Supplementary

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Appendix 1

References

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 Ac	ljusted	Observational St	udies								
						Mortality	М	L	М	S	Mortality
Yousef	2023	S	L	М	L	AoV Reintervention	М	М	М	8	AoV Reintervention
						Non-Structural Valve Dysfunction-PVL	S	S	М	8	Non-Structural Valve Dysfunction-PVL
Shih	2022	м	т	м	Т	Mortality	L	L	М	М	Mortality
5	2022		2		~	AoV Reintervention	L	М	М	М	AoV Reintervention
						Mortality	L	L	М	S	Mortality
Mehaffey	2021	s	т	s	Т	AoV Reintervention	L	М	М	S	AoV Reintervention
menancy	2021	5	-	, j	~	Stroke Hospitalization	L	М	М	S	Stroke Hospitalization
						CHF Rehospitalization	L	S	М	S	CHF Rehospitalization
Chauvette	2020	S	L	L	NI	Mortality	L	L	М	S	Mortality
						Mortality	L	L	М	М	Mortality
Tam	2020	М	L	L	L	AoV Reintervention	L	М	М	М	AoV Reintervention
						CHF Rehospitalization	L	S	М	S	CHF Rehospitalization
Tam*	2020	М	L	L	L	Mortality	L	L	М	М	Mortality
Haunschild	2019	М	L	L	М	Mortality	S	L	М	S	Mortality
						Mortality	NI	L	М	М	Mortality
						Cardiac Mortality	NI	М	М	М	Cardiac Mortality
						SVD	NI	S	NI	8	SVD
Okamoto	2016	М	L	L	L	IE	NI	S	NI	S	IE
						Major Bleeding	NI	S	NI	S	Major Bleeding
						Stroke	NI	S	NI	8	Stroke
						CHF	NI	S	NI	S	CHF
Kulik	2008	S	L	L	с	Mortality	М	L	М	С	Mortality
						CHF Composite	М	S	М	С	CHF Composite
Sommers	1997	S	L	L	NI	Mortality	L	L	М	S	Mortality
						Cardiac Mortality	L	М	М	S	Cardiac Mortality
Unmatched/Un	radjust	ed Observational	Studies								
						Mortality	S	L	L	C	Mortality
						Aov Keintervention	S	М	L	C	Ao V Reintervention
						SVD	S	М	L	С	SVD
						Non-Structural Dysfunction	S	М	L	C	Non-Structural Dysfunction
Kao	2023	C	L	8	C	Valve Thrombosis	S	M	L	C	Valve Ihrombosis
						NYHA III-IV	S	S	L	C	NYHA III-IV
						IE Min Animal and Baland Hamilton	8	8	L	C	
						Major Anticoaguiant-Related Hemormage	S	8	L	C C	Major Anticoaguiant-Related Hemorrhage
Daalamann	2016		T	T	C	Martality	5	5	L	L C	Mastality
Beckmann	2010	3	L	L	C	Montality	S	L	M	C	Montality
Conteia	2010	5	L	3		Mortality	L	L	M		Mortality
Prfiti	2015	с	L	L	М	AcV Paintervention	NI	L	s		AcV Paintervention
Panamada	2014	s	T	Т	s	Aov Kenneivennon Mortality	M	M	- 5 - M		Mortality
r charanda	2014	3	L	L	3	Mortality	M	NI	M	5	Mortality
						Beoperation**	NI	NI M	M		Reoperation**
Sakamoto	Sakamoto 2006		L	L	NI	Prosthetic Valva IE	NI	M	M		Prosthetic Valve IE
			_	Thromboembolism	NI	s	M		Thromboembolism		
I						rmomoochibolishi	INI	3	WI		rmomoochibolishi

 $Figure \ S1 \ {\rm ROBINS-I} \ {\rm assessment} \ for \ {\rm all} \ reported \ {\rm outcomes} \ {\rm within} \ {\rm each} \ of \ {\rm the} \ {\rm included} \ {\rm studies}.$

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.

Figures S2-S31. Meta-analyses for baseline characteristics

	AA	E+SAV	R		SAVR			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.1.1 Matched of Adjust	ed Obse	ervation	al stud	lles					
Okamoto 2016	73.4	11.9	58	74.7	8.5	58	4.1%	-1.30 [-5.06, 2.46]	
Haunschild 2019	67.48	10	169	67.58	9	169	14.0%	-0.10 [-2.13, 1.93]	
Chauvette (redo) 2020	63	14	21	63	14	104	1.3%	0.00 [-6.56, 6.56]	
Tam (no CABG) 2020	65.57	12.36	809	65.48	13.38	809	0.0%	0.09 [-1.17, 1.35]	
Tam (yes CABG) 2020	72.12	8.8	525	72.36	8.68	525	0.0%	-0.24 [-1.30, 0.82]	\perp
Tam 2020	68.15	11.1	1334	68.19	11.76	1334	76.5%	-0.04 [-0.91, 0.83]	
Shih 2022	63.92	12.63	54	64.94	10.84	162	4.1%	-1.02 [-4.78, 2.74]	
Subtotal (95% CI)			1636			1827	100.0%	-0.14 [-0.90, 0.62]	•
Heterogeneity: Tau ² = 0.0	00; Chi²:	= 0.63,	df=4 (P = 0.96	i); I 2 = 04	%			
Test for overall effect: Z =	= 0.36 (P	= 0.72)							
1.1.2 Unmatched/Unadju	usted Ol	oservat	ional S	tudies					
Sommers 1997	64	13	98	64	12	432	5.7%	0.00 [-2.81, 2.81]	
Kulik 2008	66.8	12.3	172	69.1	11.8	540	7.7%	-2.30 [-4.39, -0.21]	
Penaranda 2014	85.3	3.2	30	85.3	2.6	87	10.4%	0.00 [-1.27, 1.27]	-+-
Prifti 2015	67.6	10	35	69.75	7.4	20	2.9%	-2.15 [-6.79, 2.49]	
Beckmann 2016	63	13	36	71.5	11	92	2.7%	-8.50 [-13.30, -3.70]	←
Correia 2016	70.4	12.5	239	69.9	9.6	767	8.9%	0.50 [-1.22, 2.22]	_ -
Okamoto 2016	73.4	11.9	58	72.8	8.6	531	5.0%	0.60 [-2.55, 3.75]	
Haunschild 2019	67.4	10	171	68.9	11	3949	9.5%	-1.50 [-3.04, 0.04]	
Tam (no CABG) 2020	65.64	12.24	850	68.54	11.68	8764	0.0%	-2.90 [-3.76, -2.04]	
Tam (yes CABG) 2020	71.97	9.04	546	73.66	8.56	6947	0.0%	-1.69 [-2.47, -0.91]	
Tam 2020	68.12	11.1	1396	70.8	10.42	15711	12.5%	-2.68 [-3.28, -2.08]	-
Mehaffey 2021	75	7	5412	76	7	183856	13.1%	-1.00 [-1.19, -0.81]	•
Shih 2022	63.92	12.63	54	66.13	11.9	814	4.4%	-2.21 [-5.68, 1.26]	
Rao 2023	67.9	7.2	90	69.3	8.9	512	9.0%	-1.40 [-3.08, 0.28]	
Yousef 2023	62	11	131	68	12	2240	8.1%	-6.00 [-7.95, -4.05]	
Subtotal (95% CI)			7922			209551	100.0%	-1.72 [-2.61, -0.82]	◆
Heterogeneity: Tau ² = 1.5	58; Chi ≇:	= 70.25	, df = 10	2 (P < 0	.00001)	I² = 83%			
Test for overall effect: Z =	= 3.76 (P	= 0.000	02)						
									-10 -5 U 5

Test for subgroup differences: $Chi^2 = 6.95$, df = 1 (P = 0.008), l² = 85.6%

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

	AAE+S	AVR	SAV	/R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.2.1 Matched or Adjust	ted Obser	vationa	I Studies				
Okamoto 2016	11	58	11	58	1.1%	1.00 [0.47, 2.12]	
Haunschild 2019	57	169	57	169	7.0%	1.00 [0.74, 1.35]	
Chauvette (redo) 2020	6	21	44	104	1.2%	0.68 [0.33, 1.38]	
Tam (no CABG) 2020	350	809	359	809	0.0%	0.97 [0.87, 1.09]	
Tam (yes CABG) 2020	241	525	244	525	0.0%	0.99 [0.87, 1.13]	
Tam 2020	591	1334	603	1334	87.9%	0.98 [0.90, 1.07]	
Shih 2022	16	54	47	162	2.8%	1.02 [0.63, 1.64]	
Subtotal (95% CI)		1636		1827	100.0%	0.98 [0.90, 1.06]	•
Total events	681		762				
Heterogeneity: Tau ² = 0.	00; Chi² =	1.10, dt	′= 4 (P = I	0.89); I² =	0%		
Test for overall effect: Z =	= 0.54 (P =	: 0.59)					
4.0.0.11							
1.2.2 Unmatched/Unadj	usted Obs	servatio	nal Studi	es			
Sommers 1997	54	98	378	432	11.2%	0.63 [0.52, 0.76]	
Kulik 2008	53	172	136	540	8.8%	1.22 [0.94, 1.60]	—
Penaranda 2014	4	30	2	87	0.6%	5.80 [1.12, 30.08]	
Prifti 2015	6	35	2	20	0.7%	1.71 [0.38, 7.71]	
Beckmann 2016	6	36	17	92	1.9%	0.90 [0.39, 2.10]	
Correia 2016	44	239	92	767	7.3%	1.53 [1.10, 2.13]	_ _
Okamoto 2016	11	58	268	531	4.0%	0.38 [0.22, 0.64]	
Haunschild 2019	57	171	2274	3949	10.3%	0.58 [0.47, 0.72]	
Tam (no CABG) 2020	367	850	5137	8764	0.0%	0.74 [0.68, 0.80]	
Tam (yes CABG) 2020	300	546	5121	6947	0.0%	0.75 [0.69, 0.81]	
Tam 2020	667	1396	10258	15711	14.2%	0.73 [0.69, 0.77]	•
Mehaffey 2021	2163	5412	113996	183856	14.5%	0.64 [0.62, 0.67]	•
Shih 2022	16	54	549	814	5.7%	0.44 [0.29, 0.66]	
Rao 2023	56	90	401	512	11.6%	0.79 [0.67, 0.94]	
Yousef 2023	42	131	1425	2240	9.2%	0.50 [0.39, 0.65]	
Subtotal (95% CI)		7922		209551	100.0%	0.72 [0.63, 0.81]	•
Total events	3179		129798				
Heterogeneity: Tau ² = 0.	03; Chi² =	86.99,	df = 12 (P	< 0.00001	l); l² = 86	%	
Test for overall effect: Z =	= 5.14 (P =	< 0.0000)1)				

Test for subgroup differences: Chi² = 16.54, df = 1 (P < 0.0001), l² = 94.0%

Figure S3 Forest plot for male sex.

	AA	E+SAV	R		SAVR			Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI			
1.3.1 Matched or Adjust	ed Obse	ervatio	nal Stu	idies								
Okamoto 2016	1.45	0.16	58	1.38	0.16	58	16.3%	0.07 [0.01, 0.13]				
Haunschild 2019	1.9	0.2	169	1.9	0.2	169	25.1%	0.00 [-0.04, 0.04]	+			
Tam (no CABG) 2020	1.92	0.27	809	1.91	0.26	809	0.0%	0.01 [-0.02, 0.04]				
Tam (yes CABG) 2020	1.94	0.24	525	1.94	0.25	525	0.0%	0.00 [-0.03, 0.03]				
Tam 2020	1.93	0.26	1334	1.92	0.26	1334	49.6%	0.01 [-0.01, 0.03]				
Shih 2022	1.89	0.28	54	1.91	0.25	162	9.0%	-0.02 [-0.10, 0.06]				
Subtotal (95% CI)			1615			1723	100.0%	0.01 [-0.01, 0.04]	★			
Heterogeneity: Tau ² = 0.00; Chi ² = 4.71, df = 3 (P = 0.19); I ² = 36%												
Test for overall effect: Z = 1.06 (P = 0.29)												
1.3.2 Unmatched/Unadju	isted O	bserva	tional	Studies								
Sommers 1997	1.79	0.22	98	1.83	0.19	432	9.3%	-0.04 [-0.09, 0.01]				
Penaranda 2014	1.75	0.15	30	1.63	0.18	87	6.8%	0.12 [0.05, 0.19]				
Prifti 2015	1.68	0.16	35	1.67	0.2	20	3.8%	0.01 [-0.09, 0.11]				
Beckmann 2016	1.8	0.2	36	1.8	0.2	92	5.6%	0.00 [-0.08, 0.08]				
Correia 2016	1.59	0.15	239	1.57	0.13	767	13.6%	0.02 [-0.00, 0.04]				
Okamoto 2016	1.45	0.16	58	1.48	0.17	531	9.9%	-0.03 [-0.07, 0.01]				
Haunschild 2019	1.9	0.2	171	1.9	0.2	3949	12.1%	0.00 [-0.03, 0.03]	_ + _			
Tam (no CABG) 2020	1.95	0.25	850	1.96	0.26	8764	0.0%	-0.01 [-0.03, 0.01]				
Tam (yes CABG) 2020	1.96	0.26	546	1.95	0.25	6947	0.0%	0.01 [-0.01, 0.03]				
Tam 2020	1.95	0.25	1396	1.96	0.26	15711	14.6%	-0.01 [-0.02, 0.00]				
Shih 2022	1.89	0.28	54	2.03	0.24	814	5.7%	-0.14 [-0.22, -0.06]				
Rao 2023	2	0.21	90	2	0.22	512	9.3%	0.00 [-0.05, 0.05]				
Yousef 2023	1.99	0.27	131	2.03	0.27	2240	9.3%	-0.04 [-0.09, 0.01]				
Subtotal (95% CI)			2338			25155	100.0%	-0.01 [-0.03, 0.01]	•			
Heterogeneity: Tau ² = 0.0	00; Chi ^z	= 37.4	8, df = 1	10 (P < 1	0.0001); I² = 73	1%					
Test for overall effect: Z =	0.73 (P	= 0.47	7)									
									AAE+SAVR Lower AAE+SAVR Higher			
To add from a sub-supervise all forms		1.17 4	0.0 46	4 (D	0.000	17 20.0	01		ALCOARTER ALCOART ALCOART HIgher			

Test for subgroup differences: $Chi^2 = 1.63$, df = 1 (P = 0.20), $l^2 = 38.8\%$

Figure S4 Forest plot for preoperative body surface area (m²).

