Interventional procedure overview of transcatheter aortic valve implantation for native aortic valve regurgitation

Contents

Table 1 Abbreviations

Abbreviation	Definition
AF	Atrial fibrillation
aOR	Adjusted odds ratio
AR	Aortic regurgitation
AKI	Acute kidney injury
AMSTAR-2	Assessing the Methodological Quality of Systematic Reviews 2
AI	Aortic insufficiency
ASE	American Society of Echocardiography
BE	Balloon expandable
CI	Confidence interval
CMR	Cardiovascular magnetic resonance imaging
COPD	Chronic obstructive pulmonary disease
EGDs	Early generation devices
ES	Effect size
GRADE	Grading of recommendations assessment, development, and evaluation
HR	Hazard ratio
LOS	Length of hospital stay
LVEDd	Left ventricle end-diastole dimension
LVESd	Left ventricle end-systole dimension
LV	Left ventricular
LVEF	Left ventricular ejection fraction
I^2	Inconsistency test
KCCQ	Kansas City Cardiomyopathy Questionnaire
MACCE	Major adverse composite cardiac events
MI	Myocardial infarction
MR	Mitral regurgitation
MD	Mean difference
NACE	Net adverse clinical events
NA	Not available
NGDs	New-generation devices
NRD	Nationwide readmissions database
PPM	Permanent pacemaker
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PVL	Paravalvular leak
RR	Risk ratio

SAVR	Surgical aortic valve replacement
SE	Self-expandable
SMD	Standardised mean difference
STS-PROM	Society of Thoracic Surgeons Predicted Risk of Mortality
TAVI	Transcatheter aortic valve implantation
TAVR	Transcatheter aortic valve replacement
TA	Transapical
TF	Transfemoral
THV	Transcatheter heart valve
TIA	Transient ischemic attack
TR	Tricuspid regurgitation
VARC	Valve Academic Research Consortium

The condition, current treatments, unmet need and procedure

Information about the condition, current treatments, unmet need and the procedure is available in NICE's interventional procedures guidance on transcatheter aortic valve implantation for native aortic valve regurgitation.

Outcome measures

The main outcomes included device success, improvement in functional status, patient-reported outcomes, mortality rates and procedural complications.

Evidence summary

Population and studies description

This interventional procedures overview is based on 47,827 people from 5 systematic review and meta-analyses, 1 prospective case series, 1 retrospective propensity score-matched study and 3 retrospective analyses. Of these 47,827 people, 15,920 people had the procedure for AR (with either dedicated valves indicated for use in AR [referred to as on-label valves] or non-dedicated valves indicated for use in AS [referred to as off-label valves]). Of the 47,827 people,

27,851 people had SAVR, and 4,056 people had TAVI for AS. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 10 studies as the key evidence in table 2 and table 3, and lists 85 other relevant studies in table 5 in appendix B.

Table 2 presents study details.

A meta-analysis of 34 observational studies comparing effectiveness of TAVI on-label valves with off-label valves in people with high surgical risk for pure native AR was conducted according to PRISMA guidelines. Pooled estimates were calculated using a random-effects model. Subgroup analyses according to the type of valve used (that is, on-label valves [JenaValve/J-Valve] versus off-label valves) and access site (transfemoral versus transapical access) were performed. Some studies were small and retrospective which are prone to bias and confounders. There was significant heterogeneity across the available studies in terms of valves used, access site, and outcomes reported (Samimi 2025).

A systematic review and meta-analysis of 19 observational studies on TAVI for native AR (with either on-label or off-label valves) was conducted according to PRISMA guidelines. Pooled estimates were calculated using a random-effects model. NGDs were compared with EGDs. Subgroup analysis and a meta-regression were performed to study the effects of study level covariates on outcomes. There was significant heterogeneity across the available studies in terms of valves used, access site, and outcomes reported. Some studies varied in patient characteristics and some have incomplete data reporting. Most of the studies had small sample sizes, reported their outcomes peri procedurally and lack data on long-term outcomes (Rawasi 2019).

In a meta-analysis of 11 observational studies on TAVI for AR (with either on-label or off-label valves), pooled estimates were calculated a using random-effects model. A subgroup analysis of studies using EGDs and NGDs was also

performed. Studies were heterogenous with different sample sizes, inclusion criteria, patient characteristics, types of valves, and TAVI approaches. Most of the studies were multicentre studies and there might have been an overlap of people in the studies. This might have overestimated the effects of the intervention. A meta-regression was performed to study the effects of 12 covariates on 30-day all-cause mortality (Takagi 2020).

A systematic review and meta-analysis of 31 studies on NGDs (either on-label or off-label valves) was based on small retrospective observational studies with heterogenous populations. The study was conducted according to PRISMA guidelines. Most pooled studies had a low risk of bias. Authors state that there might be an overlap of study cohorts in pooled multicentre studies conducted in the same country. The study did not report results separately for valves segmented by the mechanism of action (SE and BE prostheses) because it was not possible to differentiate in the included articles (Liu 2024).

