Supplementary

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## Supplemental Figures:

| First author | Year | Domain 1-Confounding | Domain 2-Selection | Domain 3-Classification of Interventions | Domain 4-Deviations from Intended Interventions | Outcome-Specific Domains | Domain 5-Missing Data | Domain 6-Outcome Measurement | Domain 7-Reported Results | Overall Risk of Bias | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Matched or Adjusted Observational Studies** | | | | | | | | | | | |
| Yousef | 2023 | S | L | M | L | Mortality | M | L | M | S | Mortality |
| | | | | | | AoV Reintervention | M | M | M | S | AoV Reintervention |
| | | | | | | Non-Structural Valve Dysfunction-PVL | S | S | M | S | Non-Structural Valve Dysfunction-PVL |
| Shih | 2022 | M | L | M | L | Mortality | L | L | M | M | Mortality |
| | | | | | | AoV Reintervention | L | M | M | M | AoV Reintervention |
| Mehaffey | 2021 | S | L | S | L | Mortality | L | L | M | S | Mortality |
| | | | | | | AoV Reintervention | L | M | M | S | AoV Reintervention |
| | | | | | | Stroke Hospitalization | L | M | M | S | Stroke Hospitalization |
| | | | | | | CHF Rehospitalization | L | S | M | S | CHF Rehospitalization |
| Chauvette | 2020 | S | L | L | NI | Mortality | L | L | M | S | Mortality |
| Tam | 2020 | M | L | L | L | Mortality | L | L | M | M | Mortality |
| | | | | | | AoV Reintervention | L | M | M | M | AoV Reintervention |
| | | | | | | CHF Rehospitalization | L | S | M | S | CHF Rehospitalization |
| Tam* | 2020 | M | L | L | L | Mortality | L | L | M | M | Mortality |
| Haunschild | 2019 | M | L | L | M | Mortality | S | L | M | S | Mortality |
| Okamoto | 2016 | M | L | L | L | Mortality | NI | L | M | M | Mortality |
| | | | | | | Cardiac Mortality | NI | M | M | M | Cardiac Mortality |
| | | | | | | SVD | NI | S | NI | S | SVD |
| | | | | | | IE | NI | S | NI | S | IE |
| | | | | | | Major Bleeding | NI | S | NI | S | Major Bleeding |
| | | | | | | Stroke | NI | S | NI | S | Stroke |
| | | | | | | CHF | NI | S | NI | S | CHF |
| Kulik | 2008 | S | L | L | C | Mortality | M | L | M | C | Mortality |
| | | | | | | CHF Composite | M | S | M | C | CHF Composite |
| Sommers | 1997 | S | L | L | NI | Mortality | L | L | M | S | Mortality |
| | | | | | | Cardiac Mortality | L | M | M | S | Cardiac Mortality |
| **Unmatched/Unadjusted Observational Studies** | | | | | | | | | | | |
| Rao | 2023 | C | L | S | C | Mortality | S | L | L | C | Mortality |
| | | | | | | AoV Reintervention | S | M | L | C | AoV Reintervention |
| | | | | | | SVD | S | M | L | C | SVD |
| | | | | | | Non-Structural Dysfunction | S | M | L | C | Non-Structural Dysfunction |
| | | | | | | Valve Thrombosis | S | M | L | C | Valve Thrombosis |
| | | | | | | NYHA III-IV | S | S | L | C | NYHA III-IV |
| | | | | | | IE | S | S | L | C | IE |
| | | | | | | Major Anticoagulant-Related Hemorrhage | S | S | L | C | Major Anticoagulant-Related Hemorrhage |
| | | | | | | Thromboembolism | S | S | L | C | Thromboembolism |
| Beckmann | 2016 | S | L | L | C | Mortality | S | L | M | C | Mortality |
| Correia | 2016 | S | L | S | C | Mortality | L | L | M | C | Mortality |
| Prfiti | 2015 | C | L | L | M | Mortality | NI | L | S | C | Mortality |
| | | | | | | AoV Reintervention | NI | M | S | C | AoV Reintervention |
| Penaranda | 2014 | S | L | L | S | Mortality | M | L | M | S | Mortality |
| Sakamoto | 2006 | C | L | L | NI | Mortality | NI | NI | M | C | Mortality |
| | | | | | | Reoperation** | NI | M | M | C | Reoperation** |
| | | | | | | Prosthetic Valve IE | NI | S | M | C | Prosthetic Valve IE |
| | | | | | | Thromboembolism | NI | S | M | C | Thromboembolism |

**Figure S1** ROBINS-I assessment for all reported outcomes within each of the included studies.

Legend for ROBINS-I assessment: L, low risk of bias; M, moderate risk of bias; S, serious risk of bias; C, critical risk of bias; NI, no information.

Abbreviations: AoV, aortic valve; CHF, congestive heart failure; IE, infective endocarditis; NYHA, New York Heart Association functional class; PVL, paravalvular leak; SVD, structural valve deterioration.

* Distinct secondary cohort reported within the same publication.

** Long-term reoperation outcome was assumed to be related to aortic valve reintervention.


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## Figures S2-S31. Meta-analyses for baseline characteristics