	AAE	+SAV	'R	s	AVR			Mean Difference		Mean D	ifference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
1.4.1 Matched or Adjust	ed Obse	rvati	onal St	udies								
Haunschild 2019	30	6	169	29	6	169	69.5%	1.00 [-0.28, 2.28]			┼╋╾	
Chauvette (redo) 2020 Subtotal (95% CI)	28.1	3.2	21 190	26.3	7.1	104 273	30.5% 100.0%	1.80 [-0.13, 3.73] 1.24 [0.18, 2.31]			•	
Heterogeneity: Tau ² = 0.0	00; Chi =	= 0.46	6, df = 1	(P = 0.9)	50); F	² =0%						
Test for overall effect: Z =	= 2.29 (P	= 0.0	2)									
1.4.2 Unmatched/Unadj	usted Ob	serv	ational	Studies	5							
Kulik 2008	28.2	6.4	172	27.3	6.5	540	25.0%	0.90 [-0.20, 2.00]			⊢∎ −	
Penaranda 2014	27.9	4.1	30	26.1	4.3	87	20.2%	1.80 [0.08, 3.52]				
Prifti 2015	26.4	5	35	26	5	20	13.5%	0.40 [-2.35, 3.15]			•	
Beckmann 2016	34	7	36	28	5	92	14.9%	6.00 [3.50, 8.50]				
Haunschild 2019 Subtotal (95% CI)	30	6	171 444	29	5	3949 4688	26.4% 100.0%	1.00 [0.09, 1.91] 1.80 [0.44, 3.16]			•	
Heterogeneity: Tau ² = 1.6	62; Chi =	= 15.1	7, df=	4 (P = 0	.004); l² = 7	4%					
Test for overall effect: Z =	= 2.59 (P	= 0.0	10)									
									-10			10
	-								AAE+	SAVR Lower	AAE+SAVR Higher	10

Test for subgroup differences: $Chi^2 = 0.40$, df = 1 (P = 0.53), $I^2 = 0\%$

Figure S5 Forest plot for preoperative body mass index (kg/m²).

	AAE+S	AVR	SA	VR		Risk Ratio	Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI				
1.5.1 Matched or Adjust	ed Obser	vationa	I Studies								
Okamoto 2016	0	58	0	58		Not estimable					
Chauvette (redo) 2020	0	21	0	104		Not estimable					
Tam (no CABG) 2020	33	809	40	809	0.0%	0.82 [0.53, 1.29]					
Tam (yes CABG) 2020	31	525	34	525	0.0%	0.91 [0.57, 1.46]	_				
Tam 2020	64	1334	74	1334	94.8%	0.86 [0.62, 1.20]	— — ——————————————————————————————————				
Shih 2022	3	54	5	162	5.2%	1.80 [0.44, 7.28]					
Subtotal (95% CI)		1467		1658	100.0%	0.90 [0.65, 1.24]					
Total events	67		79								
Heterogeneity: Tau ² = 0.0)0; Chi = =	1.00, df	'= 1 (P =	0.32); I ^z =	0%						
Test for overall effect: Z =	0.65 (P =	0.51)									
1.5.2 Unmatched/Unadju	isted Obs	servatio	nal Stud	ies							
Penaranda 2014	6	30	11	87	5.9%	1.58 [0.64, 3.91]					
Prifti 2015	3	35	4	20	2.8%	0.43 [0.11, 1.72]	• • • • • • • • • • • • • • • • • • •				
Correia 2016	12	239	48	767	10.4%	0.80 [0.43, 1.49]					
Okamoto 2016	0	58	36	531	0.8%	0.12 [0.01, 1.99]	•				
Tam (no CABG) 2020	34	850	484	8764	0.0%	0.72 [0.52, 1.02]					
Tam (yes CABG) 2020	32	546	557	6947	0.0%	0.73 [0.52, 1.03]					
Tam 2020	66	1396	1041	15711	23.4%	0.71 [0.56, 0.91]					
Mehaffey 2021	1137	5412	35824	183856	29.9%	1.08 [1.02, 1.14]	-				
Shih 2022	3	54	41	814	4.0%	1.10 [0.35, 3.45]					
Rao 2023	6	90	53	512	7.0%	0.64 [0.29, 1.45]					
Yousef 2023	19	131	404	2240	15.9%	0.80 [0.53, 1.23]					
Subtotal (95% CI)		7445		204538	100.0%	0.86 [0.67, 1.10]	◆				
Total events	1252		37462								
Heterogeneity: Tau ² = 0.05; Chi ² = 19.01, df = 8 (P = 0.01); l ² = 58%											
Test for overall effect: Z =	1.22 (P =	0.22)									
							U.Z U.D I Z D				

Test for subgroup differences: $Chi^2 = 0.05$, df = 1 (P = 0.82), $l^2 = 0\%$

Figure S6 Forest plot for cerebrovascular disease.



Test for subgroup differences: $Chi^2 = 0.31$, df = 1 (P = 0.57), l² = 0%

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

AAE+SAVR Lower AAE+SAVR Higher



Test for subgroup differences: $Chi^2 = 3.09$, df = 1 (P = 0.08), $l^2 = 67.7\%$

Figure S8 Forest plot for smoking.

	AAE+S	AVR	SAV	R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.8.1 Matched or Adjusted Observat	ional Stud	lies					
Okamoto 2016	4	58	6	58	3.6%	0.67 [0.20, 2.24]	
Tam (no CABG; Cr >120 µM) 2020	56	809	69	809	0.0%	0.81 [0.58, 1.14]	
Tam (yes CABG; Cr >120 µM) 2020	58	525	72	525	0.0%	0.81 [0.58, 1.11]	
Tam (Cr>120 µM) 2020	114	1334	141	1334	96.4%	0.81 [0.64, 1.02]	
Tam (no CABG; Cr >180 µM) 2020	17	809	22	809	0.0%	0.77 [0.41, 1.44]	
Tam (yes CABG; Cr >180 µM) 2020	15	525	19	525	0.0%	0.79 [0.41, 1.54]	
Tam (Cr>180 µM) 2020	32	1334	41	1334	0.0%	0.78 [0.49, 1.23]	
Subtotal (95% CI)		1392		1392	100.0%	0.80 [0.64, 1.01]	◆
Total events	118		147				
Heterogeneity: Tau ² = 0.00; Chi ² = 0.0	9, df = 1 (i	P = 0.76	6); I ^z = 0%)			
Test for overall effect: Z = 1.87 (P = 0.0)6)						
1.8.2 Unmatched/Unadjusted Observ	ational S	tudies					
Penaranda 2014	0	30	3	87	0.2%	0.41 [0.02, 7.63]	• • •
Prifti 2015	2	35	0	20	0.2%	2.92 [0.15, 57.90]	
Beckmann 2016	7	36	15	92	2.3%	1.19 [0.53, 2.68]	
Correia 2016	64	239	227	767	27.4%	0.90 [0.71, 1.15]	
Okamoto 2016	4	58	61	531	1.6%	0.60 [0.23, 1.59]	
Tam (no CABG; Cr >120 µM) 2020	98	850	1117	8764	0.0%	0.90 [0.74, 1.10]	
Tam (yes CABG; Cr >120 µM) 2020	62	546	949	6947	0.0%	0.83 [0.65, 1.06]	
Tam (Cr≻120 µM) 2020	160	1396	2066	15711	66.8%	0.87 [0.75, 1.01]	
Tam (no CABG; Cr >180 µM) 2020	30	850	272	8764	0.0%	1.14 [0.79, 1.65]	
Tam (yes CABG; Cr >180 µM) 2020	19	546	234	6947	0.0%	1.03 [0.65, 1.64]	
Tam (Cr >180 µM) 2020	49	1396	506	15711	0.0%	1.09 [0.82, 1.45]	
Rao 2023	4	90	47	512	1.5%	0.48 [0.18, 1.31]	
Subtotal (95% CI)		1884		17720	100.0%	0.87 [0.77, 0.99]	◆
Total events	241		2419				
Heterogeneity: Tau ² = 0.00; Chi ² = 3.4	6, df = 6 (I	P = 0.7\$	5); I² = 0%)			
Test for overall effect: Z = 2.13 (P = 0.0	3)						
							AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 0.41$, df = 1 (P = 0.52), $l^2 = 0\%$

Figure S9 Forest plot for chronic renal failure.



Test for subgroup differences: $Chi^2 = 0.03$, df = 1 (P = 0.86), $l^2 = 0\%$

Figure S10 Forest plot for dialysis.

	AAE+S	AVR	SAV	/R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.10.1 Matched or Adjus	ted Obse	rvation	al Studies	5			
Okamoto 2016	39	58	37	58	1.5%	1.05 [0.81, 1.37]	
Haunschild 2019	150	169	144	169	15.5%	1.04 [0.96, 1.13]	- -
Chauvette (redo) 2020	13	21	61	104	0.8%	1.06 [0.73, 1.53]	
Shih 2022	44	54	128	162	4.7%	1.03 [0.89, 1.20]	
Tam (no CABG) 2020	613	809	612	809	0.0%	1.00 [0.95, 1.06]	
Tam (yes CABG) 2020	461	525	470	525	0.0%	0.98 [0.94, 1.02]	
Tam 2020	1074	1334	1082	1334	77.5%	0.99 [0.96, 1.03]	-#-
Subtotal (95% CI)		1636		1827	100.0%	1.00 [0.97, 1.04]	•
Total events	1320		1452				
Heterogeneity: Tau ² = 0.0	00; Chi ² =	1.45, dt	f= 4 (P = 0	0.84); I² =	0%		
Test for overall effect: Z =	0.20 (P =	0.84)					
1.10.2 Unmatched/Unad	justed Ob	servat	ional Stud	lies			
Penaranda 2014	23	30	65	87	2.9%	1.03 [0.81, 1.29]	
Prifti 2015	16	35	10	20	0.5%	0.91 [0.52, 1.61]	• · · · · · · · · · · · · · · · · · · ·
Beckmann 2016	24	36	67	92	2.3%	0.92 [0.70, 1.19]	
Correia 2016	138	239	338	767	7.1%	1.31 [1.15, 1.50]	
Okamoto 2016	39	58	324	531	4.0%	1.10 [0.91, 1.34]	
Haunschild 2019	152	171	3400	3949	18.3%	1.03 [0.98, 1.09]	+
Tam (no CABG) 2020	643	850	6841	8764	0.0%	0.97 [0.93, 1.01]	
Tam (yes CABG) 2020	473	546	6211	6947	0.0%	0.97 [0.94, 1.00]	
Tam 2020	1116	1396	13052	15711	23.8%	0.96 [0.94, 0.99]	
Mehaffey 2021	4765	5412	159034	183856	26.1%	1.02 [1.01, 1.03]	•
Shih 2022	44	54	693	814	7.4%	0.96 [0.84, 1.09]	
Rao 2023	67	90	385	512	7.4%	0.99 [0.87, 1.13]	
Subtotal (95% CI)		7521		206339	100.0%	1.02 [0.98, 1.06]	•
Total events	6384		177368				
Heterogeneity: Tau ² = 0.0)0; Chi = =	31.37, (df = 9 (P =	0.0003);	I² = 71%		
Test for overall effect: Z =	0.87 (P =	0.38)					
							AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 0.32$, df = 1 (P = 0.57), $l^2 = 0\%$

Figure S11 Forest plot for hypertension.

	AAE+S	AVR	SA	VR		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.11.1 Matched or Adjus	sted Obse	rvation	al Studie	s			
Okamoto 2016	13	58	10	58	1.2%	1.30 [0.62, 2.72]	
Haunschild 2019	54	169	57	169	6.9%	0.95 [0.70, 1.29]	
Chauvette (redo) 2020	6	21	16	104	1.0%	1.86 [0.82, 4.19]	
Tam (no CABG) 2020	311	809	318	809	0.0%	0.98 [0.87, 1.11]	
Tam (yes CABG) 2020	267	525	279	525	0.0%	0.96 [0.85, 1.08]	
Tam 2020	578	1334	597	1334	87.5%	0.97 [0.89, 1.05]	
Shih 2022	18	54	58	162	3.5%	0.93 [0.61, 1.43]	
Subtotal (95% CI)		1636		1827	100.0%	0.97 [0.90, 1.06]	•
Total events	669		738				
Heterogeneity: Tau ² = 0.0	00; Chi² =	3.10, df	'= 4 (P =	0.54); I ² =	0%		
Test for overall effect: Z =	0.62 (P =	0.53)					
1.11.2 Unmatched/Unad	justed Ob	oservati	ional Stu	dies			
Penaranda 2014	5	30	14	87	0.1%	1.04 [0.41, 2.63]	· · · · · · · · · · · · · · · · · · ·
Prifti 2015	8	35	5	20	0.1%	0.91 [0.35, 2.42]	·
Beckmann 2016	8	36	30	92	0.2%	0.68 [0.35, 1.34]	•
Correia 2016	42	239	99	767	0.8%	1.36 [0.98, 1.89]	
Okamoto 2016	13	58	113	531	0.3%	1.05 [0.64, 1.75]	
Haunschild 2019	54	171	1257	3949	1.6%	0.99 [0.79, 1.24]	
Tam (no CABG) 2020	329	850	3036	8764	0.0%	1.12 [1.02, 1.22]	
Tam (yes CABG) 2020	278	546	3192	6947	0.0%	1.11 [1.02, 1.21]	
Tam 2020	607	1396	6228	15711	21.0%	1.10 [1.03, 1.17]	-
Mehaffey 2021	2144	5412	63942	183856	73.9%	1.14 [1.10, 1.18]	
Shih 2022	18	54	242	814	0.5%	1.12 [0.76, 1.66]	
Yousef 2023	47	131	713	2240	1.5%	1.13 [0.89, 1.43]	
Subtotal (95% CI)		7562		208067	100.0%	1.13 [1.10, 1.16]	•
Total events	2946		72643				
Heterogeneity: Tau ² = 0.0	00; Chi ^z =	5.98, df	'= 9 (P =	0.74); I ^z =	0%		
Test for overall effect: Z =	: 8.15 (P =	0.0000	11)				

0.5 0.7 1 1.5 2 AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: Chi² = 11.18, df = 1 (P = 0.0008), I^2 = 91.1%

Figure S12 Forest plot for diabetes.

