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Associations of antidiabetic medications with abdominal aortic aneurysm growth and clinical outcomes: A systematic review and meta-analysis

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ARTICLE HIGHLIGHTS

Type of Research: Systematic review and meta-analysis

Key Findings: Thirteen studies (15 cohorts; 150,630 participants) were included. Metformin (MD -0.65 mm/year; OR 0.63) and sulfonylureas (MD -0.35 mm/year; OR 0.63) were associated with slower abdominal aortic aneurysm growth and reduced aneurysm-related events. No statistically significant association was observed for DPP-4 inhibitors (MD -0.32 mm/year).

Take home Message: Metformin, sulfonylureas—but not DPP-4 inhibitors—were significantly associated with slower abdominal aortic aneurysm growth and favorable aneurysm-related outcomes.

Table of Contents Summary

This systematic review and meta-analysis of 13 studies (15 cohorts) found that metformin and sulfonylureas were associated with slower abdominal aortic aneurysm growth and a reduced risk of aneurysm-related events.

Abstract

Objective: This review aimed to evaluate the association between different antidiabetic agents, abdominal aortic aneurysm (AAA) growth, and related events.

Methods: Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PROSPERO CRD420251115799), MEDLINE, Embase, and CENTRAL were searched to January 2026. Eligible studies evaluated antidiabetic drugs compared with not using the medication of interest and reported AAA growth and/or AAA-related events. The risk of bias was assessed using ROBINS-I and RoB 2 for nonrandomized and randomized trials, respectively. Pooled estimates (mean difference [MD]; odds ratio [OR]; hazard ratio [HR]) were calculated using inverse variance random-effects models.

Results: Thirteen studies (15 distinct cohorts; 150,630 participants) were included. Metformin was associated with slower AAA growth (MD -0.65 mm/year, 95% confidence interval [CI] -0.97 to -0.33) and lower AAA-related events (OR 0.63, 95% CI 0.41 to 0.95). Moreover, sulfonylureas reduced AAA growth (MD -0.35 mm/year, 95% CI -0.52 to -0.18) and AAA-related events (OR 0.63, 95% CI 0.52 to 0.77). Findings for dipeptidyl peptidase-4 (DPP-4) inhibitors were not statistically significant in relation to AAA growth (MD -0.32 mm/year, 95% CI -0.71 to 0.08). Metformin was not significantly associated with postoperative mortality (HR 0.86, 95% CI 0.65 to 1.13). Most studies were observational, with a moderate risk of bias, which limited causal inference.

Conclusions: Metformin and sulfonylurea were associated with reduced AAA progression, though potential confounding necessitates cautious interpretation. Evidence for other glucose-

lowering therapies remains limited. Randomized trials are required to evaluate drug-specific associations and outcomes across stratified patient groups.

Keywords: Aortic aneurysm, Abdominal; Metformin; Sulfonylurea Compounds; Dipeptidyl-Peptidase IV Inhibitors; Disease Progression

1 Background

Abdominal aortic aneurysm (AAA), an irreversible dilation of the abdominal aorta ≥ 150% of normal, is a multifactorial disease influenced by genetic and environmental risk factors, including smoking, aging, family history, and male sex[1,2] These factors are associated with aortic wall degradation through inflammatory and oxidative pathways. Chronic inflammation, a hallmark of AAA pathogenesis, involves inflammatory cytokine induction, cell adhesion molecule expression, and inflammatory cell infiltration, leading to matrix degradation and vascular wall remodeling.[3,4] Oxidative stress further exacerbates these processes, contributing to phenotype switching of vascular smooth muscle cell (VSMC) and AAA progression.[5,6] Despite advances in understanding these mechanisms, aside from surgical interventions, no pharmacological treatments have demonstrated sufficient efficacy to treat patients with AAA.[5] Previous randomized controlled trials (RCTs) of multiple drug classes—beta-blockers, angiotensin-converting enzyme inhibitors, antibiotics, mast cell stabilizers, antiplatelet inhibitors, and fibrates—have not demonstrated significant influence on AAA growth or AAA-related events.[7,8]

Interestingly, despite the well-established pro-inflammatory effects of chronic low-grade inflammation, the incidence of AAA is reportedly lower in individuals with diabetes mellitus (DM).[9,10] Morris et al.[11] reported that a genetic predisposition to type 2 diabetes does not prevent AAA development. A meta-analysis found that the AAA growth-reducing association of metformin was more pronounced in individuals without diabetes than in those with diabetes[12], suggesting that additional factors may have contributed to this observation.

Several studies have suggested that this paradox may be attributable to antidiabetic medications, including metformin, thiazolidinediones, and dipeptidyl peptidase-4 (DPP-4)

inhibitors.[13-17] Among these, metformin has been the most extensively studied; however, the current evidence remains limited and inconclusive.[18] To clarify the associations of metformin on AAA, four RCTs are underway; nonetheless, their results are expected to require several more years to become available.[19,20] To our knowledge, evidence regarding antidiabetic medications other than metformin in relation to AAA is largely derived from *in vitro* or animal studies, while clinical research remains scarce and comprehensive studies are lacking.[21] Recent studies investigating the associations of metformin with AAA have emerged[22,23], highlighting the need to reevaluate this relationship. Hence, evaluating the associations of other antidiabetic agents alongside metformin could provide a more accurate assessment of their respective associations with AAA.

Thus, we aimed to clarify the associations between antidiabetic medications—including metformin, sulfonylureas, dipeptidyl peptidase-4 (DPP-4) inhibitors, and glucagon-like peptide-1 receptor (GLP-1R) agonists—and AAA growth and AAA-related clinical events through a systematic review and meta-analysis, thereby addressing existing evidence gaps and providing insights into their potential role in AAA management.

2 Methods

2.1 Literature Search

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guideline (Supplementary Table I, online only).[24] The protocol was registered in PROSPERO (CRD420251115799). Two reviewers (YP and HWL) independently performed the literature search, study selection, data extraction, and risk-of-bias assessment. Discrepancies were resolved through discussions between the two other investigators

(YMY and Y-MA). MEDLINE, Embase, and Cochrane CENTRAL databases were searched from inception to January 26, 2026, to evaluate the associations of antidiabetic medications with AAA growth rate or related clinical outcomes. Medical subject heading on each database was "aortic aneurysm," "aortic dissection," "aortic rupture," "biguanides," "sulfonylurea," "meglitinide," "glycoside hydrolase inhibitors," "thiazolidinediones," "glucagon-like peptide," "dipeptidyl-peptidase iv inhibitors," and "sodium-glucose transporter 2 inhibitors." No language restrictions were imposed.

2.2 Study selection

Eligible studies met the following criteria: (1) population, adults (≥18 years) with AAA; (2) intervention, treatment with non-insulin antidiabetic medications, including metformin, sulfonylureas, meglitinides, alpha-glucosidase inhibitors, thiazolidinediones, DPP-4 inhibitors, GLP-1R agonists, and sodium-glucose cotransporter 2 (SGLT2) inhibitors; (3) comparator, no use of the intervention medication, without restriction to a specific comparator group; (4) outcomes, annual AAA growth rate and AAA-related events such as rupture, repair, surgical complications, or postoperative mortality; and (5) study design, clinical longitudinal comparative studies (randomized and observational). The exclusion criteria included nonhuman studies, single-arm or case studies, ongoing studies, review articles, and conference abstracts.

2.3 Data extraction and quality assessment

A standardized extraction form was used to extract data from eligible studies on first authors, publication year, country, study design, study duration, follow-up period, imaging modality, sample size, age, sex, comorbidities (including DM, hypertension, dyslipidemia, cardiovascular, and kidney diseases), smoking status, exposure/comparator definitions, and outcome details. The

risk of bias was assessed using ROBINS-I version 2[25] for nonrandomized studies and RoB 2[26] for randomized trials using standard domains and reporting overall judgments.

2.4 Study outcomes

The primary outcome was the annual AAA growth rate associated with antidiabetic medication use, summarized as the mean difference (MD) with 95% confidence interval (CI). Growth was defined as the change in diameter divided by the interscan interval (mm/year), and the values reported over the other intervals were annualized. Secondary outcomes were AAA-related clinical events (rupture, repair, perioperative complications, and postoperative mortality), expressed as odds ratios (ORs) or hazard ratios (HRs).