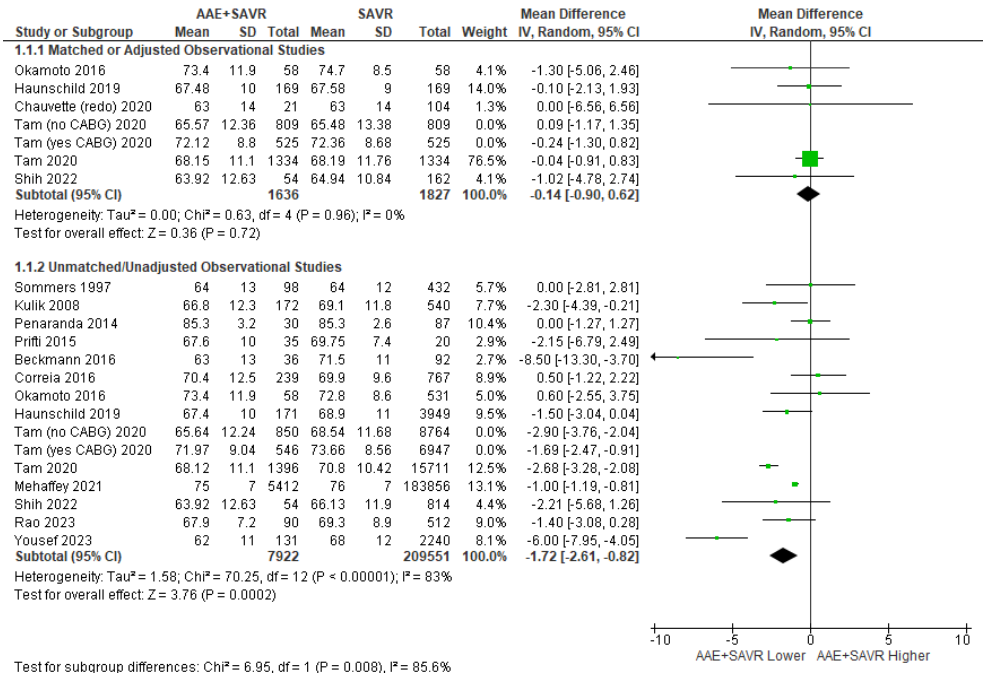


**Figure S2** Forest plot for age at time of operation (years).

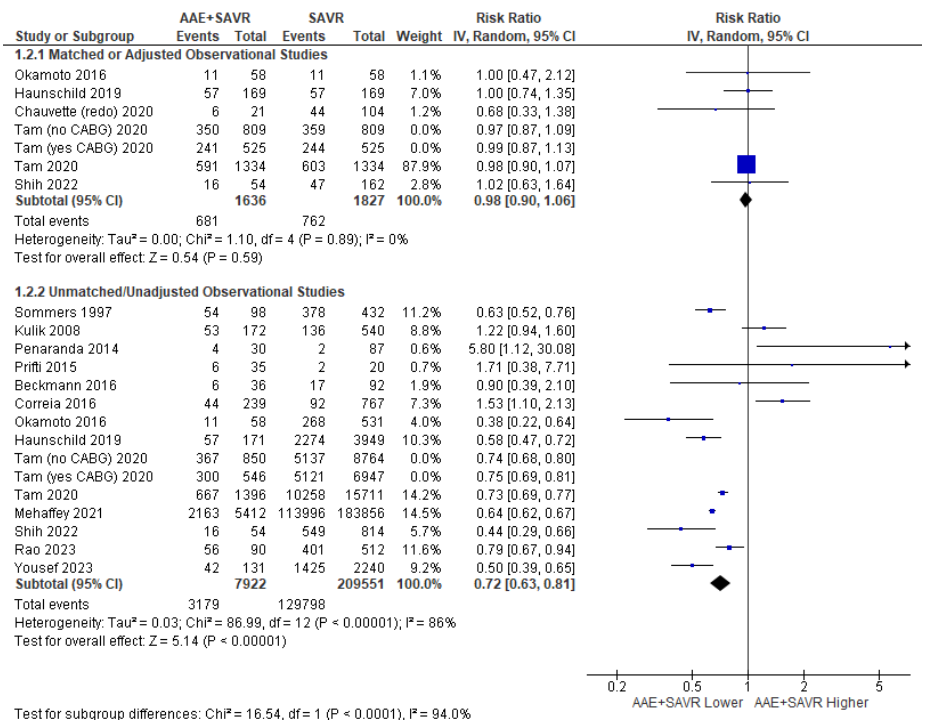


**Figure S3** Forest plot for male sex.


https://dx.doi.org/10.21037/acs-2024-aae-0023

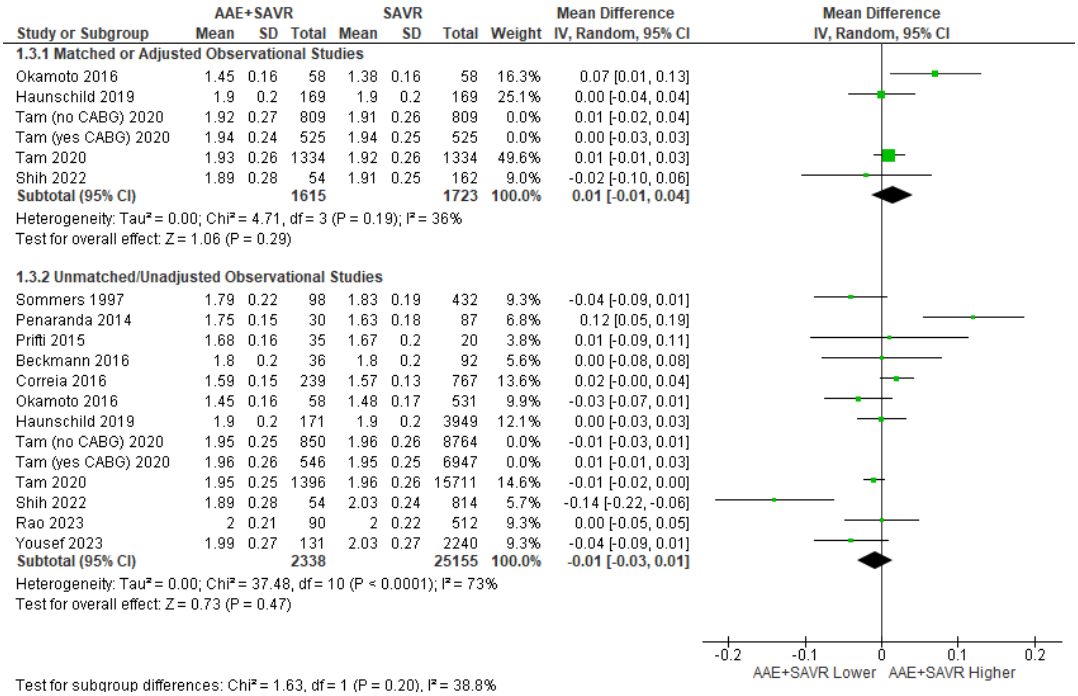


**Figure S4** Forest plot for preoperative body surface area ($m^2$).

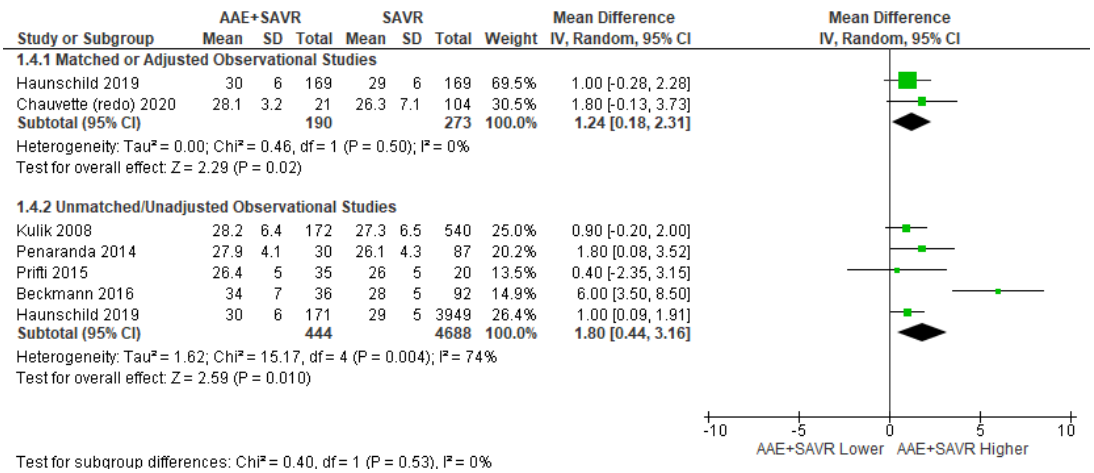


**Figure S5** Forest plot for preoperative body mass index ($kg/m^2$).


https://dx.doi.org/10.21037/acs-2024-aae-0023

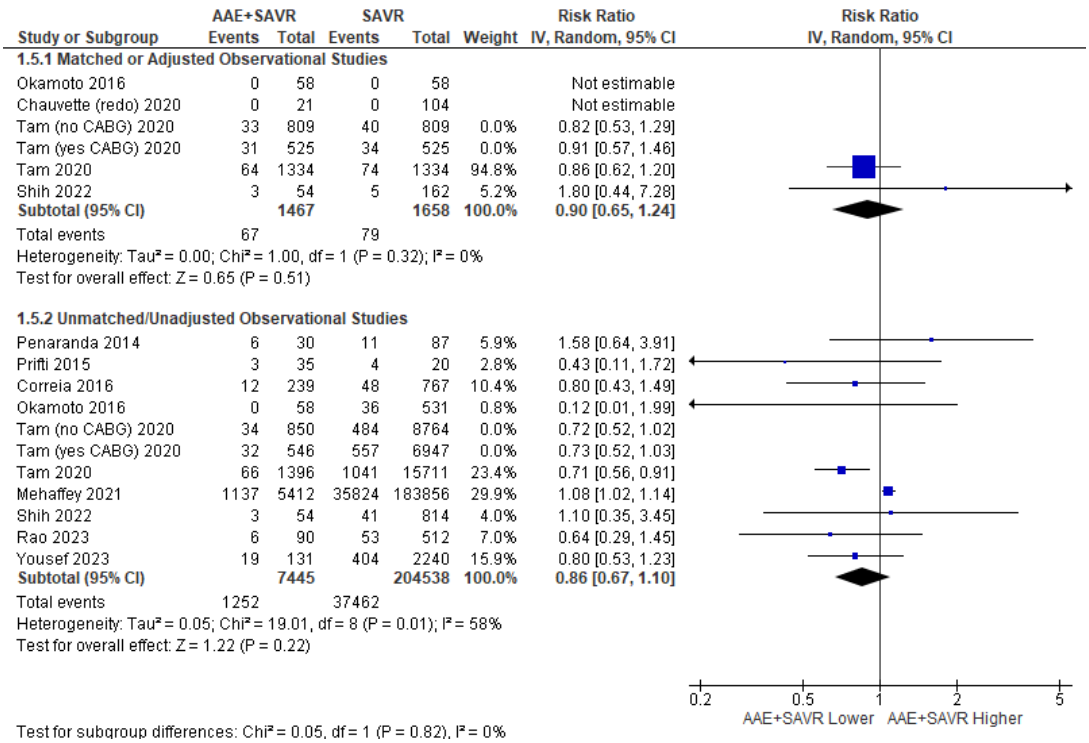


**Figure S6** Forest plot for cerebrovascular disease.

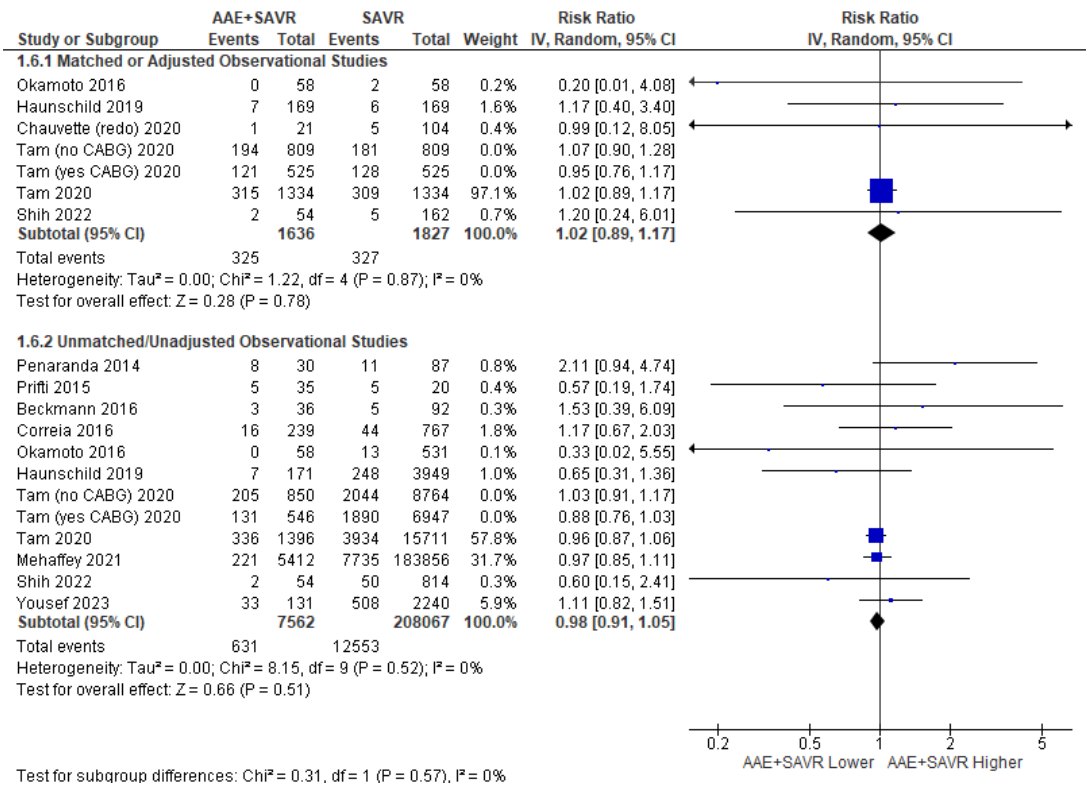


**Figure S7** Forest plot for chronic obstructive pulmonary disease (COPD).


https://dx.doi.org/10.21037/acs-2024-aae-0023

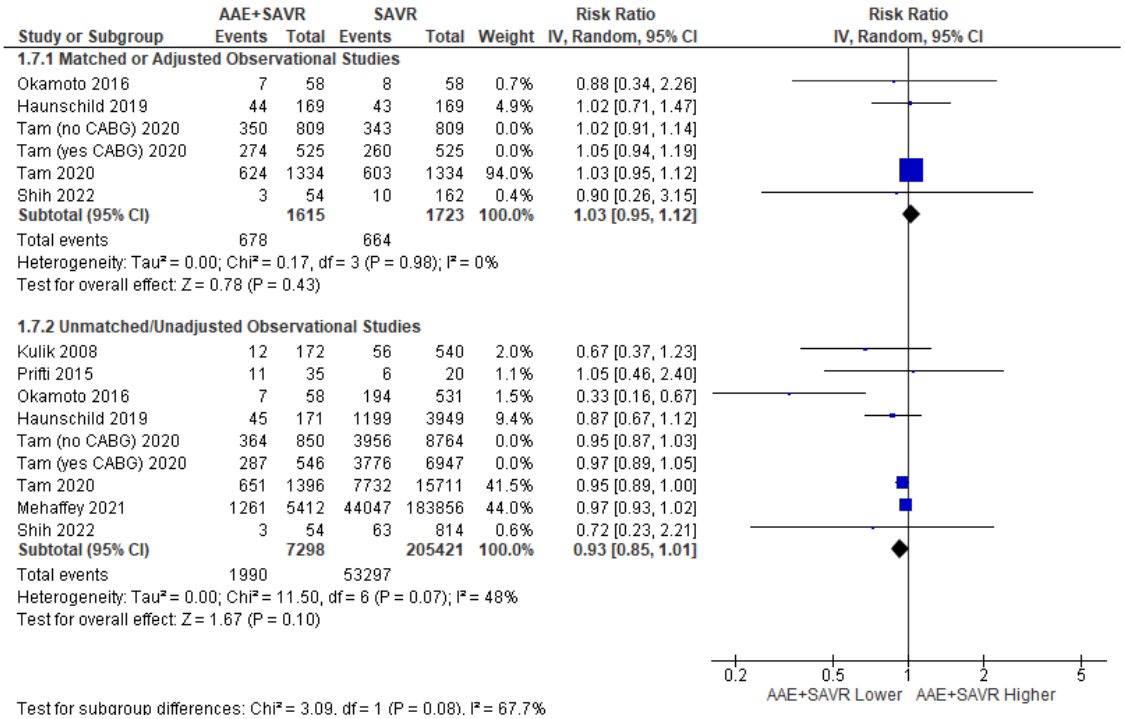


**Figure S8** Forest plot for smoking.

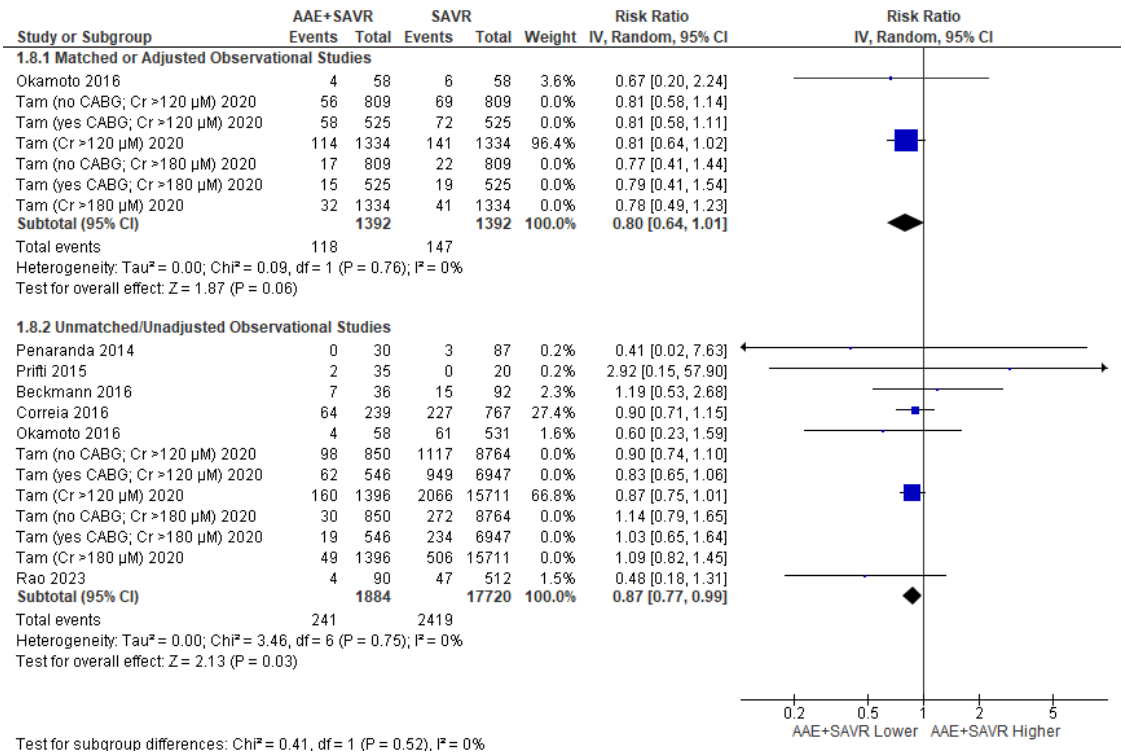


**Figure S9** Forest plot for chronic renal failure.


https://dx.doi.org/10.21037/acs-2024-aae-0023

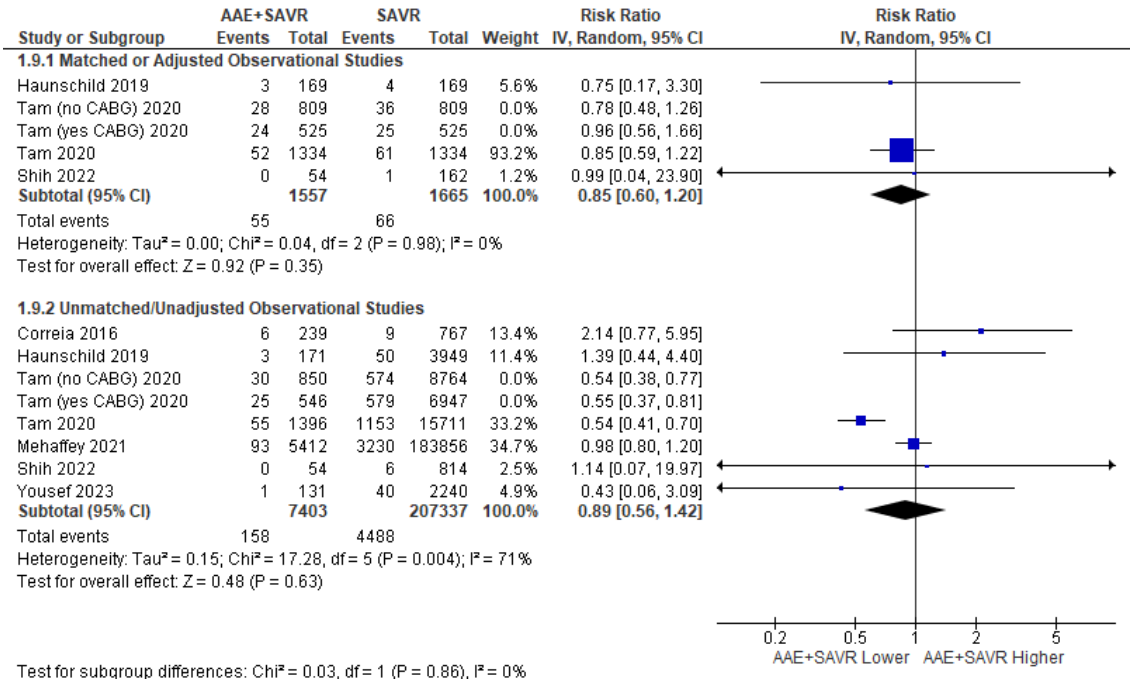


**Figure S10** Forest plot for dialysis.

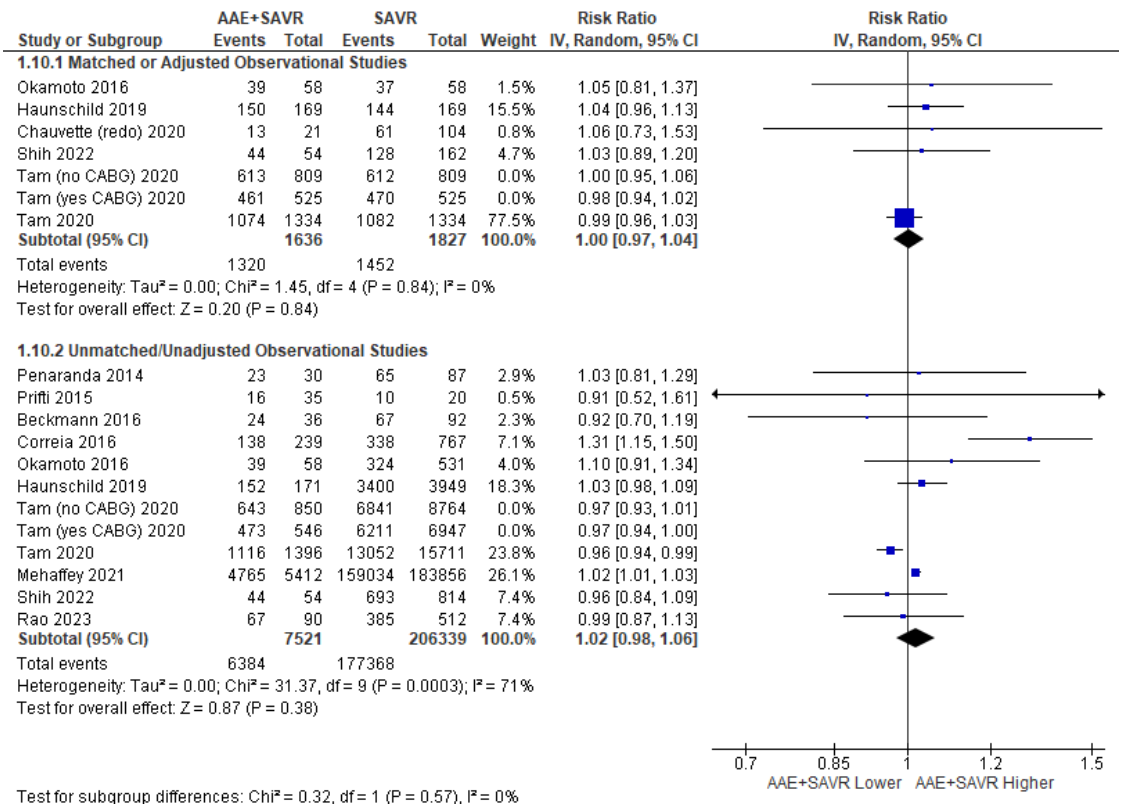


**Figure S11** Forest plot for hypertension.


https://dx.doi.org/10.21037/acs-2024-aae-0023

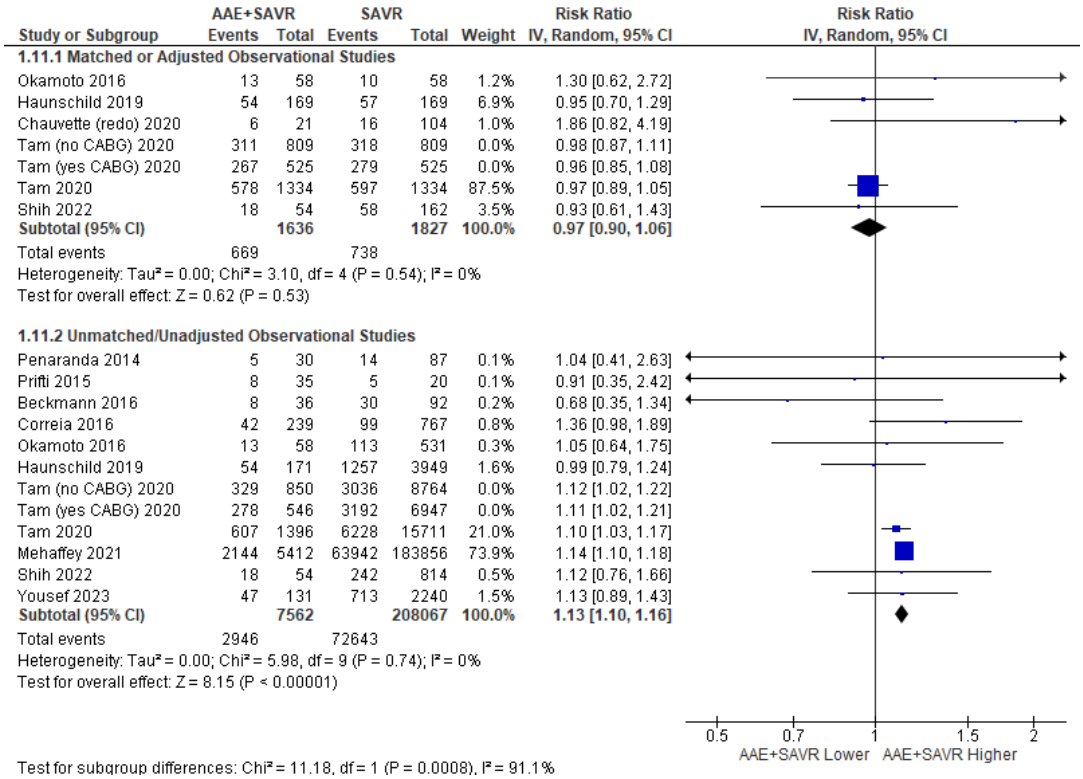