AAF+SAVR SAVR **Risk Ratio Risk Ratio** IV, Random, 95% CI Study or Subgroup Events Total Events Total Weight IV, Random, 95% Cl 1.12.1 Matched or Adjusted Observational Studies Okamoto 2016 1.80 [0.91, 3.56] 18 58 10 58 5.4% 1.13 [0.93, 1.37] Haunschild 2019 97 169 169 34.2% 86 1.00 [0.92, 1.09] Tam (no CABG) 2020 443 809 443 809 0.0% Tam (yes CABG) 2020 353 525 355 525 0.0% 0.99 [0.91, 1.08] Tam 2020 796 1334 798 1334 60.4% 1.00 [0.94, 1.06] 1.07 [0.91, 1.27] Subtotal (95% CI) 1561 100.0% 1561 Total events 911 894 Heterogeneity: Tau² = 0.01; Chi² = 4.11, df = 2 (P = 0.13); l² = 51% Test for overall effect: Z = 0.85 (P = 0.40) 1.12.2 Unmatched/Unadjusted Observational Studies Prifti 2015 11 35 4 20 1.9% 1.57 [0.58, 4.29] Okamoto 2016 18 58 104 531 8.9% 1.58 [1.04, 2.41] Haunschild 2019 97 171 2060 3949 29.3% 1.09 [0.95, 1.24] Tam (no CABG) 2020 468 850 4268 8764 0.0% 1.13 [1.06, 1.21] Tam (yes CABG) 2020 367 546 4228 6947 0.0% 1.10 [1.04, 1.17] Tam 2020 835 1396 8496 15711 37.9% 1.11 [1.06, 1.16] Rao 2023 512 21.9% 0.81 [0.66, 1.00] 48 90 336 Subtotal (95% CI) 1750 20723 100.0% 1.07 [0.93, 1.23] 11000 Total events 1009 Heterogeneity: Tau² = 0.01; Chi² = 11.94, df = 4 (P = 0.02); l² = 66% Test for overall effect: Z = 0.92 (P = 0.36) 0.7 1.5 0.5 ż

AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.97), $l^2 = 0\%$

Figure S13 Forest plot for dyslipidemia.



Test for subgroup differences: $Chi^2 = 2.13$, df = 1 (P = 0.14), l² = 53.0%

Figure S14 Forest plot for coronary artery disease.

	AAE+S	AVR	SAV	R		Risk Ratio	Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI				
1.14.1 Matched or Adjust	ted Obse	rvationa	al Studie	s							
Haunschild 2019	29	169	21	169	19.3%	1.38 [0.82, 2.32]					
Okamoto 2016	6	58	9	58	7.0%	0.67 [0.25, 1.75]					
Chauvette (redo) 2020	3	21	40	104	5.8%	0.37 [0.13, 1.09]					
Tam (no CABG) 2020	119	809	122	809	0.0%	0.98 [0.77, 1.23]					
Tam (yes CABG) 2020	81	525	85	525	0.0%	0.95 [0.72, 1.26]					
Tam 2020	200	1334	207	1334	52.9%	0.97 [0.81, 1.16]					
Shih (arrhythmia) 2022	11	54	31	162	15.0%	1.06 [0.58, 1.97]					
Subtotal (95% CI)		1636		1827	100.0%	0.97 [0.74, 1.27]	•				
Total events	249		308								
Heterogeneity: Tau ² = 0.03	3; Chi ² = {	5.50, df	= 4 (P = 0	0.24); l ² =	: 27%						
Test for overall effect: Z = 0.23 (P = 0.82)											
1.14.2 Unmatched/Unadj	usted Ob	servati	onal Stud	lies							
Kulik 2008	6	172	34	540	1.7%	0.55 [0.24, 1.30]					
Prifti 2015	2	35	1	20	0.2%	1.14 [0.11, 11.83]	• • • •				
Correia 2016	25	239	117	767	7.3%	0.69 [0.46, 1.03]					
Okamoto 2016	6	58	84	531	2.0%	0.65 [0.30, 1.43]					
Haunschild 2019	29	171	632	3949	10.5%	1.06 [0.75, 1.49]					
Tam (no CABG) 2020	125	850	1696	8764	0.0%	0.76 [0.64, 0.90]					
Tam (yes CABG) 2020	83	546	1404	6947	0.0%	0.75 [0.61, 0.92]	_				
Tam 2020	208	1396	3100	15711	72.4%	0.76 [0.66, 0.86]					
Shih (arrhythmia) 2022	11	54	201	814	4.1%	0.82 [0.48, 1.42]					
Rao 2023	6	89	51	507	1.8%	0.67 [0.30, 1.51]					
Subtotal (95% CI)		2214		22839	100.0%	0.77 [0.69, 0.86]	•				
Total events	293		4220								
Heterogeneity: Tau ² = 0.00; Chi ² = 4.82, df = 7 (P = 0.68); l ² = 0%											
Test for overall effect: Z = 4.60 (P < 0.00001)											

Test for subgroup differences: $Chi^2 = 2.32$, df = 1 (P = 0.13), $l^2 = 57.0\%$

Figure S15 Forest plot for preoperative atrial fibrillation.

AAE+SAVR Lower AAE+SAVR Higher

	AAE+S	AVR	SA	VR		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.15.1 Matched or Adjus	sted Obse	rvation	al Studie	s			
Chauvette (redo) 2020	1	21	6	104	2.2%	0.83 [0.10, 6.50]	· · · · · · · · · · · · · · · · · · ·
Haunschild 2019	23	169	19	169	29.4%	1.21 [0.69, 2.14]	
Tam (no CABG) 2020	21	809	26	809	0.0%	0.81 [0.46, 1.42]	
Tam (yes CABG) 2020	32	525	27	525	0.0%	1.19 [0.72, 1.95]	
Tam 2020	53	1334	53	1334	68.4%	1.00 [0.69, 1.45]	
Subtotal (95% CI)		1524		1607	100.0%	1.05 [0.77, 1.43]	
Total events	77		78				
Heterogeneity: Tau ² = 0.0	00; Chi ² =	0.36, dt	f= 2 (P =	0.84); I ² =	0%		
Test for overall effect: Z =	: 0.33 (P =	: 0.74)					
1.15.2 Unmatched/Unad	justed Ot	servat	ional Stu	dies			
Penaranda 2014	9	30	20	87	6.4%	1.30 [0.67, 2.55]	· · · · · · · · · · · · · · · · · · ·
Prifti 2015	0	35	2	20	0.4%	0.12 [0.01, 2.32]	•
Haunschild 2019	23	171	571	3949	14.9%	0.93 [0.63, 1.37]	
Tam (no CABG) 2020	24	850	332	8764	0.0%	0.75 [0.50, 1.12]	
Tam (yes CABG) 2020	33	546	528	6947	0.0%	0.80 [0.57, 1.12]	
Tam 2020	57	1396	860	15711	23.4%	0.75 [0.57, 0.97]	
Mehaffey 2021	777	5412	25212	183856	43.1%	1.05 [0.98, 1.12]	+■-
Yousef 2023	17	131	286	2240	11.8%	1.02 [0.64, 1.60]	
Subtotal (95% CI)		/1/5		205863	100.0%	0.95 [0.79, 1.14]	-
Total events	883		26951				
Heterogeneity: Tau ² = 0.0	32; Chi ^z =	8.81, di	f= 5 (P =	0.12); I ² =	43%		
Test for overall effect: Z =	: 0.52 (P =	: 0.60)					
							0.5 0.7 1 1.5 2
							AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 0.30$, df = 1 (P = 0.58), l² = 0%

Figure S16 Forest plot for peripheral vascular disease.

AAE+SAVR SAVR Mean Difference Mean Difference Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI 1.16.1 Matched or Adjusted Observational Studies Okamoto 2016 58 23.0% 0.40 [-2.33, 3.13] 63.1 7.8 62.7 7.2 58 11 31.2% 0.00 [-2.35, 2.35] Haunschild 2019 60 169 60 11 169 Chauvette (redo) 2020 62 5 21 60 10 104 20.8% 2.00 [-0.88, 4.88] Shih 2022 24.9% 0.83 [-1.80, 3.46] 59.16 8.81 54 58.33 7.6 162 Subtotal (95% CI) 0.71 [-0.60, 2.03] 302 493 100.0% Heterogeneity: Tau² = 0.00; Chi² = 1.18, df = 3 (P = 0.76); l² = 0% Test for overall effect: Z = 1.07 (P = 0.29) 1.16.2 Unmatched/Unadjusted Observational Studies Penaranda 2014 59 12 29 57 10 84 2.4% 2.00 [-2.86, 6.86] Prifti 2015 58 13 35 54.7 7.4 20 2.0% 3.30 [-2.09, 8.69] Beckmann 2016 58 7 36 59 13 92 4.6% -1.00 [-4.51, 2.51] 0.70 [-1.61, 3.01] Correia 2016 65.3 15.9 239 64.6 16 767 10.6% Haunschild 2019 60 11 171 59 12 3949 19.9% 1.00 [-0.69, 2.69] Shih 2022 59.16 8.81 54 56.82 9.62 814 9.5% 2.34 [-0.10, 4.78] Yousef 2023 59.3 6 131 58.7 5.9 2240 51.0% 0.60 [-0.46, 1.66] Subtotal (95% CI) 695 7966 100.0% 0.87 [0.11, 1.62] Heterogeneity: Tau² = 0.00; Chi² = 3.77, df = 6 (P = 0.71); l² = 0% Test for overall effect: Z = 2.26 (P = 0.02) -4 4 -5 ż ή AAE+SAVR Lower AAE+SAVR Higher Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.84), l² = 0%

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

	AAE+S	AVR	SA	VR		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.17.1 Matched or Adjusted Observa	tional Stu	ıdies					
Okamoto (LVEF <40%) 2016	0	58	2	58	2.6%	0.20 [0.01, 4.08]	· · · · · · · · · · · · · · · · · · ·
Tam (no CABG) 2020	347	809	363	809	0.0%	0.96 [0.86, 1.07]	
Tam (yes CABG) 2020	255	525	257	525	0.0%	0.99 [0.88, 1.12]	
Tam 2020	602	1334	620	1334	97.4%	0.97 [0.89, 1.05]	
Tam (no CABG; LVEF <50%) 2020	83	809	84	809	0.0%	0.99 [0.74, 1.32]	Т
Tam (yes CABG; LVEF <50%) 2020	78	525	64	525	0.0%	1.22 [0.90, 1.66]	
Tam (LVEF <50%) 2020	161	1334	148	1334	0.0%	1.09 [0.88, 1.34]	
Tam (no CABG; LVEF <35%) 2020	30	809	33	809	0.0%	0.91 [0.56, 1.48]	
Tam (yes CABG; LVEF <35%) 2020	27	525	21	525	0.0%	1.29 [0.74, 2.24]	
Tam (LVEF <35%) 2020	57	1334	54	1334	0.0%	1.06 [0.73, 1.52]	
Subtotal (95% CI)		1392		1392	100.0%	0.93 [0.57, 1.53]	-
Total events	602		622				
Heterogeneity: Tau ² = 0.06; Chi ² = 1.0	5, df = 1 (P = 0.30	l); l² = 5%)			
Test for overall effect: Z = 0.28 (P = 0.7	'8) `						
1.17.2 Unmatched/Unadjusted Obse	rvational	Studies					
Sommers (LVEF <40%) 1997	14	82	109	350	8.0%	0.55 [0.33, 0.91]	
Kulik (LVEF <50%) 2008	24	172	66	540	9.7%	1.14 [0.74, 1.76]	
Prifti 2015	7	35	1	20	0.7%	4.00 [0.53, 30.21]	
Prifti (LVEF <35%) 2015	7	35	1	20	0.0%	4.00 [0.53, 30.21]	
Tam (no CABG) 2020	354	850	4537	8764	0.0%	0.80 [0.74, 0.87]	
Tam (yes CABG) 2020	260	546	3859	6947	0.0%	0.86 [0.78, 0.94]	
Tam 2020	614	1396	8396	15711	27.0%	0.82 [0.77, 0.87]	•
Tam (no CABG; LVEF <50%) 2020	158	850	1550	8764	0.0%	1.05 [0.91, 1.22]	
Tam (yes CABG; LVEF <50%) 2020	96	546	1232	6947	0.0%	0.99 [0.82, 1.20]	
Tam (LVEF <50%) 2020	254	1396	2782	15711	0.0%	1.03 [0.91, 1.15]	
Tam (no CABG; LVEF <35%) 2020	57	850	512	8764	0.0%	1.15 [0.88, 1.50]	
Tam (yes CABG; LVEF <35%) 2020	30	546	408	6947	0.0%	0.94 [0.65, 1.34]	
Tam (LVEF <35%) 2020	87	1396	920	15711	0.0%	1.06 [0.86, 1.32]	
Mehaffey 2021	2208	5412	72317	183856	27.7%	1.04 [1.00, 1.07]	•
Rao 2023	17	90	92	512	8.8%	1.05 [0.66, 1.68]	
Yousef 2023	48	131	686	2240	18.1%	1.20 [0.95, 1.51]	+
Subtotal (95% CI)		7318		203229	100.0%	0.97 [0.82, 1.15]	•
Total events	2932		81667				
Heterogeneity: Tau ² = 0.03; Chi ² = 53.	24, df = 6	(P < 0.0	10001); I ^z	= 89%			
Test for overall effect: Z = 0.37 (P = 0.7	'1)						
							AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.88), I² = 0%

Figure S18 Forest plot for CHF or low LVEF.

