Supplementary

Table S1 The search strategy of MEDLINE via PubMed

#1	"Transcatheter Aortic Valve Replacement"[mh]
#2	"transcatheter aortic valve replacement"[tiab]
#3	"TAVI"[tiab]
#4	"TAVR"[tiab]
#5	#1 OR #2 OR #3 OR #4
#6	"surgical aortic valve replacement"[tiab]
#7	"SAVR"[tiab]
#8	"aortic valve stenosis/surgery"[mh]
#9	#6 OR #7 OR #8
#10	"aortic valve stenosis"[mh]
#11	"aortic valvular stenosis"[tiab]
#12	"AS"[tiab]
#13	#10 OR #11 OR #12
#14	randomized controlled trial[pt]
#15	#5 AND #9 AND #13 AND #14

Table S2 The search strategy of EMBASE

#1	exp aortic valve stenosis
#2	("aortic valve stenosis" or "AS"):ti,ab,kw.
#3	exp transcatheter aortic valve implantation
#4	("transcatheter aortic valve implantation" or "transcatheter aortic valve replacement" or "TAVR" or "TAVI").ti,ab,kw.
#5	("surgical aortic valve replacement" or "SAVR"). ti,ab,kw.
#6	Randomized controlled trial/ or Controlled clinical study/ or Randomized/
#7	("randomized controlled trial").pt. or "randomized". ti,ab,kw. or "randomly".ti,ab,kw.
#8	#1 or #2
#9	#3 or #4
#10	#6 or #7
#11	#5 and #8 and #9 and #10

Table S3 The search strategy of Cochrane CENTRAL

#1	"aortic valve stenosis" OR "AS" OR"aortic valvular stenosis":ti,ab,kw
#2	"transcatheter aortic valve replacement" OR "transcatheter aortic valve implantation" OR "TAVR" OR "TAVI":ti,ab,kw
#3	"surgical aortic valve replacement" OR "SAVR":ti,ab,kw
#4	#1 and #2 and #3

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Table S4 Definitions of outcome in each study

Trial	Death	Stroke	Disabling stroke	Rehospitalization rate	Cardiovascular mortality	Bioprosthetic valve failure
PARTNER 2A	VARC2	VARC2	VARC2	Rehospitalization for symptoms of aortic stenosis and/or complications of the valve procedure If the index hospitalization for a patient is greater than 30 days, then hospital day 31 will count as a re-hospitalization for endpoint analysis	VARC2	NA
SURTAVI	VARC2	VARC2	VARC2	VARC2	VARC2	VARC2
UK TAVI	VARC2	VARC2	VARC2	NA	VARC2	NA
NOTION	VARC2	VARC2	VARC2	VARC2	VARC2	The consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI), the European Society of Cardiology (ESC), and the European Association for Cardio-thoracic Surgery (EACTS)
PARTNER 3	VARC2	VARC2	VARC2	VARC2	VARC2	VARC3
Evoult Low Risk	VARC3	VARC3	VARC3	VARC3	VARC3	NA

VARC, Valve Academic Research Consortium.

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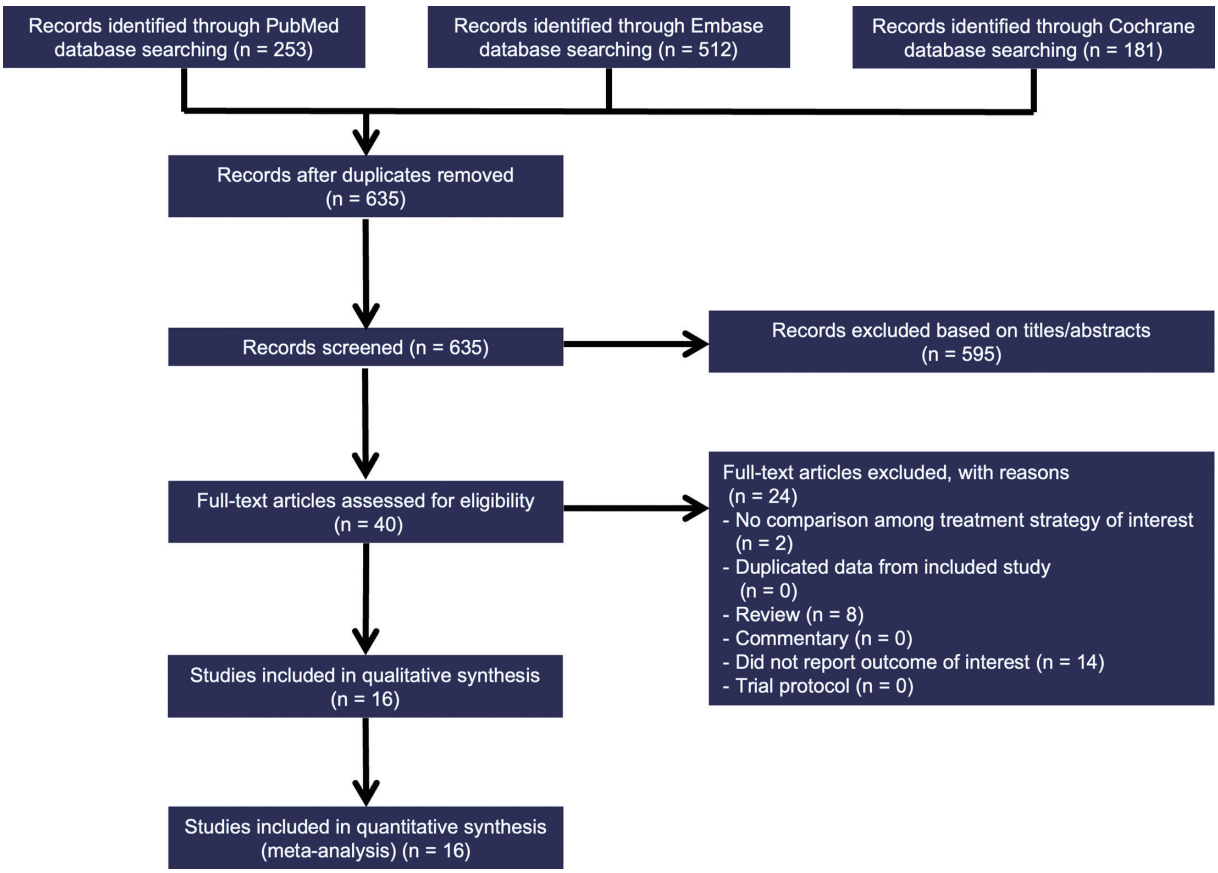

