

ORIGINAL RESEARCH

VALVULAR HEART DISEASE

Sex-Specific and Time-Dependent Outcomes After TAVR Versus SAVR



A Meta-Analysis of Randomized Trials

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ABSTRACT

BACKGROUND Sex differences in outcomes after transcatheter aortic valve replacement (TAVR) vs surgical aortic valve replacement (SAVR) have been reported, but their variation over time and across surgical risk strata remains uncertain.

OBJECTIVES The objective of the study was to evaluate sex-specific and time-dependent outcomes of TAVR vs SAVR and the influence of baseline surgical risk.

METHODS PubMed, Embase, and Cochrane Central Register of Controlled Trials were searched through January 18, 2026. Randomized controlled trials reporting sex-stratified, mortality-inclusive primary endpoints with ≥ 1 -year follow-up were included. Pooled risk ratios (RRs) were estimated using random-effects models, with prespecified analyses by sex and surgical risk and exploratory meta-regression.

RESULTS Nine trials (N = 9,583; 44.2% women) were included. In women, TAVR was associated with lower risk at 1 and 2 years vs SAVR (1 year: RR: 0.67; 95% CI: 0.55-0.81; 2 years: RR: 0.80; 95% CI: 0.69-0.94), with no significant difference at 5 years (RR: 1.03; 95% CI: 0.89-1.18). In men, no significant differences were observed across time points. By surgical risk, early benefit with TAVR in women was more evident in intermediate-high-risk patients, whereas at 5 years a higher risk with TAVR was observed in men; no clear sex differences were seen in low-risk patients. Meta-regression showed no significant effect modification by age, surgical risk, or atrial fibrillation prevalence.

CONCLUSIONS Outcomes after aortic valve replacement vary by sex, surgical risk, and time. TAVR was associated with early benefit in women, particularly in intermediate-high-risk patients, with convergence over longer follow-up, whereas men showed no significant differences across time points, with higher risk observed with TAVR at 5 years in intermediate-high-risk patients. (Sex Differences in Outcomes of Transcatheter Versus Surgical Aortic Valve Replacement: An Updated Meta-Analysis of Randomized Controlled Trials; [CRD420261287967](https://doi.org/10.1016/j.jacadv.2026.102856)) (JACC Adv. 2026;5:102856) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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**ABBREVIATIONS
AND ACRONYMS****AF** = atrial fibrillation**AS** = aortic stenosis**RCT** = randomized controlled trial**SAVR** = surgical aortic valve replacement**STS-PROM** = Society of Thoracic Surgeons Predicted Risk of Mortality**TAVR** = transcatheter aortic valve replacement**RR** = risk ratio

Calcific aortic stenosis (AS) is a leading cause of valvular heart disease worldwide, associated with substantial morbidity, mortality, and impaired quality of life.¹ Transcatheter aortic valve replacement (TAVR) is now an established alternative to surgical aortic valve replacement (SAVR) across the full spectrum of surgical risk. However, clinically meaningful sex-based differences in the presentation, management, and outcomes of AS persist.^{2,3}

Women and men with severe AS differ in clinical and pathophysiological profiles that may influence outcomes after valve replacement. Women are typically older at diagnosis, present with more advanced symptoms, and are less likely to undergo timely intervention.^{4,5} They also exhibit smaller aortic annuli, more concentric left ventricular remodeling and fibrosis, and a higher prevalence of heart failure with preserved ejection fraction.⁶⁻⁸ Subgroup analyses from the DEDICATE and PARTNER 3 trials suggest more favorable early outcomes with TAVR in women, whereas benefits in men appear attenuated.^{9,10} Prior meta-analyses support this signal,¹¹⁻¹³ but uncertainties remain regarding its durability beyond 1 year, its evolution over longer follow-up, and the modifying role of baseline surgical risk.

As TAVR expands to younger and lower-risk populations, clarifying sex-specific and time-dependent outcomes is critical for individualized valve selection. We therefore performed a meta-analysis of randomized controlled trials (RCTs) with extended follow-up comparing TAVR and SAVR reporting sex-stratified outcomes. Our aim was to evaluate differences in clinical endpoints over time and across surgical risk groups.

METHODS

STUDY DESIGN AND REGISTRATION. This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁴ The study protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; [CRD420261287967](https://doi.org/10.1186/CRD420261287967)). A completed PRISMA checklist is provided in the [Supplemental Table 1](#).

ELIGIBILITY CRITERIA. We included RCTs that enrolled adult patients (age ≥18 years) with severe AS and directly compared clinical outcomes between TAVR and SAVR. Inclusion was contingent on the study reporting sex-stratified outcomes with a

minimum follow-up duration of 12 months. No restrictions were applied based on publication date, language, or surgical risk category (eg, high, intermediate, low). We excluded nonrandomized studies, trials without a SAVR comparator arm, trials that did not report outcomes by sex subgroup, and those reporting only in-hospital or 30-day outcomes. Conference abstracts, proceedings, and other non-peer-reviewed materials were excluded because they provided insufficient data and their methodological quality could not be reliably assessed.

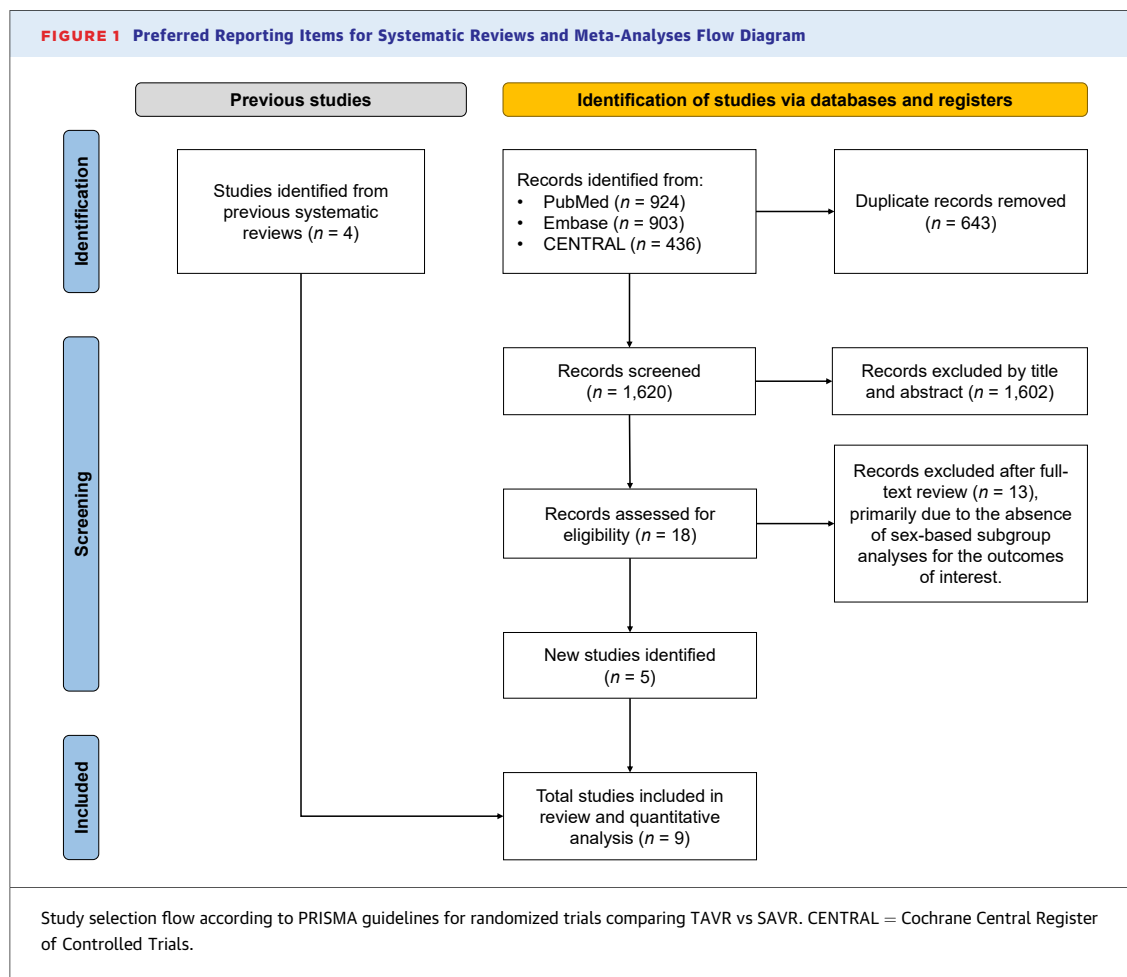
SEARCH STRATEGY AND STUDY SELECTION. A comprehensive systematic search of PubMed, Embase, and the Cochrane Central Register of Controlled Trials was performed from database inception through January 18, 2026. The search strategy utilized free-text keywords related to the core concepts: “aortic stenosis,” “transcatheter aortic valve implantation,” and “surgical aortic valve replacement.” To maximize sensitivity, the search was not limited by outcome terms. The full electronic search strategy for each database is detailed in the [Supplemental Table 2](#).