**Figure S12** Forest plot for diabetes.

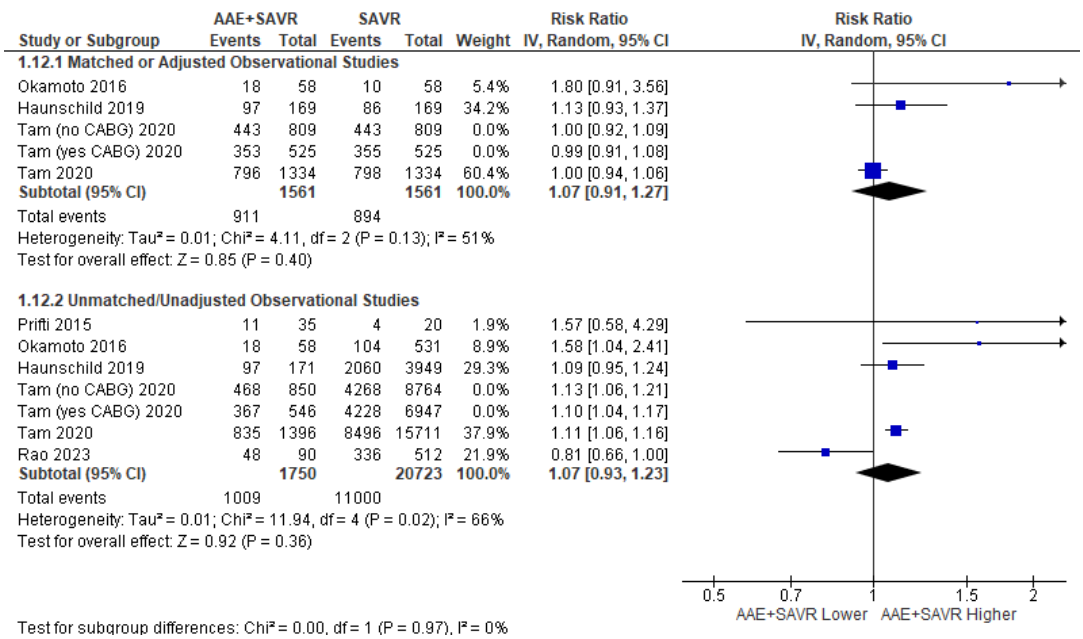


**Figure S13** Forest plot for dyslipidemia.


https://dx.doi.org/10.21037/acs-2024-aae-0023

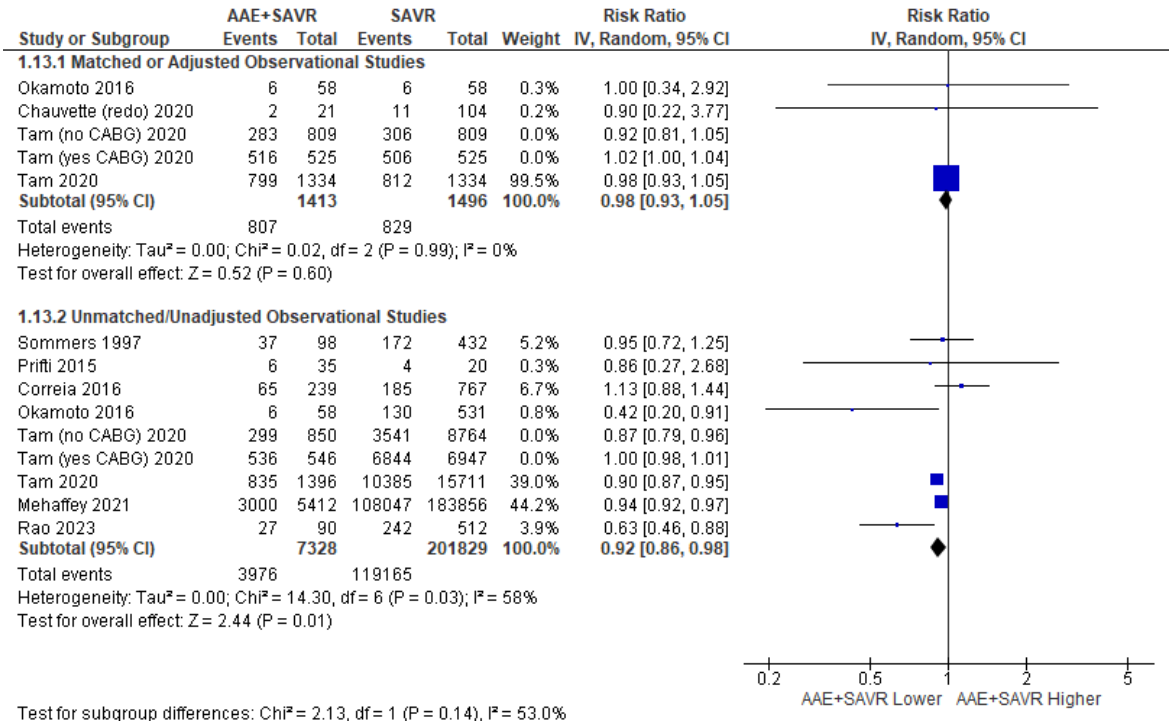


**Figure S14** Forest plot for coronary artery disease.

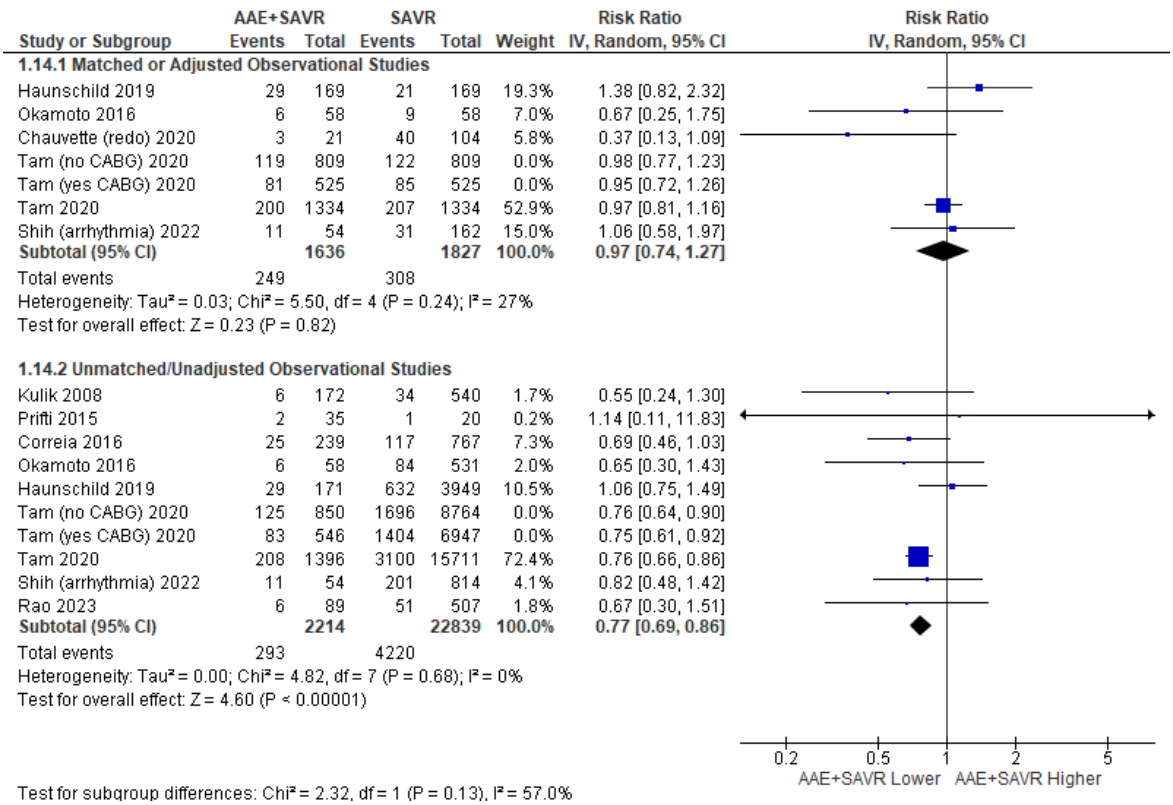


**Figure S15** Forest plot for preoperative atrial fibrillation.


https://dx.doi.org/10.21037/acs-2024-aae-0023

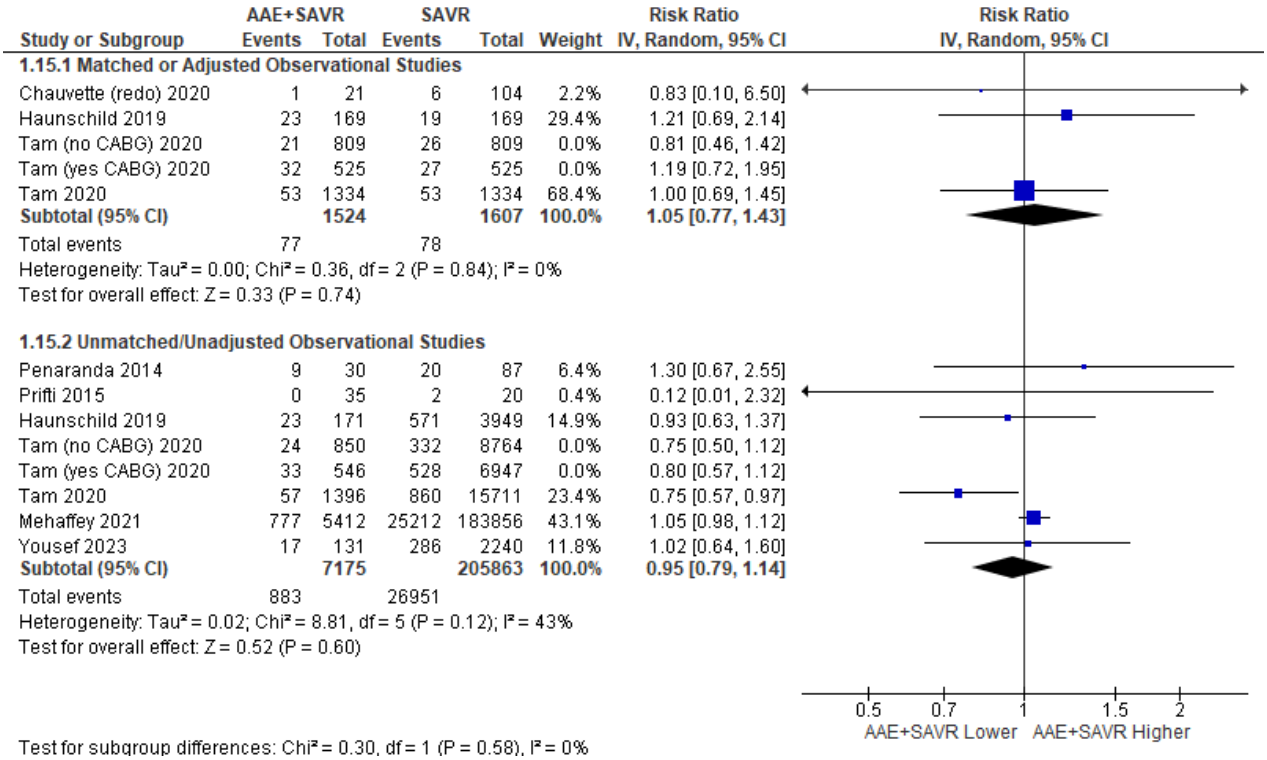


**Figure S16** Forest plot for peripheral vascular disease.

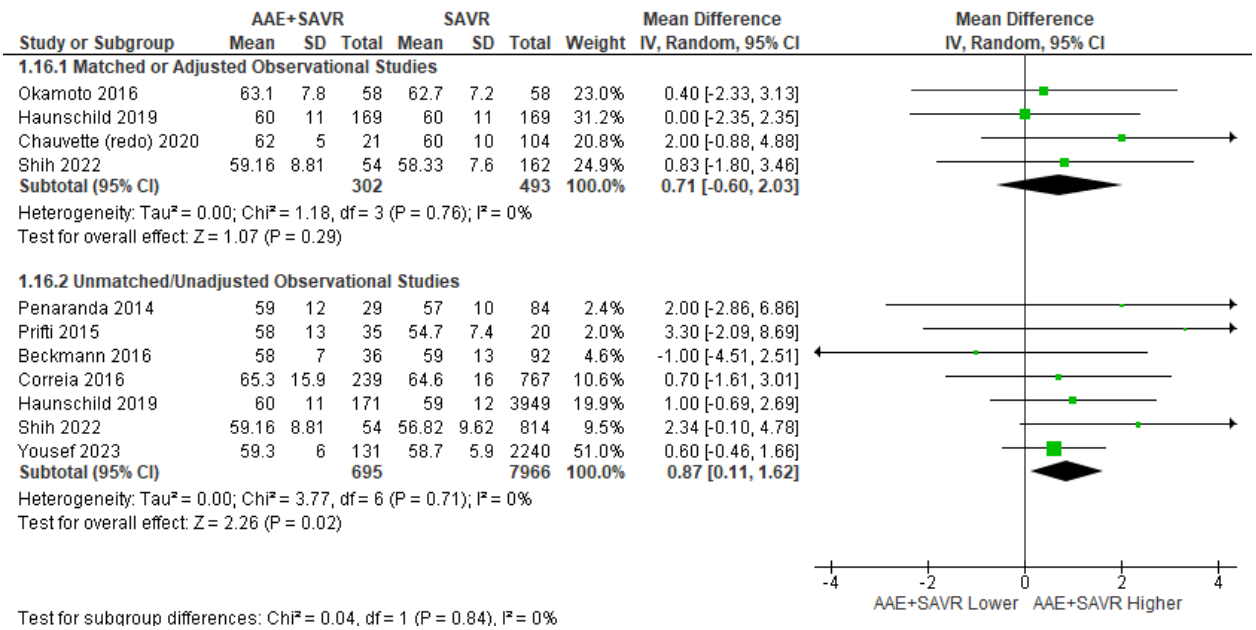


**Figure S17** Forest plot for left ventricular ejection fraction (LVEF, %).


https://dx.doi.org/10.21037/acs-2024-aae-0023

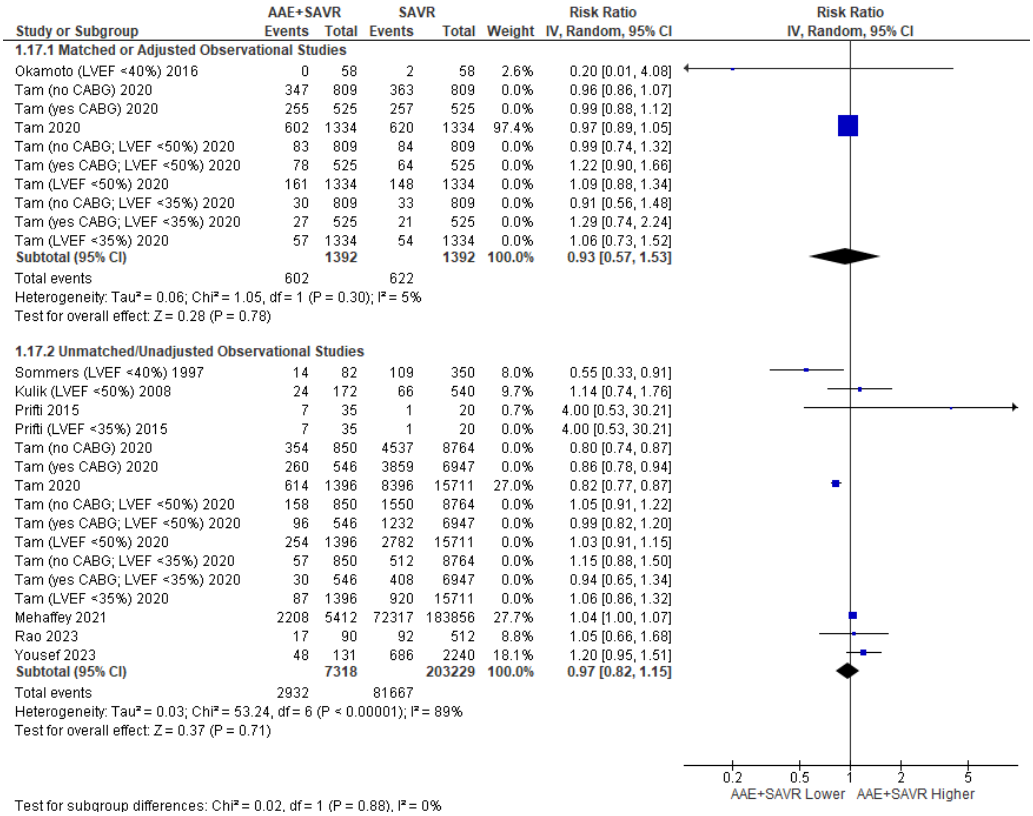


**Figure S18** Forest plot for CHF or low LVEF.

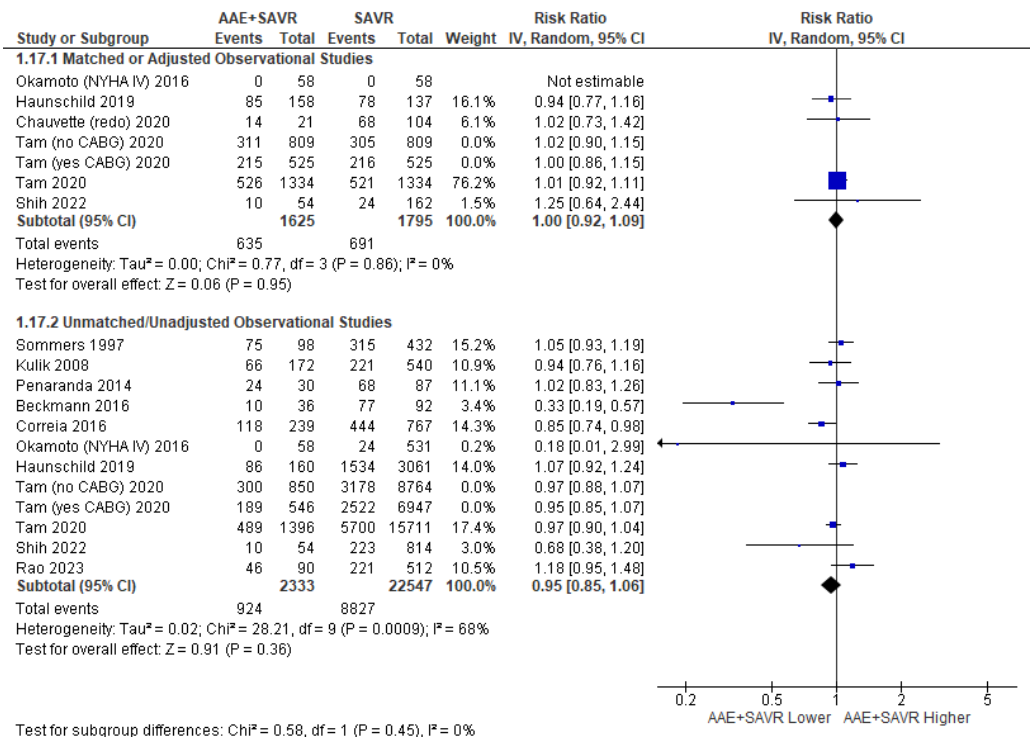


**Figure S19** Forest plot for NYHA III or IV.


https://dx.doi.org/10.21037/acs-2024-aae-0023

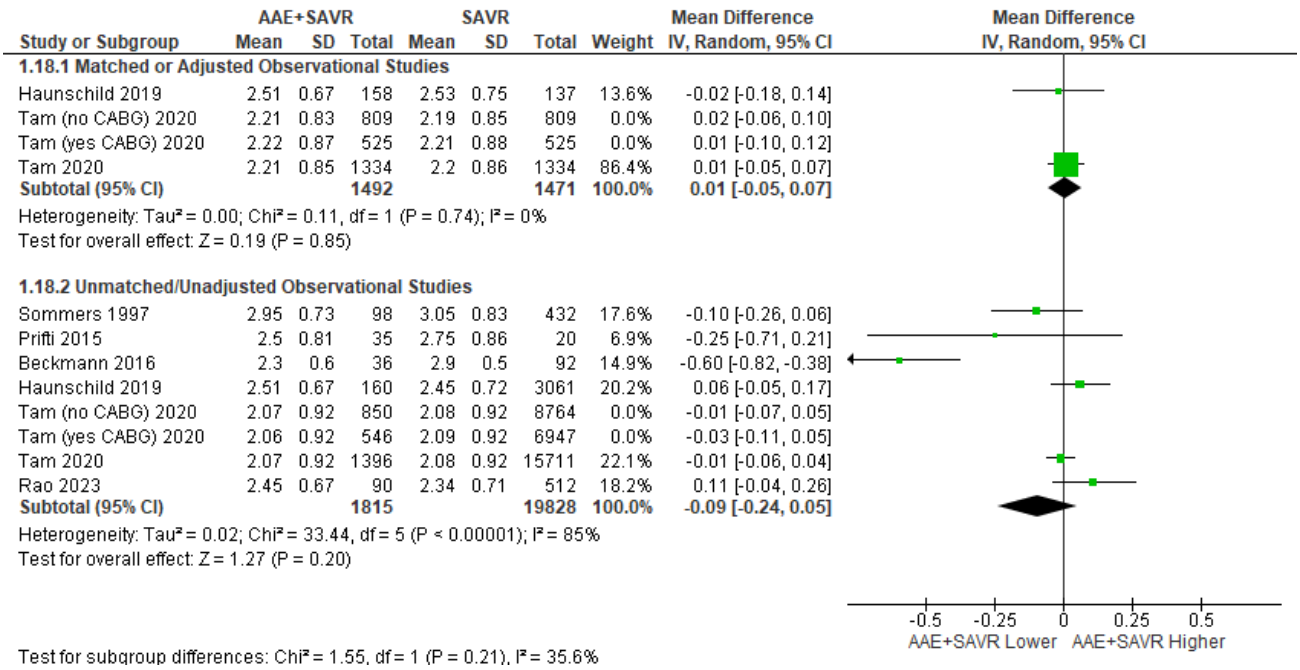


**Figure S20** Forest plot for mean NYHA grade.

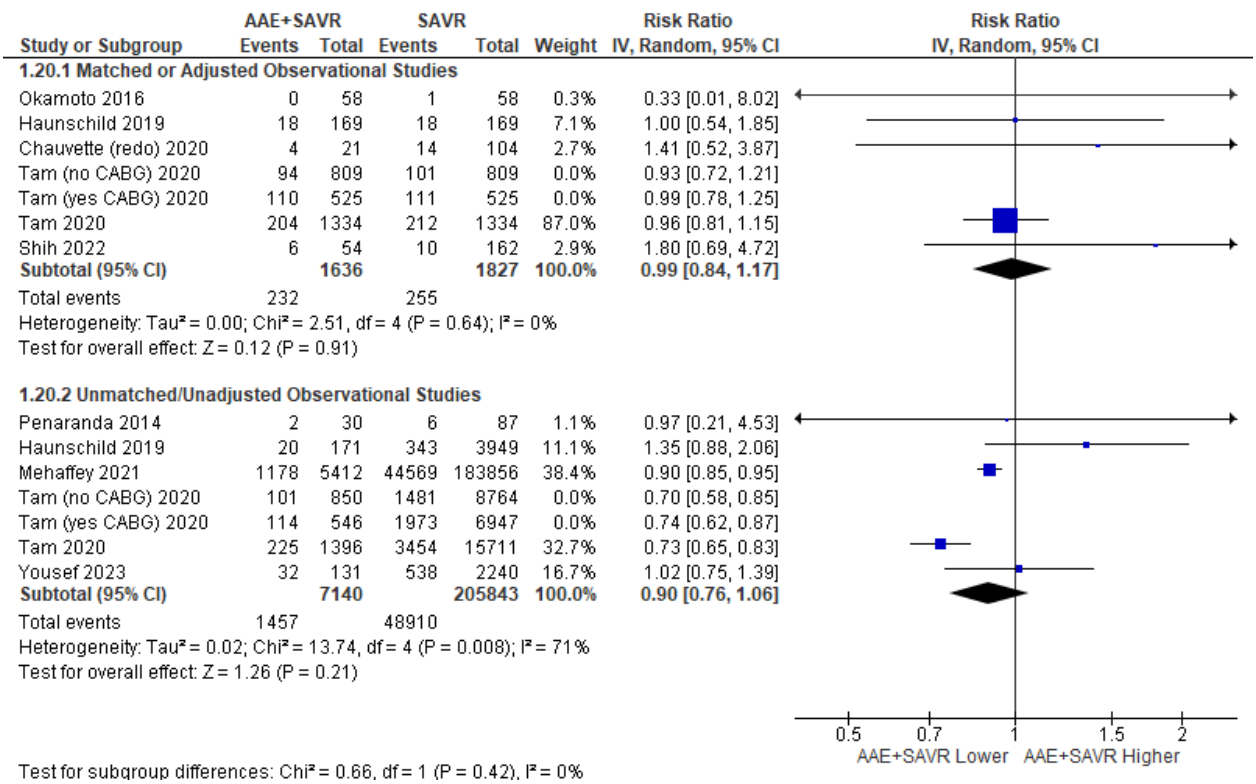


**Figure S21** Forest plot for non-elective surgery.


https://dx.doi.org/10.21037/acs-2024-aae-0023

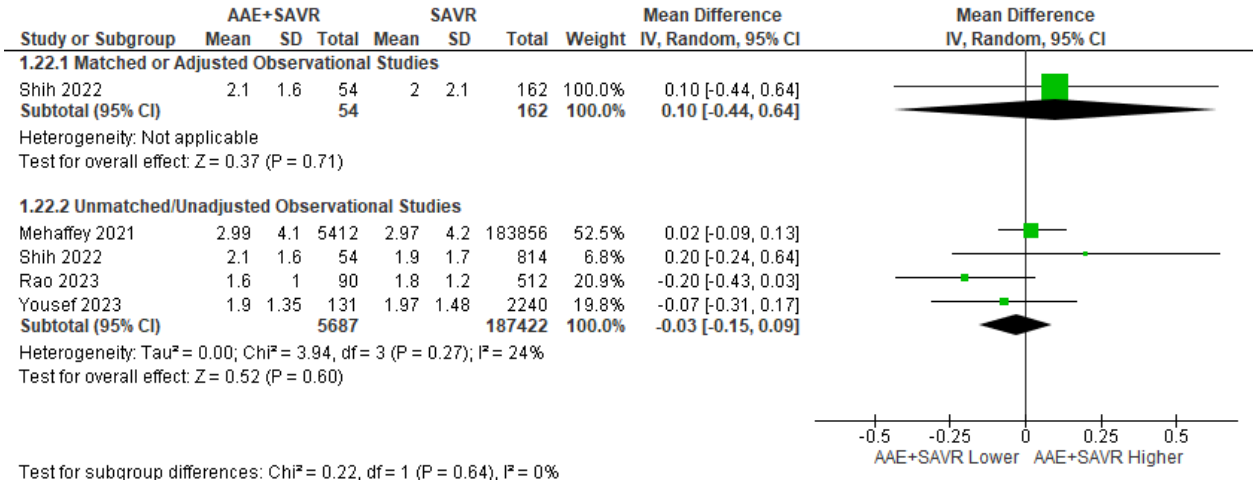


**Figure S22** Forest plot for Society of Thoracic Surgeons (STS) score (%).

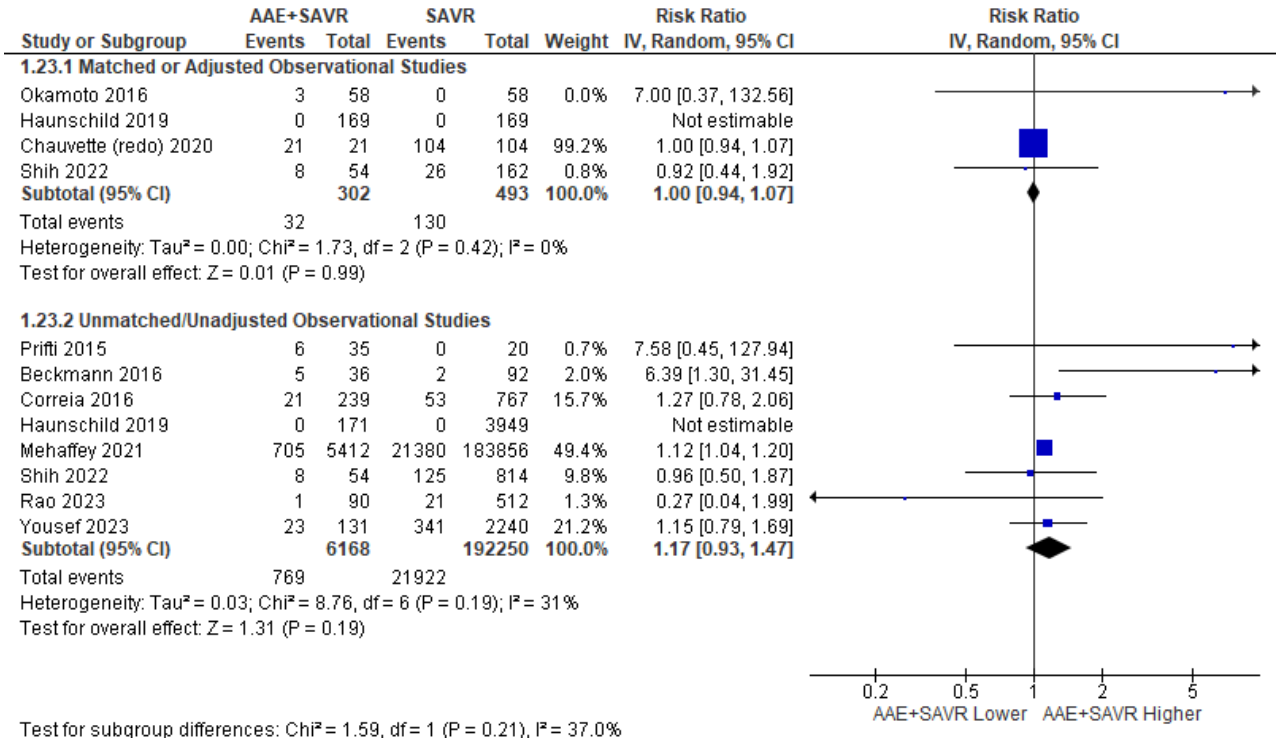