2.5 Statistical analyses

Pooled estimates for MDs, ORs, and HRs with 95% CIs were calculated using the generic inverse-variance method.[27] HRs and ORs were analyzed separately, owing to different statistical models, namely time-to-event and binary outcomes, respectively.[28] When multiple effect estimates were reported, the most fully adjusted estimate was prioritized. Heterogeneity was assessed using the chi-square test ($P < .10$) and I^2 statistics, with $I^2 > 50\%$ considered indicative of substantial heterogeneity.[29,30] To account for inherent clinical and methodological heterogeneity, all pooled estimates were calculated using random-effects models. This approach was adopted regardless of I^2 values to ensure an appropriate synthesis across diverse study characteristics.[29]

Meta-analyses were performed separately for each outcome, according to the class of antidiabetic agents. For the meta-analysis of AAA growth rates, studies on metformin, sulfonylureas, and DPP-4 inhibitors were included. Moreover, for metformin, results restricted to patients with diabetes were examined. Given the sufficient number of studies on metformin,

subgroup and sensitivity analyses were performed. Subgroup analyses were stratified according to follow-up duration (> 3 years), imaging modality (computed tomography vs. ultrasonography), and geographic region (North America vs. Europe). Random-effects meta-regression was conducted to assess the influence of baseline characteristics—including study-level demographics, comorbidities, and concomitant medication use—on the association between metformin use and AAA growth rate, accounting for between-study heterogeneity. The Knapp–Hartung method was used to evaluate individual coefficients and their corresponding confidence intervals.[31] Sensitivity analyses included (1) exclusion of studies at serious or critical risk of bias, (2) leave-one-out analysis, and (3) sequential inclusion of studies by publication year or (4) by sample size. Publication bias was assessed using a funnel plot and Egger's regression test ($P < .05$).[32,33]

Studies on both metformin and sulfonylureas were included for AAA-related events. Where feasible, analyses were also performed for metformin in populations with diabetes only. Among the AAA-related events, postoperative mortality was analyzed separately to account for differences in analytic units and comparator groups (e.g., patients without diabetes). To further assess the impact of concomitant metformin use, a post hoc analysis compared patients with diabetes treated with or without metformin versus those without diabetes. All analyses were conducted using the meta package in R software (version 4.3.1).

3 Results

3.1 Study selection

The study selection process is displayed in Figure 1. Overall, 856 records were identified through electronic database searches. After removing 137 duplicates, 719 articles remained for title and abstract screening, of which 642 were excluded based on predefined eligibility criteria.

The remaining 77 articles underwent a full-text review, resulting in the inclusion of 15 studies in the qualitative synthesis.[15,34-47] Of these, 13 studies comprising 15 distinct cohorts with 150,630 participants were included in the quantitative meta-analysis. Two studies were excluded from the quantitative synthesis because of non-comparable outcomes or insufficient data for group-level comparisons.[40,47]

3.2 Study characteristics

Table I presents the characteristics of the 15 included studies[15,34-47], published between 2010 and 2025, including five prospective cohort studies[35-38,42], eight retrospective cohort studies[15,39-41,43-45,47], one case-control study[46], and one randomized controlled trial[34]. Nine studies[15,34-41] and seven studies[34,42-47] evaluated the AAA growth rate and AAA-related clinical events, respectively; one study[34] reported both outcomes.

The mean baseline age ranged from 67.0 to 75.0 years, reflecting predominantly older adult populations; moreover, the proportion of males ranged from 69.9% to 100.0%, and all studies reported a male majority. Golledge et al.[37] divided participants into three distinct cohorts based on enrolment period and institution. Detailed baseline characteristics of the study population are presented in Supplementary Table II (online only).

3.3 Association between antidiabetic medication use and AAA growth rate

A meta-analysis of AAA growth rates focused on metformin, sulfonylureas, and DPP-4 inhibitors. Eight studies[15,34-39,41] comprising 21,132 AAA patients in the overall cohorts (combined DM and non-DM) and four studies[15,36,37,41] involving 14,295 AAA patients in DM-only cohorts, demonstrated a significant association between metformin use and reduced AAA growth. The

pooled MDs were -0.65 mm/year (95% CI: -0.97 to -0.33) in the overall cohorts and -0.36 mm/year (95% CI: -0.53 to -0.19) in the DM-only cohorts (Figure 2A).

Sulfonylureas were associated with reduced AAA progression in the overall cohorts (MD -0.35 mm/year, 95% CI: -0.52 to -0.19; Figure 2B). A cohort study by Hornby-Foster et al.[40], which was excluded from the meta-analysis owing to insufficient data for group-level comparisons, reported a significantly lower AAA growth rate in patients prescribed gliclazide compared with non-users (1.0 vs. 2.6 mm/year; P = .004). Regarding DPP-4 inhibitors, AAA growth was not significantly reduced (MD -0.32 mm/year; 95% CI: -0.71 to 0.08; Figure 2C).

Subgroup analyses exhibited no significant variation in the association of metformin with AAA growth rate across follow-up duration, imaging modality, or geographic region (Figure 3). In meta-regression, a higher proportion of male participants was associated with attenuation of the metformin-related reduction in AAA growth (P = .021; I^2 = 77.6%), whereas a higher prevalence of coronary artery disease strengthened this association (P = .013; I^2 = 77.2%; Supplementary Figure 1, online only). Other baseline factors—including the study-level prevalence of DM (P = .75) and the use of concomitant antidiabetic or cardiovascular medications—did not significantly moderate this association.

3.4 Association between antidiabetic medication use and AAA-related events

Metformin and sulfonylureas were included in the analysis of AAA-related events, including AAA rupture-related mortality, aneurysm rupture repair, and surgical complications (Figure 4A). Metformin use was significantly associated with lower AAA-related events in both the overall cohorts (OR 0.63, 95% CI: 0.41–0.95) and DM-only cohorts (OR 0.55, 95% CI: 0.31–0.99).

Sulfonylurea use was similarly associated with a lower event in the overall cohorts (OR 0.63, 95% CI: 0.52–0.77).

A separate analysis assessed postoperative mortality among metformin users in the overall cohorts and found no statistically significant association (HR 0.86, 95% CI: 0.65–1.13; Figure 4B). In patients with DM, a post hoc analysis similarly revealed no statistically significant association with metformin use (HR 0.80, 95% CI: 0.55–1.16), whereas an association was observed for non-users compared with individuals without diabetes (HR 1.09, 95% CI: 1.02–1.17).

One recent study examined the association between GLP-1R agonists and AAA-related clinical outcomes. This was not pooled in the meta-analysis due to limited data but were narratively synthesized. The study[47] reported lower odds of all-cause mortality (OR 0.54, 95% CI 0.45–0.65) and undergoing AAA repair (OR 0.66, 95% CI 0.45–0.95) in patients with DM over a 5-year follow-up period. Similar associations were observed in the non-DM cohort for both all-cause mortality (OR 0.47, 95% CI 0.30–0.74) and undergoing AAA repair (OR 0.45, 95% CI 0.21–0.96).

3.5 Quality assessment

Among the 12 observational studies, one study[39] was rated as having a serious risk of bias due to inadequate control of confounding, patient selection issues, and missing data, and one[41] was rated at low risk except for residual confounding; the remaining 10 were judged to have a moderate risk (Supplementary Figure 2A, online only). Additionally, one RCT[34] was assessed using RoB 2, demonstrating an overall low risk of bias. Visual inspection of the funnel plot suggested asymmetry, and Egger's regression test indicated a marginally significant small-study effect (P = .05; Supplementary Figure 2B, online only), suggesting the potential presence of publication bias.

3.6 Sensitivity analysis

Sensitivity analyses of AAA growth rate with metformin use demonstrated that excluding studies with a serious risk of bias, applying leave-one-out analyses, sequential inclusion by publication year, or sample size did not materially alter the findings (Supplementary Figure 3, online only).

4 Discussion

This systematic review and meta-analysis evaluated the association between antidiabetic medication use and AAA progression, focusing on AAA growth rate and AAA-related events, by incorporating recent studies and evaluating associations across diverse antidiabetic drug classes, including metformin, sulfonylureas, and DPP-4 inhibitors. This approach provides a comprehensive comparative synthesis of various antidiabetic agents, thereby broadening the evidence beyond the predominantly metformin-focused literature.

This meta-analysis suggests an association between metformin use and slower AAA progression. These findings are in line with those of previous meta-analyses reporting similar associations (AAA growth rate: -0.86 mm/year, 95% CI: -1.21 to -0.52, AAA-related events: OR 0.54, 95% CI: 0.34 to 0.86, OR 0.61, 95% CI: 0.41 to 0.92).[12,14] The favorable association between metformin use and AAA progression persisted when analyses were limited to patients with DM, with no observed heterogeneity (I^2 = 0%). This suggests a robust link within this population, independent of between-study variations. However, in the overall cohort analysis, substantial heterogeneity was observed among studies evaluating the association between metformin use and AAA growth rate. Furthermore, subgroup and meta-regression analyses did not identify covariates that significantly explained this variability, including the study-level prevalence of diabetes. Collectively, these findings suggest that although the effect size varies across the overall cohorts,

the association of metformin with attenuated AAA growth is consistently observed regardless of the proportion of participants with diabetes across studies.

In clinical practice, metformin non-users with diabetes often receive alternative glucose-lowering therapies. This complicates attribution of the observed associations to a single drug, particularly given our findings on sulfonylureas and AAA growth. However, in the study-level meta-regression analysis, no clear modifying effect was identified for concomitant antidiabetic agents or other drugs known to be associated with AAA progression. Although these findings do not exclude residual confounding, the observed associations for metformin are unlikely to be fully explained by differential use of other medication alone. Regarding demographic factors, meta-regression indicated a trend toward attenuation of the association between metformin use and slower AAA growth as the proportion of male participants increased, likely reflecting baseline sex differences in aneurysm growth rather than true sex-specific responsiveness to metformin.[48] Additionally, given the small number of studies, these findings should be interpreted with caution and regarded as hypothesis-generating rather than confirmatory. Definitive evidence regarding the clinical role of metformin in slowing AAA progression is expected from the ongoing Limiting AAA with Metformin (LIMIT) trial[49], which will help clarify the causal relevance of these observed associations.