Figure S1 Workflow for selecting eligible papers according to the PRISMA criteria in search of original studies for this meta-analysis. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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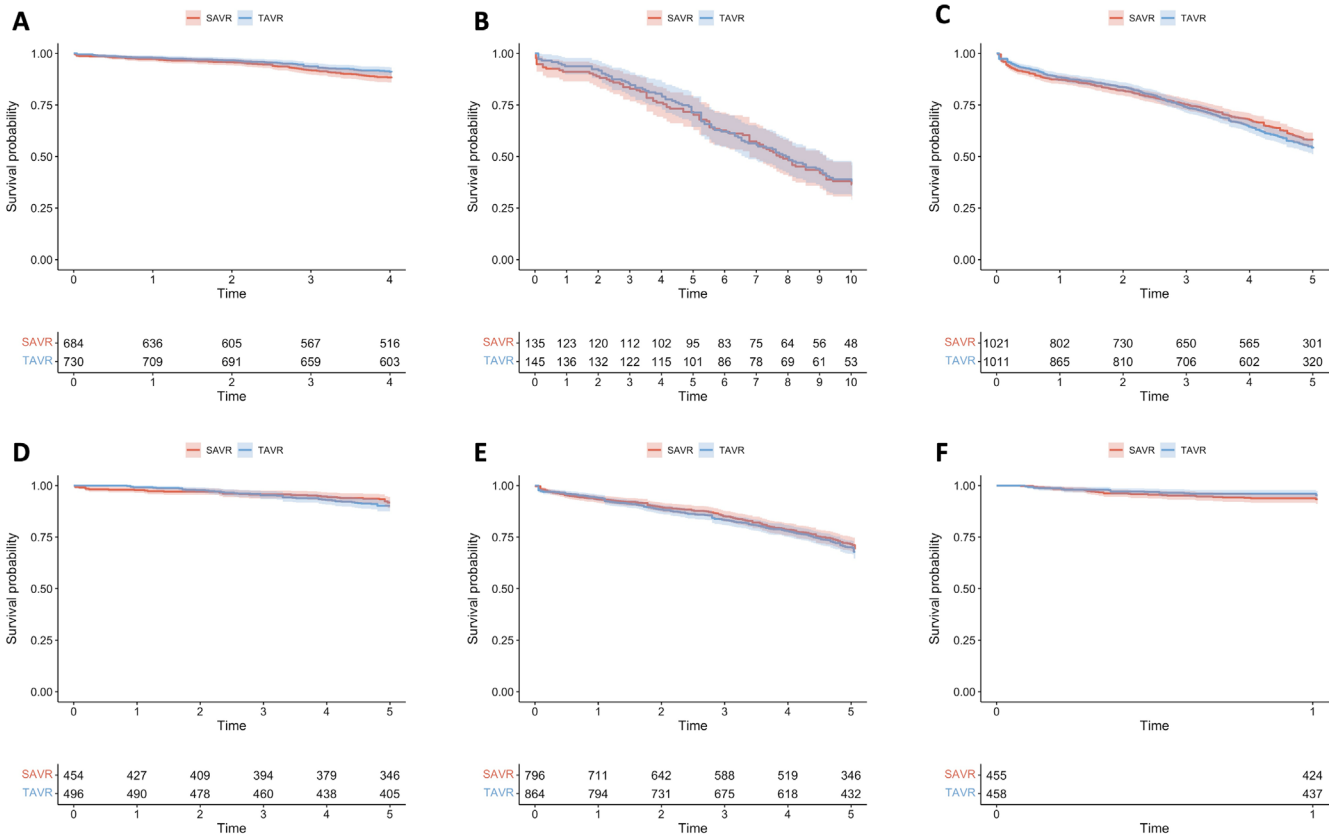

Figure S2 All-cause mortality rate: reconstructed Kaplan-Meier curves from individual studies. Kaplan-Meier analyses of all-cause mortality from individual study (A) Evolut Low Risk Trial, (B) NOTION trial, (C) PARTNER2 trial, (D) PARTNER3 trial, (E) SURTAVI trial, and (F) UKTAVI trial. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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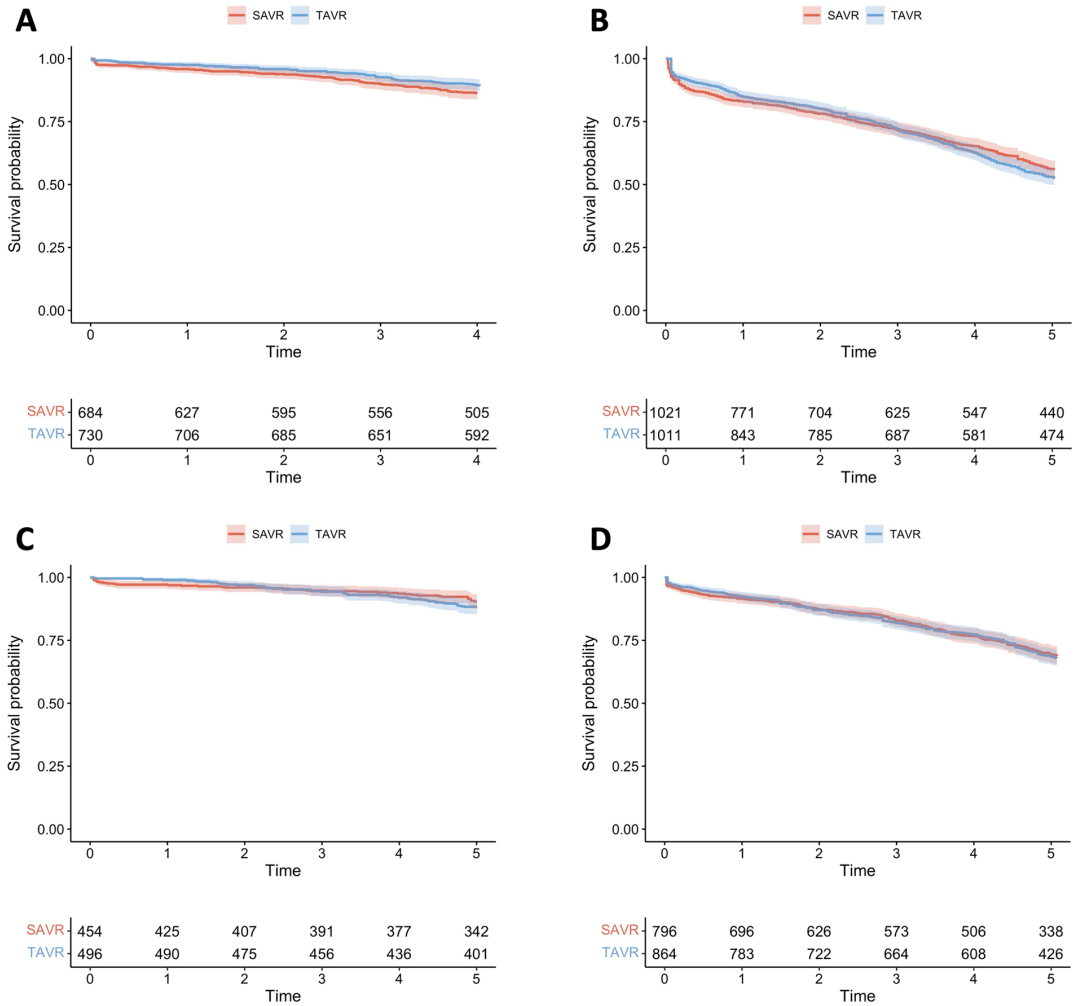