Study selection was performed independently and in duplicate by 2 reviewers (H.H. and J.H.C.). Any discrepancies were resolved through consensus or, if needed, adjudication by a senior investigator (S.W.K.). The reference lists of all included studies and relevant review articles were manually screened to identify any additional eligible trials.

DATA EXTRACTION AND OUTCOMES. Data were extracted by 1 reviewer (H.H.) and were subsequently verified in full by a second reviewer (J.H.C.). Discrepancies were resolved through discussion or consultation with the third reviewer (S.W.K.). Extracted data included: 1) study characteristics (eg, trial name, design, publication year, recruitment period, and countries involved); 2) patient demographics and baseline clinical characteristics by sex and treatment arm; 3) procedural details; and 4) sex-stratified clinical outcomes at the reported time points.

The prespecified primary outcome was the trial-defined primary endpoint of each included study, all of which incorporated mortality as a component. Outcomes were evaluated at a minimum follow-up of 1 year after the index procedure and extended to the longest available follow-up reported for each trial. Endpoint definitions adhered to the original trial protocols and, when applicable, conformed to Valve Academic Research Consortium criteria.¹⁵

RISK OF BIAS AND QUALITY ASSESSMENT. The risk of bias for each included RCT was assessed by 1



reviewer (H.H.) using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized trials,¹⁶ with verification by a second reviewer (J.H.C.). Disagreements were resolved by consensus or third-party adjudication (S.W.K.). To assess potential publication bias, funnel plots were generated for the primary outcome, and Egger linear regression test was applied statistically, contingent on the inclusion of at least 10 studies in the analysis to ensure test reliability.

STATISTICAL ANALYSIS. Primary meta-analysis.

Dichotomous outcomes were summarized as risk ratios (RRs) with corresponding 95% CIs. Pooled estimates were calculated using the Mantel-Haenszel method within a DerSimonian-Laird random-effects model. Statistical heterogeneity was assessed using the I^2 statistic, with values $\leq 25\%$, 26% to 50%, and $> 50\%$ indicating low, moderate, and substantial heterogeneity, respectively. Primary analyses were conducted separately for women and men at prespecified follow-up time points. Robustness was evaluated using leave-one-out and endpoint-

consistent sensitivity analyses. Meta-analyses were performed when ≥ 3 studies were available; analyses with fewer studies were not pooled or were presented as sensitivity analyses in the [Supplemental Material](#).

Subgroup analyses.

Subgroup analyses were conducted at the trial level according to surgical risk and valve platform (self-expanding vs balloon-expandable). Trials were stratified based on investigator-defined surgical risk, supported by reported summary risk scores, including the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM), logistic EuroSCORE, or EuroSCORE II, with STS-PROM preferentially used when available. Trials designated as low-risk and/or reporting a mean or median STS-PROM $< 4\%$ (or equivalent low-risk profiles based on EuroSCORE metrics) were classified as low surgical risk, whereas those with higher risk scores were categorized as intermediate high-risk. Within each stratum, pooled treatment effects were estimated separately for women and men, and

TABLE 1 Baseline Characteristics of the Included Trials

Trial	Centers and Countries	Recruitment Period	Trial-Defined Surgical Risk Category	TAVR/SAVR, N	TAVR Arm		
					Female, %	Age, y ^a	STS-PROM, % ^a
DEDICATE-DZHK6	38 centers in Germany	2017-2022	Low-intermediate-risk	701/713	44.0	74.3	1.8
U.S. CoreValve High Risk	45 centers in the United States	2011-2012	High-risk	394/401	46.4	83.2	7.3
Evolut Low Risk	86 centers in Australia, Canada, France, Japan, the Netherlands, New Zealand, and the United States	2016-2018	Low-risk	734/734	36.2	74.0	1.9
NOTION	3 centers in Denmark and Sweden	2009-2013	All-comers (81.8% low-risk)	145/135	46.2	79.2	2.9
SURTA VI	87 centers in the United States, Europe, and Canada	2012-2016	Intermediate-risk	879/867	42.2	79.9	4.4
PARTNER 1	25 centers in the United States, Canada, and Germany	2007-2009	High-risk	348/351	42.2	83.6	11.8
PARTNER 2	57 centers in the United States and Canada	2011-2013	Intermediate-risk	1,011/1,021	45.8	81.5	5.8
PARTNER 3	71 centers in the United States, Canada, Australia, New Zealand, and Japan	2016-2017	Low-risk	496/454	32.5	73.3	1.9
RHEIA	48 centers in Europe	2019-2023	All-comers (mostly low-risk)	215/205	100	73.1	2.1

^aValues represent mean or median.
AF = atrial fibrillation; BE = balloon-expanding; CAD = coronary artery disease; DM = diabetes mellitus; NA = not available; PPM = permanent pacemaker implantation; SAVR = surgical aortic valve replacement; SE = self-expandable; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement.

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between-subgroup differences were assessed using interaction tests.

Meta-regression. To explore between-study heterogeneity and potential effect modification, random-effects meta-regression analyses were performed using prespecified study-level covariates derived from the overall trial populations. Given the limited number of eligible trials, analyses were restricted to a small set of clinically relevant moderators to minimize overfitting and were considered exploratory. Prespecified moderators included mean age, baseline surgical risk (STS-PROM), and atrial fibrillation (AF) prevalence, selected a priori based on clinical relevance and biological plausibility.

Statistical software and significance. All analyses were performed using Review Manager (RevMan; The Cochrane Collaboration; version 5.4.1) and Stata (version 17; StataCorp). A 2-sided *P* value <0.05 was considered statistically significant.

RESULTS

STUDY SELECTION AND PATIENT CHARACTERISTICS.