Given the clinical significance of AAA-related events, the association between metformin use and postoperative mortality was investigated. Relative to non-diabetic AAA patients, postoperative mortality was not significantly lower among diabetic patients receiving metformin. Nonetheless, a higher risk was observed in those not treated with metformin, suggesting a potential benefit of metformin use in diabetic AAA patients. These findings should be interpreted cautiously because of the limited number of studies, and postoperative mortality appears to be more strongly

influenced by diabetes itself and other clinical factors, such as comorbidities, patient age, and surgical characteristics, than by metformin use.[50-56] Previous preclinical studies have demonstrated the beneficial effects of metformin on AAA. In normoglycemic mouse models of elastase-induced AAA, metformin administration was associated with medial elastin preservation, reduced VSMC loss, and decreased inflammatory cell infiltration. These effects are thought to be mediated by AMP-activated protein kinase activation and subsequent inhibition of mTOR and NF-κB signalling pathways.[15,57,58]Sulfonylureas were associated with slower AAA growth, and a lower risk of AAA-related events are comparable to those of metformin. Because sulfonylureas are commonly prescribed for diabetes, and diabetes itself has been reported to have an association with slower AAA progression, the observed benefit in the overall cohorts may reflect group differences in diabetes prevalence.[41,59] Nonetheless, the included studies did not report baseline characteristics stratified by diabetes status, limiting the ability to directly assess this possibility. Additionally, few studies assessed sulfonylurea monotherapy, and most allowed concurrent metformin use, complicating assessment of sulfonylurea-specific associations with AAA outcomes. Therefore, sulfonylurea-specific associations cannot be reliably distinguished from potential additive or class effects. In a study by Hsu et al.[59] limited to patients with diabetes and adjusted for diabetes severity, sulfonylurea use was associated with a reduced AAA risk (adjusted OR 0.82, 95% CI: 0.74–0.92), with a dose-response relationship suggesting greater benefit at higher doses.[59] Thus, sulfonylureas may be associated with a lower risk of AAA outcomes even after accounting for diabetes, warranting further investigation.

Several plausible mechanistic explanations exist for the potential effects of sulfonylureas on AAA. Sulfonylureas reduce inflammation by lowering blood glucose and by directly inhibiting inflammatory responses via the MAPK/NF-κB and NLRP3 pathways.[60-64] Whereas anti-

inflammatory effects of sulfonylureas are well documented in diabetes-related vascular complications, these exact mechanisms may contribute to their potential role in AAA progression.[65]

Although preclinical studies have demonstrated that DPP-4 inhibitors significantly suppress AAA formation and progression independent of incretin signalling[66,67], no association was identified between DPP-4 inhibitor use and AAA growth rate in the present study. Given the limited number of included studies (n=3), these results must be interpreted with caution; further evaluation of DPP-4 inhibitors is warranted. Evidence on other glucose-lowering agents and AAA progression remains limited. However, recent observational studies have reported associations between thiazolidinediones[68], and SGLT2 inhibitors[69], and GLP-1R agonists[47,70] reduced AAA occurrence risk or slower disease progression. GLP-1R agonists have been associated with a lower AAA development risk even after adjusting for metformin use[47], raising the possibility of metformin-independent association. This association may be mediated by modulation of key processes in AAA pathophysiology, including attenuation of vascular inflammation, regulation of macrophage activity, suppression of MMP activity, and preservation of elastin structure within the aortic wall[71]. For SGLT2 inhibitors, proposed biological relevance is primarily attributed to systemic anti-inflammatory, antioxidant, and blood pressure-lowering properties.[72-76] Thiazolidinediones may attenuate aortic degeneration by activating PPAR-γ, thereby suppressing inflammation and matrix degradation in the aortic wall.[77,78] Nonetheless, across antidiabetic drug classes, experimental findings provide a biological context for observed clinical associations but remain insufficient to infer causality.

The present study reaffirms the association between metformin use and attenuated AAA progression, and its potential role in preventing AAA onset. Furthermore, a favorable association

between sulfonylureas and disease progression was observed. These findings may guide the selection of antidiabetic agents in at-risk patients. Nevertheless, further studies considering combination therapies and focusing on non-metformin agents are required to clarify their differential associations.

Despite the strengths of this meta-analysis, some limitations should be acknowledged. First, most included studies were observational and retrospective, limiting causal inference and increasing the risk of selection and information bias. Specifically, DM may act as both a confounder and an effect modifier. Although adjusted estimates were prioritized, and subgroup analyses restricted to DM-only cohorts and study-level meta-regression were performed, residual confounding cannot be excluded. Notably, for metformin, analyses restricted to patients with diabetes yielded consistent results for both AAA growth and AAA-related events, partially mitigating confounding by diabetes status. Conversely, for other antidiabetic drug classes, such diabetes-restricted evaluations are largely unfeasible because reporting is limited and heterogeneous. Additionally, no eligible studies reported effect estimates specific to non-diabetic populations, limiting assessment of applicability to patients without diabetes. However, the ongoing LIMIT trial is specifically evaluating the efficacy of metformin in patients without diabetes.[52] Findings from this trial will be critical for clarifying the causal role of metformin in this population, warranting a future re-evaluation of the evidence. Studies explicitly designed to compare treated and untreated patients within diabetic populations, with detailed characterization of concomitant medication use, are needed to clarify drug-specific associations independent of the underlying influence of diabetes. Second, substantial heterogeneity existed among the studies regarding patient populations, comorbidities, medication adherence, and study design, potentially introducing residual confounding. Sample size imbalances may have biased the results; for

example, the study by van Tongeren et al.[43] included 51 metformin users, limiting statistical power and potentially reducing the precision of the estimates. Third, despite the inclusion of study-level covariates, such as the proportion of male participants, in the meta-regression, substantial residual heterogeneity (> 77%) remained. This suggests that important sources of inter-study variability were not fully captured, which may have limited the interpretability and robustness of primary meta-analytic findings. Finally, although the present study highlights the associations between metformin and sulfonylureas, data on newer antidiabetic agents, including GLP-1R agonists, remain limited.

5 Conclusions

This systematic review and meta-analysis suggests that certain antidiabetic agents, particularly metformin, are associated with slower AAA progression. Sulfonylureas were also associated with slower AAA progression, whereas their independent contributions remain unclear because of potential confounding factors. Nonetheless, evidence regarding the associations of other antidiabetic agents, including DPP-4 inhibitors, on AAA progression remains limited. Further research, including well-designed randomized controlled trials, is warranted to clarify drug-specific associations, assess outcomes in stratified risk groups, and characterize mechanisms linking glucose-lowering therapies to AAA pathophysiology.

Declaration of conflict of interest

The authors declare that this study was conducted without any commercial or financial relationships that could be construed as potential conflicts of interest.

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Ethics statement

As this study synthesized data from previously published studies, institutional ethics approval was not required. Written informed consent was not required for this study in accordance with national legislation and institutional requirements.

Data availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

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CRediT authorship contribution statement

Yoonjung Park: Writing – original draft, Methodology, Investigation, Formal analysis, Data Curation, Conceptualization. **Soyoung Kang:** Writing – original draft, Methodology, Investigation, Formal analysis, Data Curation, Conceptualization. **Hyun Woo Lee:** Methodology, Investigation, Formal analysis, and Data curation. **Jaekyu Shin:** Writing – review and editing, Supervision,

Conceptualization. **Wonseok Seol:** Investigation, Formal analysis, and Data curation. **Jiseok Lee:** Investigation, Formal analysis, and Data curation. **Yun Mi Yu:** Writing – review and editing, Supervision, Methodology, Investigation, Conceptualization. **Young-Mi Ah:** Writing – review and editing, Supervision, Methodology, Investigation, Conceptualization.

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Association of antidiabetic medication uses with abdominal aortic aneurysm: A systematic review and meta-analysis

Supplemental materials

Supplementary Table I. Checklist for Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Supplementary Table II. Baseline characteristics of the study population.

Supplementary Figure 1. Meta-regression bubble plots of the association between metformin use and AAA growth rate, stratified by baseline demographics, comorbidities, and concomitant medication use. 1) Baseline demographics and comorbidities: (A) Male proportion, (B) mean age, (C) ever smoker, (D) diabetes mellitus, (E) hypertension, (F) coronary artery disease, and (G) dyslipidemia and 2) concomitant medication use: (A) Sulfonylureas, (B) DPP-4 inhibitors, (C) thiazolidinediones, (D) insulins, (E) renin-angiotensin system inhibitors, (F) beta blockers, and (G) antiplatelets. Each bubble represents an individual study, with the size proportional to the study's weight. *P*-values for each covariate are provided within the respective panels.

Supplementary Figure 2. Assessment of study quality and publication bias. (A) Risk of Bias in Non-randomized Studies – of Intervention (ROBINS-I) summary and (B) funnel plot with Egger's test for the association between metformin use and AAA growth rate.

Supplementary Figure 3. Sensitivity analyses of metformin and AAA growth rate. (A) Excluding studies at a serious risk of bias, (B) Leave-one-out method, (C) Sequential inclusion by publication year, and (D) Sequential inclusion by sample size.