	AAE+S	AVR	SAV	'R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.17.1 Matched or Adjuste	d Observa	ational	Studies				
Okamoto (NYHA IV) 2016	0	58	0	58		Not estimable	
Haunschild 2019	85	158	78	137	16.1%	0.94 [0.77, 1.16]	
Chauvette (redo) 2020	14	21	68	104	6.1%	1.02 [0.73, 1.42]	_
Tam (no CABG) 2020	311	809	305	809	0.0%	1.02 [0.90, 1.15]	
Tam (yes CABG) 2020	215	525	216	525	0.0%	1.00 [0.86, 1.15]	
Tam 2020	526	1334	521	1334	76.2%	1.01 [0.92, 1.11]	
Shih 2022	10	54	24	162	1.5%	1.25 [0.64, 2.44]	
Subtotal (95% CI)		1625		1795	100.0%	1.00 [0.92, 1.09]	•
Total events	635		691				
Heterogeneity: Tau ² = 0.00;	$Chi^{2} = 0.7$	7, df = 3	3 (P = 0.8	36); I ^z = 0)%		
Test for overall effect: Z = 0.	06 (P = 0.	95)					
1.17.2 Unmatched/Unadjus	sted Obse	rvation	al Studie	es :			
Sommers 1997	75	98	315	432	15.2%	1.05 [0.93, 1.19]	
Kulik 2008	66	172	221	540	10.9%	0.94 [0.76, 1.16]	
Penaranda 2014	24	30	68	87	11.1%	1.02 [0.83, 1.26]	
Beckmann 2016	10	36	77	92	3.4%	0.33 [0.19, 0.57]	
Correia 2016	118	239	444	767	14.3%	0.85 [0.74, 0.98]	
Okamoto (NYHA IV) 2016	0	58	24	531	0.2%	0.18 [0.01, 2.99]	·
Haunschild 2019	86	160	1534	3061	14.0%	1.07 [0.92, 1.24]	
Tam (no CABG) 2020	300	850	3178	8764	0.0%	0.97 [0.88, 1.07]	
Tam (yes CABG) 2020	189	546	2522	6947	0.0%	0.95 [0.85, 1.07]	
Tam 2020	489	1396	5700	15711	17.4%	0.97 [0.90, 1.04]	4
Shih 2022	10	54	223	814	3.0%	0.68 [0.38, 1.20]	
Rao 2023	46	90	221	512	10.5%	1.18 [0.95, 1.48]	
Subtotal (95% CI)		2333		22547	100.0%	0.95 [0.85, 1.06]	•
Total events	924		8827				
Heterogeneity: Tau ² = 0.02;	Chi ² = 28	.21, df=	9 (P = 0	.0009); P	* = 68%		
Test for overall effect: $Z = 0$.	91 (P = 0.	36)					
							0.2 0.5 1 2 5
							AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 0.58$, df = 1 (P = 0.45), $l^2 = 0\%$

Figure S19 Forest plot for NYHA III or IV.



Test for subgroup differences: Chi² = 1.55, df = 1 (P = 0.21), l² = 35.6%

Figure S20 Forest plot for mean NYHA grade.



 $1 = 0.00, a_1 = 1, a_2 = 0.427, a_3 = 0.00, a_4 = 1, a_4 = 0.427, a_5 = 0.427, a_$

Figure S21 Forest plot for non-elective surgery.

	AAE	+SAV	R		SAVR			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.22.1 Matched or Ad	ljusted (Observ	vationa	I Studie	s				
Shih 2022	2.1	1.6	54	2	2.1	162	100.0%	0.10 [-0.44, 0.64]	
Subtotal (95% CI)			54			162	100.0%	0.10 [-0.44, 0.64]	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.37	(P = 0).71)						
1.22.2 Unmatched/Ur Mehaffey 2021 Shih 2022 Rao 2023 Yousef 2023	nadjuste 2.99 2.1 1.6 1.9	d Obs 4.1 1.6 1 1.35	ervatio 5412 54 90 131	nal Stu 2.97 1.9 1.8 1.97	dies 4.2 1.7 1.2 1.48	183856 814 512 2240	52.5% 6.8% 20.9% 19.8%	0.02 [-0.09, 0.13] 0.20 [-0.24, 0.64] -0.20 [-0.43, 0.03] -0.07 [-0.31, 0.17]	
Subtotal (95% CI) Heterogeneity: Tau² = Test for overall effect:	0.00; CI Z = 0.52	ni² = 3. (P = 0	5687 .94, df=).60)	= 3 (P =	0.27);	18/422 ² = 24%	100.0%	-0.03 [-0.15, 0.09]	-0.5 -0.25 0 0.25 0.5 AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 0.22$, df = 1 (P = 0.64), $I^2 = 0\%$

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



Test for subgroup differences: Chi² = 1.59, df = 1 (P = 0.21), l² = 37.0%

Figure S23 Forest plot for prior cardiac surgery.

	AAE+S	AVR	SAV	R		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	I	V, Random, 95% Cl		
1.24.1 Matched or Adjusted Observ	ational S	tudies								
Okamoto 2016	1	58	0	58	8.9%	3.00 [0.12, 72.15]				
Chauvette (redo) 2020	21	21	104	104	52.2%	1.00 [0.94, 1.07]		•		
Shih (replacement or repair) 2022 Subtotal (95% CI)	10	54 133	9	162 324	38.9% 100.0%	3.33 [1.43, 7.77] 1.76 [0.62, 5.00]				
Total events	32		113							
Test for overall effect: Z = 1.06 (P = 0 1 24 2 Unmatched/Unadjusted Obs	1.29) ervationa	(F = 0.0)2), (" = 7	070						
		1 Studie 25	, 3 0	20		Not optimoble				
Correia 2015	1	220	0	767	37%	9 60 10 39 734 881				
Shih (replacement or repair) 2022	10	54	30	814	87.8%	5.02 [2.60, 9.73]				
Rao 2023 Subtotal (95% CI)	1	90 418	5	512 2113	8.4% 100.0%	1.14 [0.13, 9.63] 4.54 [2.45, 8.44]				
Total events	12		35							
Heterogeneity: Tau² = 0.00; Chi² = 1. Test for overall effect: Z = 4.79 (P < 0	91, df = 2 1.00001)	(P = 0.3	38); I² = 0	%						
							AAE+SAV	R lower AAE+SAVR Higher		

Test for subgroup differences: $Chi^2 = 2.34$, df = 1 (P = 0.13), $I^2 = 57.4\%$

Figure S24 Forest plot for prior SAVR.

	AA	E+SAV	R	SAVR				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.26.1 Matched or Adju	sted Obs	servati	onal St	udies					
Okamoto 2016	92.7	24.8	58	85.1	29.9	58	55.2%	7.60 [-2.40, 17.60]	
Chauvette (redo) 2020	56.9	17.9	21	54.5	41.8	104	44.8%	2.40 [-8.70, 13.50]	
Subtotal (95% CI)			79			162	100.0%	5.27 [-2.16, 12.70]	
Heterogeneity: Tau ² = 0.	00; Chi ^z	= 0.47,	df = 1	(P = 0.5	0); l²=	:0%			
Test for overall effect: Z	= 1.39 (P	9 = 0.16	i)						
1.26.2 Unmatched/Una	ljusted (Observ	ational	Studie	s				
Kulik 2008	67.7	25.1	172	68.8	28.9	540	38.1%	-1.10 [-5.57, 3.37]	
Prifti 2015	101	22	35	116	38.7	20	6.6%	-15.00 [-33.46, 3.46]	←
Beckmann 2016	75	29	36	77	30	92	14.6%	-2.00 [-13.28, 9.28]	
Correia 2016	96.4	28.2	239	92.3	24.5	767	40.7%	4.10 [0.13, 8.07]	
Subtotal (95% CI)			482			1419	100.0%	-0.03 [-5.08, 5.02]	
Heterogeneity: Tau ² = 10	2.19; Chi	z = 6.3	3, df = 3	8 (P = 0.	10); I²	= 53%			
Test for overall effect: Z	= 0.01 (P	2 = 0.99)						
									-10 -5 0 5 10
									AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 1.34$, df = 1 (P = 0.25), $l^2 = 25.3\%$

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



Test for subgroup differences: $Chi^2 = 0.93$, df = 1 (P = 0.33), $I^2 = 0\%$

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

	AA	E+SAV	R	SAVR Mean				Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
1.27.1 Matched or Adjus	ted Ob	servatio	nal Stu	idies							
Okamoto 2016	0.61	0.2	58	0.72	0.24	58	32.9%	-0.11 [-0.19, -0.03]	_		
Chauvette (redo) 2020	0.87	0.14	21	1.18	0.14	104	33.7%	-0.31 [-0.38, -0.24]	_ 		
Shih 2022	0.7	0.229	54	0.72	0.26	162	33.3%	-0.02 [-0.09, 0.05]	_ _		
Subtotal (95% CI)			133			324	100.0%	-0.15 [-0.32, 0.03]			
Heterogeneity: Tau ² = 0.0)2; Chi ²	= 35.66	, df = 2	(P < 0.0	0001)	; I ^z = 94	%				
Test for overall effect: Z =	1.63 (P	= 0.10)									
1.27.2 Unmatched/Unadjusted Observational Studies											
Kulik 2008	0.7	0.17	172	0.72	0.34	540	29.5%	-0.02 [-0.06, 0.02]			
Beckmann 2016	0.7	0.3	36	0.7	0.2	92	7.9%	0.00 [-0.11, 0.11]			
Correia 2016	0.55	0.23	239	0.6	0.2	767	33.3%	-0.05 [-0.08, -0.02]			
Shih 2022	0.7	0.229	54	0.75	0.36	814	16.4%	-0.05 [-0.12, 0.02]			
Rao 2023	0.81	0.28	90	0.94	0.6	512	12.9%	-0.13 [-0.21, -0.05]	_		
Subtotal (95% CI)			591			2725	100.0%	-0.05 [-0.08, -0.02]	•		
Heterogeneity: Tau ² = 0.0)0; Chi ^z	= 7.03, (df = 4 (F	P = 0.13); ² = 4	43%					
Test for overall effect: Z =	2.87 (P	= 0.004	4)								
									-0.2 -0.1 0 0.1 0.2		
	-								ARETORIK LOWEL ARETORIK HIGHE		

Test for subgroup differences: Chi² = 1.18, df = 1 (P = 0.28), l² = 15.0%

Figure S27 Forest plot for aortic valve area (cm²).



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

	AAE	+SAV	/R	SAVR				Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
1.29.1 Matched or Adjusted Obs	servatior	ial St	udies								
Okamoto 2016	19.3	1.8	58	19.7	1.9	58	48.9%	-0.40 [-1.07, 0.27]			
Shih 2022	22.1	1.9	54	23.4	2.3	162	51.1%	-1.30 [-1.92, -0.68]	— —		
Subtotal (95% CI)			112			220	100.0%	-0.86 [-1.74, 0.02]			
Heterogeneity: Tau ² = 0.30; Chi ² = 3.72, df = 1 (P = 0.05); i ² = 73%											
Test for overall effect: Z = 1.91 (P	= 0.06)										
1.29.2 Unmatched/Unadjusted Observational Studies											
Beckmann 2016	19	1	36	20	1	92	34.9%	-1.00 [-1.39, -0.61]			
Shih 2022	22.1	1.9	54	24.3	2.3	814	32.4%	-2.20 [-2.73, -1.67]	←∎──		
Rao (barrel end of sizer) 2023	23.2	2.2	82	24.1	2.2	511	32.7%	-0.90 [-1.41, -0.39]			
Rao (replica end of sizer) 2023	23.1	2.1	62	23.7	2.1	494	0.0%	-0.60 [-1.15, -0.05]			
Subtotal (95% CI)			172			1417	100.0%	-1.36 [-2.12, -0.59]			
Heterogeneity: Tau ² = 0.40; Chi ² :	= 15.67,	df = 2	(P = 0.	0004); I	z = 83	7%					
Test for overall effect: Z = 3.47 (P	= 0.000	5)									
									AAE+SAVR Lower AAE+SAVR Higher		
T 16 0 0		N 10	4 (10)	0.445.17		,			the entreaction with ortheringhon		

Test for subgroup differences: Chi² = 0.69, df = 1 (P = 0.41), l² = 0%

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

	AAE+S	AVR	SAV	'R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.30.1 Matched or Adjusted Observational Studie	s						
Okamoto 2016	58	58	58	58	32.8%	1.00 [0.97, 1.03]	_ + _
Haunschild 2019	161	166	161	166	25.4%	1.00 [0.96, 1.04]	_ + _
Chauvette (redo) 2020	17	21	77	104	0.7%	1.09 [0.86, 1.39]	
Tam (no CABG) 2020	688	809	679	809	0.0%	1.01 [0.97, 1.06]	
Tam (yes CABG) 2020	460	525	457	525	0.0%	1.01 [0.96, 1.05]	
Tam 2020	1148	1334	1136	1334	37.7%	1.01 [0.98, 1.04]	
Shih 2022	49	54	142	162	3.4%	1.04 [0.93, 1.15]	
Subtotal (95% CI)		1633		1824	100.0%	1.01 [0.99, 1.03]	•
Total events	1433		1574				
Heterogeneity: Tau ² = 0.00; Chi ² = 1.07, df = 4 (P = 1	0.90); I ^z =	0%					
Test for overall effect: Z = 0.59 (P = 0.56)							
1.30.2 Unmatched/Unadjusted Observational Stud	lies						
Sommers 1997	84	98	316	432	3.2%	1.17 [1.06, 1.29]	
Penaranda 2014	30	30	87	87	9.8%	1.00 [0.95, 1.05]	_
Prifti 2015	35	35	20	20	4.9%	1.00 [0.93, 1.08]	
Beckmann 2016	36	36	92	92	11.9%	1.00 [0.96, 1.04]	_ + _
Correia 2016	170	239	528	767	0.0%	1.03 [0.94, 1.13]	
Correia (incl mixed stenosis+insufficiency) 2016	223	239	710	767	12.2%	1.01 [0.97, 1.05]	
Haunschild 2019	163	169	3513	3829	15.5%	1.05 [1.02, 1.08]	
Tam (no CABG) 2020	727	850	7486	8764	0.0%	1.00 [0.97, 1.03]	
Tam (yes CABG) 2020	479	546	5770	6947	0.0%	1.06 [1.02, 1.09]	
Tam 2020	1206	1396	13256	15711	19.1%	1.02 [1.00, 1.05]	
Shih 2022	49	54	690	814	3.8%	1.07 [0.98, 1.17]	
Rao 2023	88	90	474	512	12.1%	1.06 [1.02, 1.10]	_ _
Yousef 2023	118	131	1937	2240	7.4%	1.04 [0.98, 1.11]	+
Subtotal (95% CI)		2278		24504	100.0%	1.03 [1.01, 1.05]	◆
Total events	2032		21095				
Heterogeneity: Tau ² = 0.00; Chi ² = 16.14, df = 9 (P =	: 0.06); I ^e :	= 44%					
Test for overall effect: Z = 3.15 (P = 0.002)							
							AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: Chi² = 3.26, df = 1 (P = 0.07), l² = 69.4%

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

AAE+SAVR SAVR **Risk Ratio Risk Ratio** IV, Random, 95% CI Study or Subgroup Events Total Events Total Weight IV, Random, 95% Cl 1.31.1 Matched or Adjusted Observational Studies Okamoto 2016 8 58 9 58 0.89 [0.37, 2.14] 19.9% Shih 2022 16 54 81 162 80.1% 0.59 [0.38, 0.92] Subtotal (95% CI) 0.64 [0.43, 0.95] 112 220 100.0% Total events 24 90 Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 1 (P = 0.42); l² = 0% Test for overall effect: Z = 2.21 (P = 0.03) 1.31.2 Unmatched/Unadjusted Observational Studies Prifti 2015 9 35 9 20 19.9% 0.57 [0.27, 1.20] Shih 2022 16 54 35.4% 0.75 [0.50, 1.15] 320 814 Rao 2023 1.18 [0.89, 1.55] 37 90 179 512 44.8% Subtotal (95% CI) 179 1346 100.0% 0.87 [0.58, 1.32] Total events 62 508 Heterogeneity: Tau² = 0.08; Chi² = 5.23, df = 2 (P = 0.07); l² = 62% Test for overall effect: Z = 0.66 (P = 0.51) 0.5 0.7 1.5 Ż

AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 1.09$, df = 1 (P = 0.30), l² = 8.5%

Figure S31 Forest plot for bicuspid aortic valve.