Figure S3 Composite outcome of all-cause mortality and disabling stroke rate: reconstructed Kaplan-Meier curves from individual studies. Kaplan-Meier analyses of composite outcome including all-cause mortality and disabling stroke from individual study (A) Evolut Low Risk Trial, (B) PARTNER2 trial, (C) PARTNER3 trial, and (D) SURTAVI trial. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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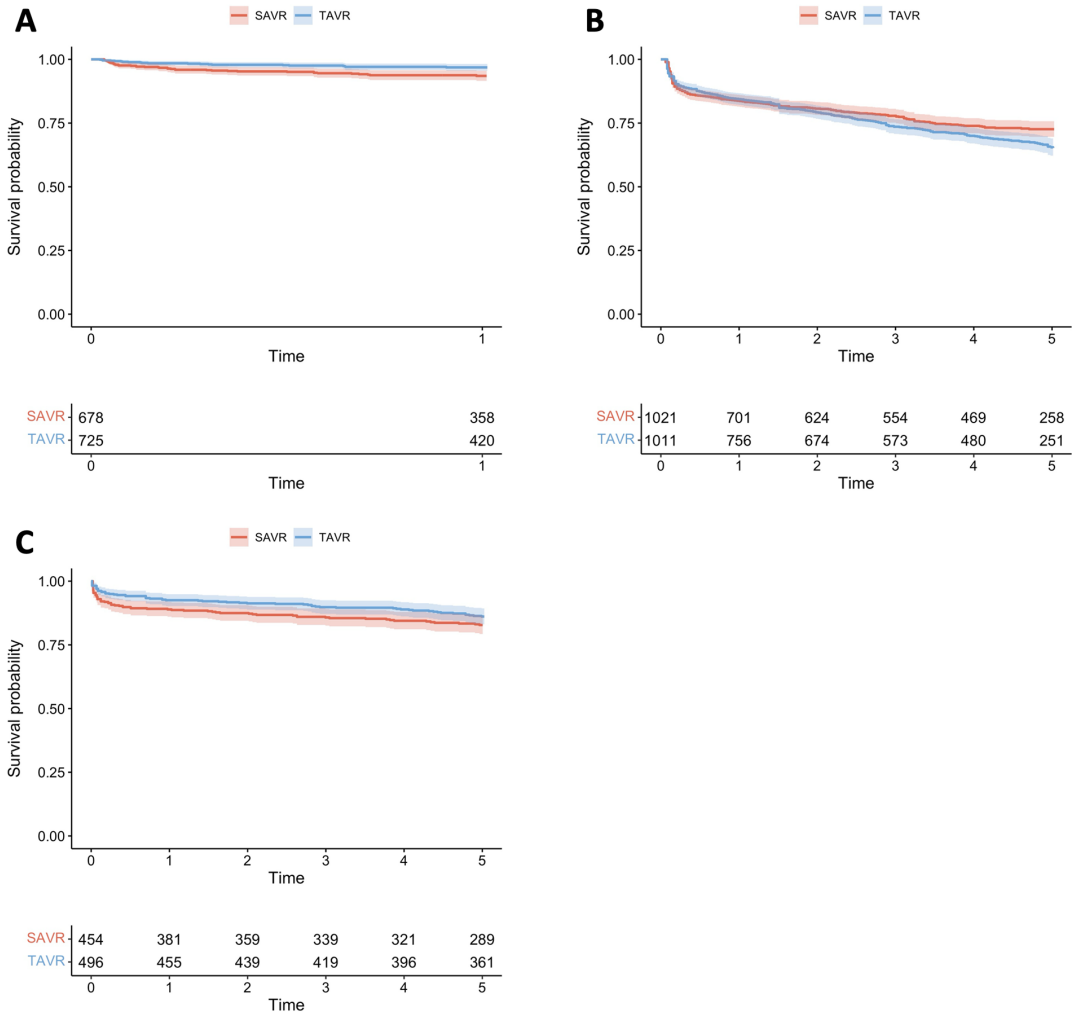

Figure S4 Heart-failure rehospitalization rates: reconstructed Kaplan-Meier curves from individual studies. Kaplan-Meier analyses of heart failure rehospitalizations from individual study (A) Evolut Low Risk Trial, (B) PARTNER2 trial, and (C) PARTNER3 trial. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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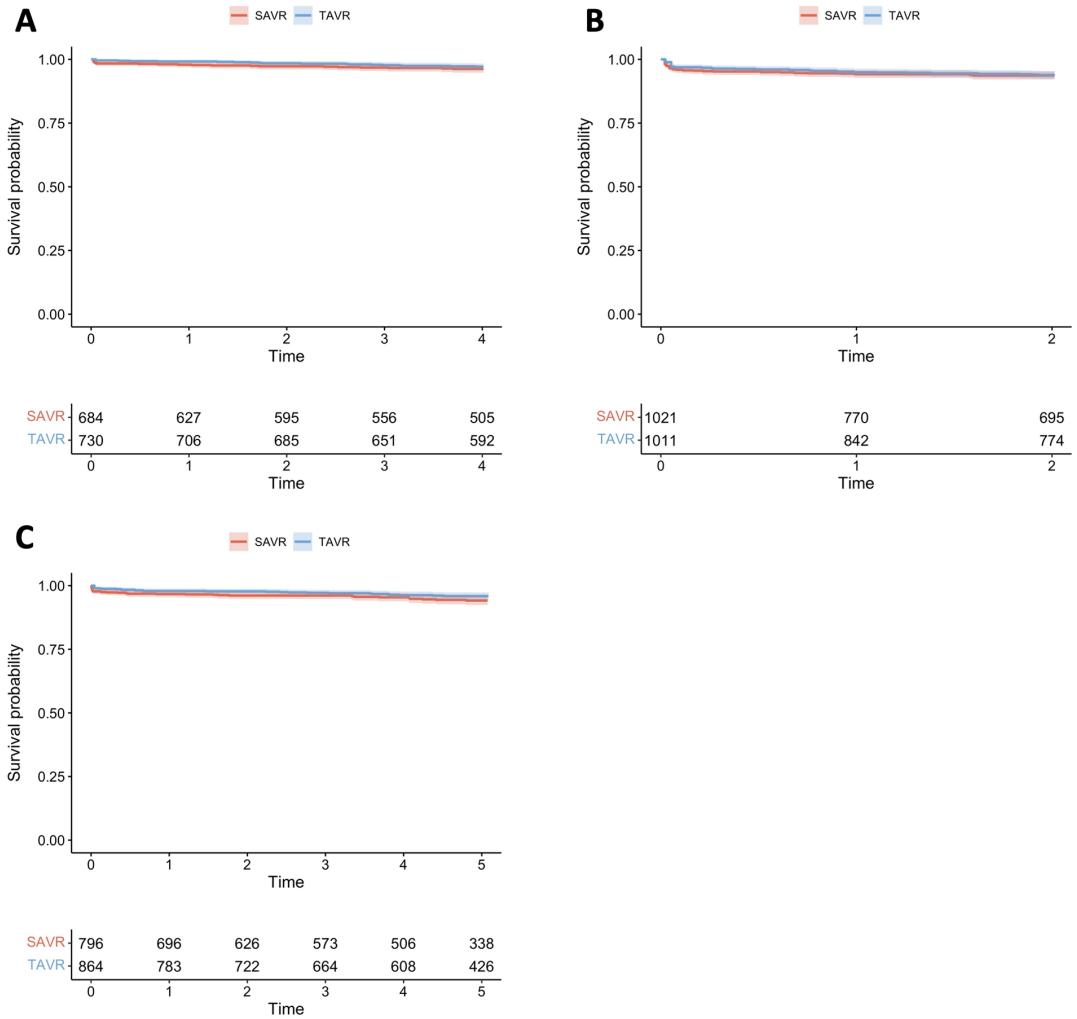

Figure S5 Disabling stroke rate: reconstructed Kaplan-Meier curves from individual studies. Kaplan-Meier analyses of disabling stroke from individual study (A) Evolut Low Risk trial, (B) PARTNER2 trial, and (C) SURTAVI trial. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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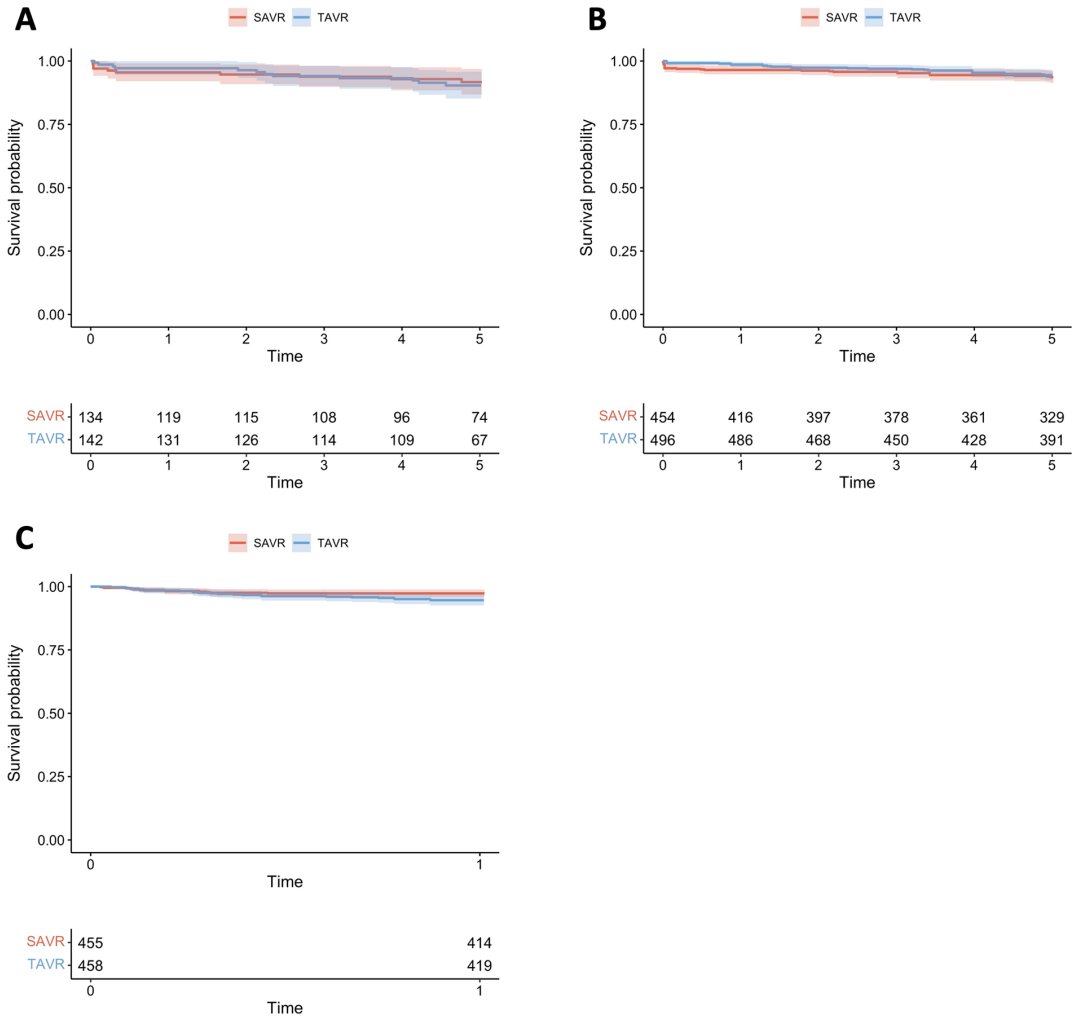