Supplementary Table 1. Checklist for Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart of the study selection process

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3 – 4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5 – 6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7 – 8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7 – 8

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7 – 8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8 – 9
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7 – 8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9 – 10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10 – 12
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10 – 12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Supplementary Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11 – 13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13 – 18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17 – 18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

Supplementary Table II. Baseline characteristics of the study population.

Study, year (country)	Group	Sample size (n)	Men (%)	Age (years), mean (SD)	Initial AAA size (mm), mean (SD)	Ever smoker (%)	Comorbidities (%)*							DM medication use (%)					Other medication use (%)		
							DM	HTN	CAD	Dyslipidemia	CVD	CKD	PAD	MFM	SU	DPP-4i	TZD	Insulins	RAS	BB	Antiplatelets
Studies of AAA growth rate																					
Eilenberg, 2025 (Austria)	AAA without DM (MFM)	30	77.0	70.9 (9.7)	42.8 (6.4)	97.0	0.0	67.0	17.0	93.0	NA	NA	NA	100.0	NA	NA	NA	NA	NA	NA	83.0
	AAA without DM (placebo)	28	89.0	69.9 (7.8)	43.6 (6.1)	86.0	4.0	86.0	18.0	100.0	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	79.0
Gellatly, 2024 (UK)	AAA; men 65 years	3,670	100.0	69.5	37.3	86.7	16.7	55.7	29.8	77.0	8.0	NA	NA	10.6	2.9	2.2	NA	1.3	50.2	27.5	62.0
Unosson, 2021 (Sweden)	AAA without DM (no MTF)	428	94.9	69.1 (5.4)	38.2 (6.1)	83.2	0.0	66.7	33.0	65.0	13.3	5.2	NA	0	0	0	NA	0	49.9	41.4	57.0
	AAA with DM (no MTF)	33	90.9	70.1 (6.9)	37.5 (6.0)	93.8	100.0	90.9	45.5	87.9	16.1	21.9¶	NA	0	21.2	9.0	NA	30.3	66.7	66.7	72.7
	AAA with DM (MTF)	65	92.3	68.5 (5.4)	36.5 (5.9)	95.2	100.0	87.3	43.5	87.7	17.5	0¶	NA	100	26.2	15.4	NA	33.8	76.9	60.0	78.5
Golledge cohort 1, 2017 (Australia, New Zealand)	AAA; multicenter	1,357	90.0	73.9 (6.3)	36.9 (6.3)	66.5	16.0	64.8	44.6	48.5	NA	NA	NA	8.7	5.7	1.0	0.1	0.8	44.3	25.6	55.0
Golledge cohort 2, 2017 (Australia, New Zealand)	AAA; multicenter	287	81.9	72.6 (7.7)	40.9 (7.3)	89.9	24.0	68.6	49.8	68.3	NA	NA	NA	13.6	7.0	2.4	0.3	1.4	53.3	34.1	75.6
Golledge cohort 3, 2017 (Australia, New Zealand)	AAA; multicenter	53	84.9	73.0 (7.6)	43.3 (5.0)	92.5	35.8	43.4	41.5	66.0	NA	NA	NA	30.2	13.2	5.7	0	3.8	17.0	20.8	71.7
Thompson (2010)	AAA; screening program	1,237	94.1	67[a] (IQR 65-71)	35[a] (IQR 31–42)	32.8[h]	NA	NA	NA	NA	NA	NA	NA	3.8	3.4	NA	NA	0.6	30.8	29.7	36.9
Bobadilla-Rosado (2024)	AAA; tertiary care facility	72	72.2	75.0 (9.1)	43.0 (16.7)[b]	NA	31.9	NA	NA	58.3	NA	NA	NA	29.2	NA	NA	NA	NA	NA	NA	NA
Hornby-Foster (2023)	AAA; surveillance program	315	81.3	80.0 (9.1)[c]	42.0 (10.6)[c]	78.0	26.0	52.0	NA	72.0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Itoga (2019)	AAA with DM	13,834	99.4	69.8 (7.8)	38.0 (7.1)	28.5[d]	100.0	NA	16.7	68.4	17.4	14.9	NA	39.7	36.7	0.4	4.9	NA	72.6	64.6	NA
Fujimura (2016)	AAA with DM	58	82.7	72.0 (7.6)[e]	40.4 (9.1)[e]	67.2	100.0	84.5	62.1	50.0	17.2	29.3	48.3	25.9	22.4	3.4	3.4	22.4	69.0	55.2	NA
Studies of AAA-related events																					
Eilenberg (2025)	AAA without DM (MFM)	30	77.0	70.9 (9.7)	42.8 (6.4)	97	0.0	67	17	93	NA	NA	NA	100.0	NA	NA	NA	NA	NA	NA	83.0
	AAA without DM (placebo)	28	89.0	69.9 (7.8)	43.6 (6.1)	86	4	86	18	100	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	79.0
Golledge, 2019 (Australia)	AAA without DM	846	79.4	73.6 (8.0)	46.6 (11.5)	86.2	0	74.0	48.7	62.8	NA	NA	NA	0	NA	NA	NA	NA	58.0	35.2	72.9
	AAA with DM (no MFM)	105	88.6	74.2 (7.2)	45.3 (10.0)	84.7	100.0	76.2[¶]	54.3	70.5[¶]	NA	NA	NA	0	NA	NA	NA	NA	74.3	40.0	72.4
	AAA with DM (MFM)	129	89.9	72.4 (6.5)	43.4 (10.3)	91.4	100.0	89.1[¶]	49.6	89.9[¶]	NA	NA	NA	100	NA	NA	NA	NA	86.0	32.6	88.4
Ahn, 2025 (USA)	AAA with DM (GLP-1)	1,401	71.6	68.7 (8.7)	NA	11.3	100.0	89.5	NA	86.6	28.7	28.3	31.1	67.7	NA	NA	NA	NA	92.9	69.7	NA
	AAA with DM (no GLP-1)	1,401	69.9	68.8 (9.8)	NA	11.1	100.0	90.7	NA	86.8	28.6	29.1	33.6	68.1	NA	NA	NA	NA	93.0	69.5	NA
	AAA with no DM (GLP-1)	336	76.8	68.0(10 .2)	NA	3.0	0	71.4	NA	69.3	24.4	22.3	21.4	NA	NA	NA	NA	NA	85.1	65.5	NA
	AAA with no DM (no GLP-1)	336	78.0	68.4 (9.8)	NA	4.2	0	69.9	NA	67.3	21.7	19.6	20.2	NA	NA	NA	NA	NA	84.5	62.8	NA
van Tongeren (2024)	AAA post-EVAR (MFM)	51	92.2	71.1 (6.71)[b]	59.3 (11.4)[b]	84.3	100.0[¶]	80.4	47.1	82.4	NA	NA	29.4	100.0	NA	NA	NA	NA	NA	72.5	84.3
	AAA post-EVAR (no MFM)	634	88.3	73.0 (7.43)[b]	60.0 (9.7)[b]	73.2	7.3[¶]	67.8	35.0	60.1	NA	NA	18.8	0	NA	NA	NA	NA	NA	46.7	74.1
Turowicz (2021)	AAA post-repair without DM	229	NA	71.0 (8.3)	61.5 (18.2)	NA	0	65.1[¶§]	31.9	45.9	NA	NA	15.3	NA	NA	NA	NA	NA	NA	NA	47.6
	AAA post-repair with DM (MFM)	54	NA	69.6 (6.8)	60.8 (12.8)	NA	100.0	50.0[§]	29.6	44.4	NA	NA	20.4	100.0	NA	NA	NA	NA	NA	NA	37.0

	AAA post-repair with DM (other glucose-lowering drugs)	23	NA	74.3 (2.4)	61.8 (23.6)	NA	100.0	95.7¶	43.5	43.5	NA	NA	13.0	0	NA	NA	NA	NA	NA	NA	47.8
Sutton (2020)	AAA without DM	56,006	100.0	70.4 (8.0)	NA	26.8	0	79.9	NA	61.0	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA
	AAA with DM (MFM)	24,361	100.0	69.7 (7.2)	NA	26.9	19.7	82.2	NA	64.5	NA	NA	NA	100.0	NA	NA	NA	NA	NA	NA	NA
	AAA with DM (no MFM)	43,073	100.0	72.3 (7.9)	NA	22.8	34.9	78.7	NA	57.1	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA
Kristensen (2017)	Case	362	83.7	73.7 (8.2)	NA	NA	100.0	NA	46.1[f]	60.8	NA	9.9[g]	NA	49.2	51.1	NA	NA	13.5	63.3	NA	71.5
	Control	3,620	83.7	73.7 (8.2)	NA	NA	100.0	NA	33.5[f]	50.1	NA	6.8[g]	NA	53.3	62.5	NA	NA	27.9	56.5	NA	60.0

Abbreviations: AAA, abdominal aortic aneurysm; AGI, alpha-glucosidase inhibitors; BB, beta blockers; CAD, coronary artery disease; CKD, chronic kidney disease; CT, computed tomography; CVD, cerebrovascular disease; DM, diabetes mellitus; DPP-4i, dipeptidyl peptidase-4 inhibitors; EVAR, endovascular aneurysm repair; HTN, hypertension; IQR, interquartile range; MFM, metformin; NA, not available; PAD, peripheral artery disease; RAS, renin-angiotensin system inhibitors; SD, standard deviation; SU, sulfonylureas; SGLT-2i, sodium-glucose transporter 2 inhibitors; TZD, thiazolidinediones; VD, vascular disease.