Figures S32-S39. Meta-analyses for operative outcomes

	AAE+S	AVR	SAVR			Risk Ratio	Risk Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl					
1.32.1 Matched or Adjusted Obs	servationa	al Studie	es									
Okamoto 2016	18	58	21	58	8.8%	0.86 [0.51, 1.43]						
Haunschild 2019	12	169	11	169	3.8%	1.09 [0.50, 2.40]						
Tam (no CABG) 2020	178	809	251	809	0.0%	0.71 [0.60, 0.84]						
Tam (yes CABG) 2020	73	525	79	525	0.0%	0.92 [0.69, 1.24]	_					
Tam 2020	251	1334	330	1334	82.8%	0.76 [0.66, 0.88]						
Shih 2022	9	54	20	162	4.5%	1.35 [0.65, 2.78]						
Subtotal (95% CI)		1615		1723	100.0%	0.80 [0.68, 0.93]	◆					
Total events	290		382									
Heterogeneity: Tau ² = 0.00; Chi ² = 3.10, df = 3 (P = 0.38); I ² = 3%												
Test for overall effect: Z = 2.83 (P	= 0.005)											
1.32.2 Unmatched/Unadjusted (bservatio	onal Stu	idies									
Sommers 1997	0	98	0	432		Not estimable						
Sakamoto (St. Jude only) 2006	24	24	104	104	20.4%	1.00 [0.94, 1.06]	+					
Sakamoto 2006	24	24	157	157	20.5%	1.00 [0.94, 1.06]	+					
Kulik 2008	74	172	217	540	10.9%	1.07 [0.88, 1.31]						
Penaranda 2014	0	30	3	87	0.1%	0.41 [0.02, 7.63]						
Prifti 2015	35	35	20	20	19.2%	1.00 [0.93, 1.08]	+					
Beckmann 2016	0	36	0	92		Not estimable						
Correia 2016	57	239	366	767	9.0%	0.50 [0.39, 0.63]	_ _					
Haunschild 2019	12	171	329	3949	2.5%	0.84 [0.48, 1.47]						
Tam (no CABG) 2020	218	850	2384	8764	0.0%	0.94 [0.84, 1.06]						
Tam (yes CABG) 2020	92	546	1166	6947	0.0%	1.00 [0.83, 1.22]						
Tam 2020	310	1396	3550	15711	17.5%	0.98 [0.89, 1.09]	-					
Rao 2023	0	90	0	512		Not estimable						
Subtotal (95% CI)		2315		22371	100.0%	0.94 [0.86, 1.03]	•					
Total events	536		4746									
Heterogeneity: Tau ² = 0.01; Chi ² :	= 33.13, d	f= 7 (P	< 0.0001); I ² = 79	%							
Test for overall effect: Z = 1.33 (P	= 0.18)											
							_ <u>_</u> <u></u> <u></u>					

Test for subgroup differences: $Chi^2 = 3.04$, df = 1 (P = 0.08), $l^2 = 67.1$ %

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

	AAE+S/	AVR	SA	/R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
1.34.1 Matched or Ad	ljusted Ol	bservat	ional Stu	dies			
Okamoto 2016	6	58	6	58	100.0%	1.00 [0.34, 2.92]	<→
Haunschild 2019	0	169	0	169		Not estimable	
Shih 2022	0	54	0	162		Not estimable	
Subtotal (95% CI)		281		389	100.0%	1.00 [0.34, 2.92]	
Total events	6		6				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.00 (P = 1.0	0)				
1.34.2 Unmatched/U	nadjusted	Obser	vational	Studies			
Kulik 2008	75	172	214	540	13.2%	1.10 [0.90, 1.34]	
Penaranda 2014	13	30	44	87	2.9%	0.86 [0.54, 1.36]	
Prifti 2015	6	35	4	20	0.5%	0.86 [0.27, 2.68]	· · · · · · · · · · · · · · · · · · ·
Correia 2016	41	239	105	767	5.4%	1.25 [0.90, 1.74]	
Haunschild 2019	0	171	0	3949		Not estimable	_
Mehaffey 2021	2307	5412	83094	183856	73.6%	0.94 [0.91, 0.97]	
Shih 2022	0	54	0	814		Not estimable	
Rao 2023	24	90	164	512	4.4%	0.83 [0.58, 1.20]	
Subtotal (95% CI)		6203		190545	100.0%	0.97 [0.90, 1.05]	-
Total events	2466		83625				
Heterogeneity: Tau² =	: 0.00; Chi	² = 5.69	, df = 5 (F	° = 0.34);	l²=12%		
Test for overall effect:	Z = 0.78 (P = 0.4	3)				
							AAE+SAVP Lower AAE+SAVP Higher

Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), l² = 0%

Figure S33 Forest plot for concomitant CABG.



Figure S34 Forest plot for concomitant mitral valve surgery.

	AAE+S/	AVR	SAV	R		Risk Ratio	Risk Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight IV, Random, 95% CI		IV, Random, 95% CI					
1.36.1 Matched or Ad	ljusted Ol	oservat										
Okamoto 2016	8	58	9	58	100.0%	0.89 [0.37, 2.14]						
Haunschild 2019	0	169	0	169		Not estimable						
Subtotal (95% CI)		227		227	100.0%	0.89 [0.37, 2.14]	-					
Total events	8		9									
Heterogeneity: Not ap	plicable											
Test for overall effect:	Z=0.26 (P = 0.7	9)									
1.36.2 Unmatched/Unadjusted Observational Studies												
Kulik 2008	1	172	29	540	23.4%	0.11 [0.01, 0.79]						
Correia 2016	4	239	36	767	76.6%	0.36 [0.13, 0.99]						
Haunschild 2019	0	171	0	3949		Not estimable						
Subtotal (95% CI)		582		5256	100.0%	0.27 [0.10, 0.73]						
Total events	5		65									
Heterogeneity: Tau² =	0.06; Chi	² = 1.09), df = 1 (l	P = 0.30	0); I² = 9%							
Test for overall effect:	Z = 2.60 (P = 0.0	09)									
							0.02 0.1 1 10 50					
							AAE+SAVR Lower AAE+SAVR Higher					

Test for subgroup differences: Chi² = 3.12, df = 1 (P = 0.08), l² = 67.9%

Figure S35 Forest plot for concomitant tricuspid valve surgery.

	AAE+SAVR				SAVR			Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl		
1.37.1 Matched or Adjusted Observation	al Studies	6									
Okamoto 2016	177	42	58	157	39	58	22.4%	20.00 [5.25, 34.75]	 ∎		
Haunschild 2019	101.18	27.4	169	76.72	22.7	169	32.6%	24.46 [19.10, 29.82]			
Chauvette (redo) 2020	146	32	21	150	71	104	17.8%	-4.00 [-23.33, 15.33]			
Shih 2022	138.17	34.91	54	102.86	33.04	162	27.1%	35.31 [24.70, 45.92]			
Subtotal (95% CI)			302			493	100.0%	21.33 [9.69, 32.97]			
Heterogeneity: Tau ² = 100.67; Chi ² = 12.70, df = 3 (P = 0.005); i ² = 76%											
Test for overall effect: Z = 3.59 (P = 0.0003	l)										
1.37.2 Unmatched/Unadjusted Observati	ional Stud	ies									
Kulik 2008	137.5	45.6	172	129.9	44.4	540	0.0%	7.60 (-0.18, 15,38)			
Kulik (excl concom procedures) 2008	119.3	44.5	94	106.9	30.8	252	11.2%	12.40 [2.63, 22.17]	_ _ _		
Penaranda 2014	145	76	30	88	31	87	3.2%	57.00 (29.03, 84.97)	_		
Prifti 2015	119.3	43	35	89	25	20	6.1%	30.30 [12.33, 48.27]	———		
Beckmann 2016	105	29	36	67	26	92	10.3%	38.00 [27.14, 48.86]			
Correia 2016	83	21	239	68.8	20.3	767	0.0%	14.20 [11.17, 17.23]			
Correia (excl concom procedures) 2016	77.4	15.5	178	55.7	11	520	16.6%	21.70 [19.23, 24.17]	+		
Haunschild 2019	101.23	27.3	171	81.27	23.6	3949	15.6%	19.96 [15.80, 24.12]	+		
Mehaffey 2021	128	51	5412	114	43	183856	17.0%	14.00 [12.63, 15.37]	•		
Rao 2023	122.8	52.7	90	105.7	40.3	512	9.9%	17.10 [5.67, 28.53]	— —		
Yousef 2023	138	64	131	96	33	2240	10.2%	42.00 [30.96, 53.04]			
Subtotal (95% CI)			6177			191528	100.0%	24.02 [18.50, 29.55]	● ●		
Heterogeneity: Tau ² = 46.36; Chi ² = 78.88,	df = 8 (P	< 0.000	01); I ^z =	90%							
Test for overall effect: Z = 8.52 (P < 0.0000	11)										
									-50 -25 0 25 50		
Taat fan auk waard diffanan aan Okiz - 0.47	46 - 4 (D	- 0.00	17 - 0.0						AAE+SAVR Lower AAE+SAVR Higher		

Test for subgroup differences: $Chi^2 = 0.17$, df = 1 (P = 0.68), $l^2 = 0\%$

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

	AAE+SAVR				SAVR			Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
1.38.1 Matched or Adjusted Observation	al Studies	;									
Okamoto 2016	126	32	58	110	34	58	21.5%	16.00 [3.98, 28.02]			
Haunschild 2019	77.7	20.3	169	55.67	14.8	169	32.6%	22.03 [18.24, 25.82]			
Chauvette (redo) 2020	114	23	21	112	51	104	19.1%	2.00 [-11.89, 15.89]			
Shih 2022	113.79	26.73	54	82.98	28.42	162	26.7%	30.81 [22.44, 39.18]			
Subtotal (95% CI)			302			493	100.0%	19.25 [10.17, 28.33]	\bullet		
Heterogeneity: Tau ² = 62.11; Chi ² = 13.17, df = 3 (P = 0.004); l ² = 77%											
Test for overall effect: Z = 4.15 (P < 0.0001)										
1.38.2 Unmatched/Unadjusted Observation	onal Stud	ies									
Sommers 1997	78	26	98	67	24	432	12.6%	11.00 [5.38, 16.62]			
Kulik 2008	94.1	26.7	172	86.5	27.9	540	0.0%	7.60 [2.97, 12.23]			
Kulik (excl concom procedures) 2008	82.1	21.3	94	72.2	20.9	252	13.2%	9.90 [4.88, 14.92]			
Penaranda 2014	74	27	30	60.5	18	87	7.9%	13.50 [3.12, 23.88]			
Prifti 2015	93	32	35	71	19	20	5.8%	22.00 [8.52, 35.48]			
Beckmann 2016	75	19	36	56	21	92	10.5%	19.00 [11.45, 26.55]			
Correia 2016	56.6	12.4	239	45.2	14.4	767	0.0%	11.40 [9.53, 13.27]			
Correia (excl concom procedures) 2016	60.5	14.4	178	41.4	10.8	520	15.8%	19.10 [16.79, 21.41]	+		
Haunschild 2019	77.7	20.2	171	58.32	17.3	3949	15.2%	19.38 [16.30, 22.46]			
Rao 2023	93.1	38.8	90	80	30.3	512	9.6%	13.10 [4.67, 21.53]			
Yousef 2023	111	51	131	74	27	2240	9.3%	37.00 [28.20, 45.80]			
Subtotal (95% CI)			863			8104	100.0%	17.70 [13.67, 21.74]	◆		
Heterogeneity: Tau ² = 25.40; Chi ² = 37.91,	df = 8 (P -	< 0.000	01); I ² =	: 79%							
Test for overall effect: Z = 8.61 (P < 0.0000	1)										

Test for subgroup differences: $Chi^2 = 0.09$, df = 1 (P = 0.76), $l^2 = 0\%$

-20 -10 0 10 20 AAE+SAVR Lower AAE+SAVR Higher

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



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.