Figure S6 All stroke rate: reconstructed Kaplan-Meier curves from individual studies. Kaplan-Meier analyses of any stroke from individual study (A) NOTION Trial, (B) PARTNER3 trial, and (C) UKTAVI trial. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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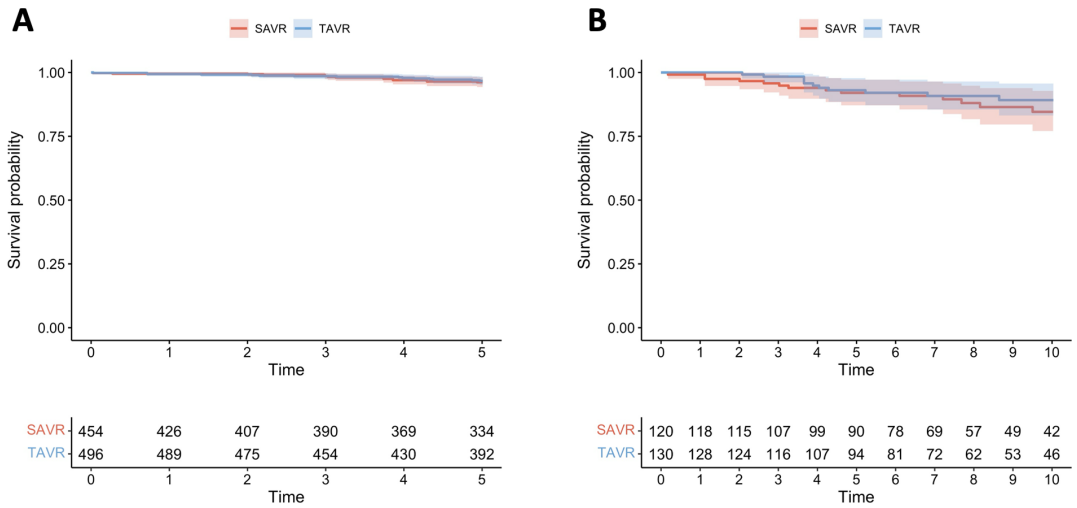

Figure S7 Bioprosthetic valve failure rates: reconstructed Kaplan-Meier curves from individual studies. Kaplan-Meier analyses of bioprosthetic valve failure from individual study (A) PARTNER3 Trial and (B) NOTION trial. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

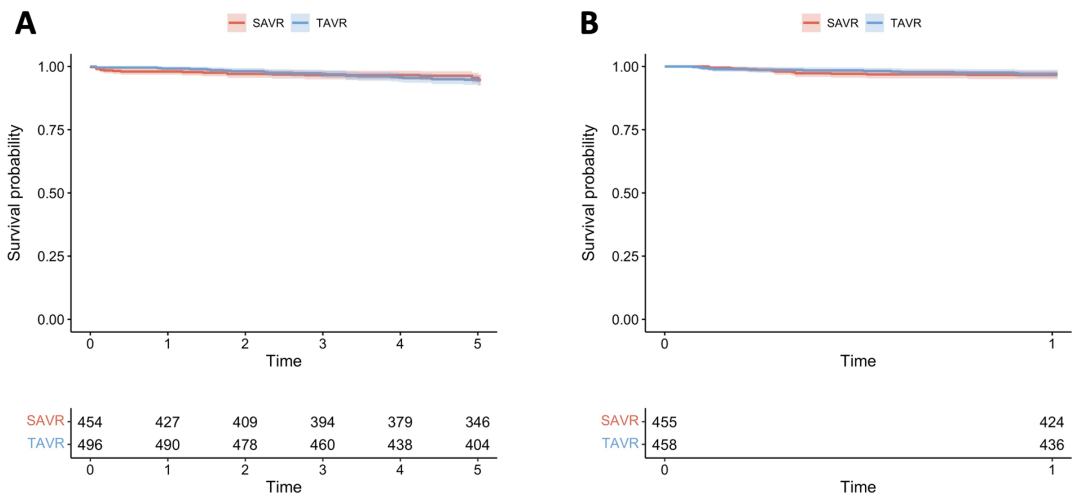

Figure S8 Cardiovascular mortality rate: reconstructed Kaplan-Meier curves from individual studies. Kaplan-Meier analyses of cardiovascular mortality from individual study (A) PARTNER3 Trial and (B) UKTAVI trial. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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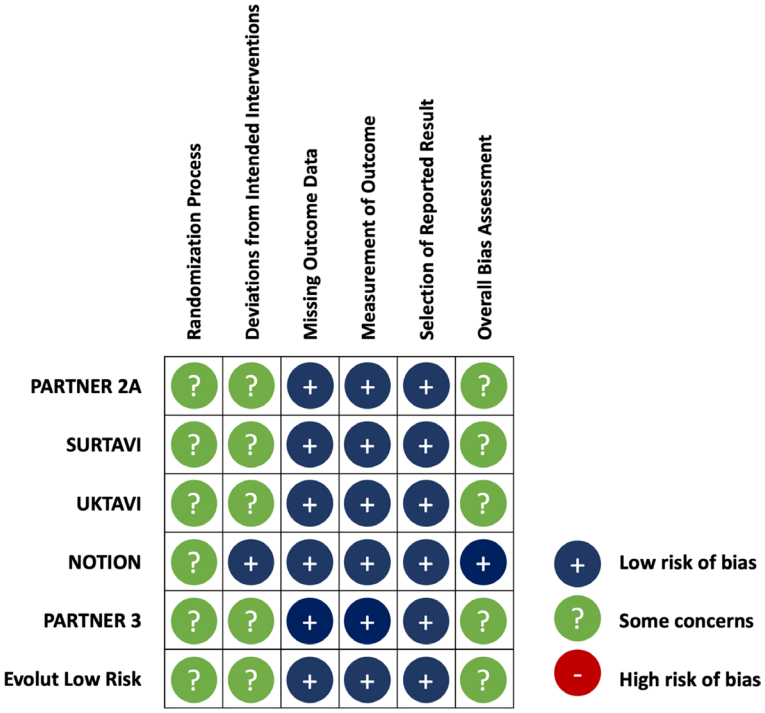

Figure S9 Risk of bias summary according to the Cochrane Collaboration Manual. PARTNER, Placement of Aortic Transcatheter Valves; SURTAVI, Surgical Replacement and Transcatheter Aortic Valve Implantation; UKTAVI, The UK Transcatheter Aortic Valve Implantation; NOTION, Nordic Aortic Valve Intervention.