[a] Mean (IQR)

[b] Mean (SD), calculated from median (IQR).

[c] SD calculated from 95% CI.

[d] Smoking status included active smokers; 60% missing data.

[e] SD calculated from standard error.

[f] Defined as myocardial infarction, congestive heart failure, peripheral arterial disease, or cerebrovascular disease.

[g] Defined as moderate to severe renal disease.

[h] Current smoker.

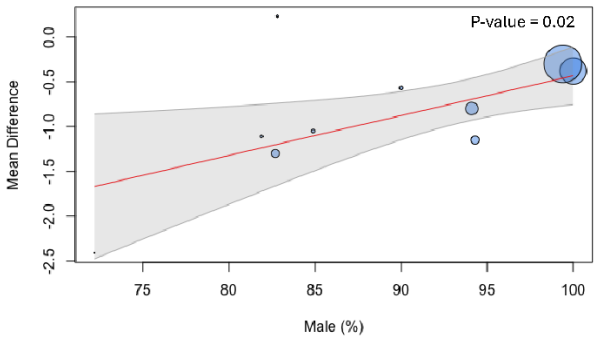
[*] Based on total population

[¶] p <.05 between groups

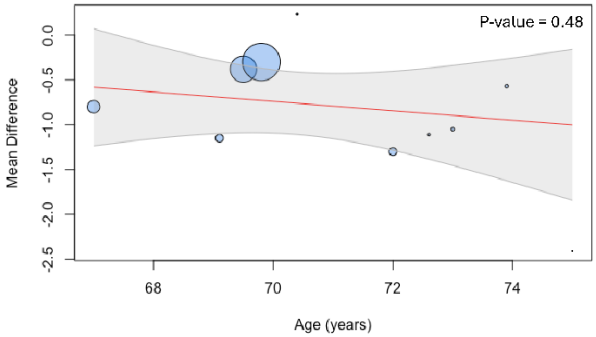
[§] p <.05 between AAA repair without DM vs. with DM + MFM

1. Baseline demographics and comorbidities

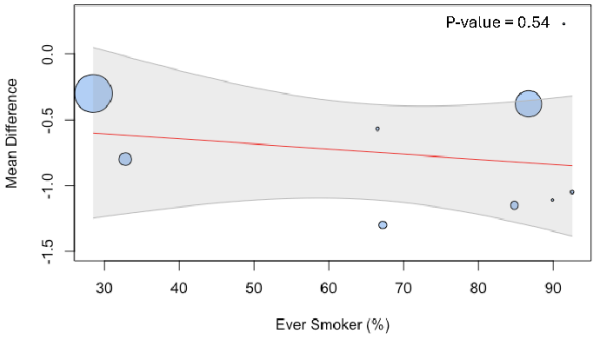
A. Male proportion



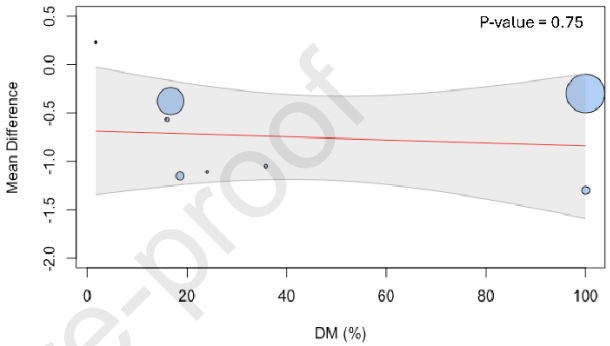
B. Mean age



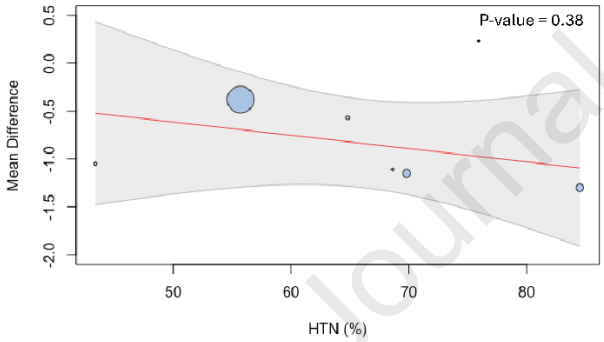
C. Ever smoker



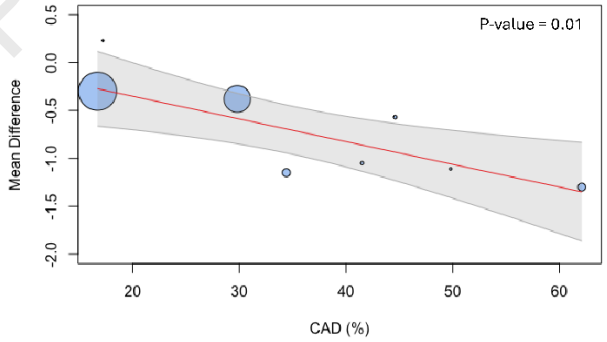
D. Diabetes mellitus



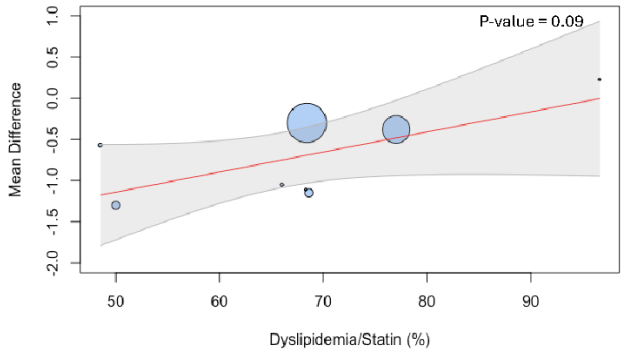
E. Hypertension



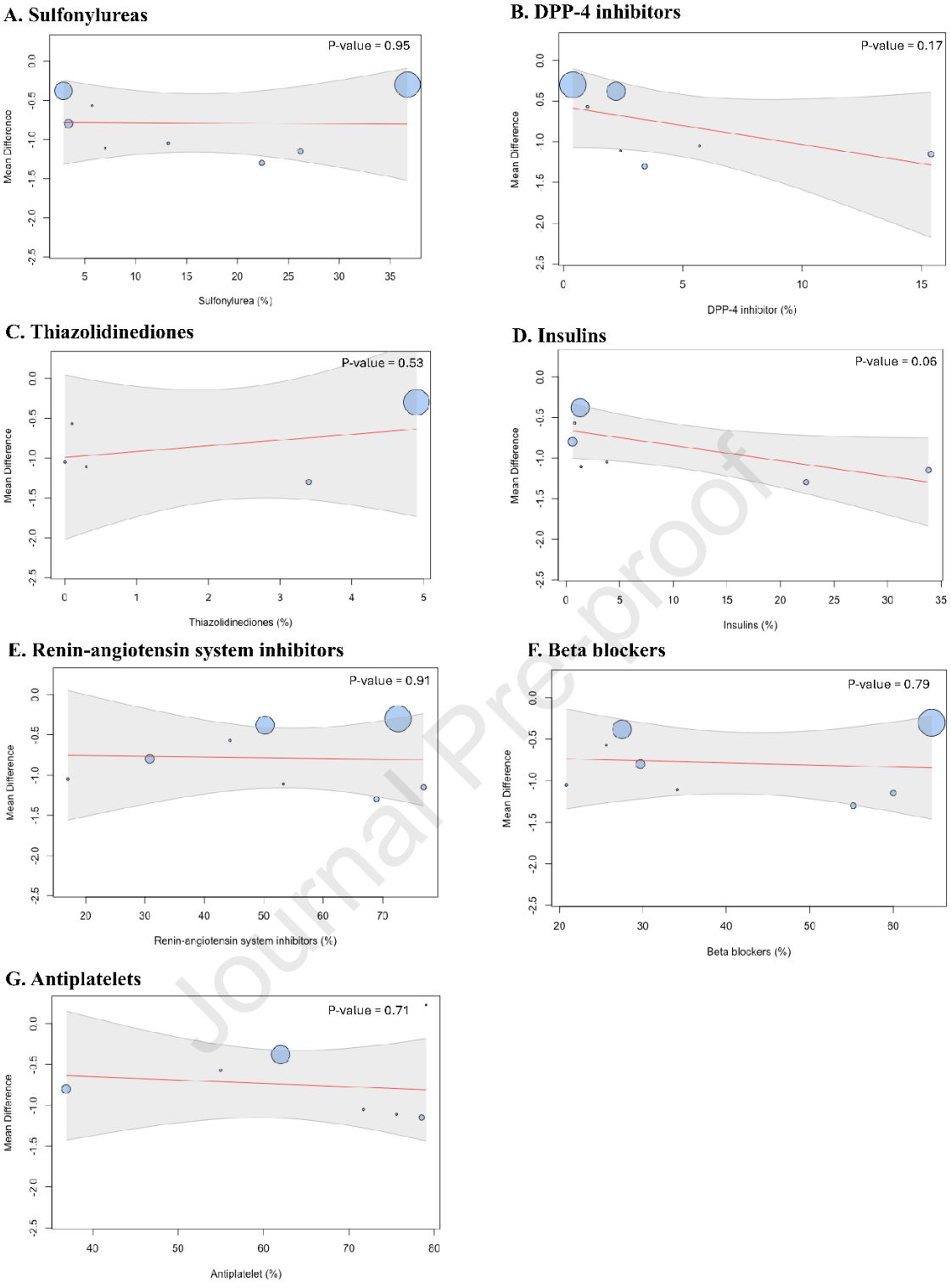
F. Coronary artery disease



G. Dyslipidemia



2. Concomitant medication use



Supplementary Figure 1. Meta-regression bubble plots of the association between metformin use and AAA growth rate, stratified by baseline demographics, comorbidities, and concomitant medication use. 1) Baseline demographics and comorbidities: (A) Male proportion, (B) mean age, (C) ever smoker, (D) diabetes mellitus, (E) hypertension, (F) coronary artery disease, and (G) dyslipidemia and 2) concomitant medication use: (A) Sulfonylureas, (B) DPP-4 inhibitors, (C) thiazolidinediones, (D) insulins, (E) renin-angiotensin system inhibitors, (F) beta blockers, and (G) antiplatelets. Each bubble represents an individual study, with the size proportional to the study's weight. *P*-values for each covariate are provided within the respective panels.