The systematic literature search identified 2,263 records. After removal of duplicates and title and abstract screening, 18 full-text articles were assessed for eligibility. Nine RCTs,^{9,10,17-23} comprising a total of 9,583 patients, met the inclusion criteria and were included in the quantitative synthesis (Figure 1). A supplementary manual review of reference lists did not identify any additional eligible studies.

The overall study population included 4,236 women (44.2%) and 5,347 men (55.8%). Baseline surgical risk, as reflected by STS-PROM scores, ranged from approximately 1.8% in low-risk trials to over 11% in high-risk populations, with corresponding variation in EuroSCORE metrics. The prevalence of cardiovascular comorbidities—including diabetes mellitus, coronary artery disease, AF, and prior stroke—was higher in intermediate-high-risk trials compared with low-risk trials. Transfemoral access was the predominant approach in the TAVR arms across studies, exceeding 90% in most contemporary trials. Trial-defined primary endpoints consistently included all-cause mortality, with most also incorporating stroke as part of composite outcomes. Only 1 included RCT was specifically designed to enroll female patients,²³ whereas the remaining trials provided sex-stratified outcomes from prespecified or post hoc subgroup analyses. A detailed summary of baseline characteristics and trial features is provided in Table 1.

RISK OF BIAS AND PUBLICATION BIAS. Risk of bias assessment using the Cochrane Risk of Bias 2.0 tool demonstrated a low-risk of bias across most domains for all included RCTs (Supplemental Table 3). No trial was judged to have a high overall risk of bias. For the primary outcome, visual inspection of funnel plots revealed no evidence of substantial publication bias (Supplemental Figure 1).

SEX-SPECIFIC OUTCOMES. One-year outcomes. At 1 year, the treatment effect differed numerically

TABLE 1 Continued

TAVR Arm								
EuroSCORE (Log or II) ^a	DM, %	CAD, %	Prior Stroke, %	AF, %	Prior PPM, %	Femoral Access, %	Valve Type	Trial-Defined Primary Outcome
2.1 (II)	33.8	34.3	6.1	28.9	5.3	97.3	BE (61.4%), SE (35.1%), other (3.5%)	All-cause mortality or fatal or nonfatal stroke
17.6 (log)	34.5	75.4	12.9	41.0	23.4	82.8	SE CoreValve	All-cause mortality
NA	31.1	NA	10.1	15.5	3.4	99.0	SE (CoreValve, Evolut R, or Evolut PRO)	All-cause mortality or disabling stroke
8.4 (log)/1.9 (II)	17.9	NA	16.6	27.8	3.4	96.5	SE CoreValve	All-cause mortality
11.9 (log)	34.4	62.5	6.6	28.1	9.8	93.6	SE CoreValve (84%) and Evolut R (16%)	All-cause mortality or disabling stroke
29.3 (log)	NA	74.9	29.3	40.8	20.0	70.1	BE SAPIEN system	All-cause mortality
NA	NA	69.2	32.1	31.0	11.7	76.3	BE SAPIEN XT	All-cause mortality or disabling stroke
1.5 (II)	31.2	27.7	3.4	15.7	2.4	100	BE SAPIEN 3	All-cause mortality, stroke, or rehospitalization
1.7 (II)	26.0	19.1	3.7	5.1	2.3	100	BE SAPIEN 3 or SAPIEN 3 Ultra	All-cause mortality, stroke, or rehospitalization

by sex; however, the interaction between sex and treatment for the primary outcome did not reach statistical significance (P for interaction = 0.07). Among women, TAVR was associated with a significant 33% relative reduction in the risk of the primary outcome compared with SAVR (RR: 0.67; 95% CI: 0.55-0.81; $P < 0.001$), with low heterogeneity across trials ($I^2 = 8\%$). In contrast, no significant treatment effect was observed among men (RR: 0.88; 95% CI: 0.70-1.09; $P = 0.23$), with moderate heterogeneity ($I^2 = 42\%$) (Figure 2A).

In prespecified subgroup analyses stratified by surgical risk, treatment effects at 1 year differed between low-risk and intermediate-high-risk populations. Among low surgical risk patients, TAVR was associated with a significant reduction in the primary outcome in both women (RR: 0.52; 95% CI: 0.38-0.71; $P < 0.0001$) and men (RR: 0.61; 95% CI: 0.45-0.82; $P = 0.001$), with no evidence of effect modification by sex (P for subgroup difference = 0.49) (Figure 2B). In contrast, among intermediate-high surgical-risk patients, a significant treatment-by-sex interaction was observed (P for subgroup difference = 0.02). In this group, TAVR was associated with a lower risk of the primary outcome in women (RR: 0.76; 95% CI: 0.61-0.95; $P = 0.01$), whereas no significant benefit was observed in men (RR: 1.08; 95% CI: 0.90-1.29; $P = 0.43$) (Figure 2C).

2-year outcomes. At 2 years, the sex-specific pattern observed at 1 year persisted, although the formal test for interaction between sex and treatment was not statistically significant (P for interaction = 0.22). Women treated with TAVR

continued to experience a significant reduction in the risk of the primary outcome compared with SAVR (RR: 0.80; 95% CI 0.69-0.94; $P = 0.007$), with no observed heterogeneity ($I^2 = 0\%$). Among men, the treatment effect remained nonsignificant (RR: 0.93; 95% CI: 0.78-1.10; $P = 0.39$) (Figure 3A).

Surgical risk-stratified analyses at 2 years demonstrated consistent findings. Among low surgical risk patients, the estimate suggested a lower risk with TAVR in women but did not reach statistical significance (RR: 0.72; 95% CI: 0.45-1.14; $P = 0.16$), whereas in men TAVR was associated with a lower risk (RR: 0.67; 95% CI: 0.50-0.91; $P = 0.01$). There was no evidence of a difference by sex (P for subgroup difference = 0.81) (Figure 3B). Among intermediate-high surgical-risk patients, TAVR remained associated with a reduced risk of the primary outcome in women (RR: 0.82; 95% CI: 0.69-0.97; $P = 0.02$), whereas no significant effect was observed in men (RR: 1.03; 95% CI: 0.90-1.19; $P = 0.67$). The subgroup comparison indicated a difference between sexes (P for subgroup difference = 0.04) (Figure 3C).

5-year outcomes. At 5 years, the early benefit of TAVR observed in women was no longer evident (RR: 1.03; 95% CI: 0.89-1.18; $P = 0.72$). Similarly, no significant difference in the primary outcome was observed among men (RR: 1.06; 95% CI: 0.99-1.14; $P = 0.11$). There was no evidence of interaction between sex and treatment at this time point (P for interaction = 0.69). Consistent with these findings, the overall pooled estimate demonstrated no significant difference between TAVR and SAVR (RR: 1.05; 95% CI: 0.98-1.12; $P = 0.17$) (Figure 4A).