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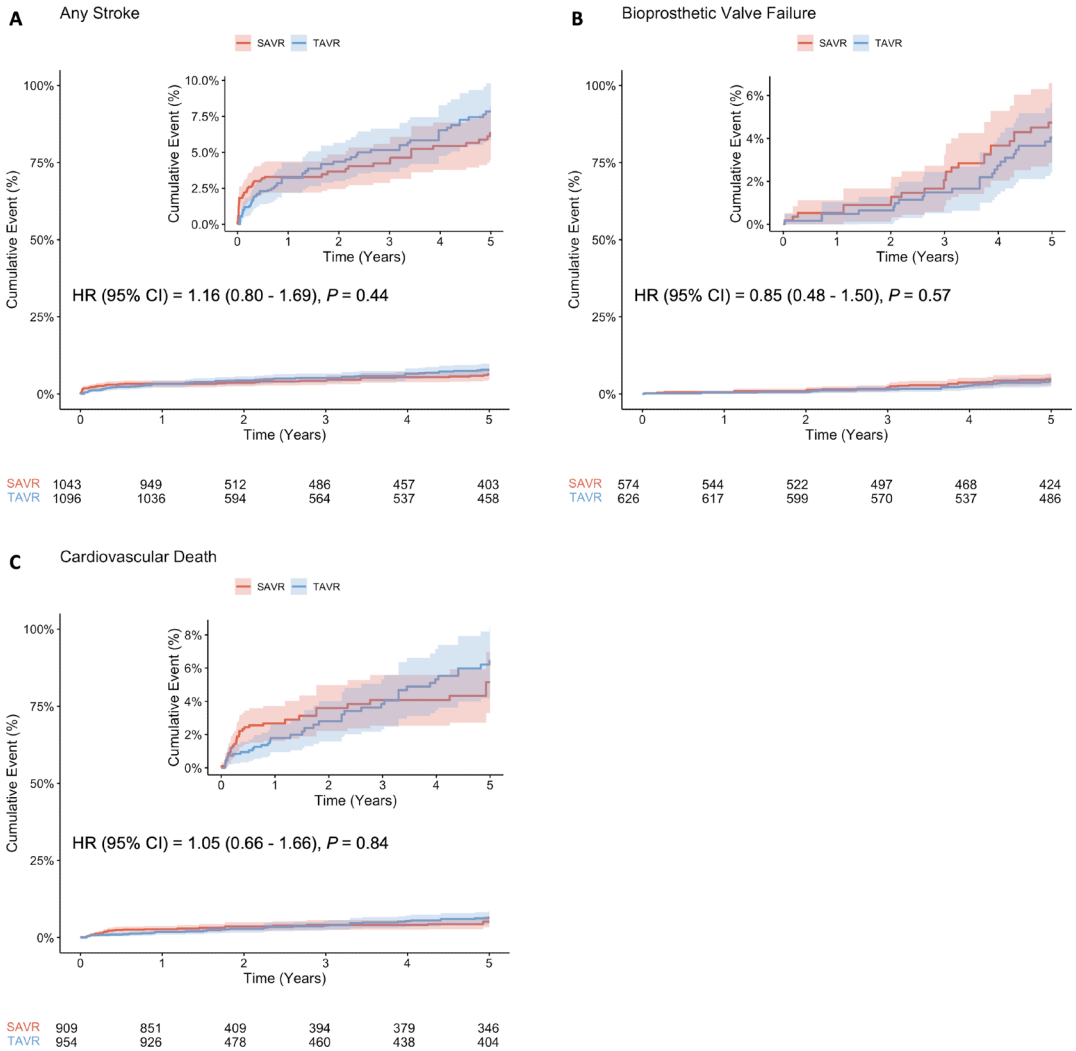

Figure S10 Rates of any stroke, bioprosthetic valve failure, and cardiovascular mortality. Kaplan-Meier analyses of (A) any stroke, (B) bioprosthetic valve failure, and (C) cardiovascular mortality. Solid lines represent the estimates, and the surrounding bands represent the 95% confidence intervals. CI, confidence interval; HR, hazard ratio; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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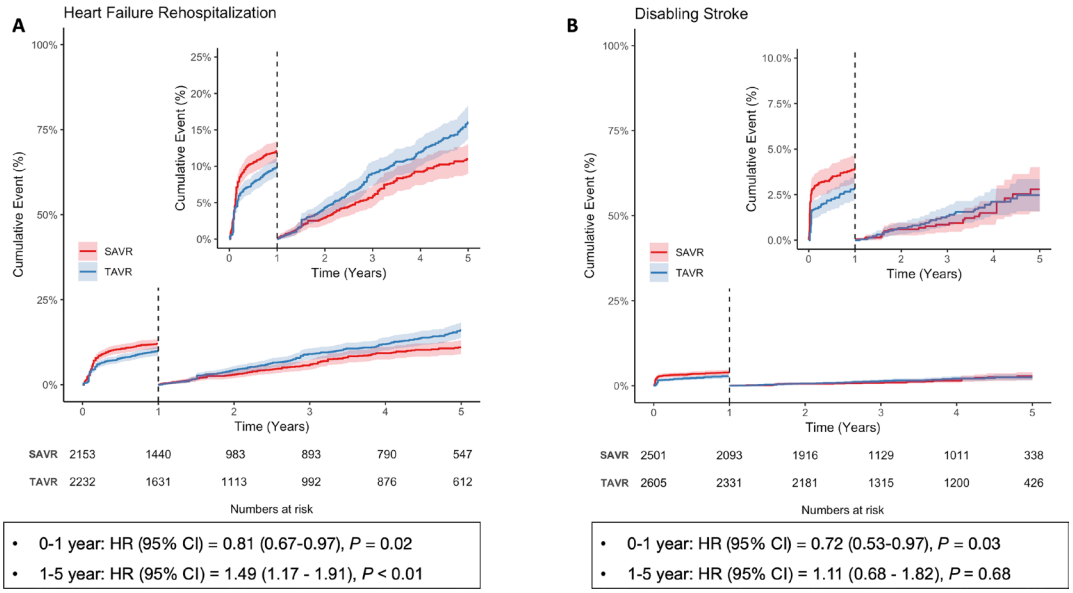