**Figure S23** Forest plot for prior cardiac surgery.


https://dx.doi.org/10.21037/acs-2024-aae-0023

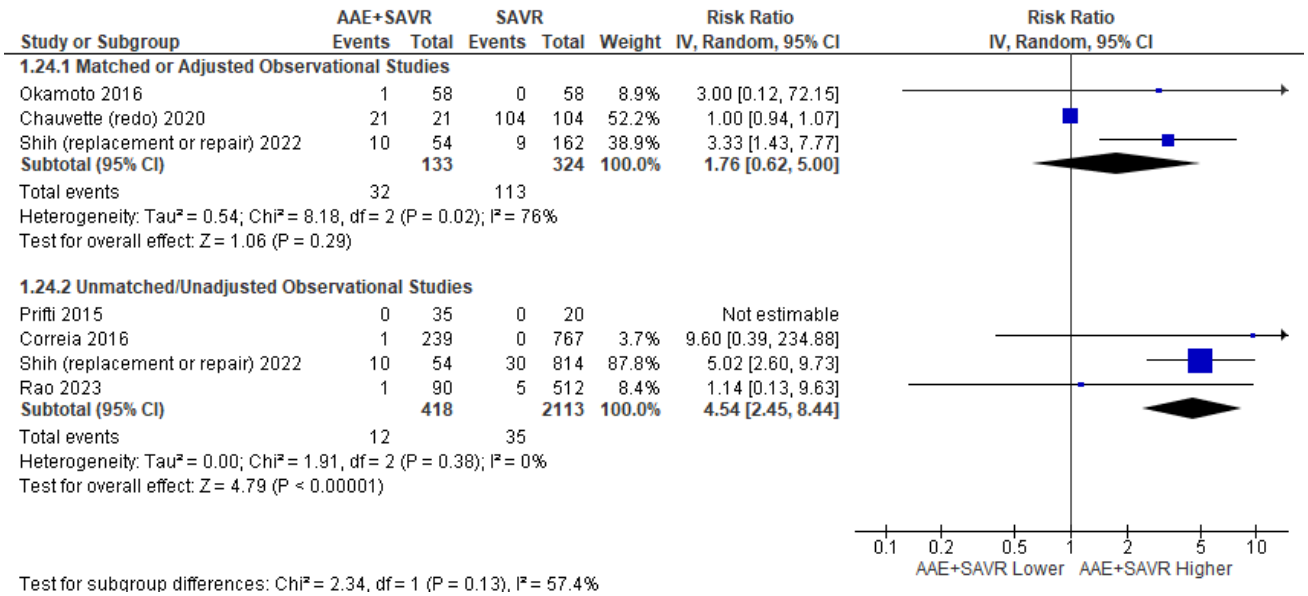


**Figure S24** Forest plot for prior SAVR.

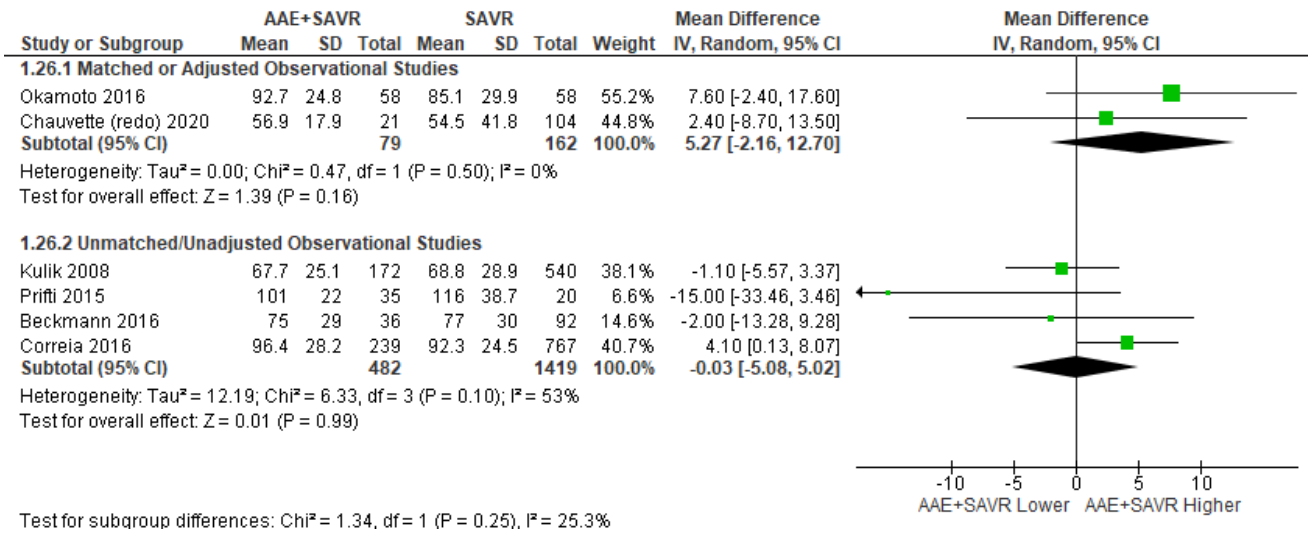


**Figure S25** Forest plot for peak aortic gradient (mm Hg).


https://dx.doi.org/10.21037/acs-2024-aae-0023

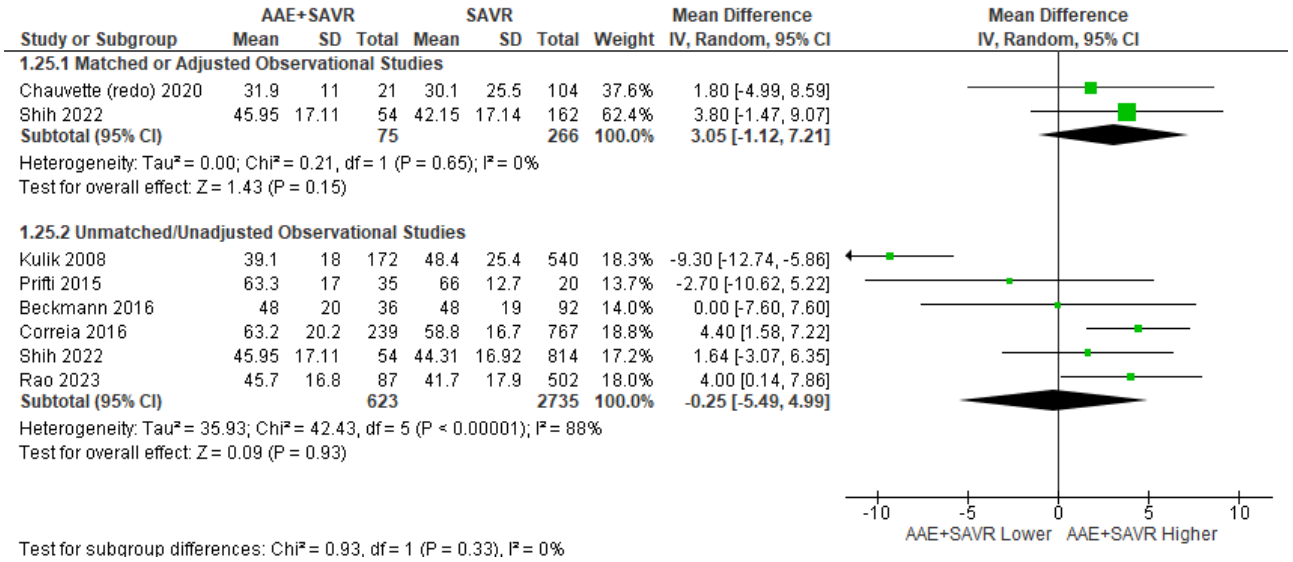


**Figure S26** Forest plot for mean aortic gradient (mm Hg).

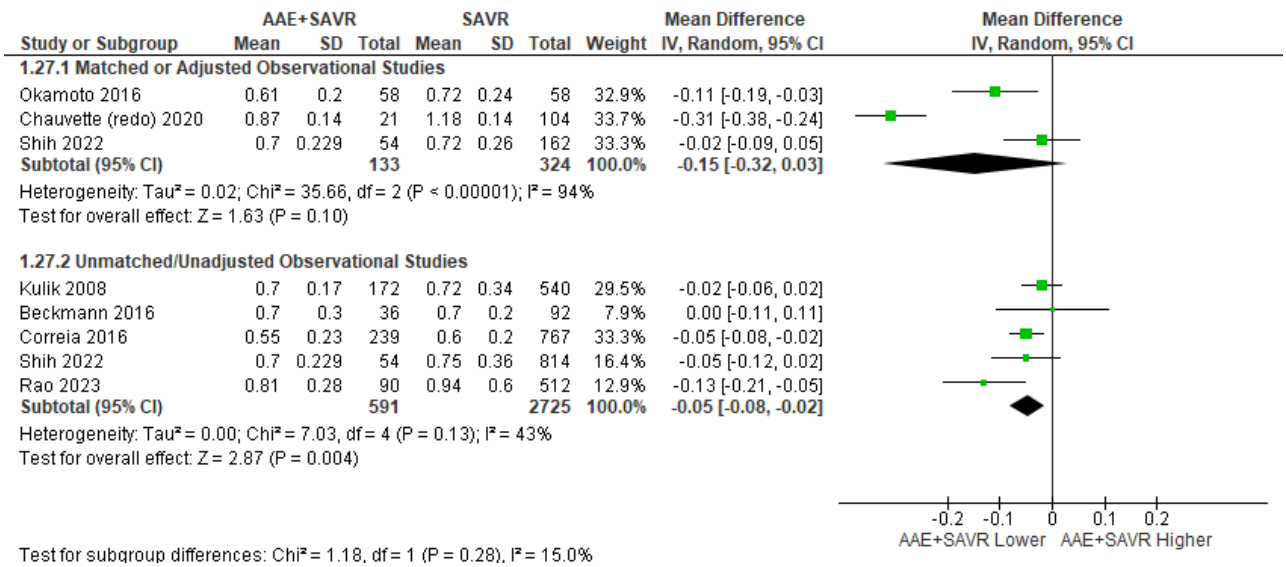


**Figure S27** Forest plot for aortic valve area ($cm^2$).


https://dx.doi.org/10.21037/acs-2024-aae-0023

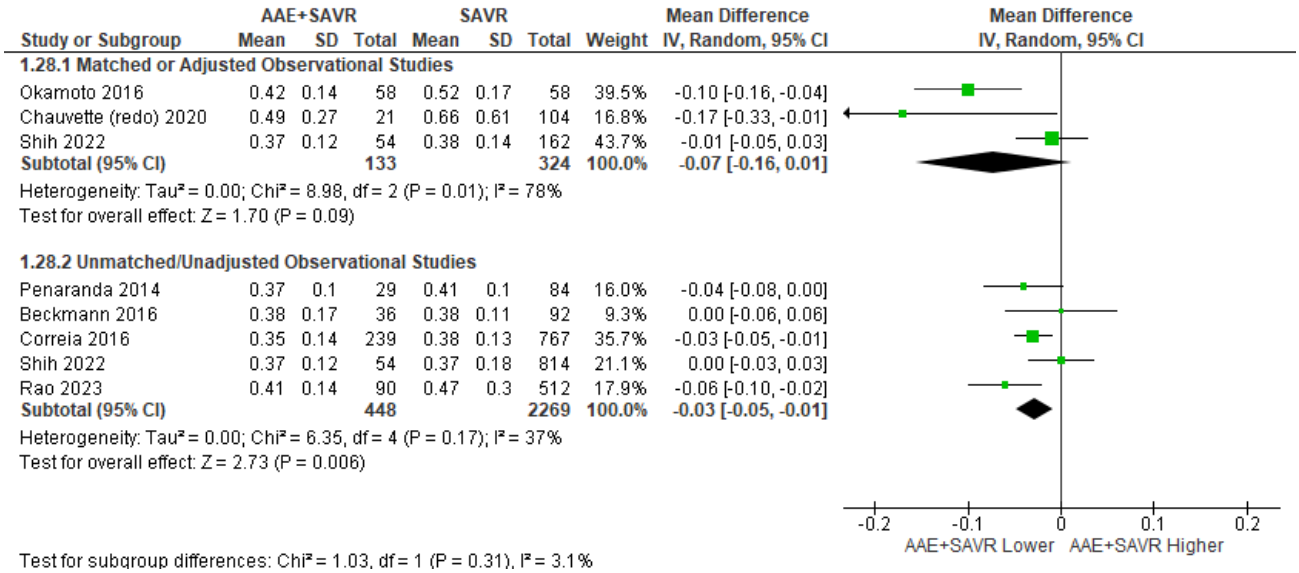


**Figure S28** Forest plot for indexed effective orifice area ($cm^2/m^2$).

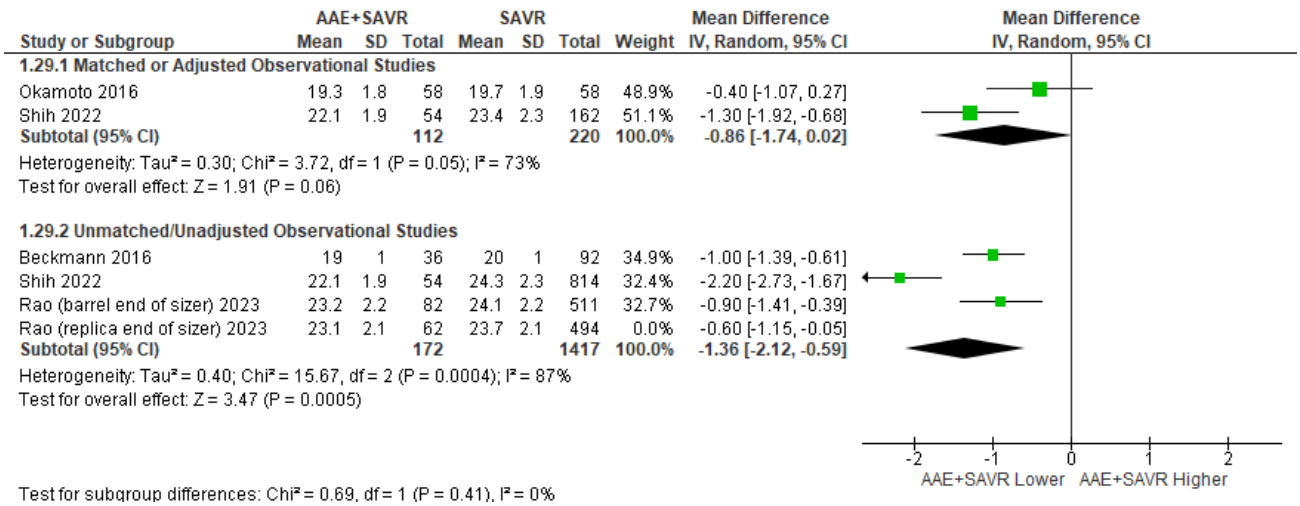


**Figure S29** Forest plot for aortic annular diameter (mm).


https://dx.doi.org/10.21037/acs-2024-aae-0023

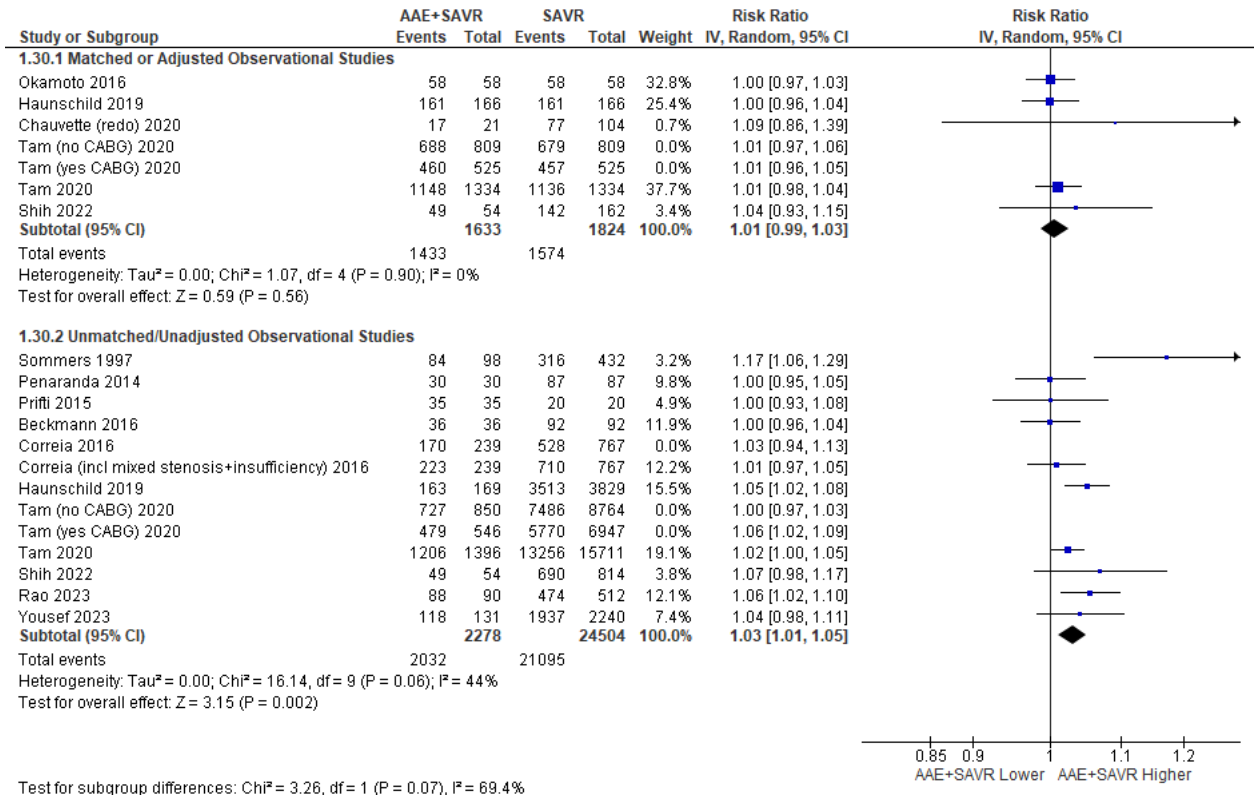


**Figure S30** Forest plot for aortic stenosis [including mixed stenosis and insufficiency] vs insufficiency.

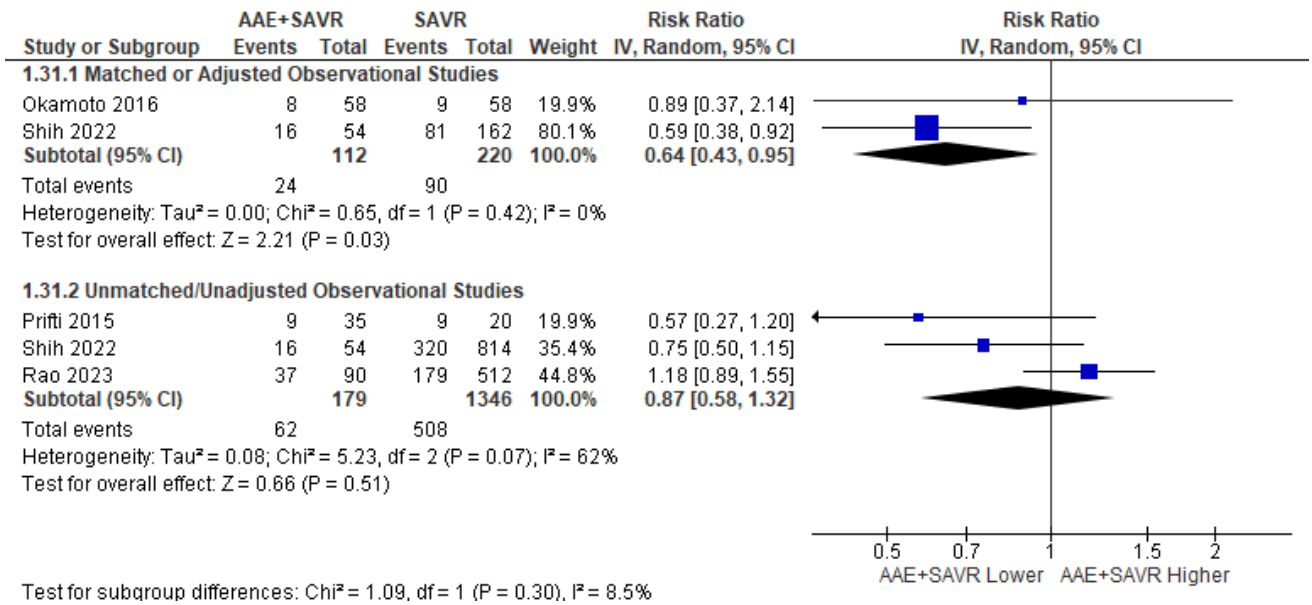


**Figure S31** Forest plot for bicuspid aortic valve.


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## Figures S32-S39. Meta-analyses for operative outcomes