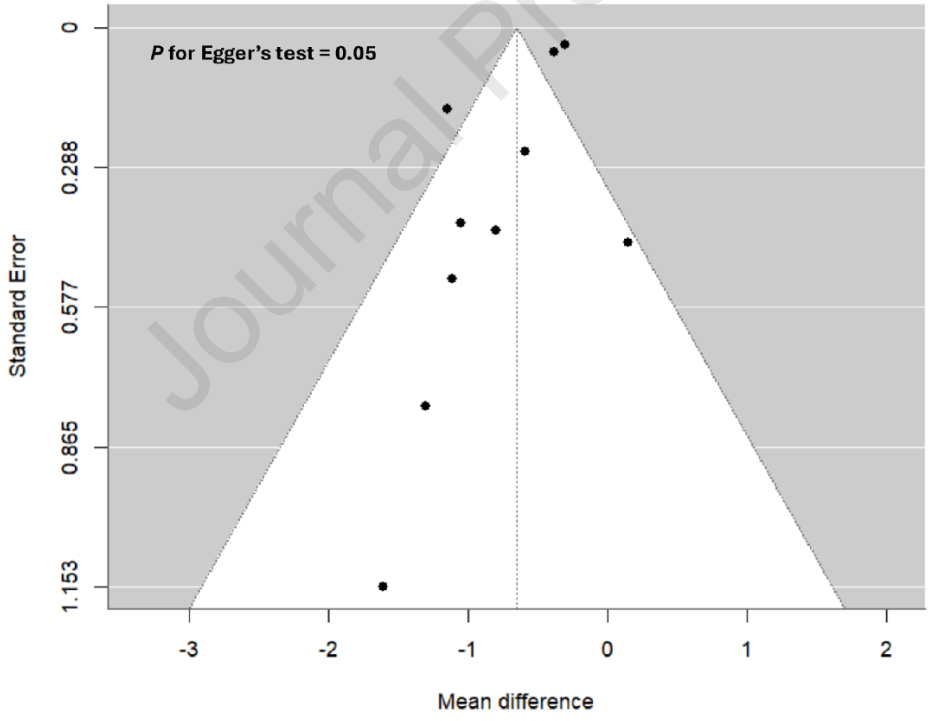
A. ROBINS-I version 2

	D1	D2	D3	D4	D5	D6	D7	Overall
Gellatly (2024)	−	+	I	+	+	+	+	I
Unosson (2021)	−	+	I	+	+	+	+	I
Golledge (2017)	−	+	I	+	+	+	+	I
Thompson (2010)	−	+	I	+	+	+	+	I
Bobadilla-Rosado (2024)	I	+	I	+	I	+	+	−
Itoga (2019)	−	+	+	+	+	+	+	−
Fujimura (2016)	−	+	I	+	+	+	+	I
Golledge (2019)	−	+	I	+	+	+	+	I
van Tongeren (2024)	−	+	I	+	+	+	+	I
Turowicz (2021)	−	+	I	+	+	+	+	I
Sutton (2020)	−	+	I	+	+	+	+	I
Kristensen (2017)	−	+	I	+	+	+	+	I

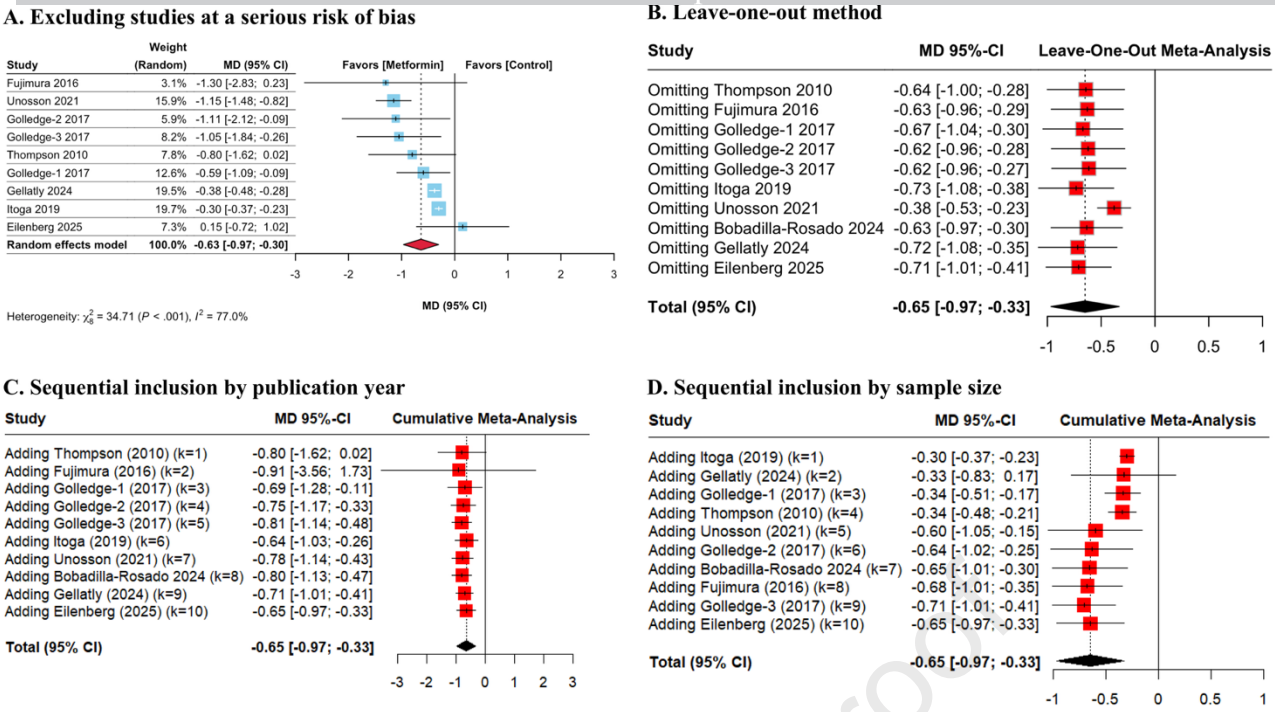
[Domains]
D1: Bias due to confounding
D2: Bias in classification of interventions
D3: Bias in selection of participants into the study or into the analysis
D4: Bias due to deviations from intended interventions
D5: Bias due to missing data
D6: Bias arising from measurement of the outcome
D7: Bias in selection of the reported result

[Judgement]
+ Low risk
− Low risk of bias except for concerns about uncontrolled confounding
I Moderate risk
− Serious risk

B. Funnel plot of Egger's test



Supplementary Figure 2. Assessment of study quality and publication bias. (A) Risk of Bias in Non-randomized Studies – of Intervention (ROBINS-I) summary and (B) funnel plot with Egger's test for the association between metformin use and AAA growth rate.



Supplementary Figure 3. Sensitivity analyses of metformin and AAA growth rate. (A) Excluding studies at a serious risk of bias, (B) leave-one-out method, (C) sequential inclusion by publication year, and (D) sequential inclusion by sample size.

Table 1. Characteristics of included studies.