Figure S11 Landmark analyses of heart failure rehospitalization and disabling stroke rates. Landmark analyses at 1 year of (A) heart failure rehospitalization and (B) disabling stroke. Solid lines represent the estimates, and the surrounding bands represent the 95% confidence intervals. CI, confidence interval; HR, hazard ratio; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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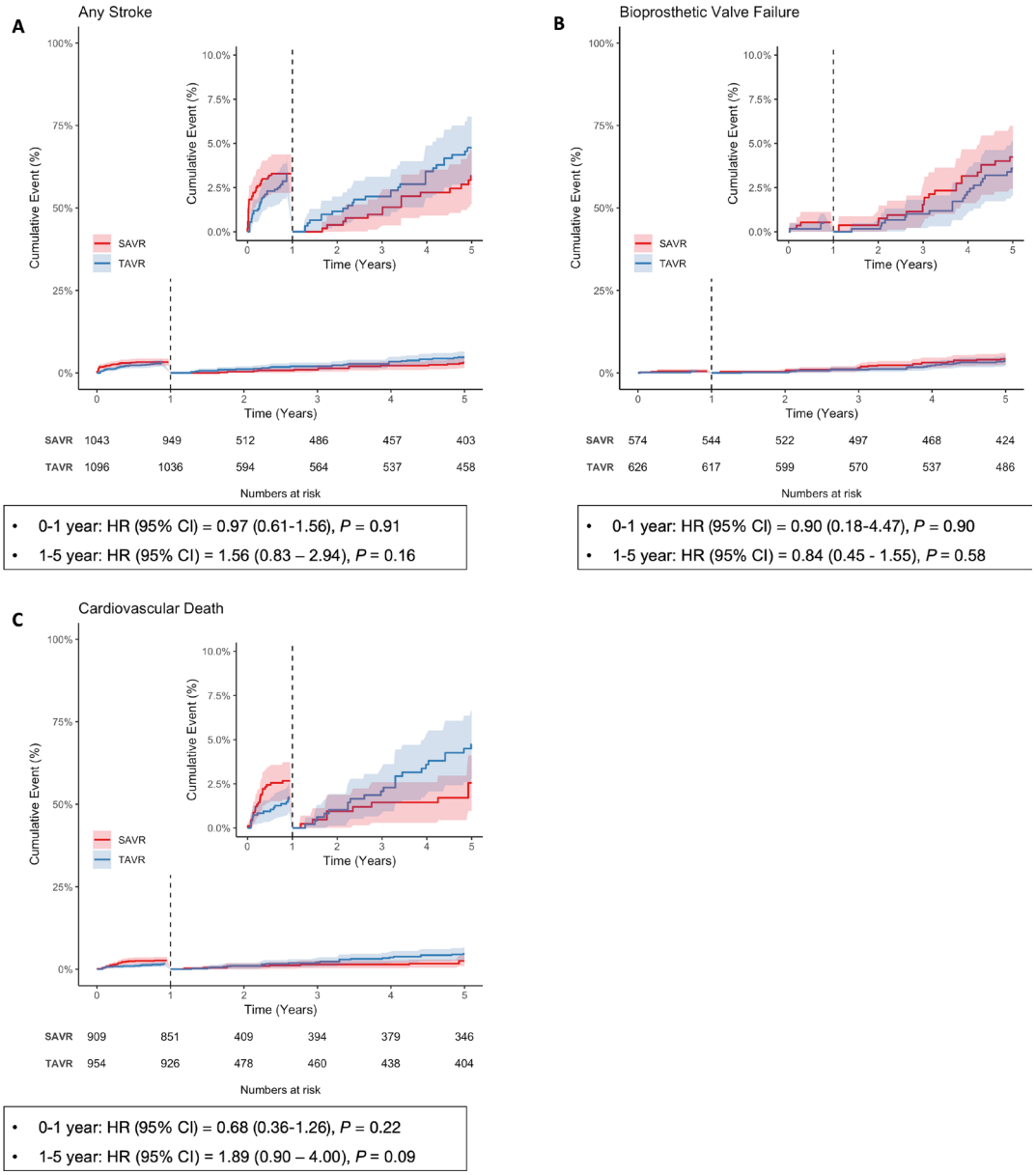

Figure S12 Landmark analyses of any stroke, bioprosthetic valve failure, and cardiovascular mortality rates. Landmark analyses at 1 year of (A) any stroke, (B) bioprosthetic valve failure, and (C) cardiovascular mortality. Solid lines represent the estimates, and the surrounding bands represent the 95% confidence intervals. CI, confidence interval; HR, hazard ratio; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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Table S5 Heterogeneity of each outcome

Outcome	Overall	0–1 year	1–5 year
All-cause Mortality	22.54	0	28.63
All-cause Mortality or Disabling Stroke	10.72	0	45.75
Bioprosthetic Valve Failure	0	0	0
Cardiovascular Mortality	0	11.77	NA
Disabling Stroke	0	12.35	0
Heart Failure Rehospitalization	86.59	69.84	65.4
Any Stroke	47.12	73.49	0

I^2 values for each outcome are summarized in the table below. NA, not available.

Table S6 Subgroup analyses for each outcome based on the TAVR valve type

Outcome	Subgroup	HR	Lower 95% CI	Upper 95% CI	P value
All-cause Mortality	Balloon-Expandable TAVR Valve	1.098	0.961	1.255	0.17
All-cause Mortality	Self-Expanding TAVR Valve	0.974	0.835	1.136	0.739
All-cause Mortality or Disabling Stroke	Balloon-Expandable TAVR Valve	1.074	0.945	1.22	0.275
All-cause Mortality or Disabling Stroke	Self-Expanding TAVR Valve	0.938	0.802	1.098	0.425
Disabling Stroke	Self-Expanding TAVR Valve	0.705	0.488	1.019	0.063
Heart Failure Rehospitalization	Balloon-Expandable TAVR Valve	1.084	0.932	1.262	0.295

CI, confidence interval; HR, hazard ratio; TAVR, transcatheter aortic valve replacement.

Table S7 Subgroup analyses for each outcome based on patient risk group

Outcome	Subgroup	HR	Lower 95% CI	Upper 95% CI	P value
All-cause Mortality	Low-Risk Patient Group	0.872	0.707	1.075	0.200
All-cause Mortality	Intermediate-Risk Patient Group	1.080	0.965	1.208	0.183
All-cause Mortality or Disabling Stroke	Low-Risk Patient Group	0.894	0.700	1.142	0.369
All-cause Mortality or Disabling Stroke	Intermediate-Risk Patient Group	1.044	0.937	1.164	0.436
Disabling Stroke	Intermediate-Risk Patient Group	0.824	0.619	1.097	0.184
Heart Failure Rehospitalization	Low-Risk Patient Group	0.664	0.502	0.877	0.004
Heart Failure Rehospitalization	Intermediate-Risk Patient Group	1.190	1.003	1.412	0.046

CI, confidence interval; HR, hazard ratio.

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Table S8 P-interaction values between subgroups

Outcomes	Number of studies	Overall outcome		Initial 1 year		Landmark analysis after 1 year	
		Valve types	Risk groups	Valve types	Risk groups	Valve types	Risk groups
All-cause Mortality	6	0.395	0.776	0.873	0.494	0.612	0.732
All-cause Mortality or Disabling Stroke	4	0.567	0.734	0.904	0.261	0.408	0.921
Bioprosthetic Valve Failure	2	NA	NA	NA	NA	NA	NA
Cardiovascular Mortality	2	NA	NA	NA	NA	NA	NA
Disabling Stroke	3	0.641	0.891	0.447	0.411	0.408	0.937
Heart Failure Rehospitalization	3	0.180	0.151	0.335	0.284	NA	NA
Any Stroke	3	0.279	0.298	0.067	0.069	NA	NA

NA, not available.