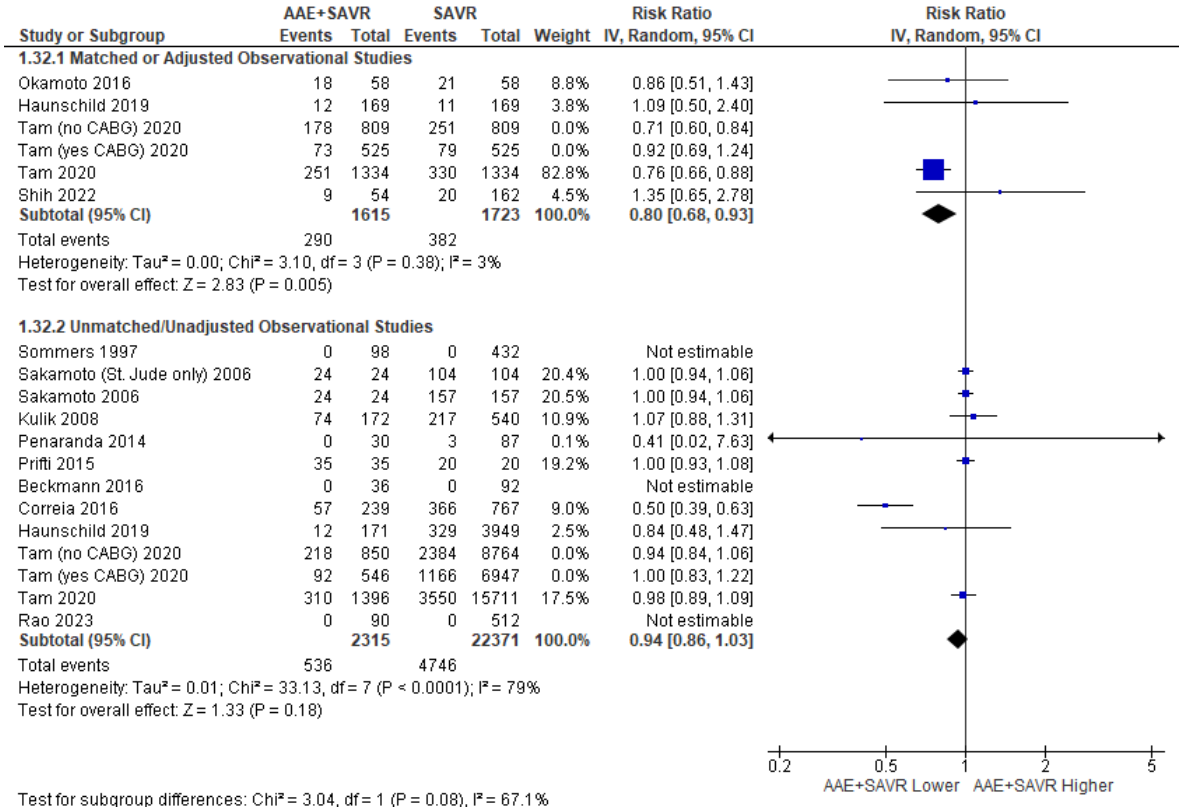


**Figure S32** Forest plot for mechanical *vs.* bioprosthetic aortic valve replacement.

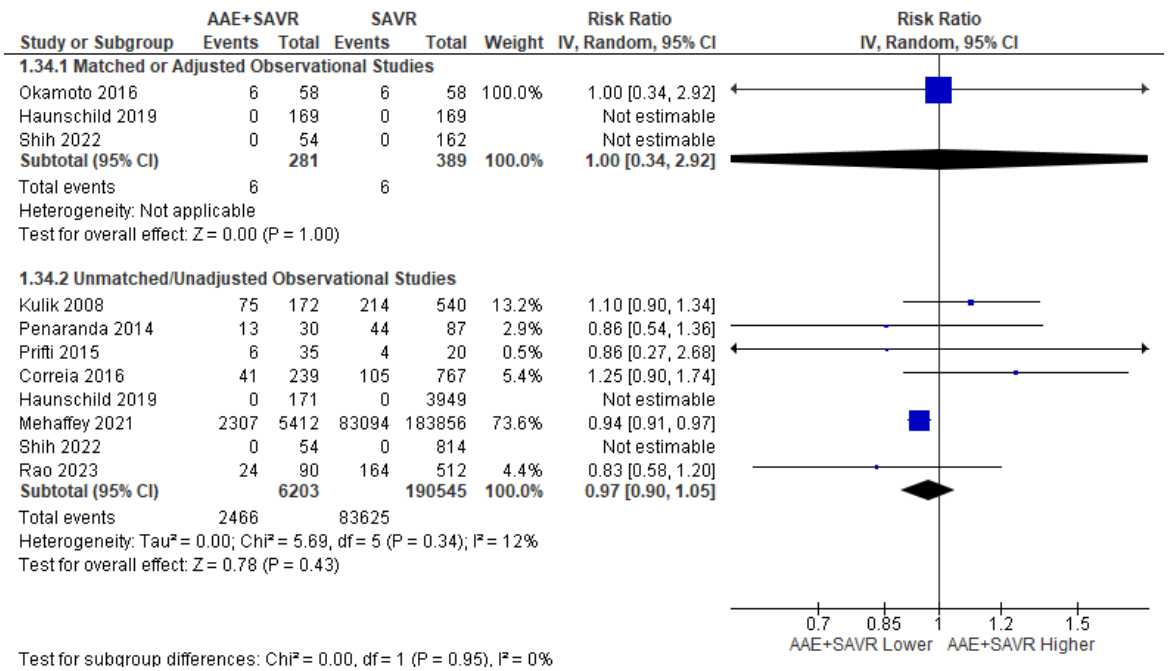


**Figure S33** Forest plot for concomitant CABG.


https://dx.doi.org/10.21037/acs-2024-aae-0023

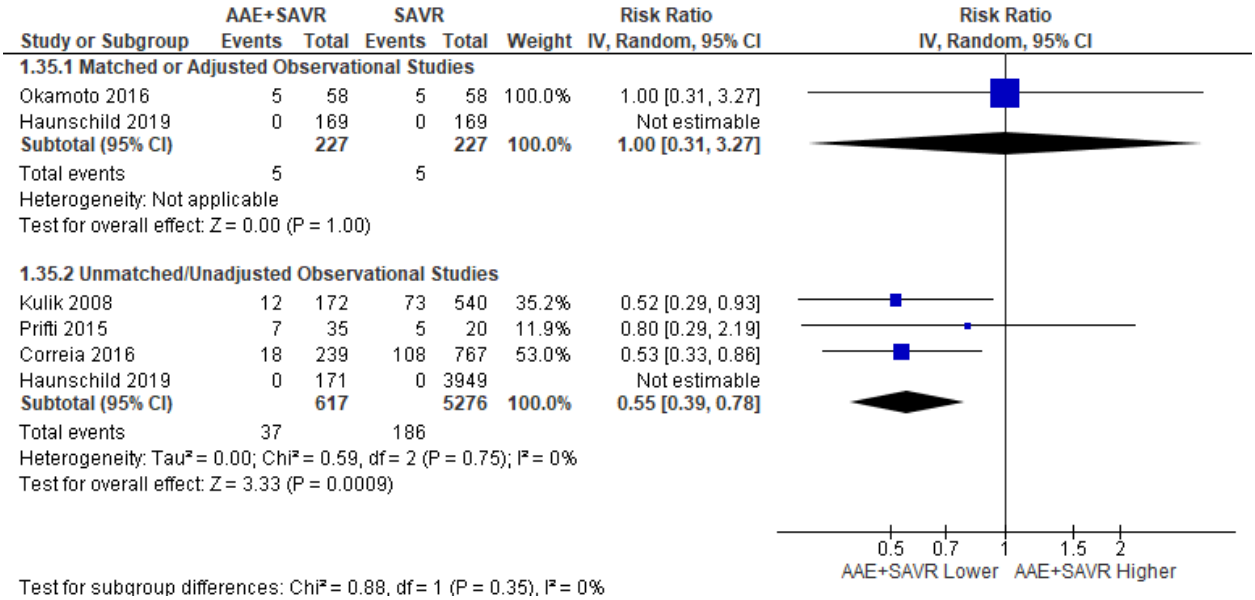


**Figure S34** Forest plot for concomitant mitral valve surgery.

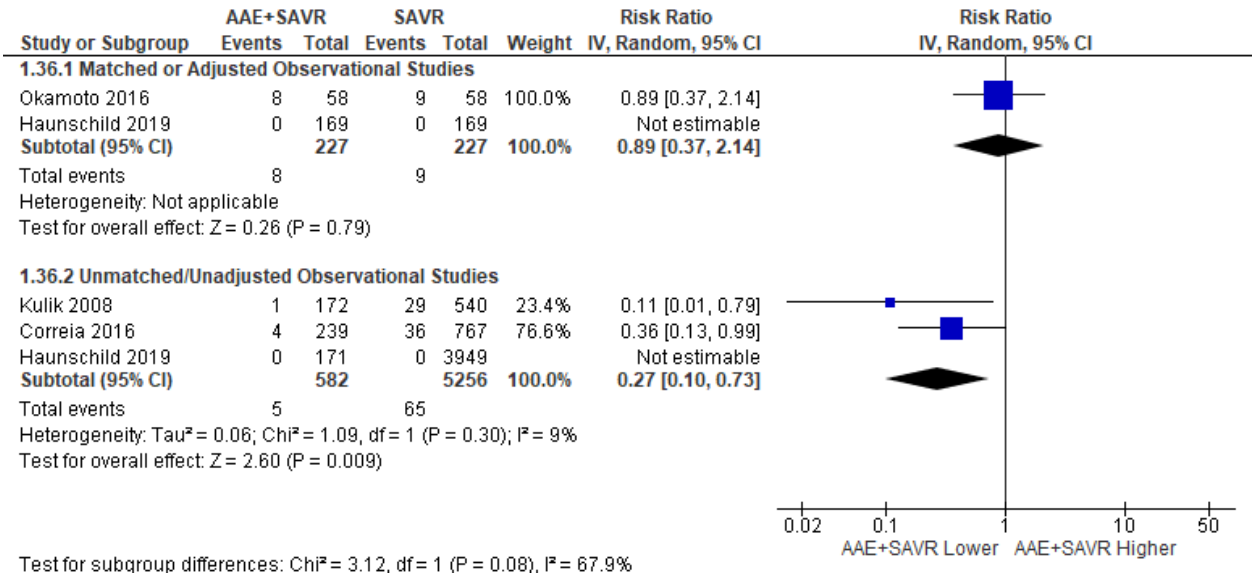


**Figure S35** Forest plot for concomitant tricuspid valve surgery.


https://dx.doi.org/10.21037/acs-2024-aae-0023

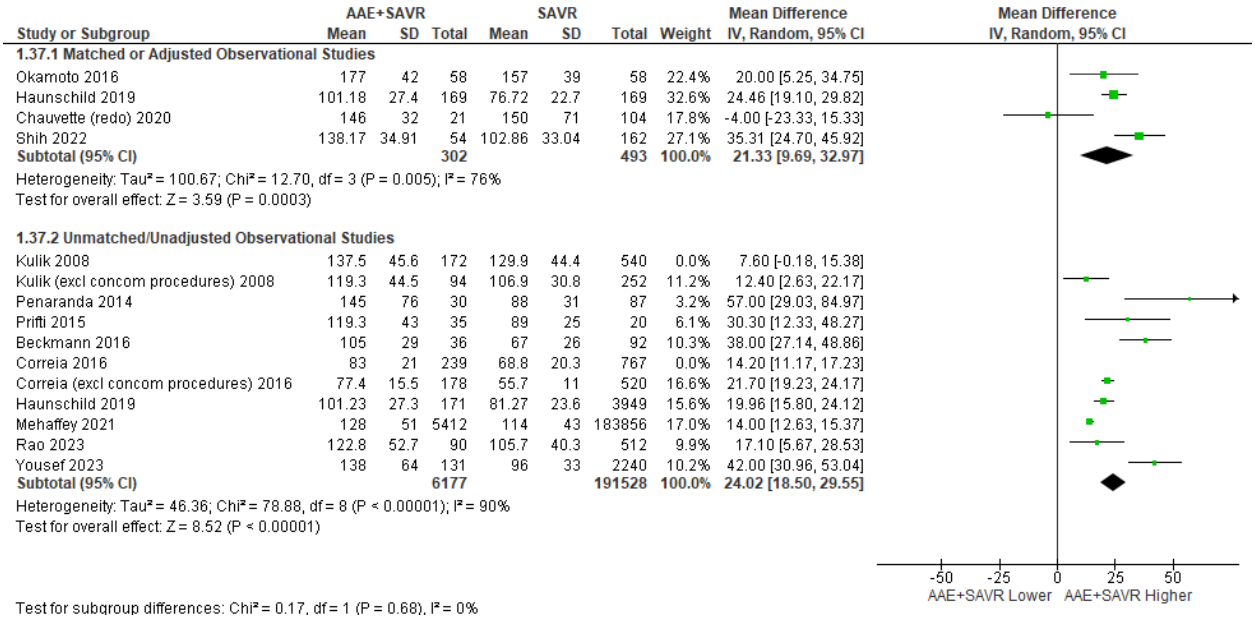


**Figure S36** Forest plot for cardiopulmonary bypass time (min).

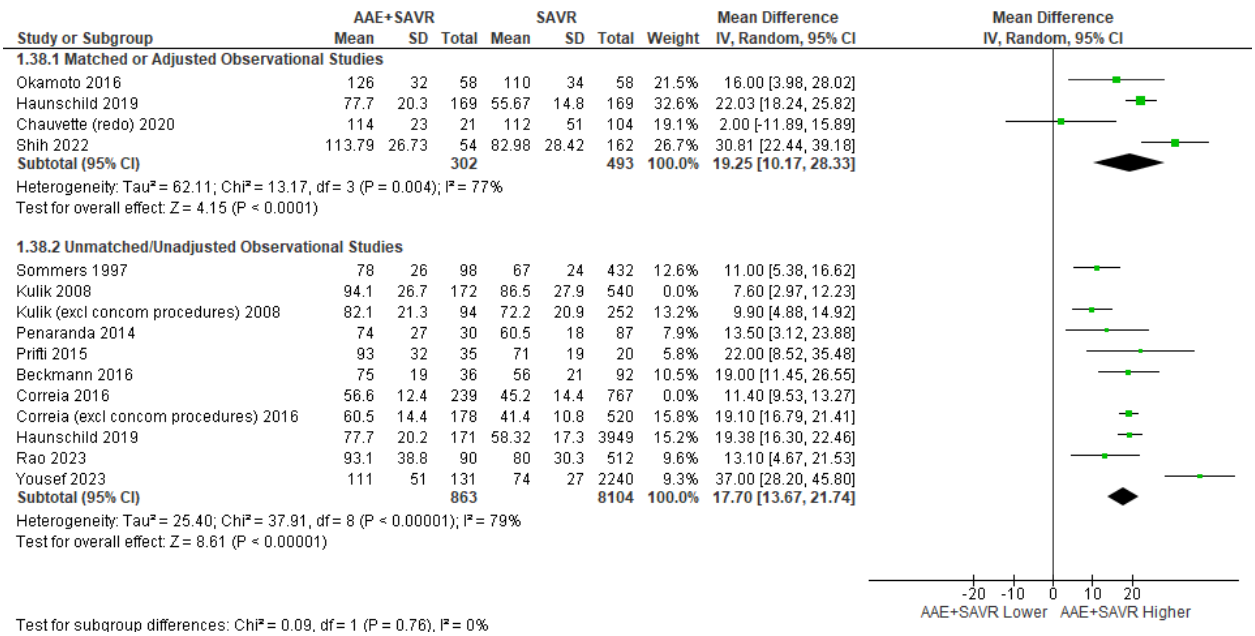


**Figure S37** Forest plot for aortic cross clamp time (min).


https://dx.doi.org/10.21037/acs-2024-aae-0023

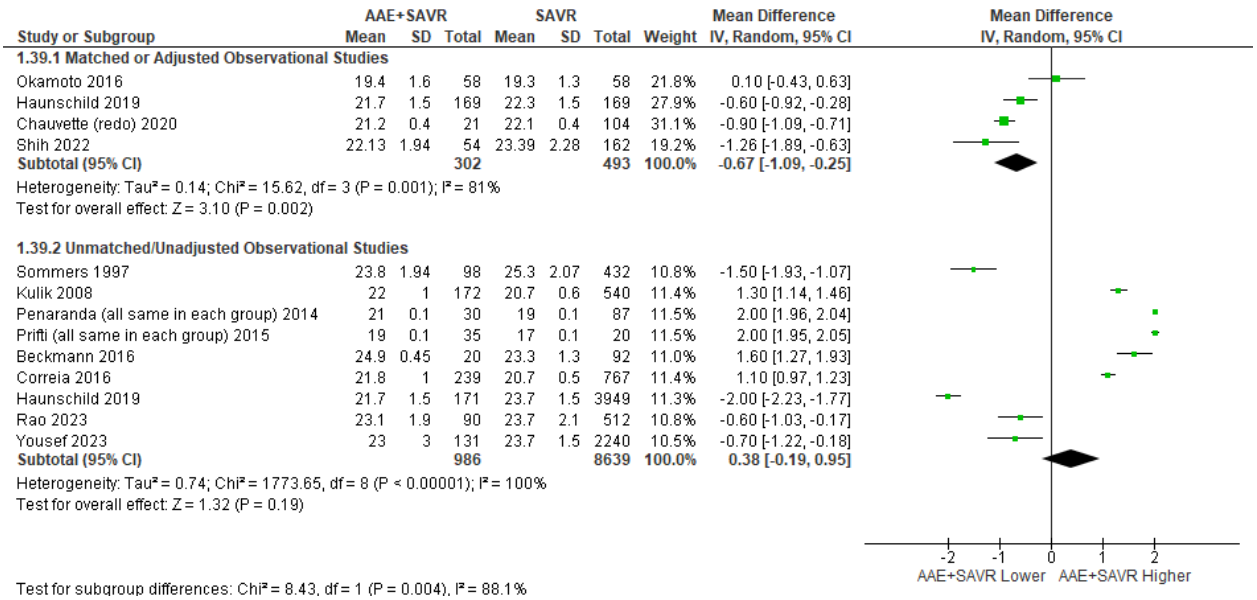


**Figure S38** Forest plot for aortic prosthesis size (mm) with arbitrary small standard deviation of 0.1 imputed for Penaranda 2014 and Prifti 2015 to allow inclusion in the pooled analysis. These studies would otherwise be excluded in the pooled analysis as each group received only one prosthesis size for these two studies resulting in zero standard deviations.

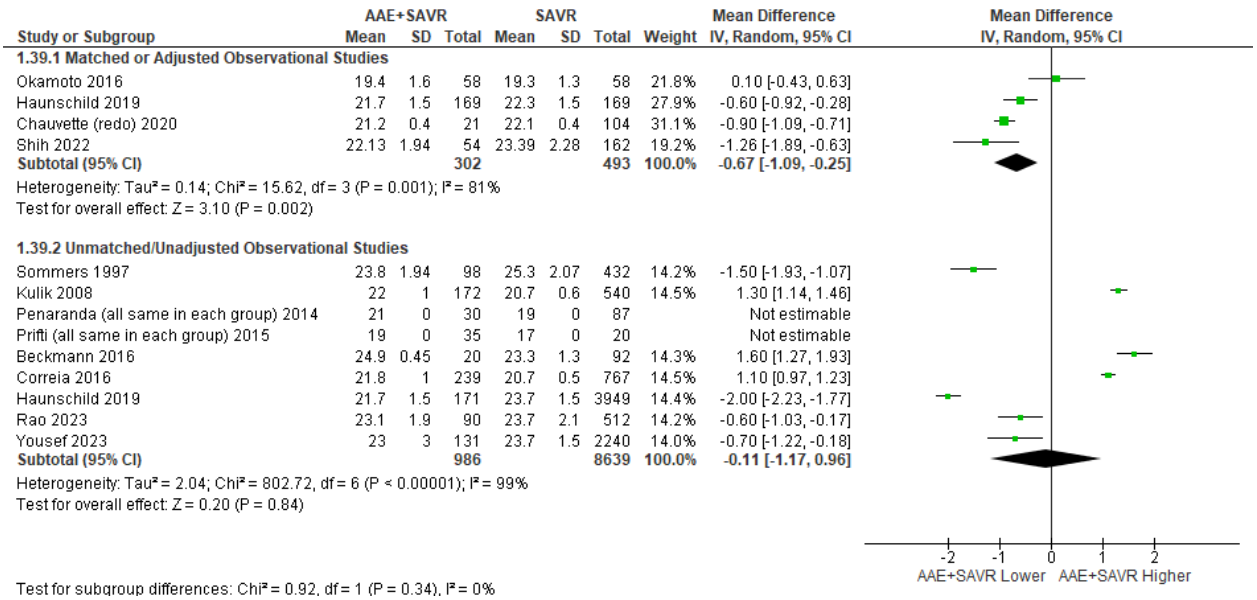


**Figure S39** Forest plot for aortic prosthesis size (mm) without imputed standard deviations from (thereby excluding) Penaranda 2014 and Prifti 2015.


