Aortic Dissection was not well predicted by diameter ≥5.5 cm [154], and aortic diameters were minimally enlarged at dissection in some MYLK mutation cases [238].
- **Molecular and Cellular Drivers of Diameter Growth:** Aneurysm growth and diameter are influenced by T- and B-cell expression, lipid-related processes [1], circulating inflammatory markers like IgG, CD38, GDF15 [10], and plasma desmosine (r=0.39) [26]. Genetic factors such as ADAMTS-4 deficiency [8] and loss of peroxiredoxin 2 (PRDX2) [22] significantly impact aortic diameter, while specific mutations (e.g., MYLK, TGFBR2) can lead to dissection at minimally enlarged diameters [238, 239].
- **Biomechanical Factors and Diameter Relationship:** Beyond simple diameter, complex biomechanical factors such as lumen volume and wall shear stress (WSS) are superior predictors of AAA enlargement (AUC 0.79 vs 0.53 for diameter alone for AAAs <50 mm) [17]. Aneurysm stiffness may not correlate with diameter [13], but local wall stress, thrombus thickness, and geometric parameters (e.g., asymmetry, tortuosity) are critical modulators of rupture risk [56, 160, 222].
- **Pharmacological and Cellular Therapies Modulating Diameter:** Various interventions have shown promise in attenuating aortic diameter expansion in animal models, including PKM2 activators [6], ADAMTS-4 deficiency [8], BP-1-102 [16], empagliflozin [18], IL-10 transfection [34], necrostatin-1s [35], AT2R agonists [39], Notch inhibitors [72], rapamycin nanoparticles [62], cyclosporine A (CsA) [251], and mesenchymal stromal cell (MSC)-derived therapies [30, 76]. However, clinical trials with doxycycline [21, 206] and ticagrelor [232] have not shown significant reduction in AAA growth by diameter.
- **Diagnostic Imaging and Measurement Precision:** Accurate measurement of aortic diameter is crucial for diagnosis, surveillance, and post-repair follow-up [7, 24, 58, 155]. While ultrasound and computed tomography (CT) are standard [54, 58], advanced techniques like 3D/4D ultrasound, image fusion [7], and vascular deformation mapping (VDM) offer more comprehensive insights into aortic wall geometry and changes beyond maximal diameter [161, 12].
- **Sex-Specific Differences in Aneurysm Progression:** Women often present with larger normalized aortic diameters for ascending aortic aneurysms (3.10±0.6 cm vs 2.75±0.5 cm in men, p≤0.001) [64] and exhibit significantly higher ascending aortic aneurysm growth rates (0.3 ± 0.5 mm/year vs 0.2 ± 0.4 mm/year in men, p=0.007) [231]. Ovariectomy increased aneurysm diameter in rats [2], and male Marfan syndrome mice showed greater diameter increase [204], suggesting hormonal influences.

- **Post-Intervention Aortic Remodeling and Complications:** After endovascular aortic aneurysm repair (EVAR), changes in aneurysm sac diameter and volume are monitored [7, 46, 49, 50, 156]. Proximal neck diameter is a critical factor influencing EVAR outcomes [63, 210, 235], with dilatation of the infrarenal neck observed post-exclusion [144, 149]. Large aneurysm diameter (≥6.0 cm) is a predictor of reintervention after EVAR [214].
- **Screening and Population-Level Risk:** Screening programs using ultrasound have identified high prevalence of AAAs, particularly in men aged ≥65 years [88, 121, 199]. Increasing infrarenal aortic diameter, even in non-aneurysmal aortas (≥30 mm), is associated with increased total and cardiovascular mortality [157, 79]. However, the risk of ruptured AAA for small and medium AAAs under surveillance is generally low (<0.5% per annum) [85].

Discussion

5.1 Principal finding

The median maximum diameter reported for ruptured abdominal aortic aneurysms was 72.0 mm, with a range of 60.0 mm to 86.0 mm [4, 9, 65, 73], underscoring diameter as a critical, albeit not sole, indicator of rupture risk.