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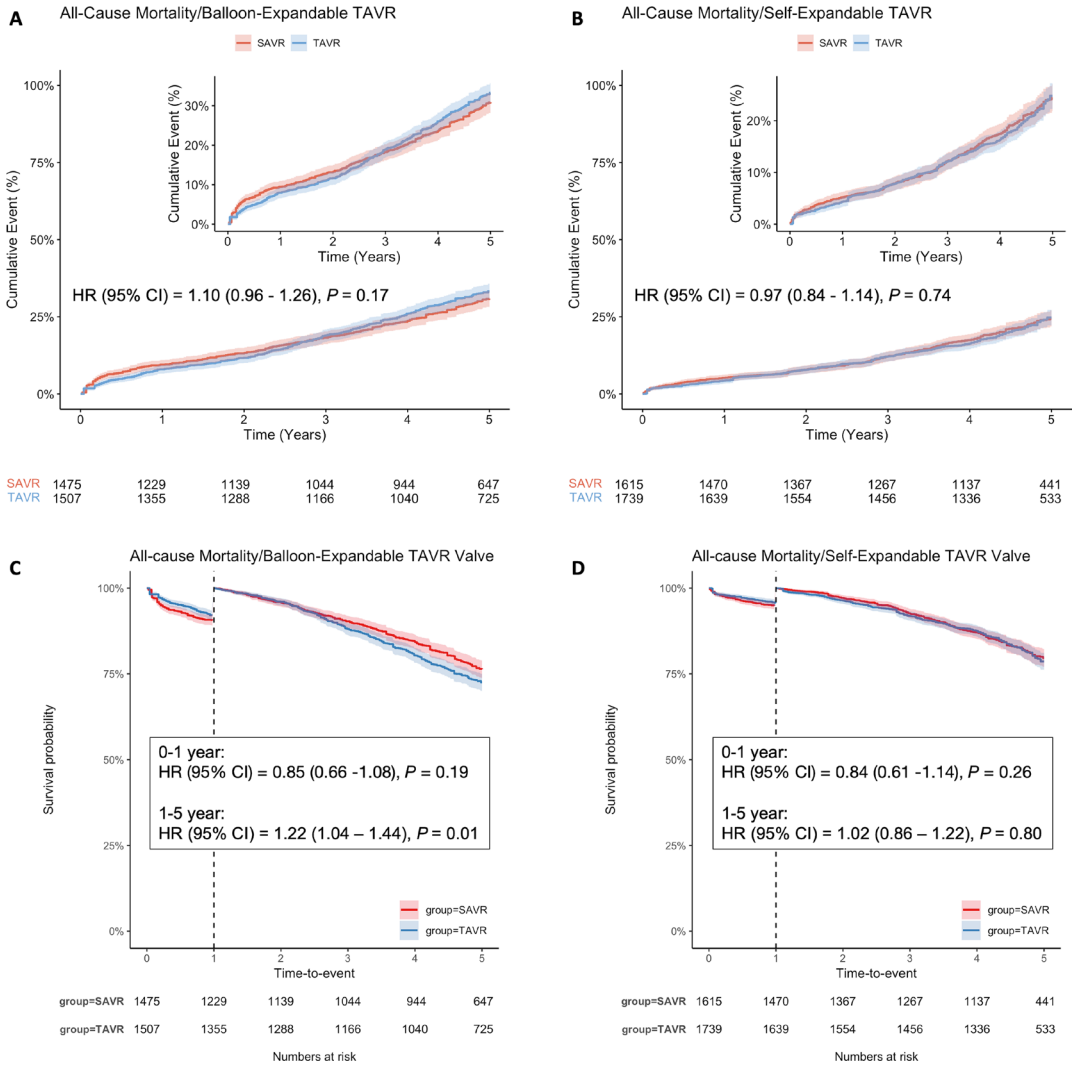

Figure S13 Subgroup analyses based on TAVR valve types. Subgroup analyses of all-cause mortality for (A) balloon-expandable TAVR valves and (B) self-expanding TAVR valves. Landmark analyses for each of the subgroup are shown in (C) and (D), in the same order. Solid lines represent the estimates, and the surrounding bands represent the 95% confidence intervals. CI, confidence interval; HR, hazard ratio; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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Table S9 Sensitivity analyses for each outcome for studies with follow-up >1 year

Outcomes	Overall				Initial 1 year				Landmark analysis after 1 year			
	HR	Lower 95% CI	Upper 95% CI	P value	HR	Lower 95% CI	Upper 95% CI	P value	HR	Lower 95% CI	Upper 95% CI	P value
All-cause Mortality	1.043	0.943	1.154	0.412	0.843	0.694	1.022	0.083	1.13	1.004	1.273	0.043
Any Stroke	0.907	0.577	1.427	0.674	0.451	0.219	0.930	0.031	1.565	0.832	2.942	0.165

CI, confidence interval; HR, hazard ratio.

Table S10 Sensitivity analyses for each outcome for studies with new generation TAVR valves

Outcomes	Overall				Initial 1 year				Landmark analysis after 1 year			
	HR	Lower 95% CI	Upper 95% CI	P value	HR	Lower 95% CI	Upper 95% CI	P value	HR	Lower 95% CI	Upper 95% CI	P value
All-cause Mortality	0.842	0.663	1.069	0.159	0.618	0.345	1.107	0.106	0.970	0.719	1.308	0.841
All-cause Mortality or Disabling Stroke	0.894	0.700	1.142	0.369	0.512	0.307	0.854	0.010	1.071	0.806	1.422	0.638
Heart Failure Rehospitalization	0.664	0.502	0.877	0.004	0.575	0.413	0.800	0.001	0.979	0.570	1.681	0.937
Any Stroke	1.171	0.770	1.780	0.461	0.390	0.161	0.948	0.038	1.458	0.694	3.064	0.319

CI, confidence interval; HR, hazard ratio.

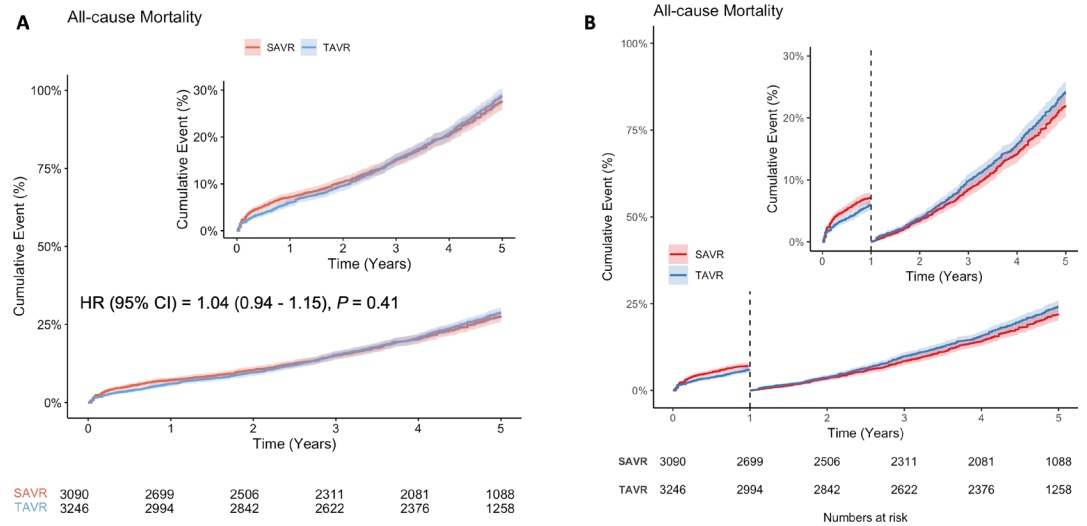

Figure S14 Sensitivity analyses with inclusion of studies reporting >1 year of follow-up. Sensitivity analyses of all-cause mortality for studies reporting >1 year of follow-up (A) all-cause mortality and (B) landmark analysis of all-cause mortality. Solid lines represent the estimates, and the surrounding bands represent the 95% confidence intervals. CI, confidence interval; HR, hazard ratio; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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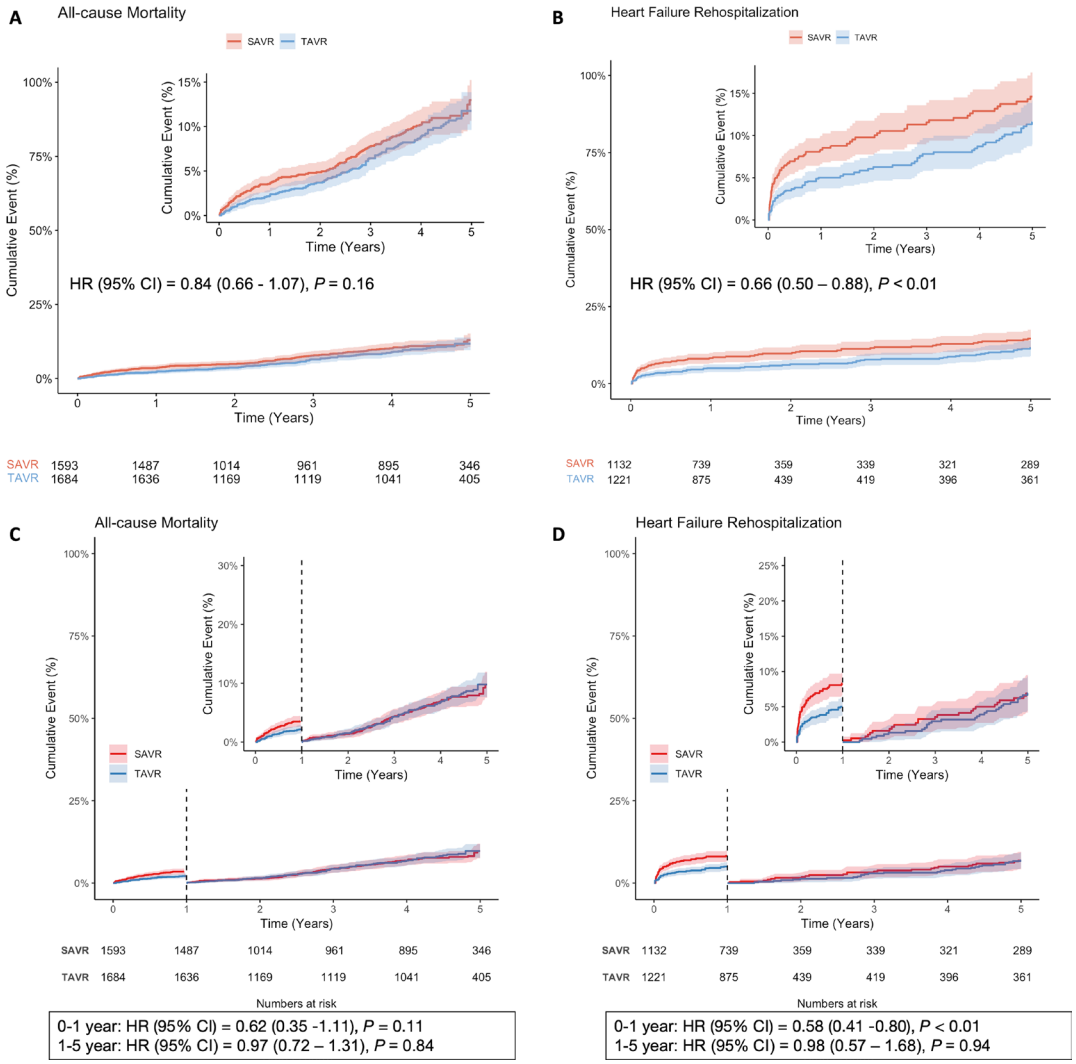