https://dx.doi.org/10.21037/acs-2024-aae-0023

## Figures S40-S55. Meta-analyses for early postoperative outcomes

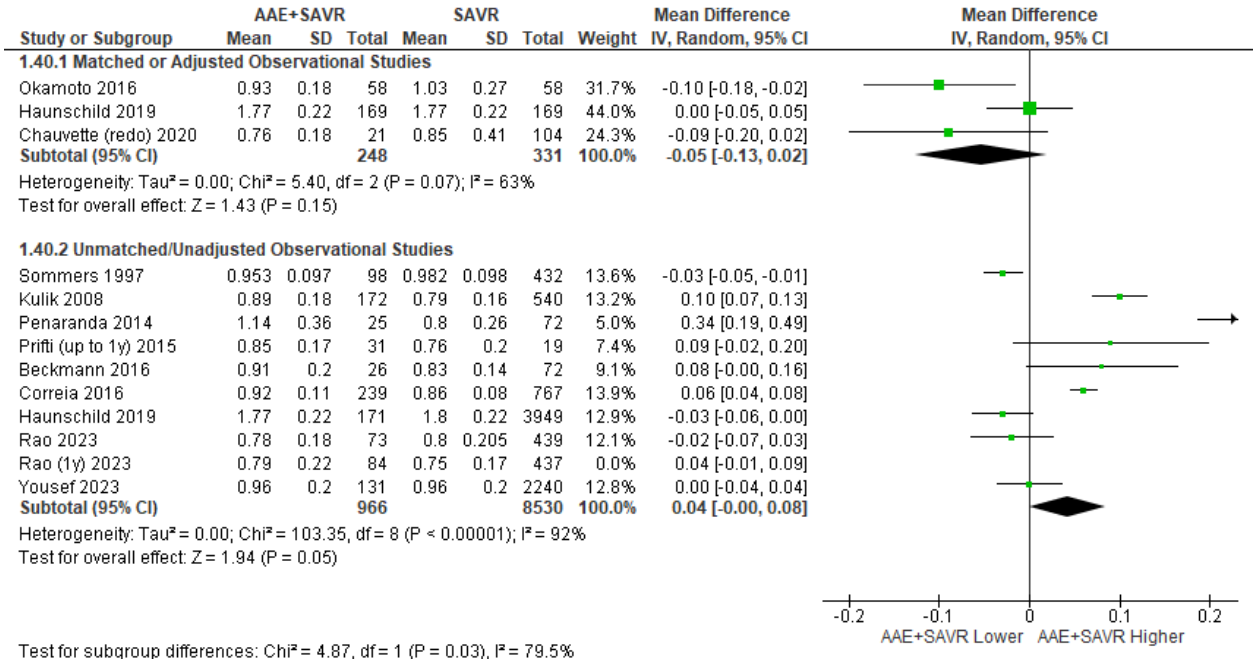


**Figure S40** Forest plot for postoperative indexed effective orifice area ($cm^2/m^2$).

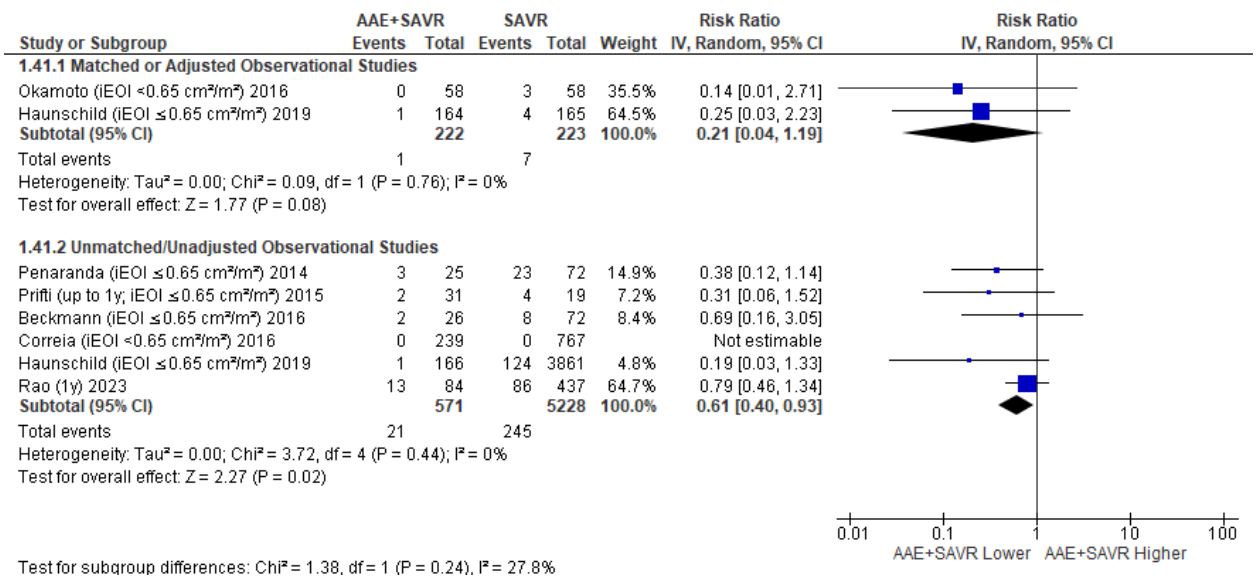


**Figure S41** Forest plot for severe patient-prosthesis mismatch (PPM).


https://dx.doi.org/10.21037/acs-2024-aae-0023

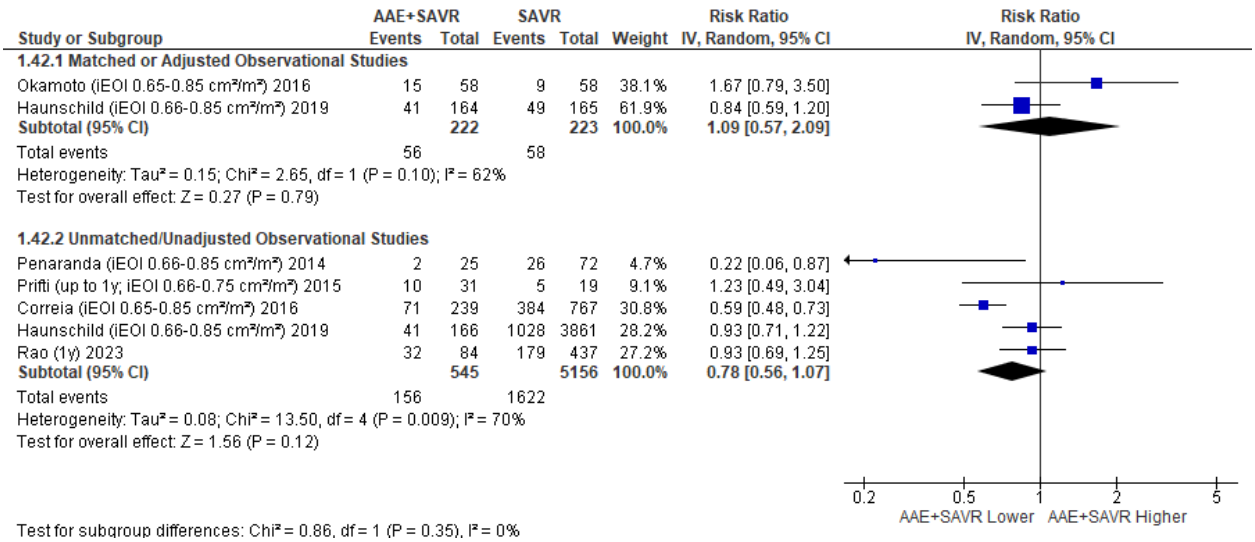


**Figure S42** Forest plot for moderate patient-prosthesis mismatch (PPM).

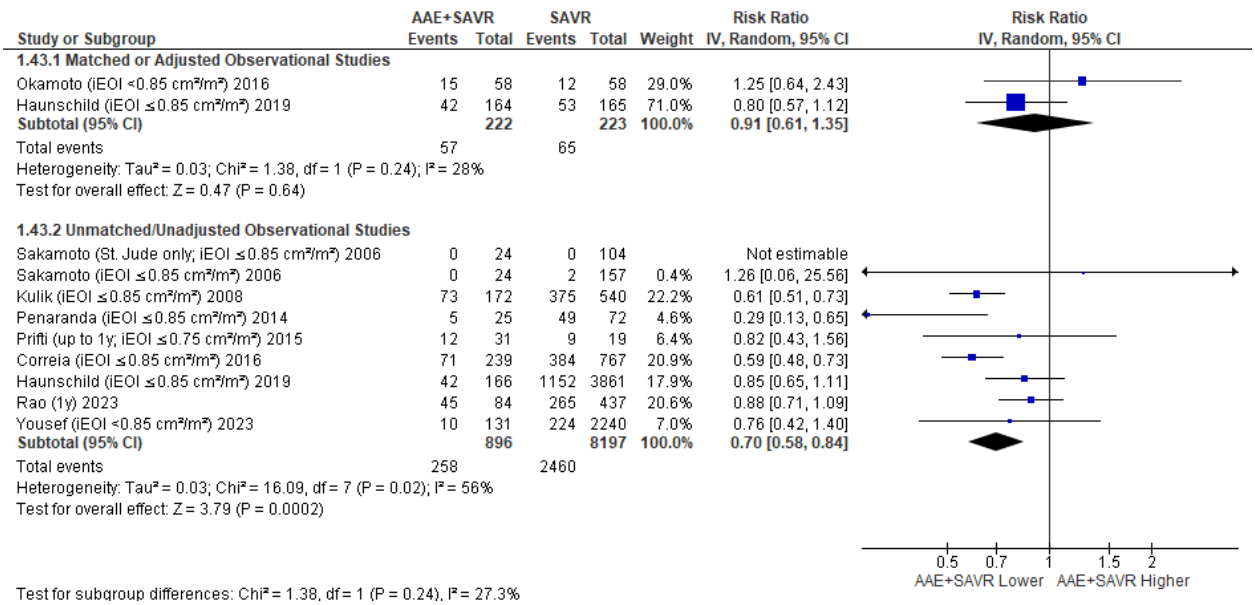


**Figure S43** Forest plot for moderate or severe patient-prosthesis mismatch (PPM).


https://dx.doi.org/10.21037/acs-2024-aae-0023

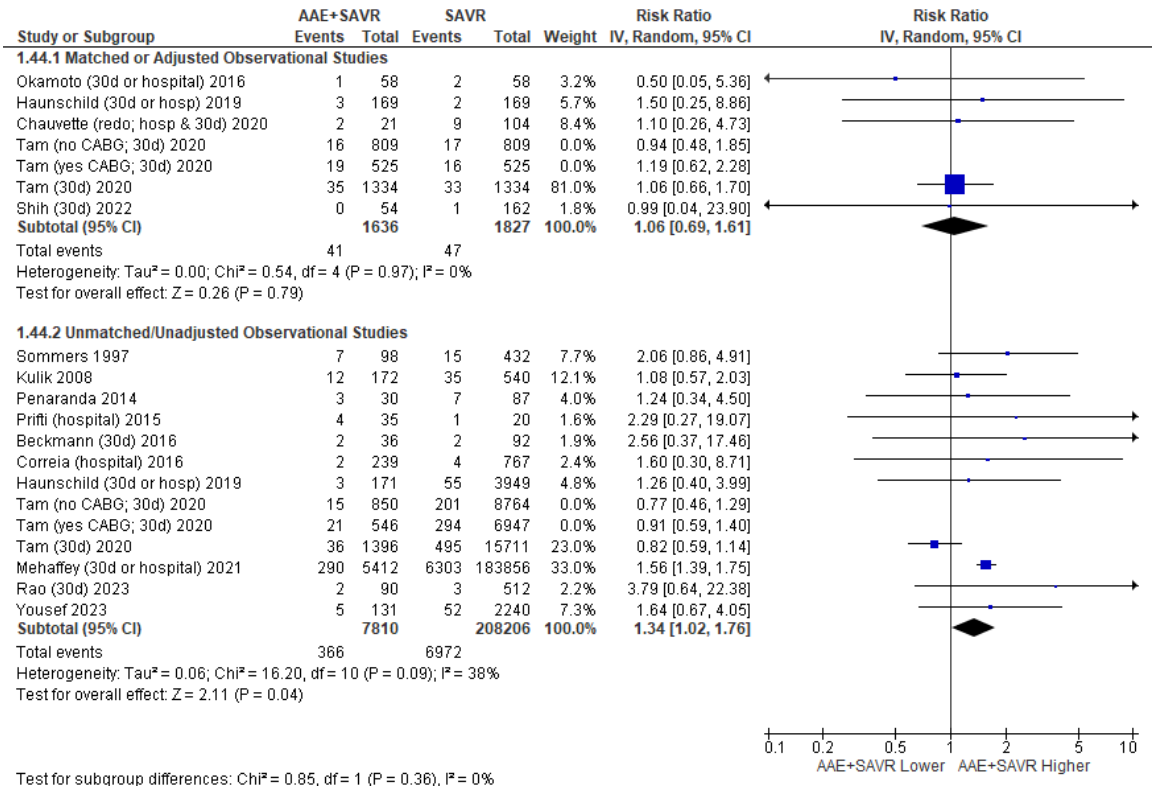


**Figure S44** Forest plot for perioperative mortality.


https://dx.doi.org/10.21037/acs-2024-aae-0023

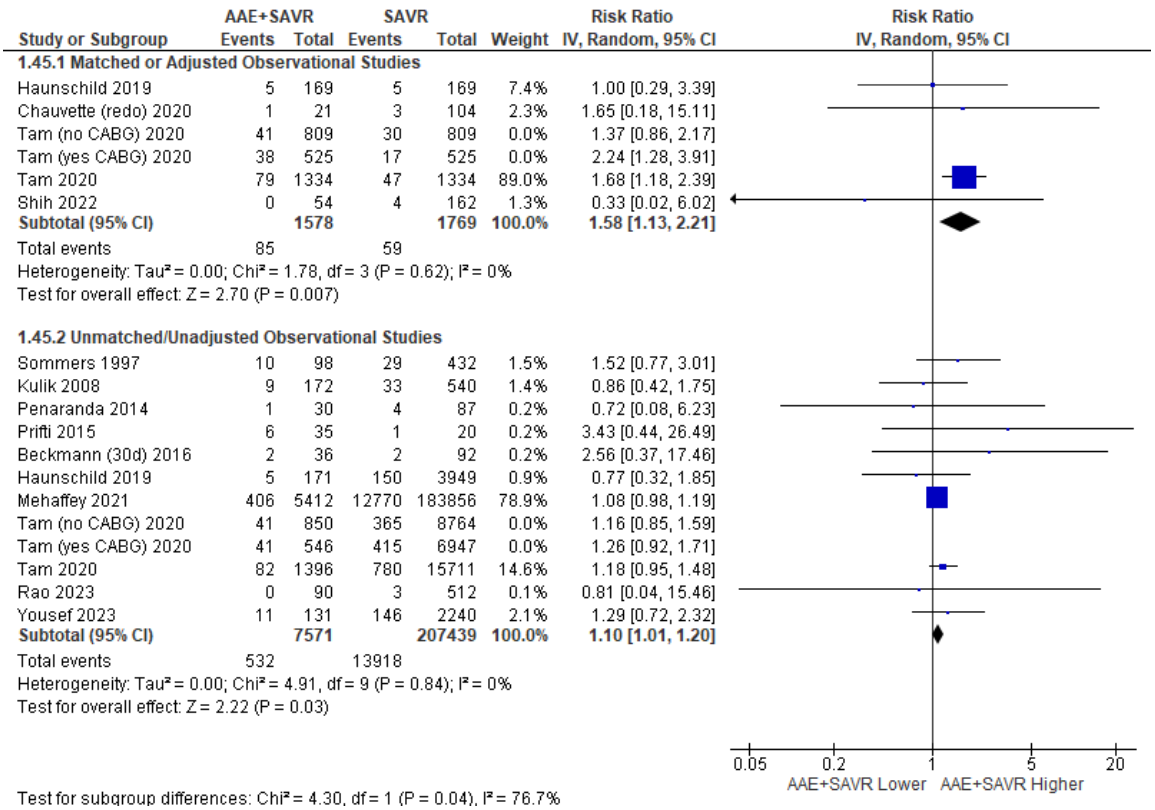


**Figure S45** Forest plot for perioperative chest reopening. Increased risk of perioperative chest reopening among the matched/adjusted studies was primarily due to the results of Tam 2020 which accounted for 89% of the weighting. Excluding Tam 2020, the pooled risk of chest reopening in the remaining matched/adjusted studies was no longer statistically significant (RR 0.97 [0.36, 2.65]).