5.2 Clinical implications

- **Rupture Risk Stratification:** Aneurysm diameter remains a primary criterion for surgical intervention decisions, particularly for AAAs, where larger diameters are strongly associated with rupture [19, 9].
- **Enhanced Monitoring Post-Repair:** Post-endovascular aortic aneurysm repair (EVAR) surveillance should incorporate not only diameter but also sac volume and neck morphology to detect complications like endoleaks and reintervention risk [156, 210, 214].
- **Sex-Specific Guidelines:** The observed sex differences in aneurysm growth rates and normalized diameters [64, 231] suggest a need for potentially tailored surveillance and intervention guidelines for women.
- **Beyond Diameter:** Clinicians should consider incorporating advanced imaging techniques and biomechanical assessments (e.g., wall stress, lumen volume, wall shear stress) to improve rupture risk prediction, especially for smaller aneurysms where diameter alone may be insufficient [17, 161].
- **Screening for Mortality Risk:** Screening for abdominal aortic aneurysms (AAAs) is vital, as even non-aneurysmal aortic diameters ≥30 mm are associated with increased mortality [157, 79].

5.3 Research implications / key gaps

- **Predictive Biomarker Validation:** Further prospective studies are needed to validate the clinical utility of circulating biomarkers (e.g., IgG, CD38, GDF15, desmosine, CatS, cystatin C) in predicting aneurysm growth and rupture in diverse patient cohorts [10, 26, 225].
- **Mechanism of Sex Differences:** Research should elucidate the precise hormonal and genetic mechanisms underlying sex-specific differences in aneurysm progression and response to therapies, particularly for ascending aortic aneurysms [2, 64, 231].
- **Advanced Imaging Integration:** Prospective trials are required to determine how advanced imaging modalities (e.g., vascular deformation mapping, 3D/4D ultrasound, shape analysis) can be integrated into routine clinical practice to improve rupture risk prediction beyond traditional diameter measurements [161, 211, 217].
- **Translational Therapeutic Efficacy:** Clinical trials are needed to translate promising animal model findings for diameter attenuation (e.g., PKM2 activators, Notch inhibitors, MSC therapies) into effective human treatments, given the limited success of some current pharmacological agents like doxycycline in clinical settings [6, 72, 183].
- **Long-Term Post-Repair Remodeling:** Longitudinal studies with standardized measurement protocols are needed to better understand the long-term remodeling of the aortic neck and sac after EVAR, and its impact on reintervention rates and overall patient outcomes [144, 149, 214].

5.4 Limitations

- **Heterogeneous Study Designs** — The diverse range of study designs, including animal models and retrospective human cohorts, limits the ability to draw universally applicable conclusions.
- **Inconsistent Reporting Metrics** — Variability in reporting specific diameter measurements (e.g., mean, median, ranges) and statistical outcomes across studies hinders direct quantitative comparison and meta-analysis.
- **Reliance on Diameter Alone** — Many studies still primarily focus on diameter as a sole predictor, potentially overlooking other crucial biomechanical and morphological factors that contribute to rupture risk.
- **Limited Long-Term Follow-up** — A number of studies, particularly animal models and early intervention reports, lack sufficient long-term follow-up to assess sustained effects on aneurysm diameter and clinical outcomes.
- **Generalizability to Diverse Populations** — Some findings are derived from specific populations (e.g., men in screening programs, Marfan syndrome patients, Asian patients), limiting generalizability to broader patient demographics.

5.5 Future directions

- **Standardized Measurement Protocols** — Develop and implement standardized protocols for aortic diameter and volume measurements across imaging modalities to improve comparability and reproducibility.
- **Integrated Risk Assessment Models** — Create comprehensive risk assessment models that combine diameter with biomechanical parameters, genetic markers, and inflammatory biomarkers for improved prediction of aneurysm events.
- **Sex-Specific Intervention Trials** — Conduct clinical trials specifically designed to evaluate sex-specific management strategies and therapeutic interventions for aortic aneurysms, considering differential growth rates and outcomes.
- **Longitudinal Biomechanical Imaging** — Utilize advanced imaging techniques to perform longitudinal 3D strain and wall stress analyses in vivo, correlating these with aneurysm growth and rupture events.
- **Translational Drug Development** — Prioritize clinical trials for novel pharmacological agents that have shown efficacy in attenuating aneurysm dilation in animal models, focusing on safety and long-term impact on diameter and outcomes.