Figure S15 Sensitivity analyses with inclusion of studies with new generation TAVR devices. Sensitivity analyses of studies with the use of new generation TAVR devices (A) all-cause mortality and (B) heart failure rehospitalization rates. (C) and (D) indicate the results of landmark analysis at 1 year. Solid lines represent the estimates, and the surrounding bands represent the 95% confidence intervals. CI, confidence interval; HR, hazard ratio; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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Table S11 Grambsch and Therneau test for time-invariant effect

Outcome	P value
All-cause Mortality	0.034
All-cause Mortality or Disabling Stroke	0.001
Bioprosthetic Valve Failure	0.421
Cardiovascular Death	0.032
Disabling Stroke	0.001
Heart Failure Rehospitalization	<0.001
Any Stroke	0.014

Table S12 The difference in restricted mean survival time for each outcome

Outcome	RMST difference (days)	Lower 95% CI (days)	Upper 95% CI (days)	P value
All-cause Mortality	6.48	–17.49	30.45	0.60
All-cause Mortality or Disabling Stroke	15.36	–12.44	43.16	0.28
Bioprosthetic Valve Failure	9.35	–11.74	30.45	0.38
Cardiovascular Death	0.92	–29.31	31.16	0.95
Disabling Stroke	17.84	–1.7	37.38	0.07
Heart Failure Rehospitalization	12.12	–26.21	50.44	0.54
Any Stroke	–9.65	–40.69	21.39	0.54

CI, confidence interval; RMST, restricted mean survival.

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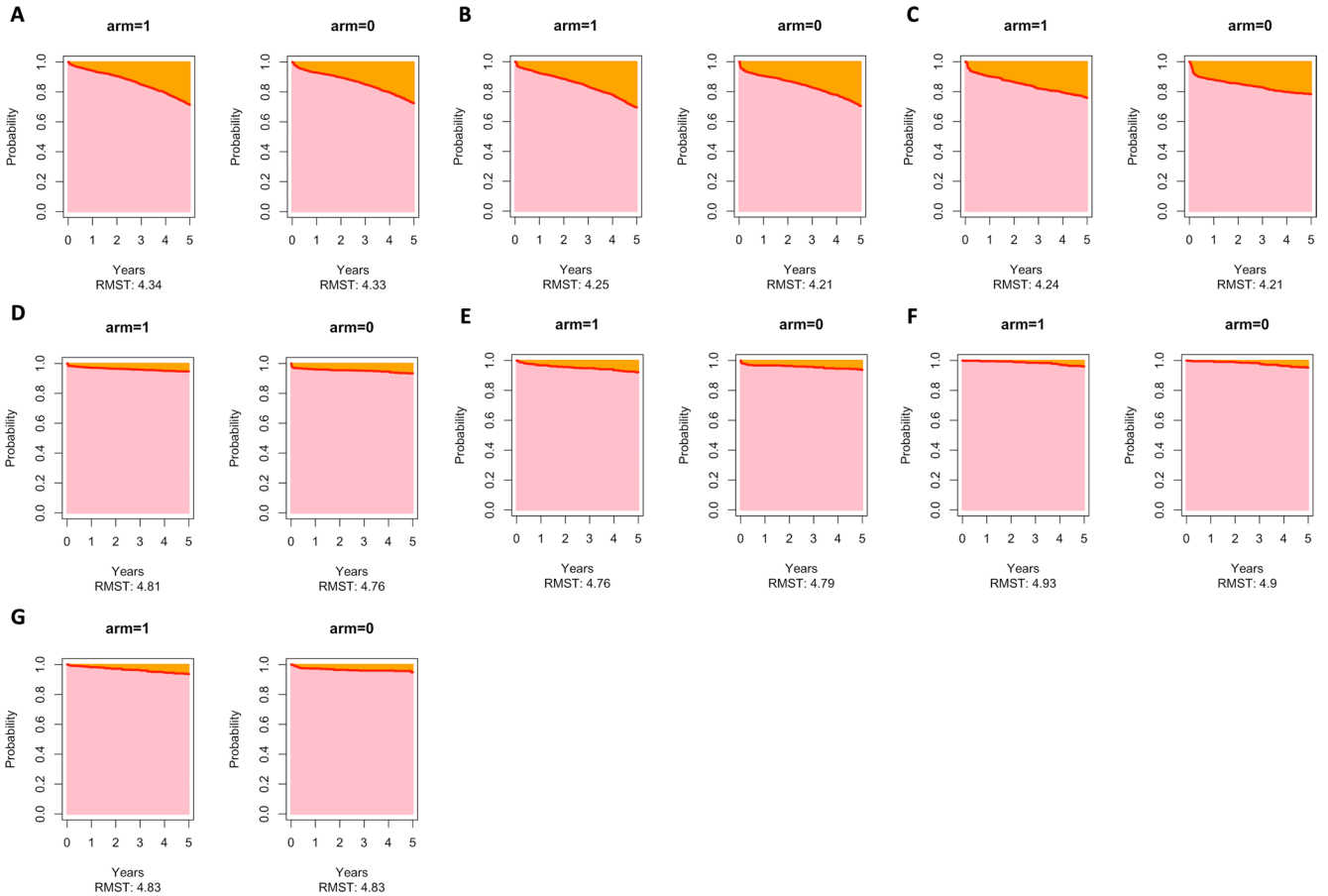

Figure S16 Restricted mean survival time as area under the Kaplan-Meier curve in each outcome. Arm 1 = transcatheter aortic valve replacement, Arm 0 = surgical aortic valve replacement. Red bold lines indicate Kaplan-Meier curve. The pink-shaded area below each Kaplan-Meier curve is restricted mean survival time with the follow-up period of 5 years. The number shown below each Kaplan Meier curve shows restricted mean survival time (years) in the corresponding treatment groups. (A) all-cause mortality, (B) all-cause mortality or disabling stroke, (C) heart-failure rehospitalization, (D) disabling stroke, (E) any stroke, (F) bioprosthetic valve failure, and (G) cardiovascular mortality. RMST, restricted mean survival time.

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