https://dx.doi.org/10.21037/acs-2024-aae-0023

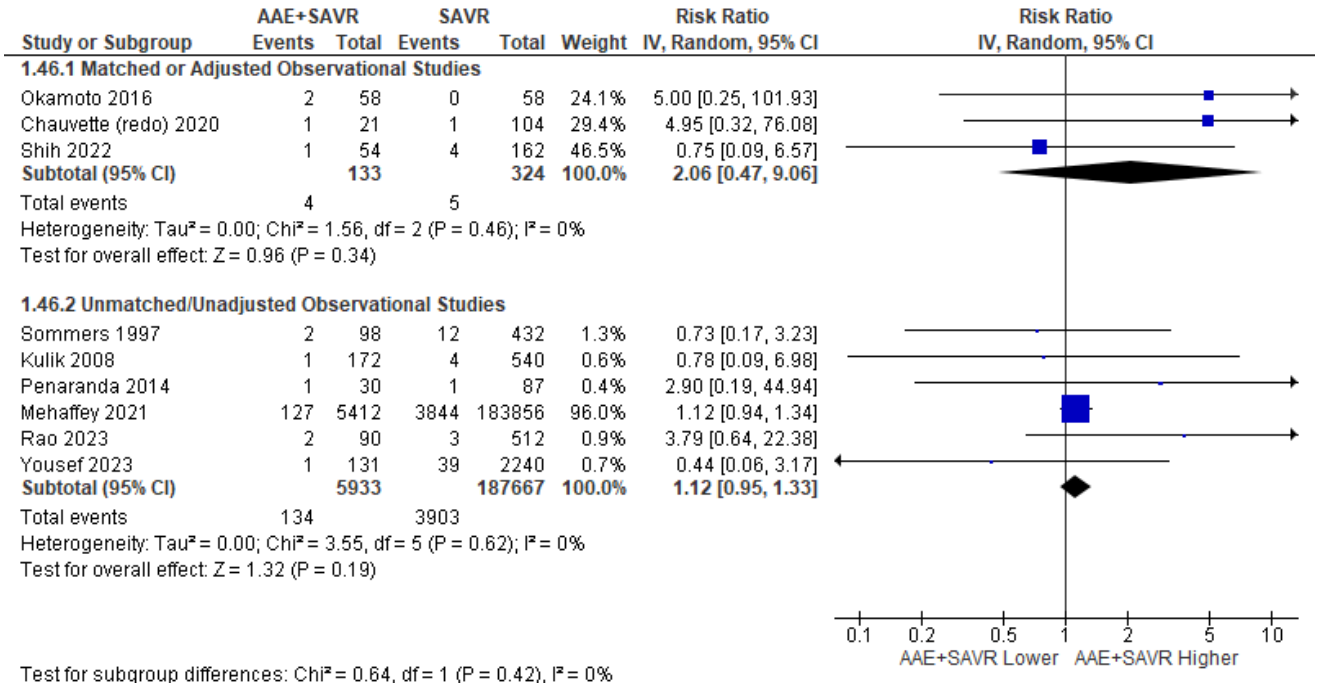


**Figure S46** Forest plot for perioperative stroke.

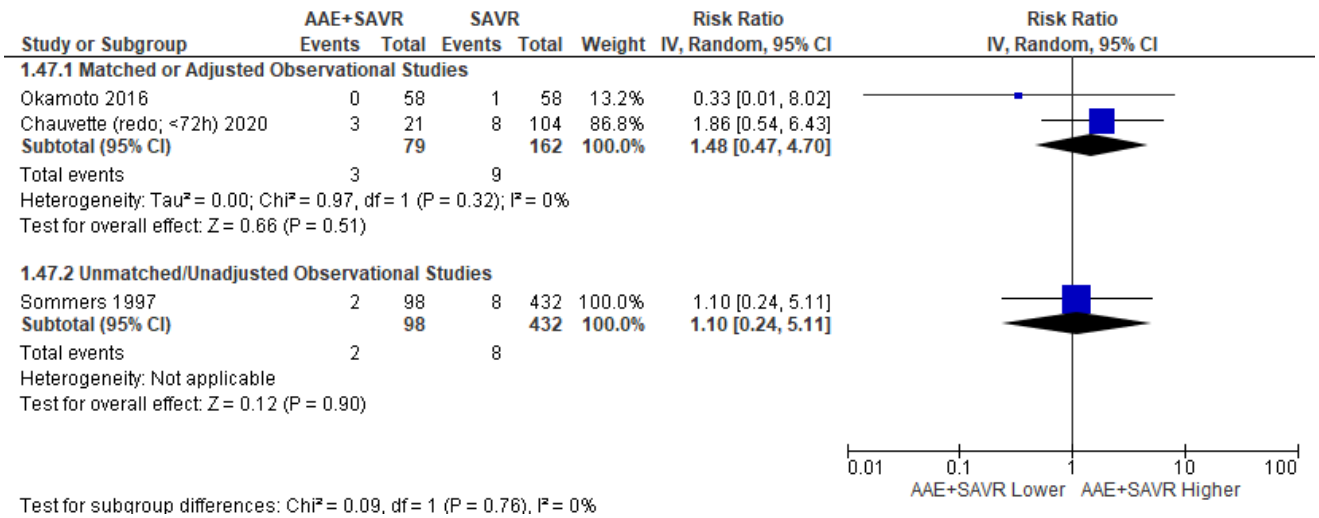


**Figure S47** Forest plot for perioperative myocardial infarction.


https://dx.doi.org/10.21037/acs-2024-aae-0023

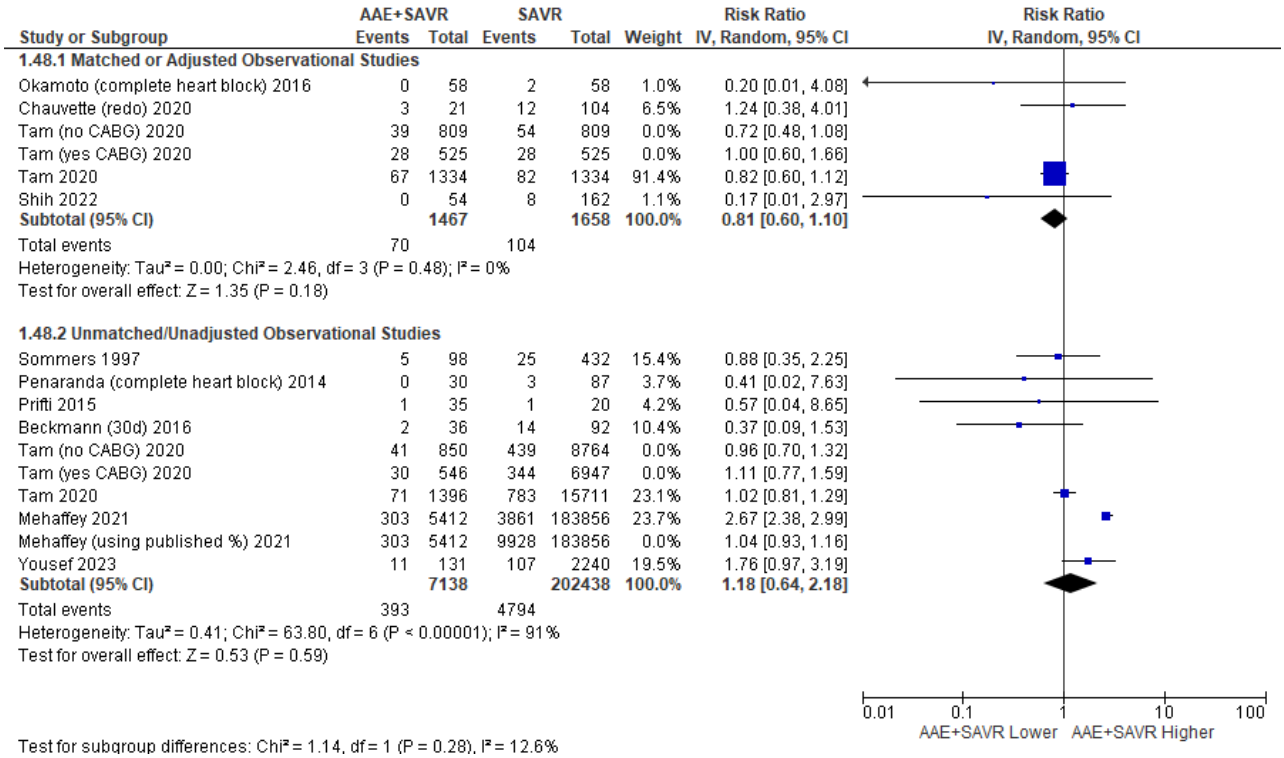


**Figure S48** Forest plot for perioperative new permanent pacemaker.

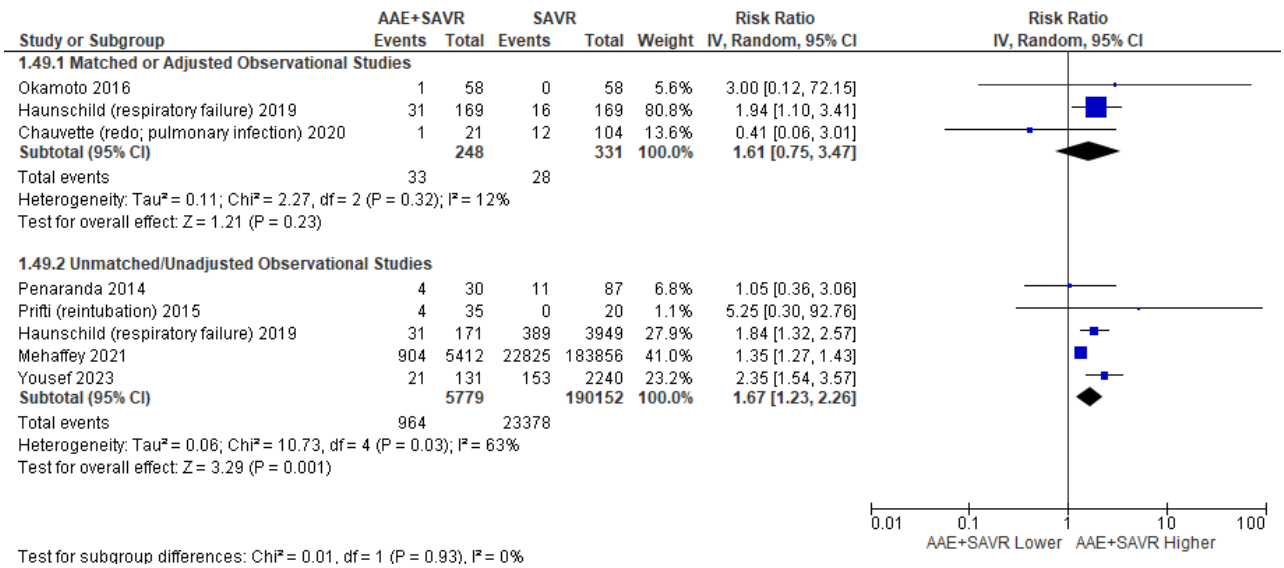


**Figure S49** Forest plot for prolonged mechanical ventilation (>24 hours) or other respiratory complications.


https://dx.doi.org/10.21037/acs-2024-aae-0023

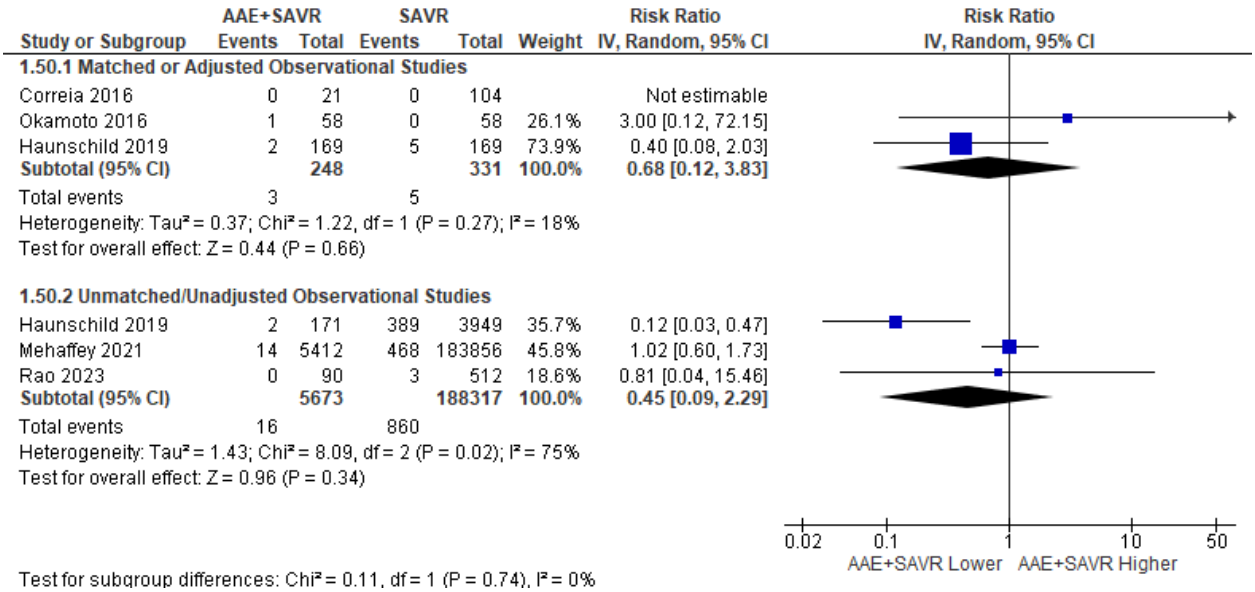


**Figure S50** Forest plot for deep sternal wound infection.

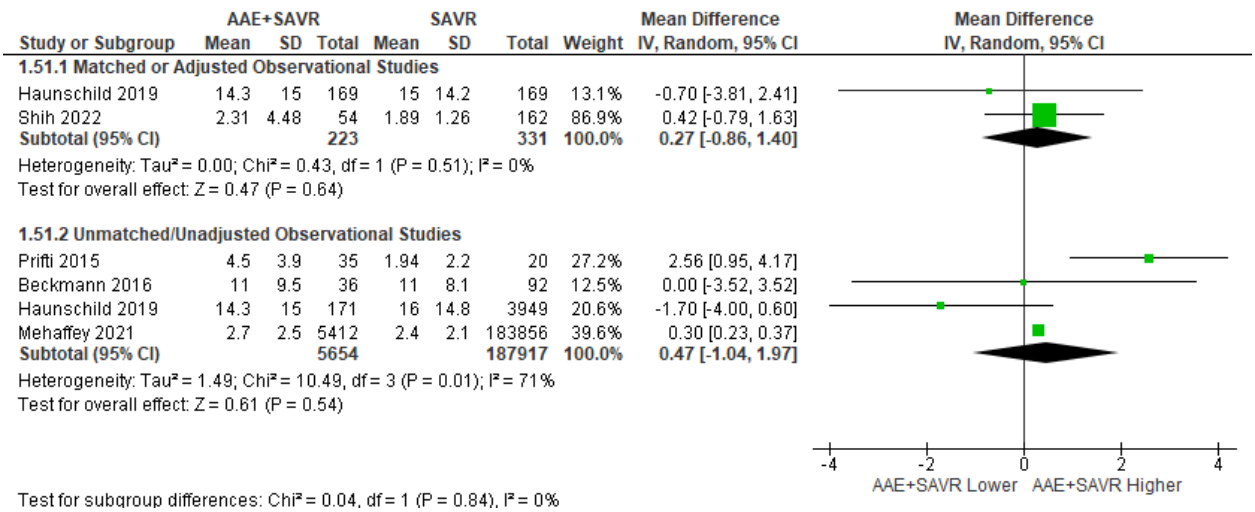


**Figure S51** Forest plot for ICU length of stay (days).


https://dx.doi.org/10.21037/acs-2024-aae-0023

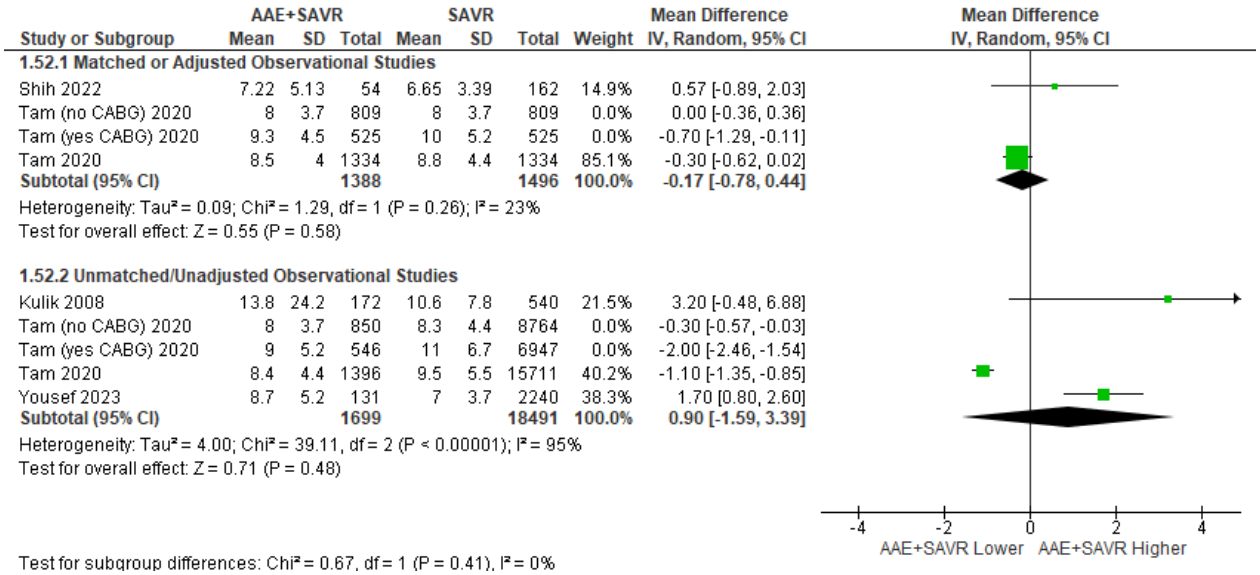


**Figure S52** Forest plot for hospital length of stay (days).

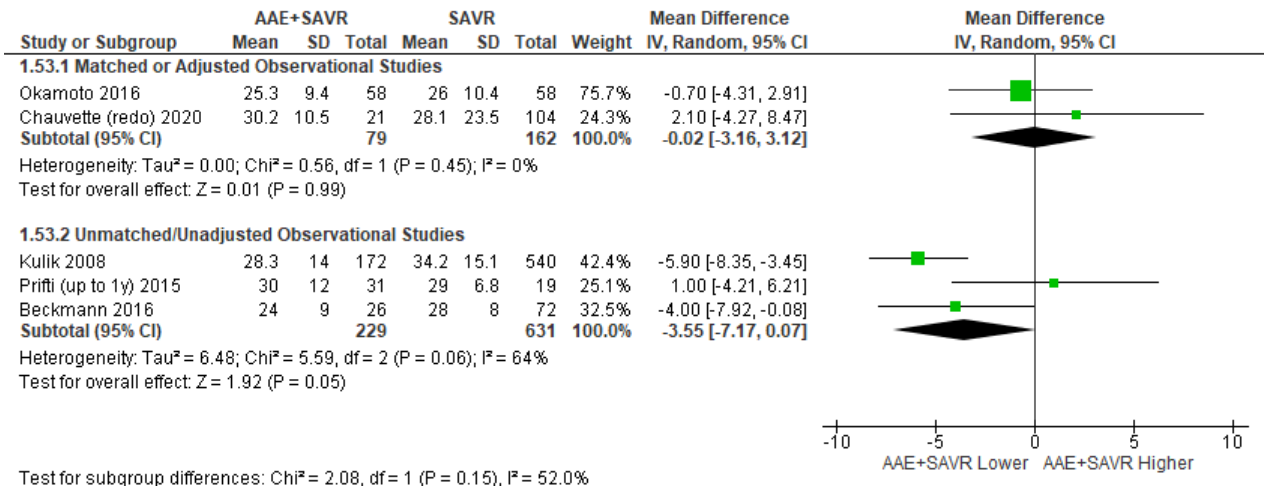


**Figure S53** Forest plot for peak transprosthetic gradient at discharge (mm Hg).


https://dx.doi.org/10.21037/acs-2024-aae-0023

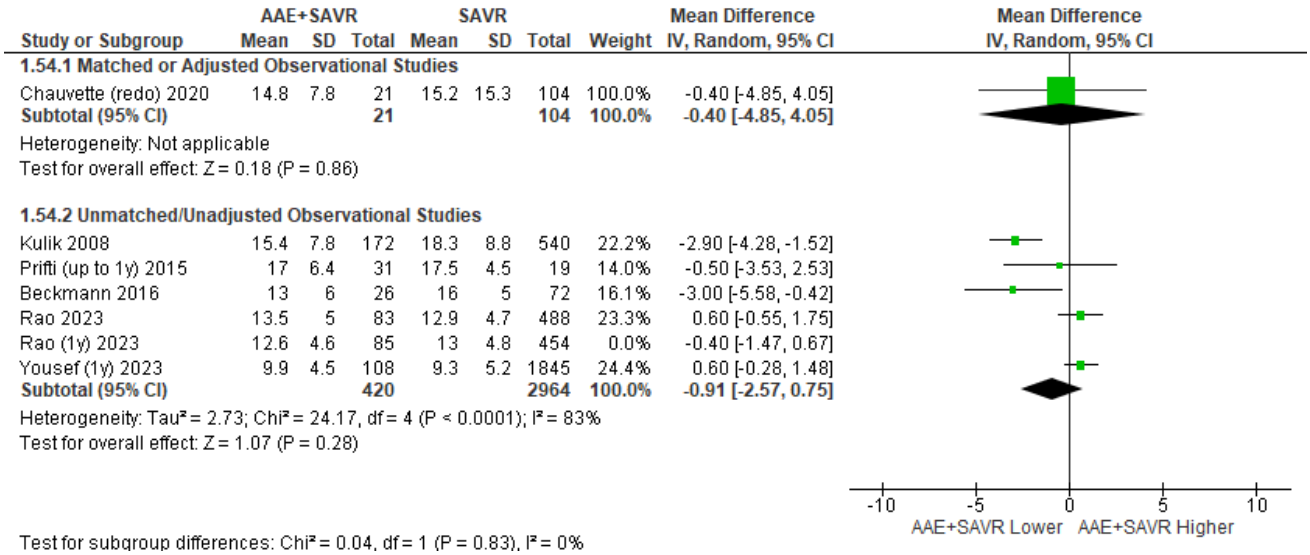


**Figure S54** Forest plot for mean transprosthetic gradient at discharge (mm Hg).

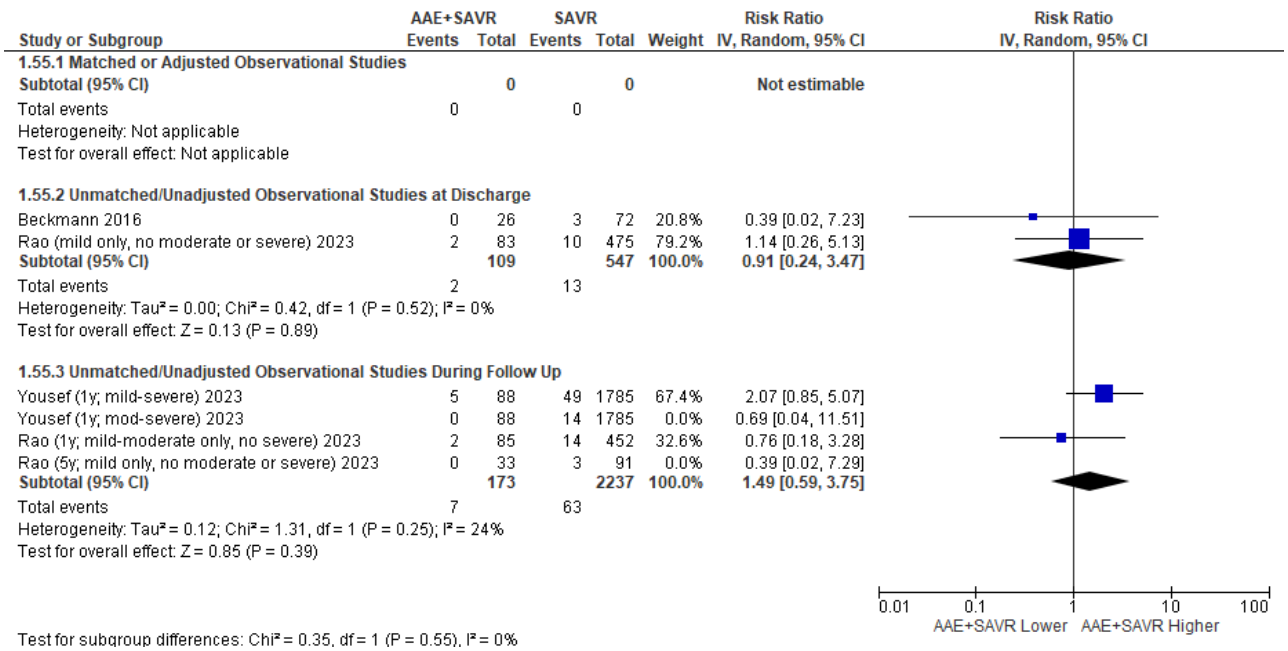


**Figure S55** Forest plot for paravalvular leak at discharge and during follow up.


https://dx.doi.org/10.21037/acs-2024-aae-0023

## Figures S56-S61. Meta-analyses of secondary outcomes lacking sufficient data

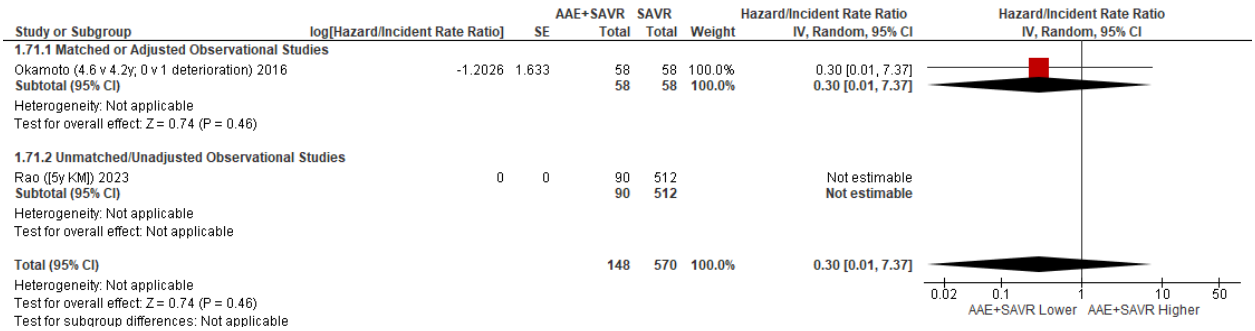


**Figure S56** Forest plot for structural valve deterioration during follow-up.

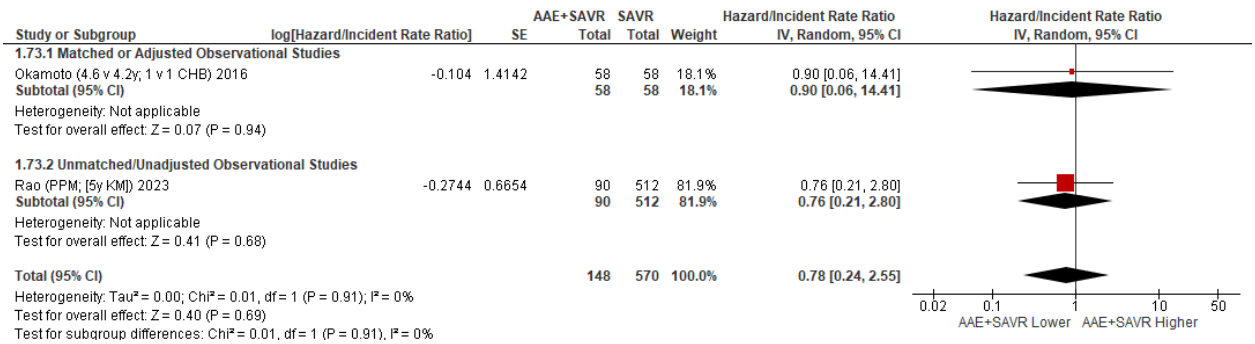


**Figure S57** Forest plot for complete heart block or permanent pacemaker insertion.

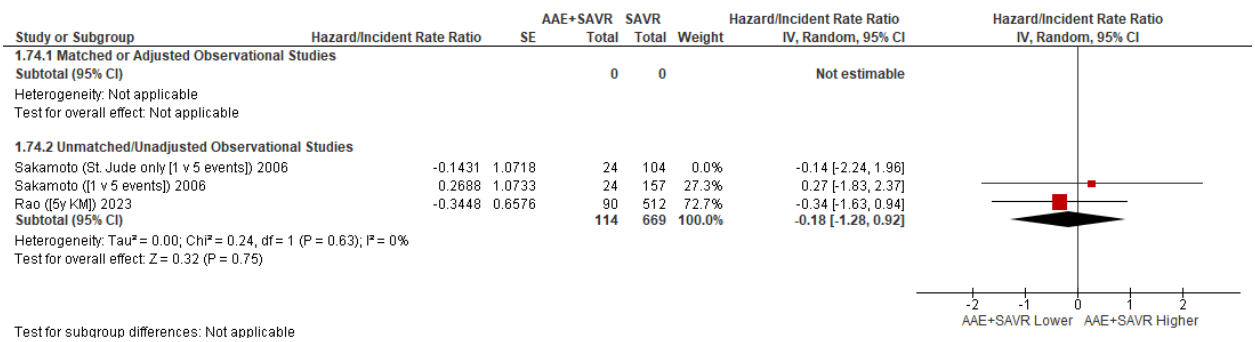


**Figure S58** Forest plot for thromboembolism during follow-up. Assumed equal follow-up lengths between groups if only overall follow-up was provided.