Study, year (country)	Study design (enrollment period)	Cohort/group definition (AAA detection method)	Number of patients[a]	Follow-up duration (years), mean (SD)	Outcomes according to antidiabetic drug use[*]
Studies of AAA growth rate					
Eilenberg, 2025 (Austria)	RCT (NA)	AAA without DM; metformin vs. placebo (CT)	45	Up to 1.5	no DM-MFM: 1.95 (1.66)[b, c] no DM-placebo: 1.80 (1.29)[b, c]
Gellatly, 2024 (UK)	Prospective cohort (2011–2019)	Screen-detected AAA; men 65 years (U)	3,663	NA	MFM: -0.38 (SE: 0.10) [†] DPP4i: -0.321 (SE: 0.10) [†] SU: -0.341 (SE: 0.18) [†]
Unosson, 2021 (Sweden)	Prospective cohort (200–2017)	Screen-detected AAA; multicenter (U)	526	3.2 (1.7)	DM-MFM: 1.1 (1.1) DM-no MFM: 1.6 (1.4) no DM-no MFM: 2.3 (2.2)
Golledge cohort 1, 2017 (Australia, New Zealand)	Prospective cohort (2002–2015)	Screen-detected AAA; multicenter (U)	1,357	3.6 (2.4)	DM-MFM: 1.03 (2.68) DM-no MFM: 1.60 (2.94) no DM-no MFM: 1.62 (2.45) DM-SU: 1.13 (3.05) DM-no SU: 1.58 (2.49) DM-DPP4i: 1.47 (1.59) DM-no DPP4i: 1.56 (2.53)
Golledge cohort 2, 2017 (Australia, New Zealand)	Prospective cohort (2002–2015)	Screen-detected AAA; multicenter (CT)	287	2.9 (2.6)	DM-MFM: 1.40 (2.99) no DM-no MFM: 2.55 (3.04) DM-no MFM: 2.18 (2.96) DM-SU: 2.25 (3.00) DM-no SU: 2.37 (3.05)
Golledge cohort 3, 2017 (Australia, New Zealand)	Prospective cohort (2009–2015)	Screen-detected AAA; multicenter (CT)	53	1	DM-MFM: 0.37 (1.28) DM-no MFM: 0.95 (1.18) no DM-no MFM: 1.46 (1.52)
Thompson, 2010 (UK)	Prospective cohort (1984–2007)	Screen-detected AAA (U)	1,237	3.4 (2.0–6.4)[e]	DM-MFM: 0.75 (2.74)[d] no MFM: 1.55 (4.48)[d] DM-SU: 0.70 (2.66)[d] no SU: 1.59 (4.49)[d]
Bobadilla-Rosado, 2024 (Mexico)	Retrospecti ve cohort (2014-2021)	AAA, stratified by DM medication (CT)	72	1.5	Pre and post follow-up MFM: 36.12 (7.04), 37.00 (4.51) no MFM: 42.05 (12.54), 45.34 (12.06)

					DM-gliclazide: 1.0 (0.4–1.6)[b,f] DM-MFM: 2.0 (0.8–3.3)[b,f] no gliclazide: 2.6[b] DM: 1.9 (1.4–2.3)[b,f] no DM: 2.9 (2.4–3.2)[b,f]
Hornby-Foster, 2023 (UK)	Retrospective cohort (2015–2020)	AAA in surveillance program (U)	434	NA	
Itoga, 2019 (USA)	Retrospective cohort (200–2013)	AAA with DM (CT/MRI/U)	13,834	4.2 (2.6)	DM-MFM: 1.2 (1.9) DM-no MFM: 1.5 (2.2)
Fujimura, 2016 (USA)	Retrospective cohort (NA)	AAA with DM (CT)	58	2.6 (2.3) [d]	DM-MFM: 0.40 (2.32)[d] DM-no MFM: 1.70 (3.28)[d] DM-SU: 1.30 (1.80)[d] DM-no SU: 1.4 (3.35)[d] DM-DPP4i: -1.0 (2.40)[d] DM-no DPP4i: 1.40 (2.99)[d]
Studies of AAA-related events					
Eilenberg, 2025 (Austria)	RCT (NA)	AAA without DM; metformin vs. placebo (CT)	50	1	AAA surgery incidence OR (95% CI)[i], ref = placebo MFM: 0.88 (0.23–3.36)[g]
Golledge, 2019 (Australia)	Prospective cohort (2002–2017)	AAA; multicenter (CT, U)	1,080	2.5 (3.1)	AAA repair or rupture-related mortality aHR (95% CI), ref = no-DM DM-MFM: 0.63 (0.44–0.93) DM-no MFM: 1.15 (0.83–1.59) OR (95% CI)[§] DM-MFM: 0.41 (0.27–0.63), ref = no MFM DM-MFM: 0.46 (0.26–0.80), ref = DM-no MFM DM-SU: 0.66 (0.40–1.09), ref = not specified
Ahn, 2025 (USA)	Retrospective cohort study (2015–2020)	AAA with DM and no-DM (NA)	3,474	5	Outcomes: all-cause mortality, AAA repair, and AAA syndrome All-cause mortality, OR (95% CI), ref: DM-no GLP-1 DM-GLP-1: 0.54 (0.45 – 0.65) AAA repair, OR (95% CI), ref: DM-no GLP-1

					DM-GLP-1: 0.66 (0.45 – 0.95) AAA syndrome, OR (95% CI), ref: DM-no GLP-1 DM-GLP-1: 0.98 (0.60 – 1.60) All-cause mortality, OR (95% CI), ref: no DM-no GLP-1 noDM-GLP-1: 0.47 (0.30 – 0.74) AAA repair, OR (95% CI), ref: no DM-no GLP-1 DM-GLP-1: 0.45 (0.21 – 0.96)
van Tongeren, 2024 (Netherlands)	Retrospective cohort (2000–2022)	AAA; post-EVAR (CT)	685	MFM: 4.0 (3.8)[h] no MFM: 5.0 (4.5)[h]	All-cause mortality aHR (95% CI), ref = no MFM MFM: 1.11 (0.66–1.88)
Turowicz, 2021 (Poland)	Retrospective cohort (NA)	AAA; post-repair (CT)	306	NA	Repair-related mortality and complications OR (95% CI) DM-MFM: 0.68 (0.34–1.34), ref = DM-no MFM and no DM DM-MFM: 0.29 (0.10–0.81), ref = DM-no MFM
Sutton, 2020 (USA)	Retrospective cohort (2000–2019)	AAA; men ≥55 years (NA)	123,440	NA	AAA surgery incidence aHR (95% CI), ref = no DM DM-MFM: 0.77 (0.73–0.81) DM-no MFM: 0.74 (0.71–0.78) All-cause mortality aHR (95% CI), ref = no DM DM-MFM: 0.88 (0.86–0.90) DM-no MFM: 1.02 (1.00–1.05) Surgery-related mortality aHR (95% CI), ref = no DM DM-MFM: 0.93 (0.86–1.02) DM-no MFM: 1.09 (1.01–1.17)

					RAAA incidence OR (95% CI), ref = DM-no MFM DM-MFM: 0.74 (0.54-1.00) aOR (95% CI), ref = DM-no MFM DM-MFM: 0.84 (0.61-1.17)
Kristensen, 2017 (Denmark)	Case-control (1998–2013)	RAAA with DM (NA)	3,982	NA	OR (95% CI)[i], ref = no SU DM-SU: 0.63 (0.51–0.78)

Abbreviations: AAA, abdominal aortic aneurysm; aHR, adjusted hazard ratio; CI, confidence interval; CT, computed tomography; DM, diabetes mellitus; DPP-4i, dipeptidyl peptidase-4 inhibitors; EVAR, endovascular aneurysm repair; IQR, interquartile range; MFM, metformin; MRI, magnetic resonance imaging; NA, not available; OR, odds ratio; RAAA, ruptured abdominal aortic aneurysms; RCT, randomized controlled trial; SD, standard deviation; SE, standard error; SGLT-2i, sodium-glucose cotransporter 2 inhibitors; SU, sulfonylurea; TZD, thiazolidinedione; TTE, transthoracic echocardiography; U, ultrasonography; UK, United Kingdom.

[a] Based on the number of subjects included in analyses of antidiabetic agents.

[b] Units converted to mm/year.

[c] Total population at 18 months used.

[d] SE is converted to SD.

[e] Result reported in mean (interquartile range).

[f] Result reported in mean (95% CI).