Conclusion

The median maximum diameter reported for ruptured abdominal aortic aneurysms was 72.0 mm, with a range of 60.0 mm to 86.0 mm [4, 9, 65, 73]. This finding highlights the critical role of diameter in assessing rupture risk for abdominal aortic aneurysms, though its generalizability is impacted by the diverse populations and methodologies across studies. The heterogeneous study designs, particularly the reliance on animal models and retrospective human cohorts, most affects certainty. A concrete next step is to develop and validate integrated risk assessment models that combine diameter with biomechanical parameters, genetic markers, and inflammatory biomarkers for improved prediction of aneurysm events.

References

SAIMSARA Session Index — session.json

Figure 1. Publication-year distribution of included originals

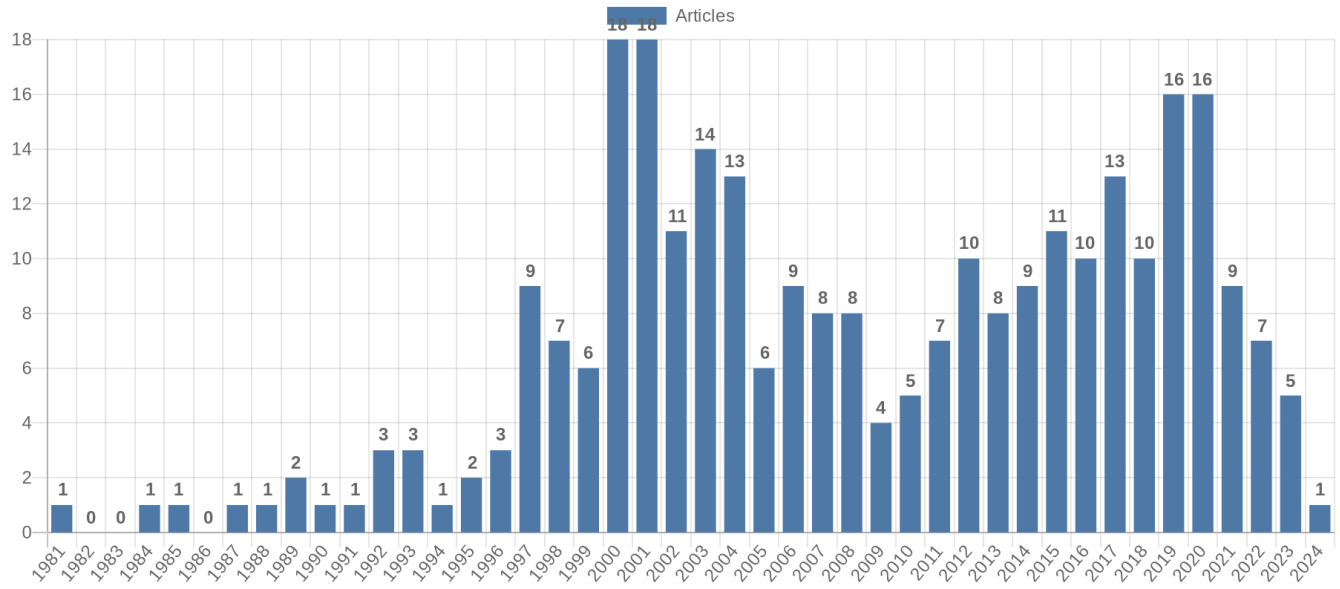