	AAE	+SAV	R	SAVR				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.39.1 Matched or Adjusted Observational	Studies								
Okamoto 2016	19.4	1.6	58	19.3	1.3	58	21.8%	0.10 [-0.43, 0.63]	_ _
Haunschild 2019	21.7	1.5	169	22.3	1.5	169	27.9%	-0.60 [-0.92, -0.28]	
Chauvette (redo) 2020	21.2	0.4	21	22.1	0.4	104	31.1%	-0.90 [-1.09, -0.71]	+
Shih 2022	22.13	1.94	54	23.39	2.28	162	19.2%	-1.26 [-1.89, -0.63]	_
Subtotal (95% CI)			302			493	100.0%	-0.67 [-1.09, -0.25]	◆
Heterogeneity: Tau ² = 0.14; Chi ² = 15.62, df =	: 3 (P = 0	0.001)	I ² = 81	%					
Test for overall effect: Z = 3.10 (P = 0.002)									
4 20 2 Upmatched/Upadjusted Observation	ol Etudi								
1.59.2 Onmatched/onaujusted Observation		es	~~						_
Sommers 1997	23.8	1.94	98	25.3	2.07	432	14.2%	-1.50 [-1.93, -1.07]	_ _
Kulik 2008	22	1	172	20.7	0.6	540	14.5%	1.30 [1.14, 1.46]	+
Penaranda (all same in each group) 2014	21	0	30	19	0	87		Not estimable	
Prifti (all same in each group) 2015	19	0	35	17	0	20		Not estimable	
Beckmann 2016	24.9	0.45	20	23.3	1.3	92	14.3%	1.60 [1.27, 1.93]	
Correia 2016	21.8	1	239	20.7	0.5	767	14.5%	1.10 [0.97, 1.23]	-
Haunschild 2019	21.7	1.5	171	23.7	1.5	3949	14.4%	-2.00 [-2.23, -1.77]	
Rao 2023	23.1	1.9	90	23.7	2.1	512	14.2%	-0.60 [-1.03, -0.17]	
Yousef 2023	23	3	131	23.7	1.5	2240	14.0%	-0.70 [-1.22, -0.18]	— •—
Subtotal (95% CI)			986			8639	100.0%	-0.11 [-1.17, 0.96]	
Heterogeneity: Tau ² = 2.04; Chi ² = 802.72, df	= 6 (P <	0.000	01); l² =	= 99%					
Test for overall effect: Z = 0.20 (P = 0.84)									
								_	
									-z -1 U 1 Z

Test for subgroup differences: $Chi^2 = 0.92$, df = 1 (P = 0.34), $l^2 = 0\%$

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

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

	AA	E+SAV	2		SAVR			Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
1.40.1 Matched or Adjust	sted Obs	servatio	nal Stu	idies							
Okamoto 2016	0.93	0.18	58	1.03	0.27	58	31.7%	-0.10 [-0.18, -0.02]	e		
Haunschild 2019	1.77	0.22	169	1.77	0.22	169	44.0%	0.00 [-0.05, 0.05]	_		
Chauvette (redo) 2020	0.76	0.18	21	0.85	0.41	104	24.3%	-0.09 [-0.20, 0.02]			
Subtotal (95% CI)			248			331	100.0%	-0.05 [-0.13, 0.02]			
Heterogeneity: Tau ² = 0.00; Chi ² = 5.40, df = 2 (P = 0.07); I ² = 63%											
Test for overall effect: Z =	: 1.43 (P	= 0.15)									
1.40.2 Unmatched/Unad	ljusted (Observa	tional	Studies							
Sommers 1997	0.953	0.097	98	0.982	0.098	432	13.6%	-0.03 [-0.05, -0.01]			
Kulik 2008	0.89	0.18	172	0.79	0.16	540	13.2%	0.10 [0.07, 0.13]			
Penaranda 2014	1.14	0.36	25	0.8	0.26	72	5.0%	0.34 [0.19, 0.49]			
Prifti (up to 1y) 2015	0.85	0.17	31	0.76	0.2	19	7.4%	0.09 [-0.02, 0.20]			
Beckmann 2016	0.91	0.2	26	0.83	0.14	72	9.1%	0.08 [-0.00, 0.16]			
Correia 2016	0.92	0.11	239	0.86	0.08	767	13.9%	0.06 [0.04, 0.08]			
Haunschild 2019	1.77	0.22	171	1.8	0.22	3949	12.9%	-0.03 [-0.06, 0.00]			
Rao 2023	0.78	0.18	73	0.8	0.205	439	12.1%	-0.02 [-0.07, 0.03]			
Rao (1y) 2023	0.79	0.22	84	0.75	0.17	437	0.0%	0.04 [-0.01, 0.09]			
Yousef 2023	0.96	0.2	131	0.96	0.2	2240	12.8%	0.00 [-0.04, 0.04]			
Subtotal (95% CI)			966			8530	100.0%	0.04 [-0.00, 0.08]	\bullet		
Heterogeneity: Tau ² = 0.0	00; Chi²∘	= 103.3	5, df = 8	3 (P ≤ 0.	.00001)	; I ^z = 92	%				
Test for overall effect: Z =	: 1.94 (P	= 0.05)									
									AAE+SAVR Lower AAE+SAVR Higher		

Test for subgroup differences: $Chi^2 = 4.87$, df = 1 (P = 0.03), l² = 79.5%

Figure S40 Forest plot for postoperative indexed effective orifice area (cm²/m²).



Test for subgroup differences: Chi² = 1.38, df = 1 (P = 0.24), l² = 27.8%

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



Test for subgroup differences: $Chi^2 = 0.86$, df = 1 (P = 0.35), $I^2 = 0\%$

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

	AAE+SAVR		SAVR			Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
1.43.1 Matched or Adjusted Observational Studies									
Okamoto (iEOI <0.85 cm²/m²) 2016	15	58	12	58	29.0%	1.25 [0.64, 2.43]			
Haunschild (iEOI ≤0.85 cm²/m²) 2019	42	164	53	165	71.0%	0.80 [0.57, 1.12]			
Subtotal (95% CI)		222		223	100.0%	0.91 [0.61, 1.35]			
Total events	57		65						
Heterogeneity: Tau ² = 0.03; Chi ² = 1.38, df = 1 (P = 0.3)	24); I 2 = 28	3%							
Test for overall effect: Z = 0.47 (P = 0.64)									
4 42 0 Homestele d'Alex directed Obergenetics - L Studi									
1.43.2 Unmatched/Unadjusted Observational Studie	es	~ .							
Sakamoto (St. Jude only; iEOI ≤0.85 cm²/m²) 2006	0	24	0	104	~	Not estimable			
Sakamoto (IEOI ≤0.85 cm³/m²) 2006	U 	24	2	157	0.4%	1.26 [0.06, 25.56]			
Kulik (iEOI ≤0.85 cm²/m²) 2008	73	172	375	540	22.2%	0.61 [0.51, 0.73]			
Penaranda (iEOi ≤0.85 cm²/m²) 2014	5	25	49	- 72	4.6%	0.29 [0.13, 0.66]	•		
Prifti (up to 1y; iEOI ≤0.75 cm²/m²) 2015	12	31	9	19	6.4%	0.82 [0.43, 1.56]			
Correia (iEOI ≤0.85 cm²/m²) 2016	71	239	384	767	20.9%	0.59 [0.48, 0.73]			
Haunschild (iEOI ≤0.85 cm²/m²) 2019	42	166	1152	3861	17.9%	0.85 [0.65, 1.11]			
Rao (1y) 2023	45	84	265	437	20.6%	0.88 [0.71, 1.09]			
Yousef (IEOI <0.85 cm*/m*) 2023	10	131	224	2240	7.0%	0.76 [0.42, 1.40]			
Subtotal (95% CI)		890		8197	100.0%	0.70 [0.58, 0.84]	-		
lotal events	258		2460						
Heterogeneity: $Iau^2 = 0.03$; $Chi^2 = 16.09$, $df = 7$ (P = 0).U2); I* = 5	56%							
Test for overall effect: Z = 3.79 (P = 0.0002)									
							0.5 0.7 1 1.5 2		
Test for subgroup differences: Ohi7 – 4-30, df – 4 /D –	0.040 18-						AAE+SAVR Lower AAE+SAVR Higher		
restion subgroup dilierences: ChF = 1.38, dt = 1 (P =	÷ U.∠4), I* =	= 27.3%)						

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

	AAE+S	AVR	SAV	/R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.44.1 Matched or Adjusted Observa	tional St	udies					
Okamoto (30d or hospital) 2016	1	58	2	58	3.2%	0.50 [0.05, 5.36]	• •
Haunschild (30d or hosp) 2019	3	169	2	169	5.7%	1.50 [0.25, 8.86]	
Chauvette (redo; hosp & 30d) 2020	2	21	9	104	8.4%	1.10 [0.26, 4.73]	
Tam (no CABG; 30d) 2020	16	809	17	809	0.0%	0.94 [0.48, 1.85]	
Tam (yes CABG; 30d) 2020	19	525	16	525	0.0%	1.19 [0.62, 2.28]	L
Tam (30d) 2020	35	1334	33	1334	81.0%	1.06 [0.66, 1.70]	_
Shih (30d) 2022	0	54	1	162	1.8%	0.99 [0.04, 23.90]	·
Subtotal (95% CI)		1636		1827	100.0%	1.06 [0.69, 1.61]	-
Total events	41		47				
Heterogeneity: Tau ² = 0.00; Chi ² = 0.5/	4, df = 4 (P = 0.97	7); I² = 0%)			
Test for overall effect: Z = 0.26 (P = 0.7	9)						
1.44.2 Unmatched/Unadjusted Obser	vational	Studies	6				
Sommers 1997	7	98	15	432	7.7%	2.06 [0.86, 4.91]	
Kulik 2008	12	172	35	540	12.1%	1.08 [0.57, 2.03]	
Penaranda 2014	3	30	7	87	4.0%	1.24 [0.34, 4.50]	
Prifti (hospital) 2015	4	35	1	20	1.6%	2.29 [0.27, 19.07]	
Beckmann (30d) 2016	2	36	2	92	1.9%	2.56 [0.37, 17.46]	
Correia (hospital) 2016	2	239	4	767	2.4%	1.60 [0.30, 8.71]	
Haunschild (30d or hosp) 2019	3	171	55	3949	4.8%	1.26 [0.40, 3.99]	
Tam (no CABG; 30d) 2020	15	850	201	8764	0.0%	0.77 [0.46, 1.29]	
Tam (yes CABG; 30d) 2020	21	546	294	6947	0.0%	0.91 [0.59, 1.40]	
Tam (30d) 2020	36	1396	495	15711	23.0%	0.82 [0.59, 1.14]	
Mehaffey (30d or hospital) 2021	290	5412	6303	183856	33.0%	1.56 [1.39, 1.75]	
Rao (30d) 2023	2	90	3	512	2.2%	3.79 [0.64, 22.38]	
Yousef 2023	5	131	52	2240	7.3%	1.64 [0.67, 4.05]	
Subtotal (95% CI)		7810		208206	100.0%	1.34 [1.02, 1.76]	◆
Total events	366		6972				
Heterogeneity: Tau ² = 0.06; Chi ² = 16.2	20, df = 1	0 (P = 0	1.09); I 2 = 1	38%			
Test for overall effect: Z = 2.11 (P = 0.0	4)						

Test for subgroup differences: Chi² = 0.85, df = 1 (P = 0.36), l² = 0\%

Figure S44 Forest plot for perioperative mortality.



Test for subgroup differences: $Chi^2 = 4.30$, df = 1 (P = 0.04), $I^2 = 76.7\%$

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]).



Test for subgroup differences: Chi² = 0.64, df = 1 (P = 0.42), l² = 0%

Figure S46 Forest plot for perioperative stroke.



Test for subgroup differences: Chi² = 0.09, df = 1 (P = 0.76), l² = 0%

Figure S47 Forest plot for perioperative myocardial infarction.

	AAE+S	AVR	SA	VR		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	
1.48.1 Matched or Adjusted Observation	al Studies							
Okamoto (complete heart block) 2016	0	58	2	58	1.0%	0.20 [0.01, 4.08]	· · · ·	
Chauvette (redo) 2020	3	21	12	104	6.5%	1.24 [0.38, 4.01]		
Tam (no CABG) 2020	39	809	54	809	0.0%	0.72 [0.48, 1.08]		
Tam (yes CABG) 2020	28	525	28	525	0.0%	1.00 [0.60, 1.66]		
Tam 2020	67	1334	82	1334	91.4%	0.82 [0.60, 1.12]		
Shih 2022	0	54	8	162	1.1%	0.17 [0.01, 2.97]		
Subtotal (95% CI)		1467		1658	100.0%	0.81 [0.60, 1.10]	•	
Total events	70		104					
Heterogeneity: Tau ² = 0.00; Chi ² = 2.46, df	= 3 (P = 0	.48); l²:	= 0%					
Test for overall effect: Z = 1.35 (P = 0.18)								
1.48.2 Unmatched/Unadjusted Observati	onal Stud	ies						
Sommers 1997	5	98	25	432	15.4%	0.88 [0.35, 2.25]		
Penaranda (complete heart block) 2014	0	30	3	87	3.7%	0.41 [0.02, 7.63]		
Prifti 2015	1	35	1	20	4.2%	0.57 [0.04, 8.65]		
Beckmann (30d) 2016	2	36	14	92	10.4%	0.37 [0.09, 1.53]		
Tam (no CABG) 2020	41	850	439	8764	0.0%	0.96 [0.70, 1.32]		
Tam (yes CABG) 2020	30	546	344	6947	0.0%	1.11 [0.77, 1.59]		
Tam 2020	71	1396	783	15711	23.1%	1.02 [0.81, 1.29]	+	
Mehaffey 2021	303	5412	3861	183856	23.7%	2.67 [2.38, 2.99]	•	
Mehaffey (using published %) 2021	303	5412	9928	183856	0.0%	1.04 [0.93, 1.16]		
Yousef 2023	11	131	107	2240	19.5%	1.76 [0.97, 3.19]		
Subtotal (95% CI)		7138		202438	100.0%	1.18 [0.64, 2.18]	•	
Total events	393		4794					
Heterogeneity: Tau ² = 0.41; Chi ² = 63.80, d	lf=6 (P ≺	0.0000	1); I ^z = 91	%				
Test for overall effect: Z = 0.53 (P = 0.59)								
								H

Test for subgroup differences: Chi² = 1.14, df = 1 (P = 0.28), l² = 12.6%

Figure S48 Forest plot for perioperative new permanent pacemaker.



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

	AAE+S	AVR	SA	VR		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
1.50.1 Matched or Ad									
Correia 2016	0	21	0	104		Not estimable			
Okamoto 2016	1	58	0	58	26.1%	3.00 [0.12, 72.15]			\rightarrow
Haunschild 2019 Subtotal (95% CI)	2	169 248	5	169 331	73.9% 100.0%	0.40 [0.08, 2.03] 0.68 [0.12, 3.83]			
Total events	3		5						
Heterogeneity: Tau ² =	0.37; Chi	i ^z = 1.22	2, df = 1 (i	= 0.27);	I ² = 18%				
Test for overall effect:	Z=0.44 ((P = 0.6	6)						
1.50.2 Unmatched/Ur	nadjusted	Obser	vational	Studies					
Haunschild 2019	2	171	389	3949	35.7%	0.12 [0.03, 0.47]	-		
Mehaffey 2021	14	5412	468	183856	45.8%	1.02 [0.60, 1.73]			
Rao 2023	0	90	3	512	18.6%	0.81 [0.04, 15.46]			
Subtotal (95% CI)		5673		188317	100.0%	0.45 [0.09, 2.29]			
Total events	16		860						
Heterogeneity: Tau ² =	1.43; Chi	i ^z = 8.09), df = 2 (i	P = 0.02);	I² = 75%				
Test for overall effect:	Z = 0.96 ((P = 0.3	4)						
							0.02		50
							0.01	AAE+SAVR Lower AAE+SAVR Higher	00

Test for subgroup differences: Chi² = 0.11, df = 1 (P = 0.74), l² = 0%

Figure S50 Forest plot for deep sternal wound infection.