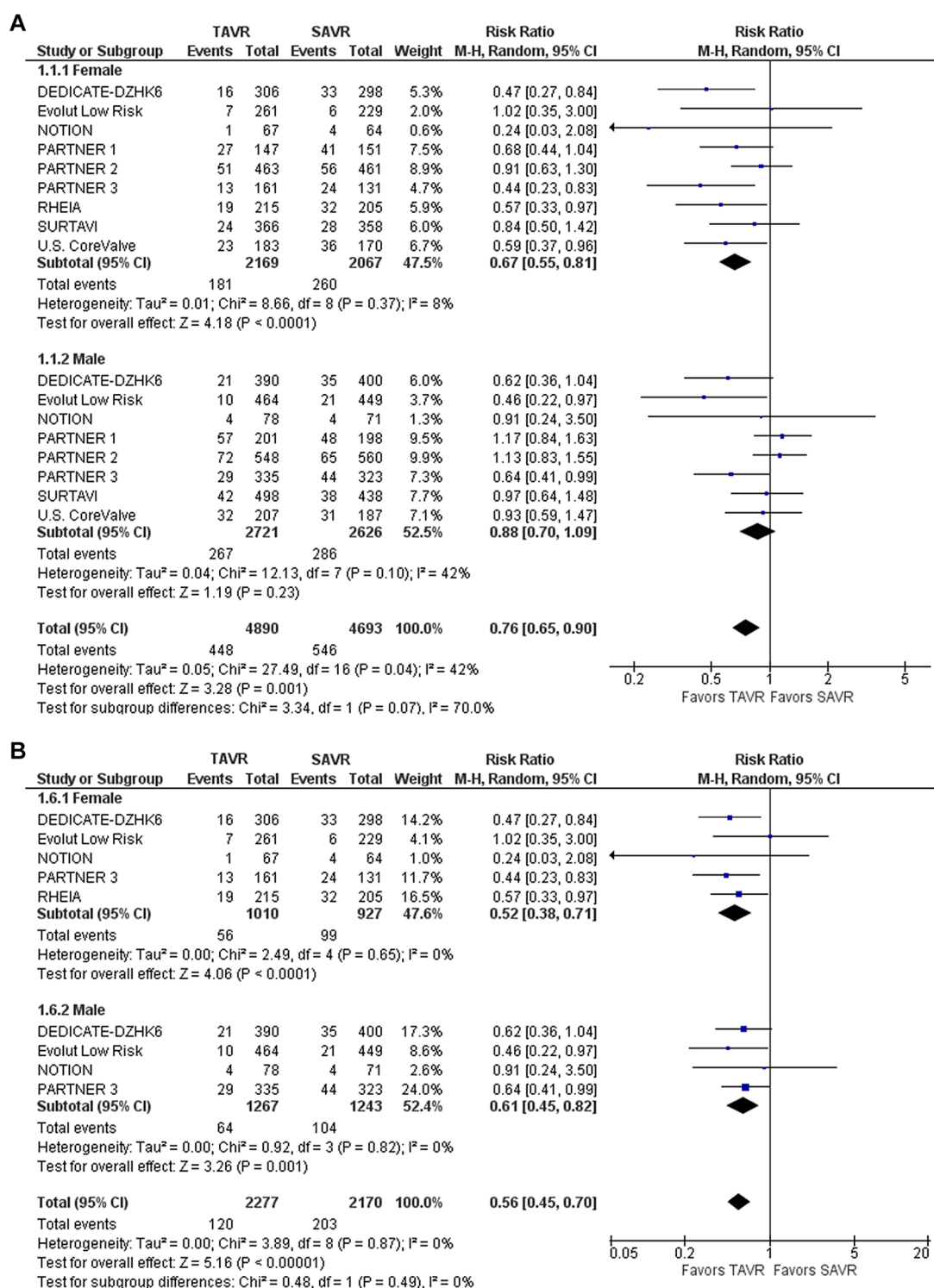
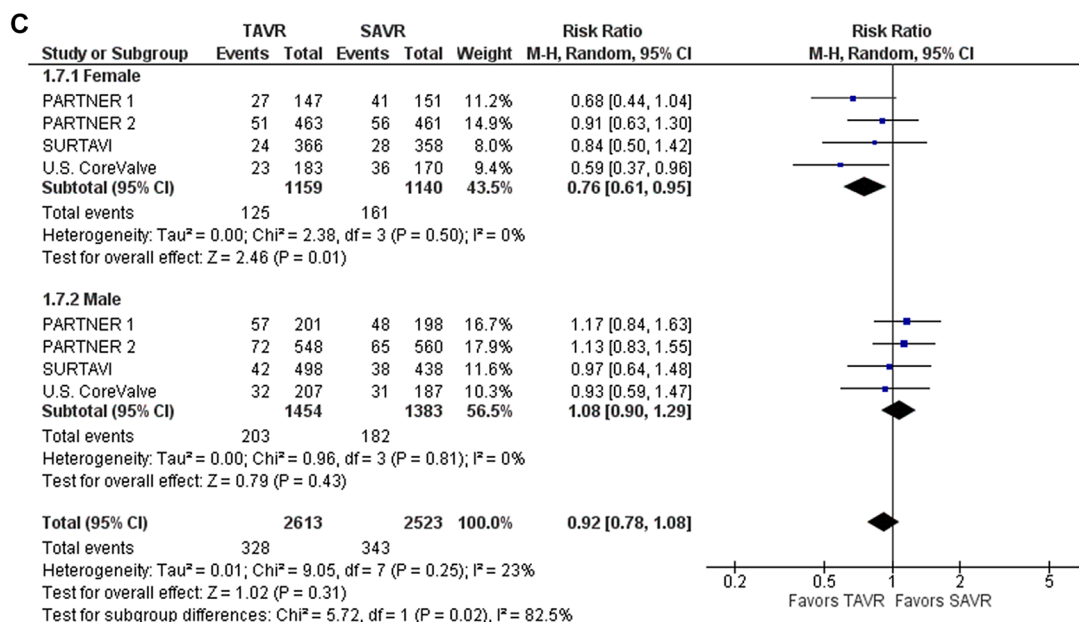
FIGURE 2 One-Year Outcomes Stratified by Sex