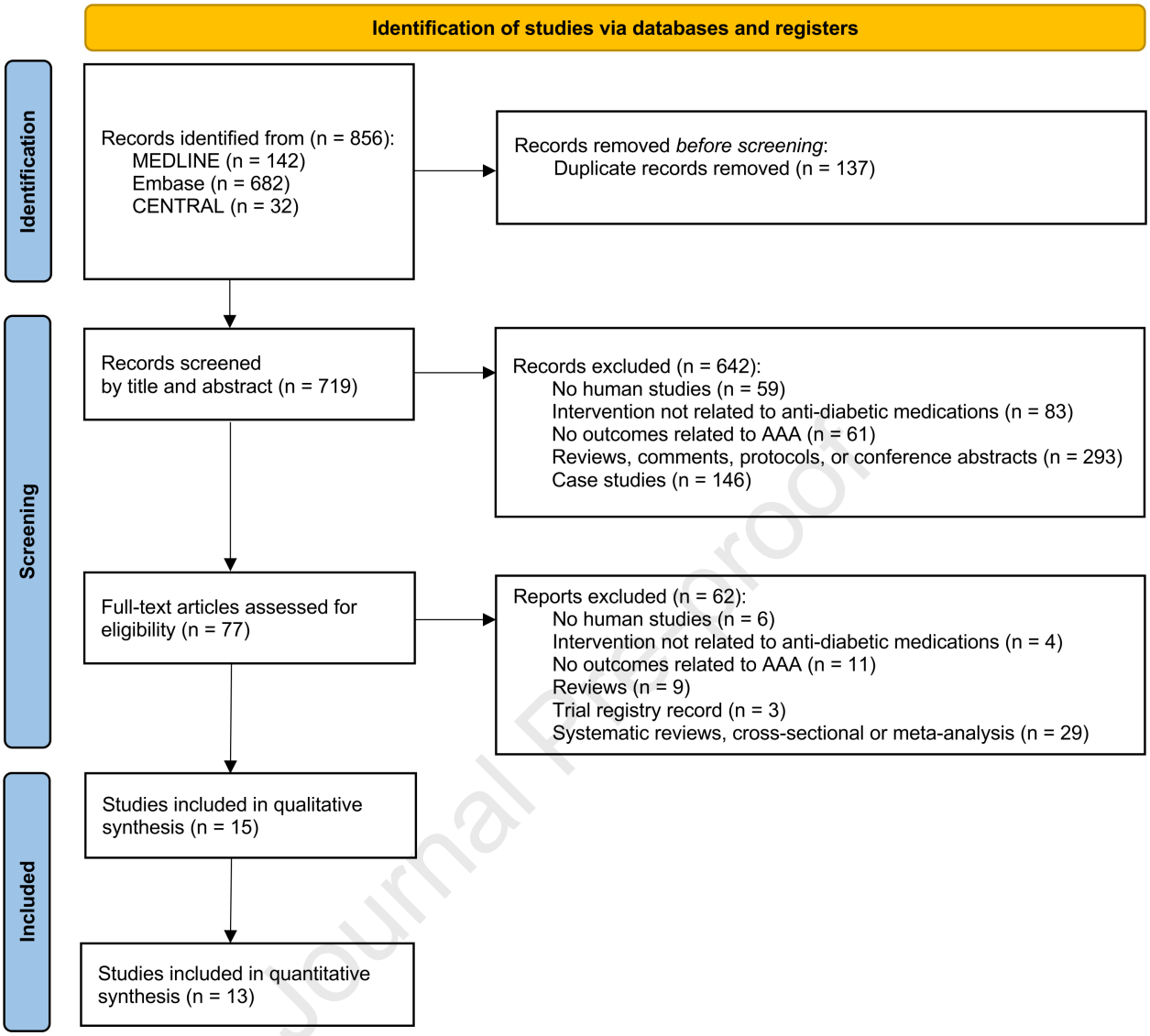
[g] Total population at 12 months used.

[h] Median (IQR) is converted to mean (SD).

[i] OR calculated by authors from reported data, not directly provided in the original study.

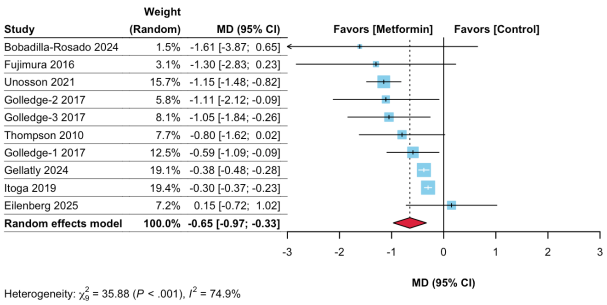
[*] For studies of AAA growth rate, outcomes are expressed as the annual AAA growth rate (mm/year), mean (SD).

[†] Analyses of AAA growth rate using a multivariable model.



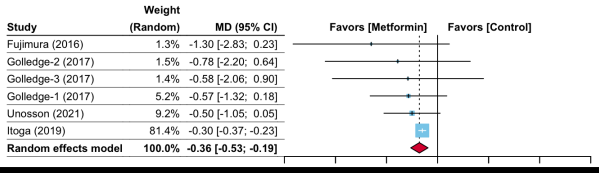
A. Metformin

a) Overall

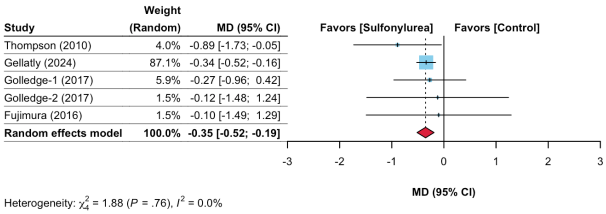


Heterogeneity: $\chi^2_9 = 35.88$ ($P < .001$), $I^2 = 74.9\%$

b) DM-only cohorts

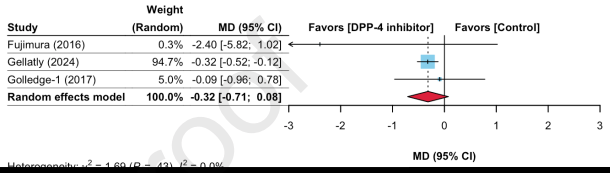


B. Sulfonylureas – overall



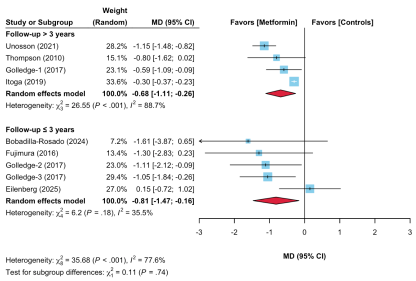
Heterogeneity: $\chi^2_4 = 1.88$ ($P = .76$), $I^2 = 0.0\%$

C. DPP-4 inhibitors - overall

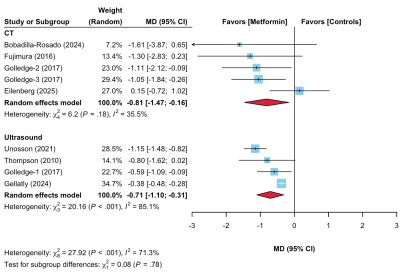


Heterogeneity: $\chi^2_2 = 1.69$ ($P = .43$), $I^2 = 0.0\%$

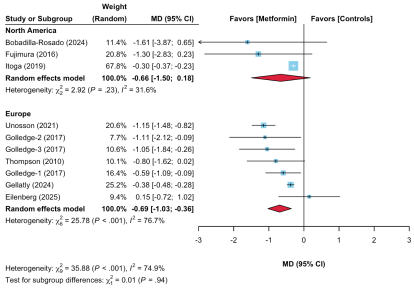
A. Follow-up duration



B. Imaging modality

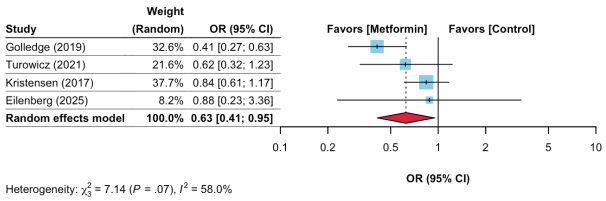


C. Geographic region



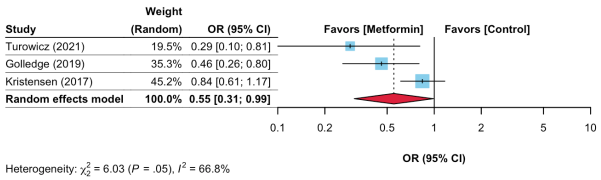
A. AAA-related events

a) Metformin – overall



Heterogeneity: $\chi^2_3 = 7.14$ ($P = .07$), $I^2 = 58.0\%$

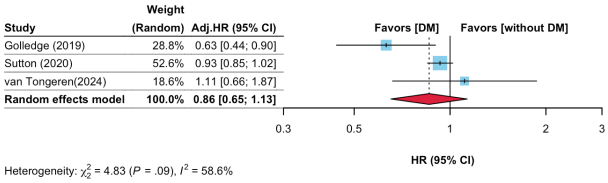
b) Metformin – DM-only cohort



Heterogeneity: $\chi^2_2 = 6.03$ ($P = .05$), $I^2 = 66.8\%$

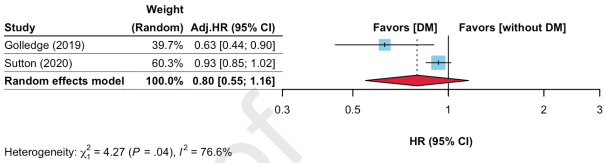
B. Postoperative mortality

a) Metformin – overall



Heterogeneity: $\chi^2_2 = 4.83$ ($P = .09$), $I^2 = 58.6\%$

b) Diabetes with metformin



Heterogeneity: $\chi^2_1 = 4.27$ ($P = .04$), $I^2 = 76.6\%$

[redacted]

Legends for Figures

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram of included studies evaluating the association between antidiabetic medication use and abdominal aortic aneurysm (AAA) growth or AAA-related events.

Figure 2. Forest plots of mean differences in abdominal aortic aneurysm growth rate associated with antidiabetdic medications. (A) Metformin, (B) sulfonylureas, and (C) dipeptidyl peptidase-4 (DPP-4) inhibitors. In this figure, "overall" indicates the combined diabetes medllitus (DM) and non-DM cohorts.

Figure 3. Subgroup analysis of metformin stratified by (A) follow-up duration (> 3 years), (B) imaging modality (CT vs. ultrasound), and (C) geographic region (North America and Europe). The study by Golledge et al. (2017), conducted in Australia and New Zealand, was grouped with European studies due to limited regional data.

Figure 4. Forest plot of abdominal aortic aneurysm (AAA)-related outcomes associated with antidiabetic medication use. (A) AAA-related events and (B) postoperatvie mortality. In this figure, "overall" indicates the combined diabetes mellitus (DM) and non-DM cohorts.