A large multicentre prospective case series of 180 people (the JenaValve ALIGN-AR pivotal trial) in the USA assessed on-label use of TAVI in people with severe symptomatic AR and at high risk of surgery. Findings were compared with a pre-specified performance goal, and analysis was on early outcomes (Vahl 2024).

A small retrospective cohort study with long-term follow up (median 5.7 years) in China assessed TAVI with an on-label valve (J-valve) in 36 people with pure native AR. Follow-up assessments were done through telephone interviews or outpatient visits. Potential limitations of this study include bias and confounding factors such as age and cardiovascular comorbidities (Li F 2024).

The PANTHEON study was a retrospective international registry analysis that assessed NGDs (both on-label and off-label valves segmented by the mechanism of action SE and BE). The study was in people with severe pure native AR for whom surgery was considered high risk or whose native aortic

valve regurgitation was considered inoperable. TF approach was the most common approach used. Different types of valves were used and only 10% were JenaValve Trilogy THV, which is a dedicated on-label valve for native AR. Echocardiographic outcomes were not reported, so the rate of moderate-to-severe AR at follow up is unknown (Polleti 2023).

One retrospective analysis with a small sample size and short follow-up period assessed TAVI with off-label NGDs in different risk groups. People were classified into different risk groups based on STS scores and not on EuroSCORE (Da-Wei 2024).

A systematic review and meta-analysis of 6 observational studies comparing TAVI with various types of valves to SAVR in people with pure native AR followed the Cochrane Handbook for Systematic Reviews of Intervention, AMSTAR-2 guidelines and reported it according to the PRISMA guidelines. The Newcastle–Ottawa scale was used to assess the quality of included studies, and all included studies posed a low risk of bias. The strength of evidence was assessed using the GRADE scale. Heterogeneity was assessed using inconsistent test. Meta-analysis was done using the random-effects model and subgroup analysis was done depending on the approach of TAVI (TF and TA) and the country of origin. The efficacy of TAVI and SAVR in people with different surgical risk was not analysed. (Elkasaby 2024).

A retrospective propensity score-matched study comparing TAVI for treatment of AR with TAVI for treatment of AS used NRD codes for diagnosis of AR. Procedural and echocardiographic outcomes were not assessed in this study because of a lack of data. People were either symptomatic or had a compelling indication for valvular replacement. They were of similar age in both groups and had similar comorbidities (the Elixhauser comorbidity index [to predict in-hospital mortality] was comparable). Details of valves used were not available in the article (Ullah 2024).