	AAE	+SAV	R		SAVR Mean Difference				Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI			
1.51.1 Matched or Ad	ljusted (Obser	vationa	I Studie	s								
Haunschild 2019	14.3	15	169	15	14.2	169	13.1%	-0.70 [-3.81, 2.41]	_				
Shih 2022	2.31	4.48	54	1.89	1.26	162	86.9%	0.42 [-0.79, 1.63]		— ——— —			
Subtotal (95% CI)			223			331	100.0%	0.27 [-0.86, 1.40]					
Heterogeneity: Tau ² =	0.00; Cl	hi² = 0	.43, df=	= 1 (P =	0.51);	I ² = 0%							
Test for overall effect:	Z = 0.47	' (P = 0).64)										
1.51.2 Unmatched/Ur	nadjuste	d Obs	ervatio	onal Stu	dies								
Prifti 2015	4.5	3.9	35	1.94	2.2	20	27.2%	2.56 [0.95, 4.17]		_			
Beckmann 2016	11	9.5	36	11	8.1	92	12.5%	0.00 [-3.52, 3.52]					
Haunschild 2019	14.3	15	171	16	14.8	3949	20.6%	-1.70 [-4.00, 0.60]	_				
Mehaffey 2021	2.7	2.5	5412	2.4	2.1	183856	39.6%	0.30 [0.23, 0.37]					
Subtotal (95% CI)			5654			187917	100.0%	0.47 [-1.04, 1.97]					
Heterogeneity: Tau² =	1.49; C	hi² = 1	0.49, dt	f= 3 (P :	= 0.01)); I ² = 71%							
Test for overall effect:	Z = 0.61	(P = 0).54)										
									-4				
									-4	AAE+SAVR Lower AAE+SAVR Higher			

Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.84), l² = 0%

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



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

	AAE	+SAV	R	5	SAVR			Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
1.53.1 Matched or Adjust	sted Obs	servati	onal S	tudies							
Okamoto 2016	25.3	9.4	58	26	10.4	58	75.7%	-0.70 [-4.31, 2.91]			
Chauvette (redo) 2020 Subtotal (95% Cl)	30.2	10.5	21 79	28.1	23.5	104 162	24.3% 100.0%	2.10 [-4.27, 8.47] -0.02 [-3.16, 3.12]			
Heterogeneity: Tau ² = 0.0	00; Chi ^z :	= 0.56	df = 1	(P = 0.4	5); l² =	0%					
Test for overall effect: Z =	= 0.01 (P	= 0.99))								
1.53.2 Unmatched/Unadjusted Observational Studies											
Kulik 2008	28.3	14	172	34.2	15.1	540	42.4%	-5.90 [-8.35, -3.45]			
Prifti (up to 1y) 2015	30	12	31	29	6.8	19	25.1%	1.00 [-4.21, 6.21]			
Beckmann 2016 Subtotal (95% CI)	24	9	26 229	28	8	72 631	32.5% 100.0%	-4.00 [-7.92, -0.08] - 3.55 [-7.17, 0.07]			
Heterogeneity: Tau ² = 6.4	48; Chi ≇÷	= 5.59	df = 2	(P = 0.0	6); I ^z =	64%					
Test for overall effect: Z =	= 1.92 (P	= 0.05	i)								
									-10 -5 0 5 10		
	-								AAE+SAVR Lower AAE+SAVR Higher		

Test for subgroup differences: $Chi^2 = 2.08$, df = 1 (P = 0.15), $I^2 = 52.0\%$

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

	AAE	+SAV	'R	S	AVR			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.54.1 Matched or Adjus	sted Obs	ervat	ional S	tudies					
Chauvette (redo) 2020 Subtotal (95% Cl)	14.8	7.8	21 21	15.2	15.3	104 104	100.0% 100.0%	-0.40 [-4.85, 4.05] - 0.40 [-4.85, 4.05]	
Heterogeneity: Not applic	cable								
Test for overall effect: Z =	: 0.18 (P	= 0.8	6)						
1.54.2 Unmatched/Unad	justed C)bser	vationa	al Studie	s				
Kulik 2008	15.4	7.8	172	18.3	8.8	540	22.2%	-2.90 [-4.28, -1.52]	
Prifti (up to 1y) 2015	17	6.4	31	17.5	4.5	19	14.0%	-0.50 [-3.53, 2.53]	
Beckmann 2016	13	6	26	16	5	72	16.1%	-3.00 [-5.58, -0.42]	
Rao 2023	13.5	5	83	12.9	4.7	488	23.3%	0.60 [-0.55, 1.75]	
Rao (1y) 2023	12.6	4.6	85	13	4.8	454	0.0%	-0.40 [-1.47, 0.67]	
Yousef (1y) 2023	9.9	4.5	108	9.3	5.2	1845	24.4%	0.60 [-0.28, 1.48]	
Subtotal (95% CI)			420			2964	100.0%	-0.91 [-2.57, 0.75]	-
Heterogeneity: Tau ² = 2.7	73; Chi ≃ ∍	= 24.1	7, df=	4 (P ≤ 0	.0001); l² = 83	3%		
Test for overall effect: Z =	: 1.07 (P	= 0.2	8)						
									-10 -5 0 5 10
				=					AAE+SAVR Lower AAE+SAVR Higher

Test for subgroup differences: $Chi^2 = 0.04$, df = 1 (P = 0.83), $I^2 = 0\%$

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

	AAE+SAVR		SAVR		Risk Ratio		Risk Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI					
1.55.1 Matched or Adjusted Observational Studie	S											
Subtotal (95% CI)		0		0		Not estimable						
Total events	0		0									
Heterogeneity: Not applicable												
Test for overall effect: Not applicable												
1.55.2 Unmatched/Unadjusted Observational Studies at Discharge												
Beckmann 2016	0	26	3	72	20.8%	0.39 [0.02, 7.23]						
Rao (mild only, no moderate or severe) 2023 Subtotal (95% CI)	2	83 109	10	475 547	79.2%	1.14 [0.26, 5.13]						
Total events	2	100	13	041	100.070	0101 [0124, 0141]						
Heterogeneity: Tau ² = 0.00; Chi ² = 0.42; df = 1 (P = 0.52); P = 0%												
Test for overall effect: Z = 0.13 (P = 0.89)												
1.55.3 Unmatched/Unadjusted Observational Stu	dies Duri	ng Follo	w Up									
Yousef (1y; mild-severe) 2023	5	88	49	1785	67.4%	2.07 [0.85, 5.07]	+-=					
Yousef (1y; mod-severe) 2023	0	88	14	1785	0.0%	0.69 [0.04, 11.51]						
Rao (1y; mild-moderate only, no severe) 2023	2	85	14	452	32.6%	0.76 [0.18, 3.28]						
Rao (5y; mild only, no moderate or severe) 2023	0	33	3	91	0.0%	0.39 [0.02, 7.29]						
Subtotal (95% CI)		173		2237	100.0%	1.49 [0.59, 3.75]						
Total events	7		63									
Heterogeneity: Tau ² = 0.12; Chi ² = 1.31, df = 1 (P =	0.25); I ² =	24%										
Test for overall effect: Z = 0.85 (P = 0.39)												
							'0.01 0.1 i 10 100'					
Test for subgroup differences: Chi ² = 0.35, df = 1 (F	P = 0.55),	I² = 0%					AAE+SAVR Lower AAE+SAVR Higher					

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

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

Study or Subgroup	log[Hazard/Incident Rate Ratio]	SE	AAE+SAVR Total	SAVR Total	Weight	Hazard/Incident Rate Ratio IV, Random, 95% Cl	Hazard/Incident Rate Ratio IV, Random, 95% Cl
1.71.1 Matched or Adjusted Observational St	udies						
Okamoto (4.6 v 4.2y; 0 v 1 deterioration) 2016 Subtotal (95% CI)	-1.2026	1.633	58 58	58 58	100.0% 100.0%	0.30 [0.01, 7.37] 0.30 [0.01, 7.37]	
Heterogeneity: Not applicable Test for overall effect: Z = 0.74 (P = 0.46)							
1.71.2 Unmatched/Unadjusted Observational	Studies						
Rao ((5y KM)) 2023 Subtotal (95% CI)	0	0	90 90	512 512		Not estimable Not estimable	
Heterogeneity: Not applicable Test for overall effect: Not applicable							
Total (95% CI) Heterogeneity: Not applicable Toot for everyll offect: 7 = 0.74 (P = 0.48)			148	570	100.0%	0.30 [0.01, 7.37]	0.02 0.1 1 10 50
Test for subgroup differences: Not applicable							AAE+SAVR Lower AAE+SAVR Higher

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

			AAE+SAVR	SAVR		Hazard/Incident Rate Ratio	Hazard/Incident Rate Ratio
Study or Subgroup	log[Hazard/Incident Rate Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.73.1 Matched or Adjusted Observati	ional Studies						
Okamoto (4.6 v 4.2y; 1 v 1 CHB) 2016 Subtotal (95% CI)	-0.104	1.4142	58 58	58 58	18.1% 18.1%	0.90 [0.06, 14.41] 0.90 [0.06, 14.41]	•
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.07 (P = 0.94	4)						
1.73.2 Unmatched/Unadjusted Observ Rao (PPM; (5y KM)) 2023 Subtotal (95% Cl) Heterogeneity: Not applicable Test for overall effect: Z = 0.41 (P = 0.66	vational Studies -0.2744 3)	0.6654	90 90	512 512	81.9% <mark>81.9%</mark>	0.76 [0.21, 2.80] 0.76 [0.21, 2.80]	*
Total (95% Cl) Heterogeneity: Tau ² = 0.00; Chi ² = 0.01, Test for overall effect: Z = 0.40 (P = 0.69 Test for subgroup differences: Chi ² = 0.	, df = 1 (P = 0.91); I ^z = 0% 3) .01, df = 1 (P = 0.91), I ^z = 0%		148	570	100.0%	0.78 [0.24, 2.55]	0.02 0.1 10 50 AAE+SAVR Lower AAE+SAVR Higher

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

			AAE+SAVR	SAVR		Hazard/Incident Rate Ratio	Hazard/Incide	nt Rate Ratio
Study or Subgroup	Hazard/Incident Rate Ratio	SE	Total	Total	Weight	IV, Random, 95% Cl	IV, Randon	n, 95% CI
1.74.1 Matched or Adjusted Observational Stu	dies							
Subtotal (95% CI)			0	0		Not estimable		
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
1.74.2 Unmatched/Unadjusted Observational S	Studies							
Sakamoto (St. Jude only [1 v 5 events]) 2006	-0.1431	1.0718	24	104	0.0%	-0.14 [-2.24, 1.96]		
Sakamoto ([1 v 5 events]) 2006	0.2688	1.0733	24	157	27.3%	0.27 [-1.83, 2.37]		-
Rao ([5y KM]) 2023	-0.3448	0.6576	90	512	72.7%	-0.34 [-1.63, 0.94]		
Subtotal (95% CI)			114	669	100.0%	-0.18 [-1.28, 0.92]		
Heterogeneity: Tau ² = 0.00; Chi ² = 0.24, df = 1 (F	'= 0.63); I ² = 0%							
Test for overall effect: Z = 0.32 (P = 0.75)								
						-	-2 -1 0	1 2
							AAE+SAVR Lower	AAE+SAVR Higher

Test for subgroup differences: Not applicable

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

Study or Subgroup	Ibgroup log[Hazard/Incident Rate Ratio]				Weight	Hazard/Incident Rate Ratio IV, Random, 95% Cl	Hazard/Incident Rate Ratio IV, Random, 95% Cl
1.75.1 Matched or Adjusted Observation	al Studies						
Okamoto (4.6 v 4.2y; 0 v 0 strokes) 2016	-0.104	2	58	58	0.1%	0.90 [0.02, 45.42]	← · · · · · · · · · · · · · · · · · · ·
Mehaffev (3.3 v 3.4v: [HR]) 2021	-0.0101	0.054	5412	183856	99.9%	0.99 (0.89, 1.10)	
Subtotal (95% CI)			5470	183914	100.0%	0.99 [0.89, 1.10]	-
Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, df	f= 1 (P = 0.96); I ² = 0%						
Test for overall effect: Z = 0.19 (P = 0.85)							
1.75.2 Unmatched/Unadjusted Observati	ional Studies						\perp
Mehaffey (3.3 v 3.4y; [HR]) 2021	0.01	0.0552	5412	183856	100.0%	1.01 [0.91, 1.13]	
Subtotal (95% CI)			5412	183856	100.0%	1.01 [0.91, 1.13]	\bullet
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.18 (P = 0.86)							
							0.7 0.03 I 1.2 1.3 AAE+SAVR Lower AAE+SAVR Higher
Test for subgroup differences: Chi ² = 0.07	, df = 1 (P = 0.79), I² = 0%						ALCONTREME ALCONTRIGIE

Figure S59 Forest plot for stroke during follow-up.