FIGURE 2 Continued



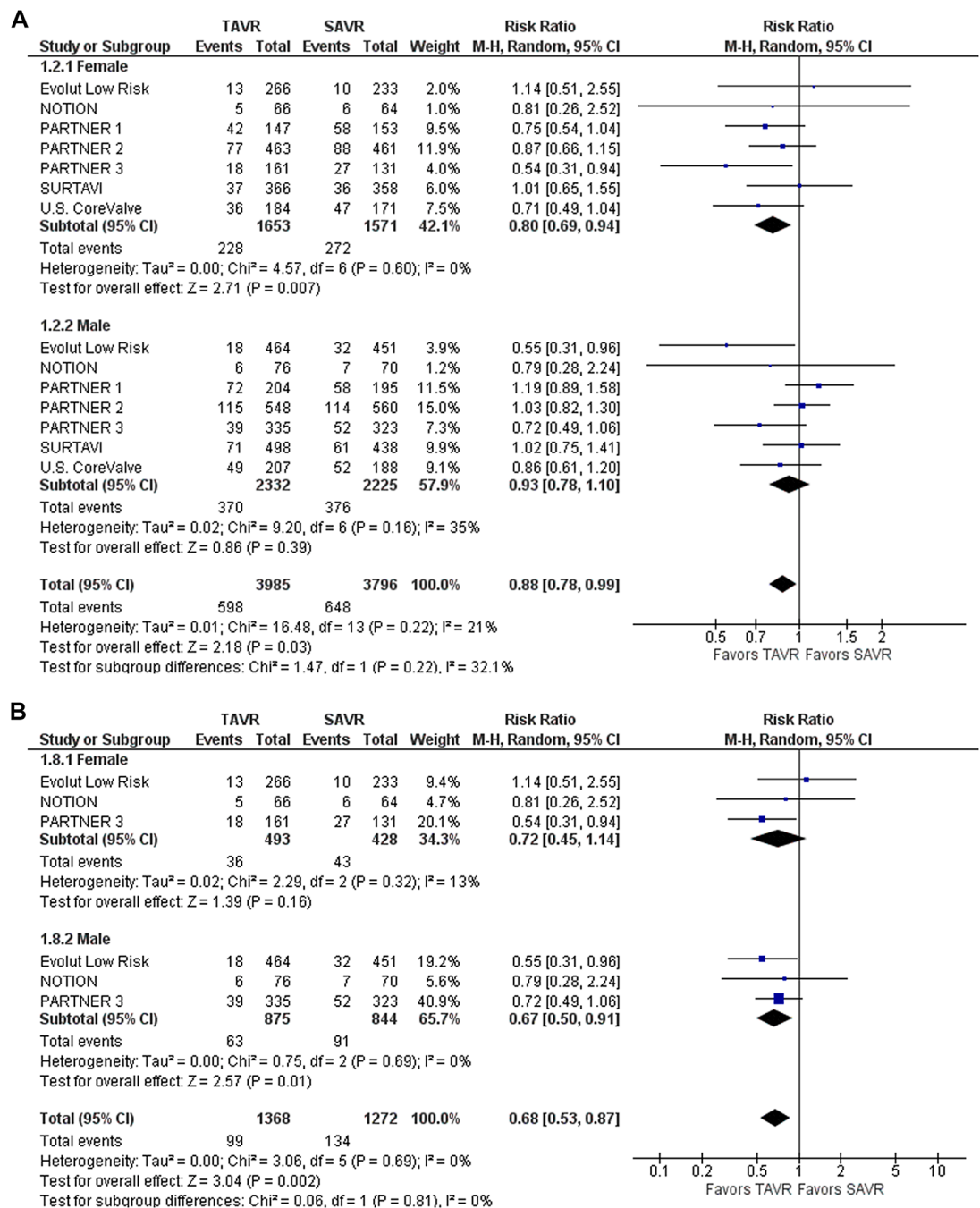
Risk-stratified analyses at 5 years showed no significant differences between TAVR and SAVR in low surgical-risk patients for either women (RR: 0.85; 95% CI: 0.64-1.12; $P = 0.24$) or men (RR: 0.93; 95% CI: 0.78-1.11; $P = 0.43$) (Figure 4B). In contrast, among intermediate-high surgical-risk patients, long-term outcomes favored SAVR, driven primarily by men (RR: 1.09; 95% CI: 1.00-1.18; $P = 0.04$), whereas outcomes in women were directionally similar but not statistically significant (RR: 1.08; 95% CI: 0.93-1.25; $P = 0.33$), with no evidence of sex-based heterogeneity (P for subgroup difference = 0.91) (Figure 4C).

VALVE PLATFORM-STRATIFIED ANALYSES. In subgroup analyses stratified by valve platform (self-expanding vs balloon-expandable), the overall pattern of sex-specific, time-dependent treatment effects remained consistent. At 1 year, women derived a significant benefit with TAVR in both self-expanding (RR: 0.70; 95% CI: 0.50-0.98; $P = 0.04$) and balloon-expandable valve trials (RR: 0.63; 95% CI: 0.48-0.83; $P = 0.001$), whereas no significant effect was observed in men (Supplemental Figure 2). At 2 years, the benefit in women persisted in balloon-expandable valve trials but not in self-expanding valve trials; however, there was no

significant interaction between valve type and treatment effect (Supplemental Figure 3). By 5 years, no significant differences were observed between TAVR and SAVR in either sex across both valve platforms (Supplemental Figure 4). Across all time points, tests for subgroup differences were not statistically significant, suggesting no clear evidence that valve type modified the sex-specific treatment effect.

SENSITIVITY ANALYSIS. Leave-one-out sensitivity analyses of the overall cohort, including both sexes and across all follow-up time points, showed that the pooled effect estimates were not materially influenced by any single trial.

Sensitivity analyses using more consistent endpoints showed broadly similar patterns. For all-cause mortality, women had a lower risk with TAVR at 1 year, with no significant differences at 2 and 5 years, whereas no significant differences were observed in men across time points. For the composite of all-cause mortality or disabling stroke, no significant differences were observed at 1 and 2 years in either sex. At 5 years, a higher risk with TAVR was observed in women, whereas no statistically significant difference was observed in men (Supplemental Figures 5 and 6).

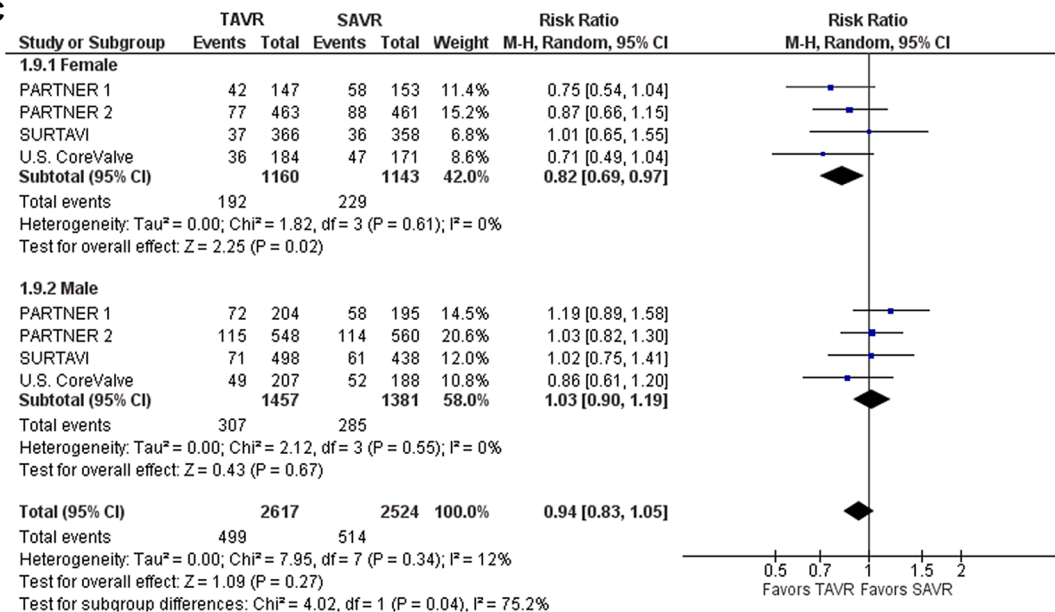
FIGURE 3 2-Year Outcomes Stratified by Sex

Forest plots of 2-year outcomes comparing TAVR vs SAVR, stratified by sex: (A) overall cohort, (B) low surgical risk trials, and (C) intermediate-high surgical risk trials. Abbreviations as in [Figure 2](#).

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FIGURE 3 Continued

C



Further stratification of the intermediate-high surgical-risk group into intermediate and high-risk categories (2 trials per subgroup) showed no significant sex-specific differences among intermediate-risk patients at 1 and 2 years. In high-risk patients, lower risk with TAVR was observed in women but not in men at early follow-up. At 5 years, a higher risk with TAVR was observed in both sexes in the intermediate-risk group, whereas no significant differences were observed in high-risk patients (Supplemental Figures 7 to 9).