Figure 2. Study-design distribution of included originals

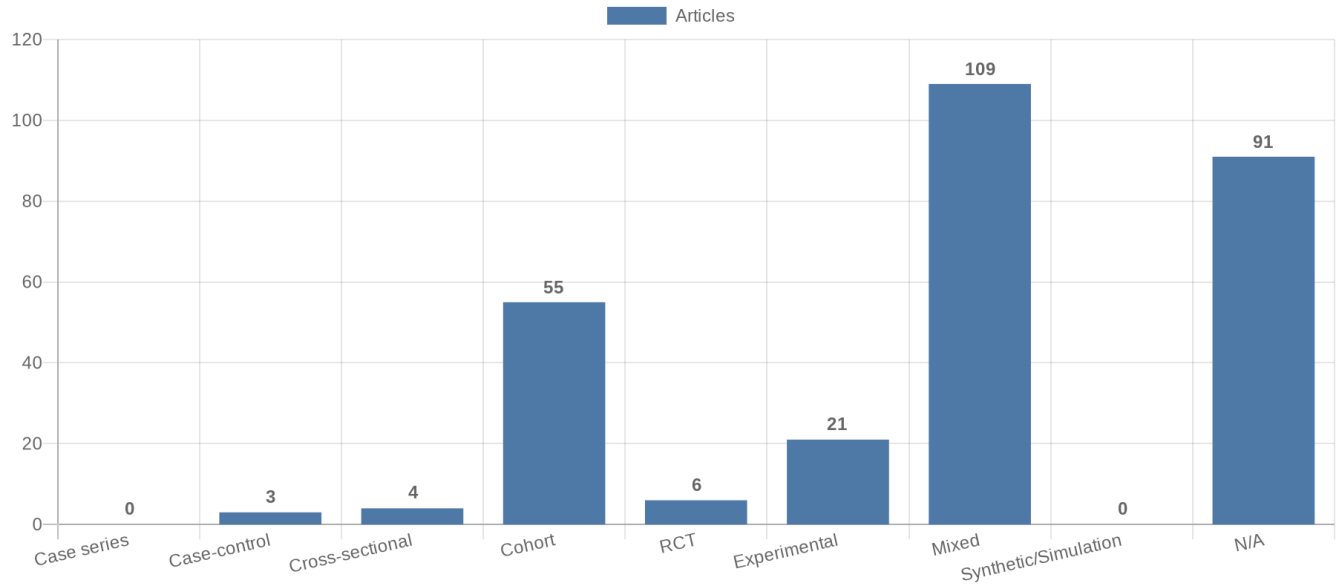


Figure 3. Study-type (directionality) distribution of included originals

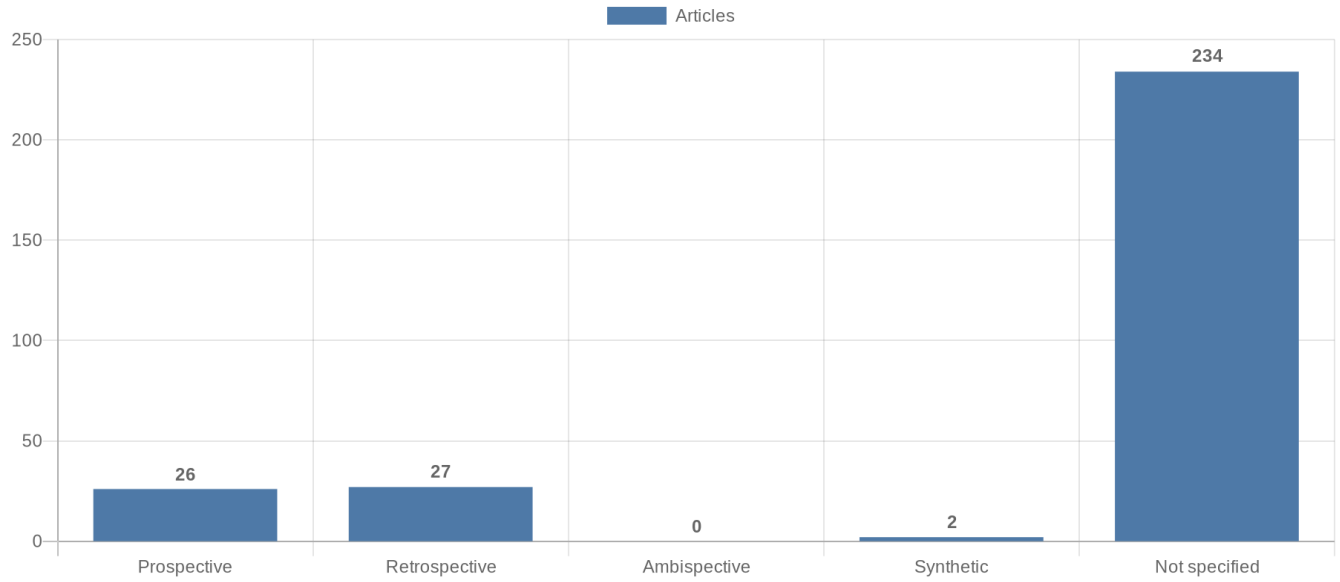


Figure 4. Main extracted research topics

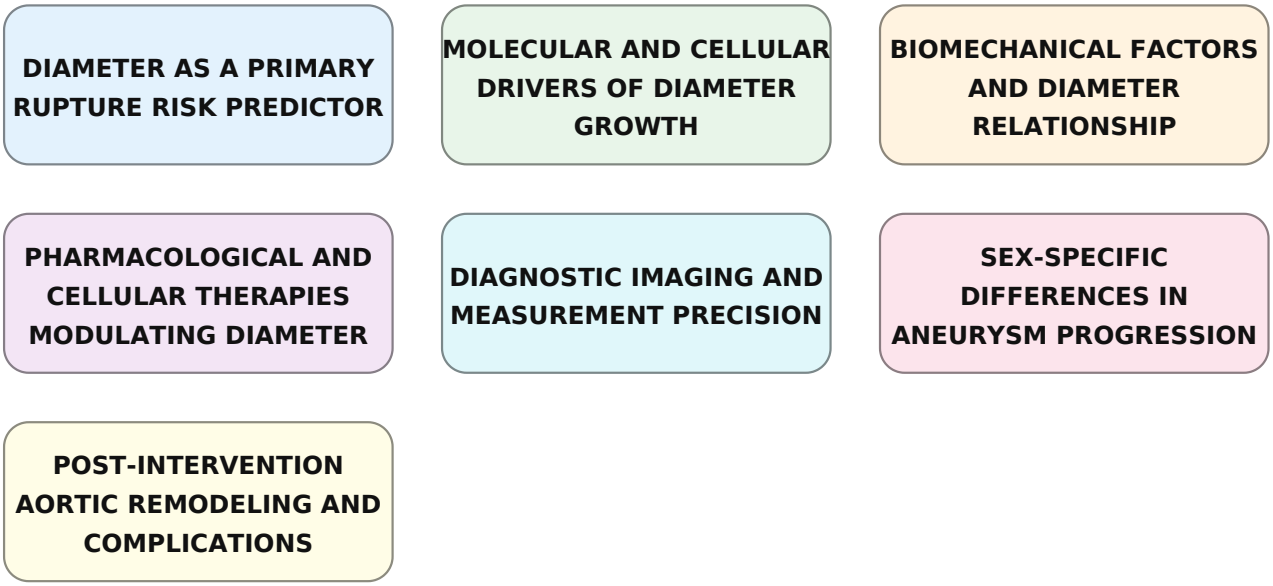


Figure 5. Limitations of current studies (topics)

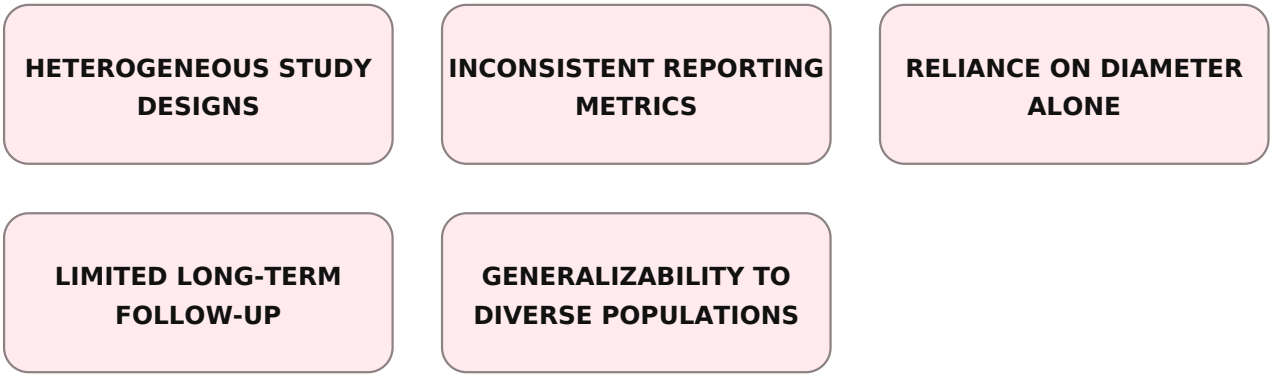


Figure 6. Future research directions (topics)