https://dx.doi.org/10.21037/acs-2024-aae-0023

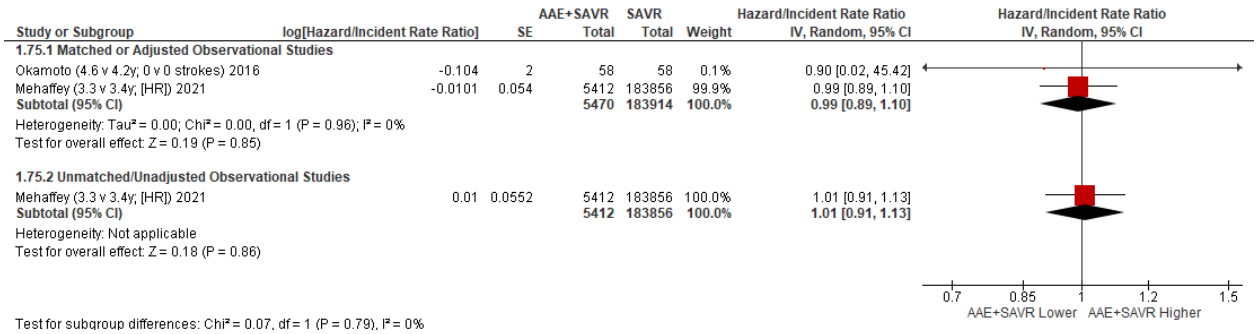


**Figure S59** Forest plot for stroke during follow-up.

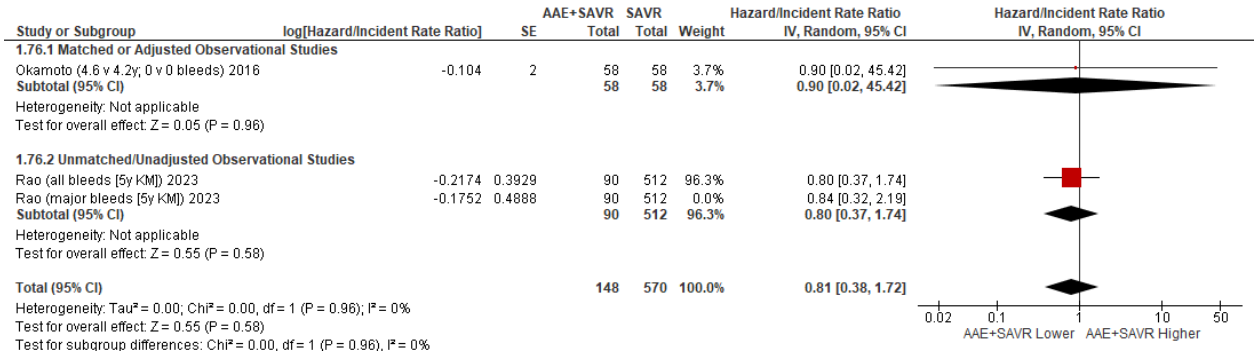


**Figure S60** Forest plot for bleeding during follow-up.

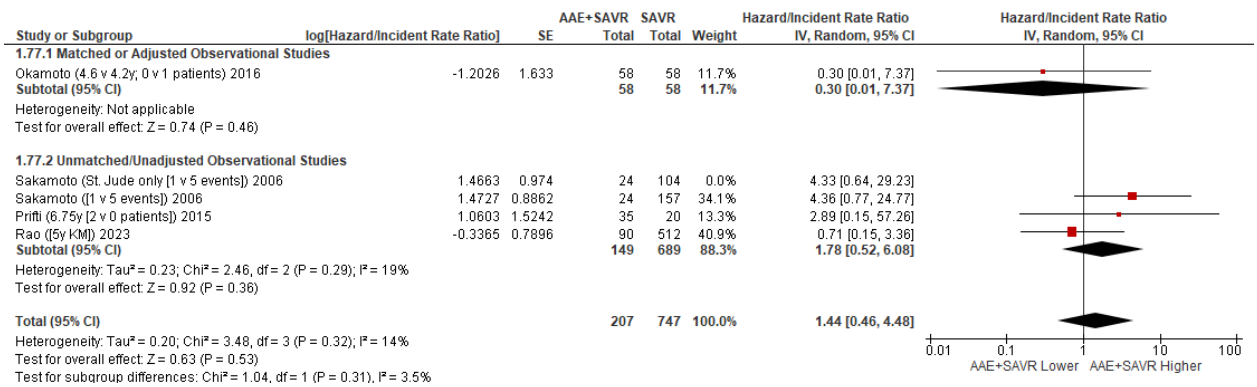


**Figure S61** Forest plot for endocarditis during follow-up.


https://dx.doi.org/10.21037/acs-2024-aae-0023

## Figures S62-S63. Summaries of sensitivity analyses

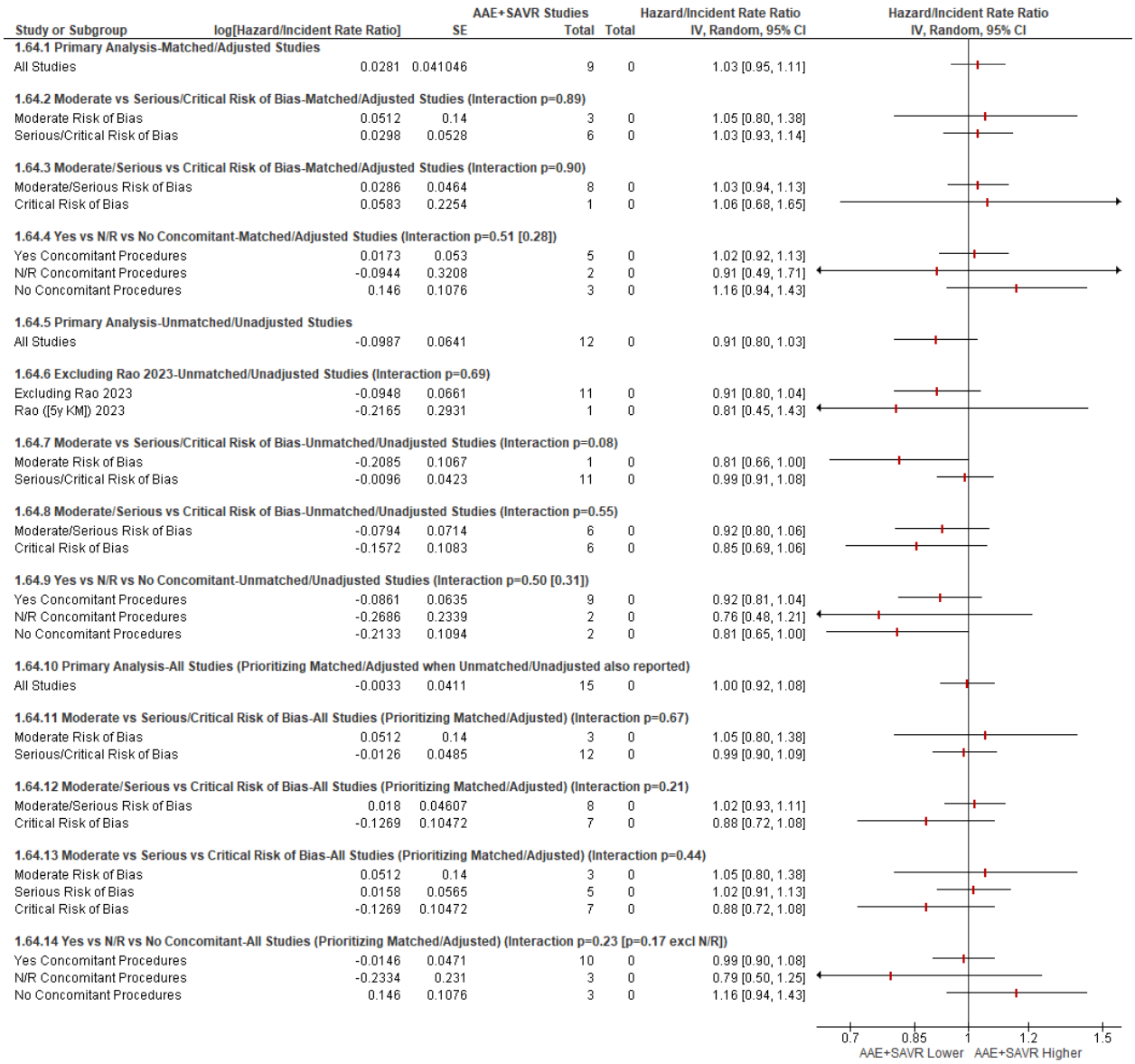


**Figure S62** Sensitivity analyses for mid-term mortality.


https://dx.doi.org/10.21037/acs-2024-aae-0023

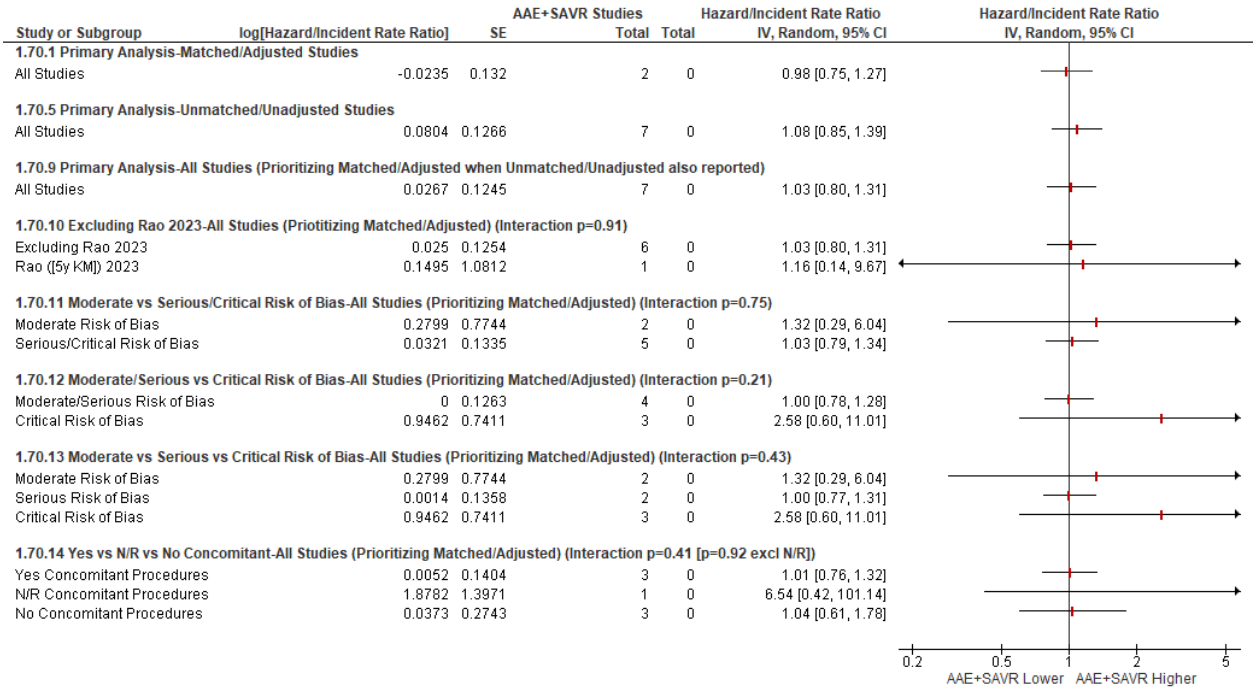


**Figure S63** Sensitivity analyses for aortic valve reintervention.


https://dx.doi.org/10.21037/acs-2024-aae-0023

**Supplemental Tables:**

**Table S1** Characteristics of included studies (detailed)

| First author | Year | Cohort size | Group | | Group number, n (%) | | Age (year) | | Male sex (%) | | Body surface area ($m^2$) | | Cerebrovascular disease (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE |
| Matched or adjusted observational studies | | | | | | | | | | | | | | |
| Yousef | 2023 | 2371 | AAE + AVR | Isolated AVR | 131 (5.5%) | 2240 (94.5%) | 62.0 [55.0–70.0] | 68.0 [60.0–76.0] | 32.1 | 63.6 | 1.99±0.27 | 2.03±0.27 | 14.5 | 18.0 |
| Shih | 2022 | 216 | AAE + AVR | Isolated AVR | 54 (25%) | 162 (75%) | 63.92±12.63 | 64.94±10.84 | 29.6 | 29.0 | 1.89±0.28 | 1.91±0.25 | 5.6 | 3.1 |
| Mehaffey | 2021 | 189268 | AAE + AVR | AVR | 5412 (2.9%) | 183856 (97.1%) | 75 [70–79] | 76 [71–81] | 40.0 | 62.0 | – | – | 21.0 | 19.4 |
| Chauvette | 2020 | 125 | AAE + Redo AVR | Redo AVR | 21 (16.8%) | 104 (83.2%) | 63±3 | 63±3 | 28.6 | 42.3 | – | – | 0.0 | 0.0 |
| Tam | 2020 | 1618 | AAE + AVR | Isolated AVR | 809 (50%) | 809 (50%) | 65.57±12.36 | 65.48±13.38 | 43.3 | 44.4 | 1.92±0.27 | 1.91±0.26 | 4.1 | 4.9 |
| Tam* | 2020 | 1050 | AAE + AVR + CABG | AVR + CABG | 525 (50%) | 525 (50%) | 72.12±8.80 | 72.36±8.68 | 54.1 | 53.5 | 1.94±0.24 | 1.94±0.25 | 5.9 | 6.5 |
| Haunschild | 2019 | 338 | AAE + AVR | AVR | 169 (50%) | 169 (50%) | 67.48±10 | 67.58±9 | 34.0 | 34.0 | 1.9±0.2 | 1.9±0.2 | – | – |
| Okamoto | 2016 | 116 | AAE + AVR | AVR | 58 (50%) | 58 (50%) | 73.4±11.9 | 74.7±8.5 | 19.0 | 19.0 | 1.45±0.16 | 1.38±0.16 | 0.0 | 0.0 |
| Kulik | 2008 | 712 | AAE + AVR | AVR in SAR | 172 (24.2%) | 540 (75.8%) | 66.8±12.3 | 69.1±11.8 | 30.8 | 25.2 | – | – | – | – |
| Sommers | 1997 | 530 | AAE + Medtronic Hancock II bioAVR | Medtronic Hancock II bioAVR | 98 (18%) | 432 (82%) | 64±13 | 64±12 | 55.0 | 87.0 | 1.79±0.22 | 1.83±0.19 | – | – |
| Unmatched/unadjusted observational studies | | | | | | | | | | | | | | |
| Rao | 2023 | 602 | Aortic root, STJ, or annular enlargement + Medtronic Avalus AVR | Medtronic Avalus AVR | 90 (15.0%)** | 512 (85.0%) | 67.9±7.2 | 69.3±8.9 | 62.2 | 78.3 | 2.00±0.21 | 2.00±0.22 | 1.1 | 4.7 |
| Beckmann | 2016 | 128 | AAE + bioAVR in SAR | Corcym Perceval bioAVR in SAR | 36 (28.1%) | 92 (71.9%) | 62 (37–92) | 79 (37–91) | 16.7 | 18.5 | 1.8±0.2 | 1.8±0.2 | – | – |
| Correia | 2016 | 1006 | AAE + AVR in SAR | AVR in SAR | 239 (23.8%) | 767 (76.2%) | 70.4±12.5 | 69.9±9.6 | 18.4 | 12.0 | 1.59±0.15 | 1.57±0.13 | 5.0 | 6.3 |
| Prifti | 2015 | 55 | AAE + 19 mm supraannular AVR | 17 mm supraannular AVR | 35 (63.6%) | 20 (36.4%) | 67.6±10 | 69.75±7.4 | 17.0 | 10.0 | 1.68±0.16 | 1.67±0.2 | 8.6 | 20.0 |
| Penaranda | 2014 | 117 | AAE + 21 mm AVR | 19 mm AVR | 30 (25.6%) | 87 (74.4%) | 83.8 (80.2–93.4) | 84.1 (80.1–92.7) | 13.0 | 2.0 | 1.7 (1.5–2.1) | 1.6 (1.2–2.1) | 20.0 | 13.0 |
| Sakamoto | 2006 | 128 | AAE + St Jude mechAVR | St Jude mechAVR | 24 (18.75%) | 104 (81.25%) | 52.6±11.9† | | 72.7† | | 1.60±0.15† | | – | – |


https://dx.doi.org/10.21037/acs-2024-aae-0023

**Table S1** (*continued*)

| First author | Year | Renal failure (%) | | Dialysis (%) | | Coronary artery disease (%) | | COPD (%) | | Smoking (%) | | Diabetes (%) | | Hypertension (%) | | Urgent status (%) | | Emergent Status (%) | | Urgent/Emergent Status (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE |
| Matched or adjusted observational studies | | | | | | | | | | | | | | | | | | | | | |
| Yousef | 2023 | – | – | 0.8 | 1.8 | – | – | – | – | – | – | 35.9 | 31.8 | – | – | – | – | – | – | 24.4 | 24.0 |
| Shih | 2022 | – | – | 0.0 | 0.6 | – | – | 3.7 | 3.1 | 5.6 | 6.2 | 33.3 | 35.8 | 81.5 | 79.0 | 11.1 | 6.2 | 0 | 0 | 11.1 | 6.2 |
| Mehaffey | 2021 | – | – | 1.7 | 1.8 | 55.4 | 58.8 | – | – | 23.3 | 24.0 | 39.6 | 34.7 | 88.1 | 86.5 | 21.7 | 24.2 | 0 | 0 | 21.7 | 24.2 |
| Chauvette | 2020 | – | – | – | – | 10.0 | 11.0 | 3.0 | 5.0 | – | – | 28.0 | 15.0 | 62.0 | 59.0 | – | – | – | – | 19.0 | 13.0 |
| Tam | 2020 | – | – | 3.5 | 4.4 | 35.0 | 37.8 | 24.0 | 22.4 | 43.3 | 42.4 | 38.4 | 39.3 | 75.8 | 75.6 | 11.6 | 12.5 | 0 | 0 | 11.6 | 12.5 |
| Tam* | 2020 | – | – | 4.6 | 4.8 | 98.3 | 96.4 | 23.0 | 24.4 | 52.2 | 49.5 | 50.9 | 53.1 | 87.8 | 89.5 | 21.0 | 21.1 | 0 | 0 | 21.0 | 21.1 |
| Haunschild | 2019 | – | – | 2.0 | 2.0 | – | – | 4.0 | 4.0 | 26.0 | 25.0 | 32.0 | 34.0 | 89.0 | 85.0 | 11.0 | 11.0 | 0 | 0 | 11.0 | 11.0 |
| Okamoto | 2016 | 6.9 | 10.3 | – | – | 10.3 | 10.3 | 0.0 | 3.4 | 12.1 | 13.8 | 22.4 | 17.2 | 67.2 | 63.8 | – | – | – | – | 0.0 | 1.7 |
| Kulik | 2008 | – | – | – | – | – | – | – | – | 12.8 | 10.4 | – | – | – | – | – | – | – | – | – | – |
| Sommers | 1997 | – | – | – | – | 38.0 | 40.0 | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Unmatched/unadjusted observational studies | | | | | | | | | | | | | | | | | | | | | |
| Rao | 2023 | 4.4 | 9.2 | – | – | 30.0 | 47.3 | – | – | – | – | – | – | 74.4 | 75.2 | – | – | – | – | – | – |
| Beckmann | 2016 | 19.0 | 16.0 | – | – | – | – | 8.0 | 5.0 | – | – | 22.0 | 33.0 | 66.0 | 73.0 | – | – | – | – | – | – |
| Correia | 2016 | 26.8 | 29.6 | 2.5 | 1.2 | 27.2 | 24.1 | 6.7 | 5.7 | – | – | 17.6 | 12.9 | 57.7 | 44.1 | – | – | – | – | – | – |
| Prifti | 2015 | 5.7 | 0.0 | – | – | 17.1 | 20.0 | 14.3 | 25.0 | 31.4 | 30.0 | 23.0 | 25.0 | 46.0 | 50.0 | – | – | – | – | – | – |
| Penaranda | 2014 | 0.0 | 3.0 | – | – | – | – | – | – | – | – | 17.0 | 16.0 | 77.0 | 75.0 | – | – | – | – | 7.0 | 7.0 |
| Sakamoto | 2006 | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |


https://dx.doi.org/10.21037/acs-2024-aae-0023

**Table S1** (*continued*)

| First author | Year | EuroSCORE II (%) | | STS score (%) | | Previous cardiac surgery (%) | | Previous SAVR (%) | | Preoperative LVEF (%) | | Preoperative LVEF (< 35%) (%) | | Preoperative NYHA ≥3 (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE |
| Matched or adjusted observational studies | | | | | | | | | | | | | | | |
| Yousef | 2023 | – | – | 1.7 [1.1–2.9] | 1.7 [1.1–3.1] | 17.6 | 15.2 | – | – | 60.0 [55.0–63.0] | 58.0 [55.0–63.0] | – | – | – | – |
| Shih | 2022 | – | – | 2.1±1.6 | 2.0±2.1 | 14.8 | 16.1 | – | – | 59.16±8.81 | 58.33±7.6 | – | – | 18.5 | 14.8 |
| Mehaffey | 2021 | – | – | 2.99±4.1 | 2.97±4.2 | 13.0 | 11.6 | – | – | – | – | – | – | – | – |
| Chauvette | 2020 | 13.8±1.6 | 10.4±1.6 | – | – | 100.0 | 100.0 | 100.0 | 100.0 | 62±1 | 60±1 | – | – | 67.0 | 65.0 |
| Tam | 2020 | – | – | – | – | 0.0 | 0.0 | 0.0 | 0.0 | – | – | 4 | 4 | 38.4 | 37.7 |
| Tam* | 2020 | – | – | – | – | 0.0 | 0.0 | 0.0 | 0.0 | – | – | 5 | 5 | 40.2 | 41.1 |
| Haunschild | 2019 | – | – | – | – | 0.0 | 0.0 | 0.0 | 0.0 | 60±11 | 60±11 | – | – | 51.0 | 47.0 |
| Okamoto | 2016 | – | – | – | – | 5.2 | 0.0 | 1.7 | 0.0 | 63.1±7.8 | 62.7±7.2 | – | – | – | – |
| Kulik | 2008 | – | – | – | – | – | – | – | – | – | – | – | – | 38.4 | 40.9 |
| Sommers | 1997 | – | – | – | – | – | – | – | – | – | – | – | – | 77.0 | 73.0 |
| Unmatched/unadjusted observational studies | | | | | | | | | | | | | | | |
| Rao | 2023 | – | – | 1.6±1.0 | 1.8±1.2 | 1.1 | 4.1 | 1.1 | 1.0 | – | – | – | – | 51.1 | 43.1 |
| Beckmann | 2016 | – | – | – | – | 14.0 | 2.0 | – | – | 60 (42–70) | 60 (25–90) | – | – | 28.0 | 84.0 |
| Correia | 2016 | – | – | – | – | 8.8 | 6.9 | 0.4 | 0.0 | 65.3±15.9 | 64.6±16.0 | – | – | 49.4 | 57.9 |
| Prifti | 2015 | – | – | – | – | 17.1 | 0.0 | 0.0 | 0.0 | 58±13 | 54.7±7.4 | 20 | 5 | – | – |
| Penaranda | 2014 | – | – | NS | | 10.0 | 8.0 | – | – | 64 (30–78) | 63 (13–78) | – | – | 80.0 | 78.0 |
| Sakamoto | 2006 | – | – | – | – | – | – | – | – | – | – | – | – | – | – |


https://dx.doi.org/10.21037/acs-2024-aae-0023

**Table S1** (*continued*)

| First author | Year | Preoperative mean aortic gradient (mmHg) | | Preoperative iEOA (cm^2/m^2) | | Preoperative aortic annulus diameter (mm) | | Aortic stenosis (%) | | Aortic insufficiency (%) | | Mixed aortic valve disease (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE |
| Matched or adjusted observational studies | | | | | | | | | | | | | |
| Yousef | 2023 | – | – | – | – | – | – | 90.1 | 86.5 | 32.1 | 37.1 | – | – |
| Shih | 2022 | 45.95±17.11 | 42.15±17.14 | 0.37±0.12 | 0.38±0.14 | – | – | 90.7 | 87.7 | – | – | – | – |
| Mehaffey | 2021 | – | – | – | – | – | – | – | – | – | – | – | – |
| Chauvette | 2020 | 31.9±2.4 | 30.1±2.5 | 0.49±0.06 | 0.66±0.06 | – | – | 82.0 | 74.0 | – | – | – | – |
| Tam | 2020 | – | – | – | – | – | – | 85.0 | 83.9 | – | – | – | – |
| Tam* | 2020 | – | – | – | – | – | – | 87.6 | 87.0 | – | – | – | – |
| Haunschild | 2019 | – | – | – | – | – | – | 95.0 | 95.0 | 4.0 | 4.0 | – | – |
| Okamoto | 2016 | – | – | 0.42±0.14 | 0.52±0.17 | 19.3±1.8 | 19.7±1.9 | 74.1 | 74.1 | 0.0 | 0.0 | 25.9 | 25.9 |
| Kulik | 2008 | 39.1±18.0 | 48.4±25.4 | – | – | – | – | – | – | – | – | – | – |
| Sommers | 1997 | – | – | – | – | – | – | 57.0 | 42.0 | 14.0 | 27.0 | 29.0 | 31.0 |
| Unmatched/unadjusted observational studies | | | | | | | | | | | | | |
| Rao | 2023 | 46±17 | 42±18 | 0.41±0.14 | 0.47±0.30 | 23.2 | 24.1 | 88.9 | 82.2 | 2.2 | 7.0 | 8.9 | 10.4 |
| Beckmann | 2016 | 48±20 | 48±19 | 0.38±0.17 | 0.38±0.11 | 19 (17–21) | 20 (17–22) | 100.0 | 100.0 | – | – | – | – |
| Correia | 2016 | 63.2 ±20.2 | 58.8±16.7 | 0.35±0.14 | 0.38±0.13 | – | – | 71.1 | 68.8 | 6.3 | 7.4 | 22.2 | 23.7 |
| Prifti | 2015 | 63.3±17 | 66±12.7 | – | – | – | – | 100.0 | 100.0 | – | – | – | – |
| Penaranda | 2014 | – | – | 0.40 (0.14–0.53) | 0.41 (0.16–0.64) | 19 | 19 | 100.0 | 100.0 | – | – | 30.0 | 17.0 |
| Sakamoto | 2006 | – | – | – | – | – | – | 8.6† | | 50† | | 33.6† | |


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**Table S1** (*continued*)

| First author | Year | BAV (%) | | Mechanical valve (%) | | Mean implanted valve size (mm) | | Concomitant valve surgery (%) | | Concomitant CABG (%) | | Concomitant other procedure(s) (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE | AAE | No AAE |
| Matched or adjusted observational studies | | | | | | | | | | | | | |
| Yousef | 2023 | – | – | 25[†] | | 23.0 [21.0–25.0] | 25.0 [23.0–25.0] | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Shih | 2022 | 30.2 | 50.0 | 19.6 | 12.4 | 22.13±1.94 | 23.39±2.28 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Mehaffey | 2021 | – | – | – | – | 23.0[‡] | 23.0[‡] | 0.0 | 0.0 | 42.6 | 45.2 | 0.0 | 0.0 |
| Chauvette | 2020 | – | – | – | – | 21.2±0.4 | 22.1±0.4 | – | – | – | – | – | – |
| Tam | 2020 | – | – | 22.0 | 31.0 | – | – | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Tam* | 2020 | – | – | 13.9 | 15.0 | – | – | 0.0 | 0.0 | 100.0 | 100.0 | 0.0 | 0.0 |
| Haunschild | 2019 | – | – | 7.0 | 6.5 | 21 [21–23] | 23 [21–23] | 0.0 | 0.0 | 0.0 | 0.0 | 33.0 | 17.0 |
| Okamoto | 2016 | 13.8 | 15.5 | 31.0 | 36.0 | 19.4±1.6 | 19.3±1.3 | 22.4 | 24.1 | 10.3 | 10.3 | 24.1 | 31.0 |
| Kulik | 2008 | – | – | 43.0 | 40.2 | 22.0 | 20.7 | 7.6 | 18.9 | 43.6 | 39.6 | – | – |
| Sommers | 1997 | – | – | 0.0 | 0.0 | 23.8±1.94 | 25.2±2.07 | – | – | – | – | – | – |
| Unmatched/unadjusted observational studies | | | | | | | | | | | | | |
| Rao | 2023 | 41.1 | 35.0 | 0.0 | 0.0 | 23.1±1.9 | 23.7±2.1 | 0.0 | 0.0 | 26.7 | 32.0 | 46.7 | 31.6 |
| Beckmann | 2016 | – | – | 0.0 | 0.0 | – | 23.07 | – | – | – | – | 6.0 | 33.0 |
| Correia | 2016 | 15.3[†] | | 23.8 | 47.7 | 21.8±1.0 | 20.7±0.5 | 9.2 | 18.8 | 17.2 | 13.7 | 59.0 | 68.2 |
| Prifti | 2015 | 25.7 | 45.0 | 100.0 | 100.0 | 19 | 17 | 20.0 | 25.0 | 17.1 | 20.0 | – | – |
| Penaranda | 2014 | – | – | 0.0 | 3.0 | 21 | 19 | – | – | 43.0 | 51.0 | 16.7 | 21.8 |
| Sakamoto | 2006 | – | – | 100.0 | 100.0 | 24.1[†] | | 28.9[†] | | 0.0 | 0.0 | 3.1[†] | |

Continuous variables are presented as mean ± standard deviation, median (range), or median [interquartile range]. *, distinct secondary cohort reported within the same publication; **, of 90 patients within the intervention arm, only 27 patients (30%) had a confirmed AAE and 3 patients (3.3%) within the intervention arm had an aortic root replacement; [†], demographic information derived from the overall cohort of the respective study; [‡], median implanted valve size. AAE, aortic annular enlargement; BAV, bicuspid aortic valve; bioAVR, bioprosthetic aortic valve replacement; AVR; aortic valve replacement; COPD, chronic obstructive pulmonary disease; iEOA, indexed effective orifice area; LVEF, left ventricular ejection fraction; mechAVR, mechanical aortic valve replacement; NS, no statistically significant difference in STS score between ARE and no ARE groups; SAR, small aortic root; SAVR, surgical aortic valve replacement; STJ, sinotubular junction.


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**Table S2** GRADE domain–specific judgements for midterm mortality, aortic valve reintervention, and heart failure

| Outcome | AAE + SAVR | SAVR | Studies | Design | Risk of bias | Unexplained heterogeneity | Indirectness | Imprecision | Publication bias | Large effect | Dose response | Plausible residual confounding | Overall quality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Midterm mortality | | | | | | | | | | | | | |
| Matched or adjusted | 7445 | 188,557 | 9* | Low quality | – | –** | – | – | – | N/A | N/A | N/A | Low |
| Unmatched/unadjusted | 7834 | 208,363 | 12* | Very low quality | Downgrade | –** | – | – | – | N/A | N/A | N/A | Very low |
| Aortic valve reintervention | | | | | | | | | | | | | |
| Matched or adjusted | 6221 | 184,665 | 2 | Low quality | – | –** | – | – | – | N/A | N/A | N/A | Low |
| Unmatched/unadjusted | 6596 | 196,363 | 7 | Very low quality | Downgrade | –** | – | – | – | N/A | N/A | N/A | Very low |
| Heart failure | | | | | | | | | | | | | |
| Matched or adjusted | 6451 | 185,263 | 4 | Low quality | Downgrade | –** | – | – | – | N/A | N/A | N/A | Very low |
| Unmatched/unadjusted | 6443 | 193,021 | 4 | Very low quality | Downgrade | –** | – | – | – | N/A | N/A | N/A | Very low |

GRADE Working Group grades of evidence—high quality: further research is very unlikely to change our confidence in the estimate of effect; moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low quality: we are very uncertain about the estimate. *, separate estimate from secondary cohort of Tam *et al.* considered as same study; **, the vast majority of heterogeneity was felt to be explained by the risk of bias observed within each of the subsets of examined studies. GRADE, Grading of Recommendations Assessment, Development and Evaluation; AAE, aortic annular enlargement; SAVR, surgical aortic valve replacement; N/A, not applicable; –, no change to overall quality rating.


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## Appendix 1: Detailed risk of bias assessment

Only three included studies reported on outcomes at moderate risk of bias (1-3). All three studies were designed with extensive propensity score matching that addressed the relevant a priori-specified baseline confounders that could bias the selection of patients for or against receiving an AAE procedure at the time of SAVR. The remaining studies and their reported outcomes of interest were either at severe or critical risk of bias (4-15). These ratings were primarily driven by unclear or incomplete accounting methods for confounding variables or the complete absence of matching or adjustment of outcomes. Notably, in the studies by Rao et al. (12) Beckmann et al., (4) Correia et al. (6), and Kulik et al. (8), there were also critical issues regarding the composition of the intervention group (12) and the imbalance of important concomitant procedures (4,6,8,12).

The study by Sakamoto et al. did not provide information regarding baseline characteristics, intraoperative details and perioperative outcomes to be able to compare the characteristics of the St. Jude mechanical AVR with AAE versus St. Jude mechanical AVR without AAE groups (13). However, the data regarding mid-term mortality and aortic valve reintervention are described by Sakamoto et al. These outcomes are reported for the distinct groups of interest, i.e., AAE and St. Jude mechanical AVR and St. Jude mechanical AVR without AAE (13). As such, these estimates remain in the mid-term outcomes syntheses.

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