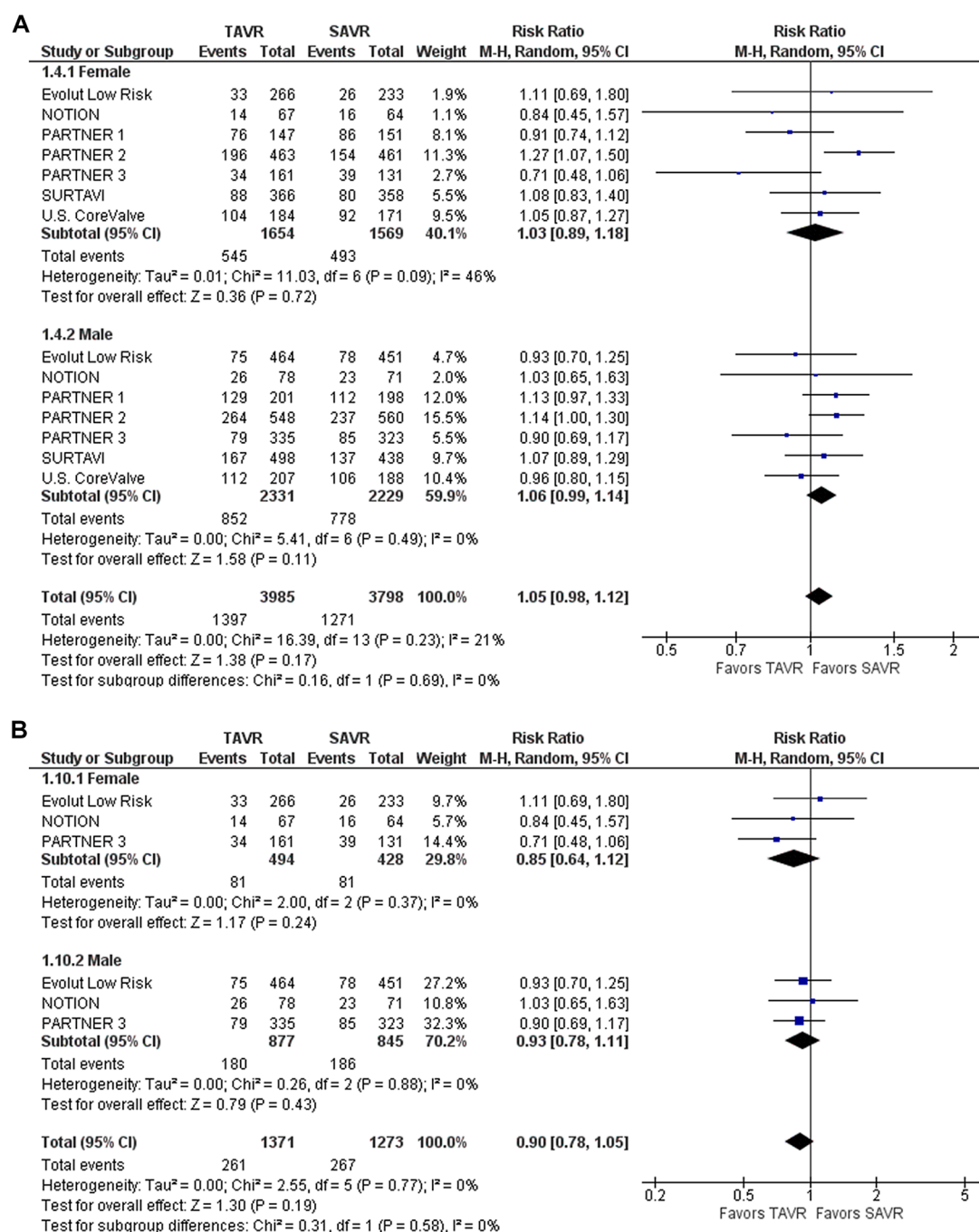
META-REGRESSION. In exploratory univariate random-effects meta-regression (Table 2, Figure 5), none of the prespecified study-level moderators were significantly associated with the treatment effect for the trial-defined primary endpoint. The mean age was not associated with the log RR (β -0.0001 per year; 95% CI: -0.0083 to 0.0080 ; $P = 0.98$). Similarly, baseline surgical risk, assessed by the mean STS-PROM score, showed no significant association with treatment effect (β 0.0035 ; 95% CI: -0.0083 to 0.0154 ; $P = 0.56$). The proportion of patients with AF was also not associated with outcome differences between TAVR and SAVR (β 0.0005 per percentage point; 95% CI: -0.0025 to 0.0035 ; $P = 0.73$). Residual heterogeneity remained moderate across all models

(residual I^2 range, 55.2%-57.9%), indicating that these moderators did not explain between-study variability.

DISCUSSION

The Central Illustration summarizes the principal findings of this meta-analysis. In this pooled analysis of contemporary randomized trials, several key findings emerged. First, outcomes appeared to differ by sex and varied over time following aortic valve replacement. Women showed a lower risk of the primary endpoint with TAVR compared with SAVR at 1 and 2 years, with convergence by 5-year follow-up. In contrast, men showed no significant differences at 1, 2, or 5 years. Second, these patterns varied by surgical risk. Among low-risk patients, outcomes were generally similar between TAVR and SAVR in both sexes, with no significant differences by 5 years. Among intermediate-high-risk patients, lower risk with TAVR was observed in women at early and midterm follow-up, whereas at 5 years a higher risk with TAVR was observed in men. Collectively, these findings suggest that the comparative effectiveness of TAVR and SAVR may vary according to sex, baseline surgical risk, and duration of follow-up.

FIGURE 4 5-Year Outcomes Stratified by Sex

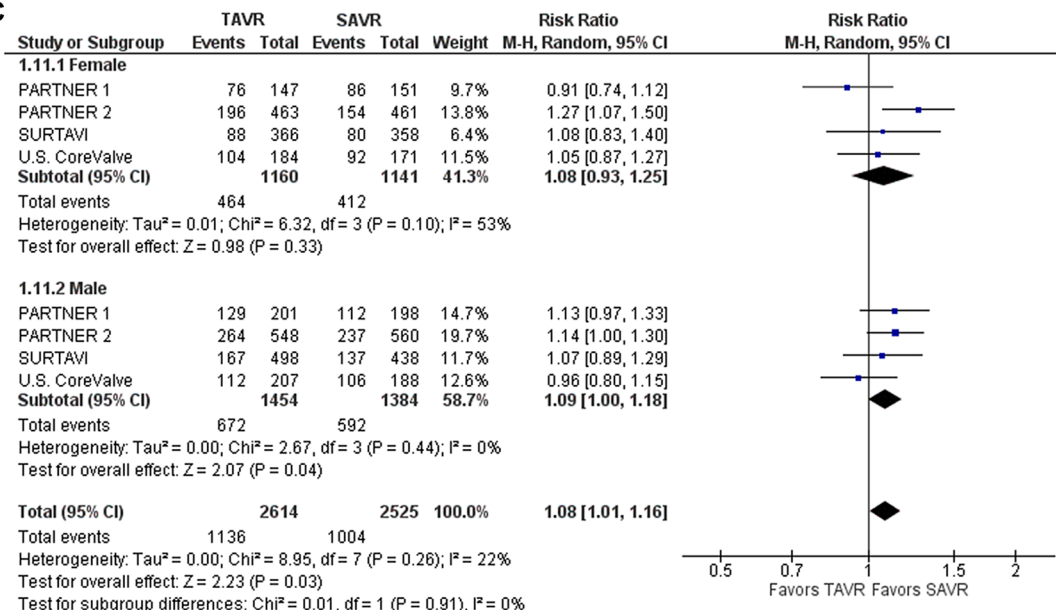


Forest plots of 5-year outcomes comparing TAVR vs SAVR, stratified by sex: (A) overall cohort, (B) low surgical risk trials, and (C) intermediate-high surgical risk trials. Abbreviations as in [Figure 2](#).