Study or Subgroup	log[Hazard/Incident Rate Ratio]	\$E	AAE+SAVR Total	SAVR Total	Weight	Hazard/Incident Rate Ratio IV, Random, 95% CI	Hazard/Incident Rate Ratio IV, Random, 95% CI
Okamoto (4.6 v 4.2y; 0 v 0 bleeds) 2016 Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect 7 = 0.05 (P = 0.96)	-0.104	2	58 58	58 58	3.7% 3.7%	0.90 [0.02, 45.42] 0.90 [0.02, 45.42]	
1.76.2 Unmatched/Unadjusted Observat Rao (all bleeds (5y KMJ) 2023 Rao (major bleeds (5y KMJ) 2023 Subtotal (95% CI) Heterogeneity. Not applicable Test for overall effect. Z = 0.55 (P = 0.58)	ional Studies -0.2174 -0.1752	0.3929 0.4888	90 90 90	512 512 512	96.3% 0.0% 96.3%	0.80 [0.37, 1.74] 0.84 [0.32, 2.19] 0.80 [0.37, 1.74]	-
Total (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, di Test for overall effect: Z = 0.55 (P = 0.58) Test for subgroup differences: Chi ² = 0.00	f = 1 (P = 0.96); I ^z = 0%), df = 1 (P = 0.96), I ^z = 0%		148	570	100.0%	0.81 [0.38, 1.72]	0.02 0.1 10 50 AAE+SAVR Lower AAE+SAVR Higher

Figure S60 Forest plot for bleeding during follow-up.

Study or Subgroup log[Hazard/Inciden	t Rate Ratio]	SE	AAE+SAVR Total	SAVR Total	Weight	Hazard/Incident Rate Ratio IV, Random, 95% CI	Hazard/Incid IV, Rando	ent Rate Ratio om, 95% Cl
1.77.1 Matched or Adjusted Observational Studies								
Okamoto (4.6 v 4.2y; 0 v 1 patients) 2016 Subtotal (95% CI)	-1.2026	1.633	58 58	58 58	11.7% 11.7%	0.30 [0.01, 7.37] 0.30 [0.01, 7.37]	•	
Heterogeneity: Not applicable Test for overall effect: Z = 0.74 (P = 0.46)								
1.77.2 Unmatched/Unadjusted Observational Studies								
Sakamoto (St. Jude only [1 v 5 events]) 2006	1.4663	0.974	24	104	0.0%	4.33 [0.64, 29.23]		
Sakamoto ([1 v 5 events]) 2006	1.4727	0.8862	24	157	34.1%	4.36 [0.77, 24.77]	-	
Prifti (6.75y (2 v 0 patients)) 2015	1.0603	1.5242	35	20	13.3%	2.89 [0.15, 57.26]		•
Rao ((5y KMI) 2023	-0.3365	0.7896	90	512	40.9%	0.71 (0.15, 3,36)		
Subtotal (95% CI)			149	689	88.3%	1.78 [0.52, 6.08]		
Heterogeneity: Tau² = 0.23; Chi² = 2.46, df = 2 (P = 0.29); l² = 19% Test for overall effect: Z = 0.92 (P = 0.36)								
Total (95% CI)			207	747	100.0%	1.44 [0.46, 4.48]	-	
Heterogeneity: Tau ² = 0.20; Chi ² = 3.48, df = 3 (P = 0.32); I ² = 14%								
Test for overall effect: Z = 0.63 (P = 0.53)							AAE+SAVR Lower	AAE+SAVR Higher
Test for subgroup differences: Chi ² = 1.04, df = 1 (P = 0.31), l ² = 3.59	%							, the oriting to the

Figure S61 Forest plot for endocarditis during follow-up.

Figures S62-S63. Summaries of sensitivity analyses

		,	AAE+SAVR Studies	1	Hazard/Incident Rate Ratio	Hazard/Incident Rate Ratio
Study or Subgroup	log[Hazard/Incident Rate Ratio]	SE	Total	Total	IV, Random, 95% CI	IV, Random, 95% Cl
All Studioc	ed/Adjusted Studies	0.041046	0	0	1 02 00 05 1 111	
Air atudies	0.0281	0.041040	5	0	1.03 [0.85, 1.11]	
1.64.2 Moderate vs Serious/Cri	tical Risk of Bias-Matched/Adjuste	ed Studies (I	nteraction p=0.89)			
Moderate Risk of Bias	0.0512	0.14	3	0	1.05 [0.80, 1.38]	
Serious/Critical Risk of Bias	0.0298	0.0528	6	0	1.03 [0.93, 1.14]	
1.64.3 Moderate/Serious vs Cri	tical Risk of Bias-Matched/Adjuste	d Studies (I	nteraction p=0.90)			
Moderate/Serious Risk of Bias	0.0286	0.0464		0	1.03 [0.94, 1.13]	— + —
Critical Risk of Bias	0.0583	0.2254	1	0	1.06 [0.68, 1.65]	
1.64.4 Yes vs N/R vs No Concor	nitant-Matched/Adjusted Studies	Interaction I	p=0.51 [0.28])			
Yes Concomitant Procedures	0.0173	0.053	5	0	1.02 [0.92, 1.13]	— + —
N/R Concomitant Procedures	-0.0944	0.3208	2	0	0.91 [0.49, 1.71]	< <u>+</u> + →
No Concomitant Procedures	0.146	0.1076	3	0	1.16 [0.94, 1.43]	
1.64.5 Primary Analysis-Unmat	ched/Unadiusted Studies					
All Studies	-0.0987	0.0641	12	0	0.91 [0.80, 1.03]	
1.64.6 Excluding Rao 2023-Unn	natched/Unadjusted Studies (Inter	action p=0.6	59)	-		
Excluding Rao 2023	-0.0948	0.0661	11	0	0.91 [0.80, 1.04]	
Rao ([59 KM]) 2023	-0.2165	0.2931	1	U	0.81 [0.45, 1.43]	· · ·
1.64.7 Moderate vs Serious/Cri	tical Risk of Bias-Unmatched/Una	ljusted Stud	lies (Interaction p=0.	.08)		
Moderate Risk of Bias	-0.2085	0.1067	1	0	0.81 [0.66, 1.00]	
Serious/Critical Risk of Bias	-0.0096	0.0423	11	0	0.99 [0.91, 1.08]	
1 64 8 Moderate/Serious vs Cri	tical Risk of Rias-Unmatched/Una	liusted Stud	lies (Interaction n=0	55)		
Moderate/Serious Rick of Rise	-0 0794	0 0714	nes (interaction p=0.	.55)	0.02.00.00.1.061	
Critical Risk of Bias	-0.1572	0.1083	6	0	0.85 [0.69, 1.06]	
				-	,	
1.64.9 Yes vs N/R vs No Concor	nitant-Unmatched/Unadjusted Stu	dies (Interac	ction p=0.50 [0.31])			
Yes Concomitant Procedures	-0.0861	0.0635	9	0	0.92 [0.81, 1.04]	
No Concomitant Procedures	-0.2000	0.2339	2	0	0.70 [0.40, 1.21] 0.81 [0.65, 1.00]	·
	0.2100	0.1004	-	0	0.01 [0.00] 1.00]	
1.64.10 Primary Analysis-All St	udies (Prioritizing Matched/Adjust	ed when Un	matched/Unadjusted	l also re	eported)	
All Studies	-0.0033	0.0411	15	0	1.00 [0.92, 1.08]	
1.64.11 Moderate vs Serious/C	ritical Risk of Bias-All Studies (Pri	pritizing Mat	ched/Adjusted) (Inte	raction	p=0.67)	
Moderate Risk of Bias	0.0512	0.14	3	0	1.05 [0.80, 1.38]	
Serious/Critical Risk of Bias	-0.0126	0.0485	12	0	0.99 [0.90, 1.09]	
1 64 12 Modorato/Sorious vs C	ritical Diek of Dias All Studios (Dri	oritizing Mat	chod/Adjustod) (Into	raction	n=0.24)	
Moderate/Serious Pick of Pice	n n10	0.04607	oncurrujusteu) (illte	nacaon n	1 02 00 03 1 111	
Critical Risk of Bias	-0.1269	0.10472	7	0	0.88 [0.72, 1.08]	+ ` _
4 G4 42 Modorate un Canicus	Critical Diak of Dias All Churthand	Deioeiti-i •	Jotobod (A Surstand) 4		ion n=0 (4)	
1.04.15 Moderate Vs Serious Vs Moderate Rick of Picc	S CHUCAI RISK OF BIAS-All STUDIES (watched/Adjusted) (II	nteracti	011 p=0.44) 1 05 (0 00 - 1 00)	
Serious Risk of Rise	0.0512	0.14	3 F	0	1.00 [0.80, 1.38] 1.00 [0.80, 1.38]	'
Critical Risk of Bias	-01269	0.10472	5	0	0.88 [0.72, 1.08]	+ ` _
1.64.14 Yes vs N/R vs No Conco	omitant-All Studies (Prioritizing Ma	tched/Adjus	sted) (Interaction p=0	1.23 [p=1	U.1 / excl N/R])	
Yes Concomitant Procedures	-0.0146	0.0471	10	0	0.99 [0.90, 1.08]	
No Concomitant Procedures	-U.2334 0.146	0.∠31 0.1076	3	0	0.79 [0.50, 1.25] 1 1 16 [0.94, 1.43]	· · ·
sonoonmanti loosuul65	0.140	5.1010	5	0	1.10 [0.34, 1.40]	
						AAE+SAVR Lower AAE+SAVR Higher

Figure S62 Sensitivity analyses for mid-term mortality.

			AAE+SAVR Studies		Hazard/Incident Rate Ratio	Hazard/Incident Rate Ratio
Study or Subgroup	log[Hazard/Incident Rate Ratio]	SE	Total	Tota	I IV, Random, 95% CI	I IV, Random, 95% CI
1.70.1 Primary Analysis-Matche	ed/Adjusted Studies					
All Studies	-0.0235	0.132	2	0	0.98 [0.75, 1.27]	I − † −
1.70.5 Primary Analysis-Unmat	ched/Unadiusted Studies					
All Studies	0.0804	0.1266	7	(1.08 [0.85, 1.39]	I -+
1.70.9 Primary Analysis-All Stu	dies (Prioritizing Matched/Adjuste	d when	Unmatched/Unadjuste	ed also	o reported)	
All Studies	0.0267	0.1245	7	(1.03 [0.80, 1.31]	ı — — —
1.70.10 Excluding Rao 2023-All	Studies (Priotitizing Matched/Adju	isted) (li	nteraction p=0.91)			
Excluding Rao 2023	0.025	0.1254	6	0) 1.03 [0.80, 1.31]	ı — ∔ —
Rao ([5y KM]) 2023	0.1495	1.0812	1	0	1.16 [0.14, 9.67]	· ← + →
1.70.11 Moderate vs Serious/Ci	ritical Risk of Bias-All Studies (Pri	oritizing	Matched/Adjusted) (Ir	iterac	tion p=0.75)	
Moderate Risk of Bias	0.2799	0.7744	2	0) 1.32 [0.29, 6.04]	
Serious/Critical Risk of Bias	0.0321	0.1335	5	0) 1.03 [0.79, 1.34]	I — I — I — I
1.70.12 Moderate/Serious vs Ci	ritical Risk of Bias-All Studies (Pri	oritizing	Matched/Adjusted) (Ir	nterac	tion p=0.21)	
Moderate/Serious Risk of Bias	0	0.1263	4	0) 1.00 (0.78, 1.28)	
Critical Risk of Bias	0.9462	0.7411	3	(2.58 [0.60, 11.01]	i —
1.70.13 Moderate vs. Serious vs	Critical Risk of Rias-All Studies (I	Prioritizi	ng Matched/Adjusted) (Inte	raction p=0.43)	
Moderate Risk of Riss	n 2700	0 7744	ng materioantajaotoa ז	, (co.		
Serious Risk of Bias	0.0014	0.1358	2	í	1 00 0 77 1 31	
Critical Risk of Bias	0.9462	0.7411	3	Ċ	2.58 [0.60, 11.01]	
1.70.14 Yes vs N/R vs No Conco	mitant-All Studies (Prioritizing Ma	tched/A	djusted) (Interaction p)=0.41	[p=0.92 excl N/R])	
Yes Concomitant Procedures	0.0052	0.1404	3	0) 1.01 [0.76, 1.32]	
N/R Concomitant Procedures	1.8782	1.3971	1	0) 6.54 [0.42, 101.14]	
No Concomitant Procedures	0.0373	0.2743	3	() 1.04 [0.61, 1.78]	I — I
						0.2 0.5 1 2 5
						AAE+SAVR Lower AAE+SAVR Higher

Figure S63 Sensitivity analyses for aortic valve reintervention.

Supplemental Tables:

Table S1 Char	Fable S1 Characteristics of included studies (detailed)													
First author	Year	Cohort	Group		Group number, r	ר (%)	Age (year)		Male se	ex (%)	Body surface a	rea (m²)	Cerebro disease	vascular ; (%)
		size	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE
Matched or a	djusted	observatio	onal 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/u	nadjuste	ed observa	ational 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^{\dagger}		$1.60\pm0.15^{\dagger}$		-	-

Table S1 (continued)																					
First author	Year	Renal fa	illure (%)	Dialysis	(%)	Coronary disease (/ artery (%)	COPD (%	6)	Smoking	(%)	Diabetes	s (%)	Hyperter	nsion (%)	Urgent status (%	6)	Emerger Status (9	nt %)	Urgent/E Status (9	Emergent %)
		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 a	djusted	observatio	onal 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/u	inadjust	ed observ	ational studi	es																	
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	_	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table S1 (continu	Fable S1 (continued)														
First author	Year	EuroSCORE II	(%)	STS score (%)		Previous surgery (9	cardiac %)	Previous	SAVR (%)	Preoperative LVEF	- (%)	Preopera LVEF (< 3	ative 35%) (%)	Preopera NYHA ≥3	itive 3 (%)
		AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE
Matched or adju	usted observ	ational 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/una	djusted obs	ervational 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	-	_	-	-	-	-	-	-	-	-	-	-	-	_

Table S1 (com	tinued)												
	Maran	Preoperative mean a	aortic gradient (mmHg)	Preoperative iEOA	(cm^2/m^2)	Preoperative aortic	annulus diameter (mm)	Aortic steno	osis (%)	Aortic insuff	iciency (%)	Mixed aortic va	lve disease (%)
First author	Year	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE
Matched or a	djusted obs	ervational 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/u	inadjusted c	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^{\dagger}		50^{\dagger}		33.6 [†]	

Table S1 (contin	ued)												
First suth su	Ma a r	BAV (%)		Mechanica	Il valve (%)	Mean implanted val	ve size (mm)	Concomita	nt valve surgery (%)	Concomita	ant CABG (%)	Concomita	nt other procedure(s) (%)
First author	rear	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE	AAE	No AAE
Matched or adj	usted obser	vational studie	es										
Yousef	2023	-	-	25^{\dagger}		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/una	adjusted ob	servational stu	ıdies										
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^{\dagger}		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.

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; moderate 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.

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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