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FIGURE 4 Continued

C



Our findings are broadly consistent with, and extend, prior randomized evidence and meta-analyses examining sex-specific outcomes after aortic valve replacement.^{9,11,12,17} The RHEIA trial—the first randomized study conducted exclusively in women—reported a lower incidence of its composite primary endpoint at 1 year with TAVR compared with SAVR.²³ Importantly, this difference was largely driven by reductions in rehospitalization, whereas individual hard endpoints, including mortality and stroke, did not differ significantly between strategies. Accordingly, these data do not support a mortality or stroke benefit of TAVR in women, suggesting that early advantages may primarily reflect reduced morbidity rather than improved survival.

More recent randomized trials in patients with small aortic annuli—a population that disproportionately includes women—further highlight the importance of sex-related anatomical factors. In the VIVA trial, early outcomes were comparable between TAVR and SAVR, although the study was underpowered due to early termination.²⁴ The SMART trial demonstrated noninferiority between self-expanding and balloon-expandable TAVR platforms in this population.²⁵ Although not directly informing long-term comparisons between TAVR and SAVR, these studies support the role of anatomy in shaping procedural performance and early outcomes.

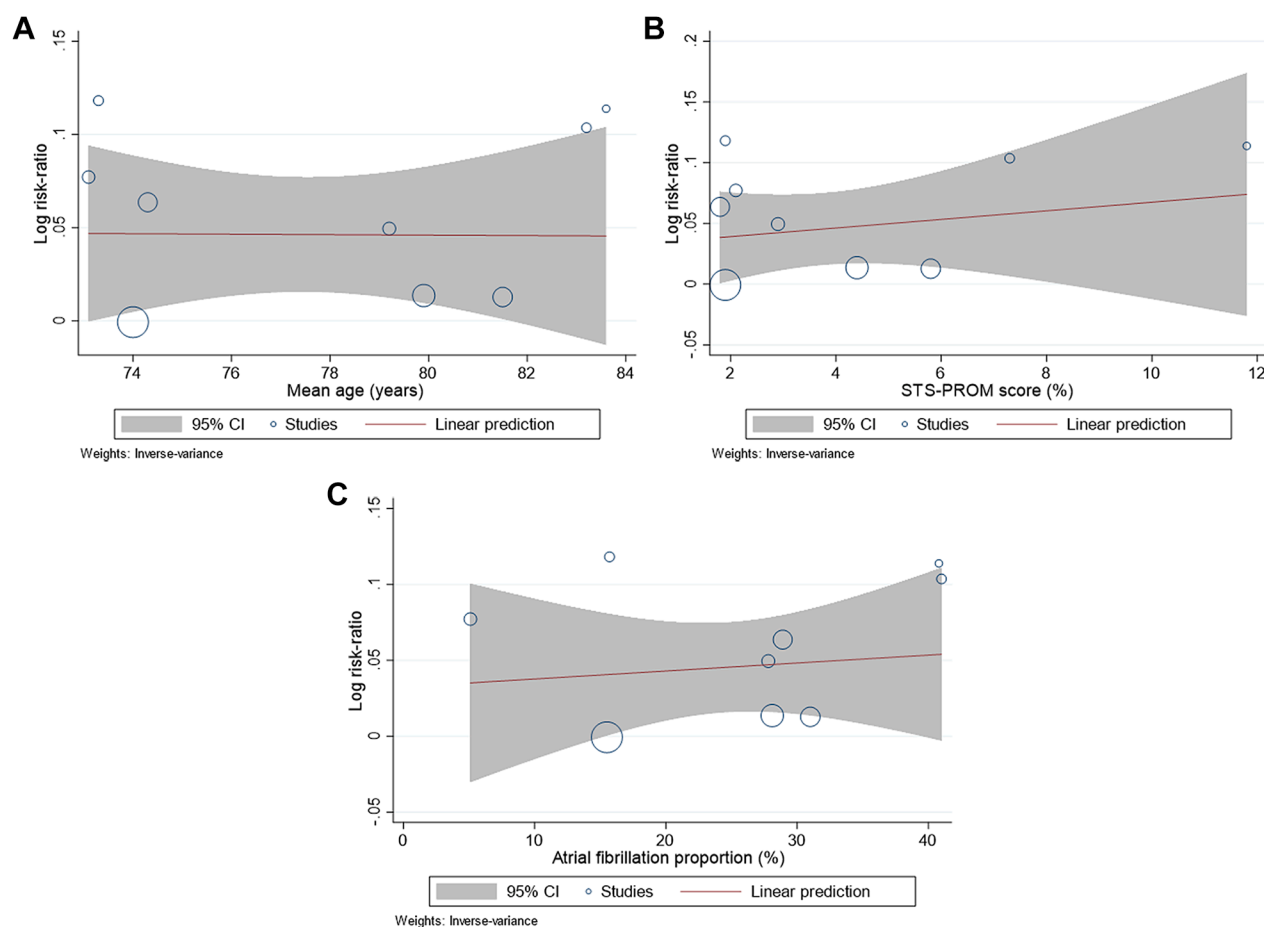
Surgical risk may help contextualize the observed sex-related patterns. In lower-risk populations,

TABLE 2 Univariate Meta-Regression Analyses for the Primary Outcome in Women

Moderator	β Coefficient (95% CI)	P Value	No. of Studies	τ^2	Residual I^2 (%)
Mean age (years)	−0.0001 (−0.0083 to 0.0080)	0.976	9	0.0012	57.9
STS-PROM score (%)	0.0035 (−0.0083 to 0.0154)	0.559	9	0.0010	56.3
Atrial fibrillation proportion (%)	0.0005 (−0.0025 to 0.0035)	0.730	9	0.0010	55.2

Abbreviation as in Table 1.

FIGURE 5 Meta-Regression in Female Subgroup



Univariate meta-regression analyses in women evaluating associations between treatment effect and (A) mean age, (B) STS-PROM score, and (C) atrial fibrillation prevalence. STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality.

where procedural risk is reduced and life expectancy is longer, outcomes between TAVR and SAVR were broadly similar across sexes over time. In contrast, in intermediate-high-risk patients, early differences were more apparent in women, which may reflect differences in anatomical characteristics, procedural risk profiles, and recovery trajectories. The absence of similar early patterns in men, together with the emergence of less favorable longer-term outcomes with TAVR in higher risk patients, suggests that factors such as baseline comorbidity burden and valve durability may play a more prominent role over time.

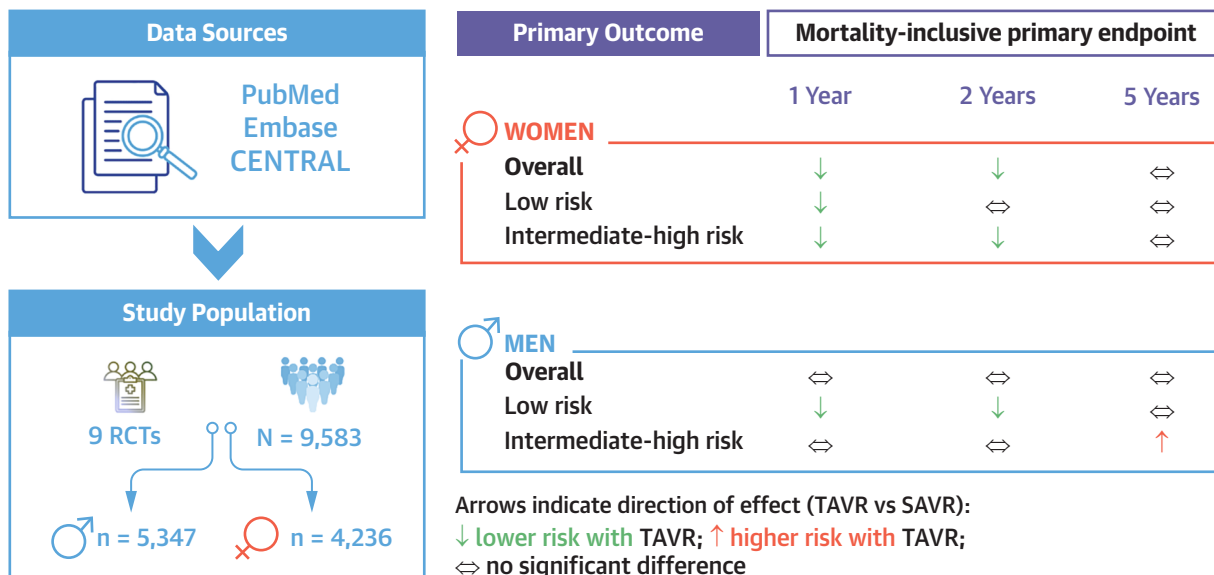
The early reduction in the primary endpoint with TAVR in women is likely multifactorial. Women undergoing SAVR have historically had higher perioperative risk, including bleeding, acute kidney injury,

and prosthesis-patient mismatch—risks that may be mitigated with a less invasive approach.^{26,27} Sex-related differences in ventricular remodeling, vascular compliance, and recovery may also contribute.²⁸ Consistent with this, valve platform-stratified analyses showed similar sex-specific patterns across self-expanding and balloon-expandable valves, with no significant interaction. Although effect sizes in women were numerically greater in balloon-expandable trials at some time points, this did not translate into a significant difference, suggesting that these effects are unlikely to be device-driven.

From an echocardiographic perspective, the DEDICATE subgroup analysis demonstrated comparable improvements in valve hemodynamics between

CENTRAL ILLUSTRATION Sex-Specific and Time-Dependent Outcomes After TAVR vs SAVR

Sex-Specific Differences in Outcomes After TAVR vs SAVR



- Women showed lower risk with TAVR at 1 to 2 years, with no significant difference by 5 years.
- Men showed no significant differences at 1, 2, or 5 years.
- Findings varied by surgical risk, with early differences more apparent in intermediate-high-risk patients, particularly in women. A higher risk with TAVR at 5 years was observed in intermediate-high-risk men.

Hendrianus H, et al. JACC Adv. 2026;5(7):102856.

This illustration depicts time-dependent, sex-specific outcomes of TAVR vs SAVR for the trial-defined mortality-inclusive endpoint. CENTRAL = Cochrane Central Register of Controlled Trials; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; RCTs = randomized controlled trials.

sexes, with no differences in gradients or residual regurgitation.²⁹ However, effective orifice area was larger after TAVR than SAVR in women, but not in men. In the female cohort of the RHEIA trial, very small annuli were uncommon, reflected by low use of small prostheses.²³ Valve hemodynamics were satisfactory in both arms, with mean gradients <15 mm Hg and valve area >1.7 cm². These findings are consistent with the VIVA trial, which included predominantly small annuli and similarly showed comparable hemodynamics between TAVR and SAVR.²⁴

The attenuation of early benefits over time warrants careful interpretation. Rather than loss of TAVR efficacy, this likely reflects increasing influence of competing risks, including age, comorbidities, and long-term valve performance.³⁰ In men, the absence

of early benefit and a late signal favoring SAVR may relate to differences in life expectancy, baseline risk, and valve durability. Sex-related differences in disease progression and postintervention remodeling may also contribute.³¹ However, given the exploratory nature of these analyses and limited power for long-term sex-specific comparisons, these findings should be considered hypothesis-generating.

From a clinical perspective, these results underscore the importance of individualized treatment selection that accounts for both short- and long-term considerations. For women—particularly those at intermediate or high surgical risk—TAVR may offer meaningful early and mid-term advantages in composite clinical outcomes, whereas longer-term outcomes appear broadly comparable between

treatment strategies. For men, outcomes were generally similar between TAVR and SAVR across time points, although a higher risk with TAVR was observed at 5 years in intermediate-high-risk patients. Importantly, these findings do not support a sex-based treatment mandate but instead reinforce the need for shared decision-making that integrates patient sex, surgical risk, anatomical characteristics, comorbidity burden, life expectancy, and patient preferences.

STUDY LIMITATIONS. Several limitations warrant consideration. First, sex-specific effects were derived largely from subgroup analyses of trials not powered to detect differences between women and men; only 1 trial was specifically designed for this purpose,²³ increasing the risk of chance findings, particularly at longer follow-up. In addition, sex-based comparisons relied on study-level subgroup estimates rather than within-trial interaction effects, and interaction *P* values were based on pooled subgroup comparisons, which may be more susceptible to bias. Second, the primary endpoint consisted of trial-defined mortality-inclusive outcomes that varied across studies, potentially influencing results, particularly if driven by nonfatal components. Moreover, sex-stratified data were largely limited to primary endpoints, restricting assessment of secondary outcomes. Third, the absence of individual patient-level data precluded adjustment for anatomical, procedural, and device-related factors that may differ by sex. Fourth, effect estimates were based on RRs rather than HRs—more appropriate for time-to-event data—because HRs were inconsistently reported across trials. Although analyses at prespecified time points (1, 2, and 5 years) may partially mitigate this limitation, they were conducted as independent cross-sectional meta-analyses, which do not fully account for censoring, and not all trials contributed data at each time point. Finally, as a study-level meta-analysis with a limited number of trials (*N* = 9), the findings should be considered hypothesis-generating. Statistical power to detect modest effect modification was limited, and meta-regression was constrained by the small number of studies and reliance on study-level covariates.

CONCLUSIONS

In this meta-analysis of randomized trials, outcomes after aortic valve replacement appeared to differ by

sex and varied over time. Women showed a lower risk of the mortality-inclusive primary endpoint with TAVR compared with SAVR at 1 and 2 years, with no significant difference by 5 years. Men showed no significant differences across time points. Findings varied by surgical risk, with early differences more apparent in intermediate-high-risk populations, particularly in women. At 5 years, a higher risk with TAVR was observed in intermediate-high-risk men. Overall, these findings suggest that the relative effectiveness of TAVR and SAVR may vary according to sex, baseline risk, and duration of follow-up.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND

MEDICAL KNOWLEDGE: Sex-specific and time-dependent patterns in outcomes after aortic valve replacement support an individualized approach to treatment selection. Women may have lower risk with TAVR at early follow-up, particularly in intermediate-high-risk patients, with no significant difference at longer follow-up. In men, outcomes are generally similar between TAVR and SAVR across time points, although a higher risk with TAVR was observed at 5 years in intermediate-high-risk patients. These findings highlight the importance of considering sex and surgical risk in clinical decision-making.

TRANSLATIONAL OUTLOOK: Future studies incorporating patient-level data are needed to better understand mechanisms underlying sex-specific differences and to evaluate long-term valve durability across treatment strategies.

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APPENDIX For supplemental tables and figures, please see the online version of this paper.