Figure 1 Flow chart of study selection

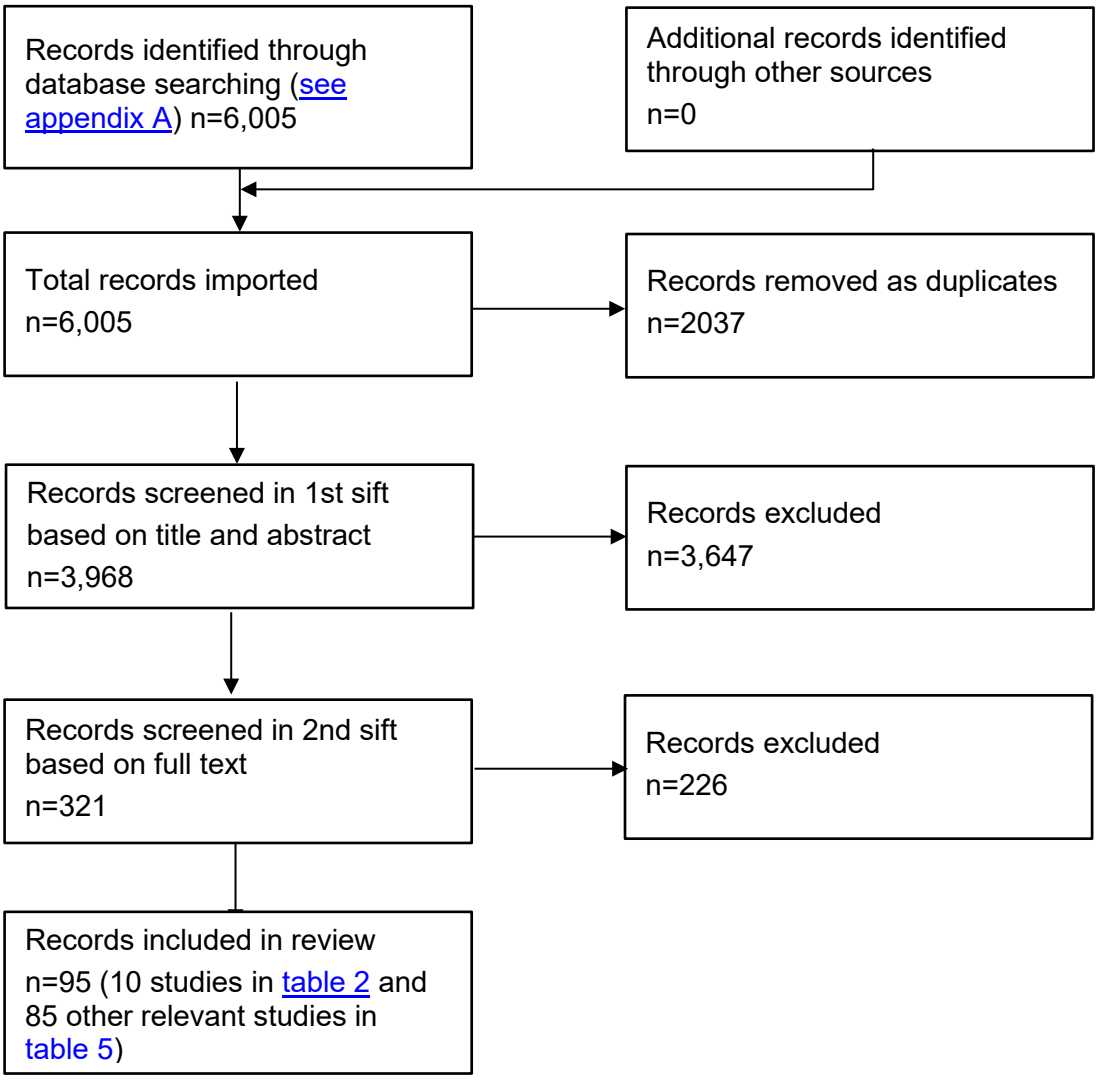

Table 2 Study details

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
1	Samimi S 2025 USA	34 studies (n=2,162 people with high surgical risk with pure severe native AR). (19 multicentre and 15 single centre studies). Mean age: 75.4 years. Gender: 43% women. Mean logistic EuroSCORE I: 24.2%; STS score: 5.6%.	Systematic review and meta-analysis Databases searched: PubMed, EMBASE, and Cochrane Central	Studies on people with pure native AR without significant aortic stenosis undergoing TAVR (with on-label JenaValve/J-Valve or off-label valves), reporting at least 1 outcome were included. Studies on people with bioprosthetic valves or mixed aortic stenosis and regurgitation as well as studies with fewer than 10 people who did not report the desired outcomes specified by valve type were excluded.	**TAVI** **Dedicated on-label versus off-label valves** Valves used Dedicated on-label valves (20 studies, 55%, n=1,193): JenaValve (8 studies, n=588) and J-Valve (12 studies, n=605) Off-label valves (various types of valves used: CoreValve, Evolut R, Sapien XT, 3, Ultra, Acurate Neo and Neo 2; 15 studies, 45%, n=969) Access site:	30 days and 1 year.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
					transfemoral access (16 studies, n=1,114) transapical access (15 studies, n=652)	
2	Rawasia WF 2019 USA	19 studies (n=998 people with pure native AR) 13 full studies and 6 abstracts. Mean age: ranged from 68 to 84 years, mean logistic EUROSCORE ranged from 9.8 to 34.0.	Systematic review and meta-analysis Databases searched: MEDLINE, Scopus, and Cochrane CENTRAL	Studies in English with at least 5 people undergoing TAVR for pure native AR and reporting at least one of the endpoints were included. Case reports and editorials were excluded. In case of serial publications, only the most recent one was included.	**TAVI** **NGDs versus EGDs** Valves used: new-generation (purpose-specific valves: JenaValve, ACCURATE TA; non-purpose-specific valves: CoreValve, Sapien XT, Direct Flow]) or (early generation [CoreValve and Sapien XT) Access route: TF or TA access. Valve size: not reported.	Varied across studies. 30 days to 1 year

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
3	Takagi H 2020 Japan	11 studies (n=911 people undergoing TAVI for AR) Age: range 73 to 75 years.	Systematic review and meta-analysis of single-arm studies. Databases searched: Medline and EMBASE, up to July 2018	Studies with more than 20 people undergoing TAVI for AR were included.	**TAVI** **NGDs versus EGDs** Access route: TF or TA access. NGDs were used in 7 studies (SAPIEN 3, JenaValve, J-Valve, Accurate, Direct Flow, Engager, Evolut R, Lotus, Portico). EGDs were used in 5 studies (CoreValve, SAPIEN, SAPIEN XT). 2 studies (Yoon 2017, de Backer 2018) compared NGD and EGDs. 1 compared off-label with on-label valves (Frerker 2015).	Varied across studies. 30 days to 1 year

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
					1 compared TAVI for AR with TAVI for AS or TAVI for AS plus concomitant-grade of AR (Testa 2014). 5 studies (Silaschi 2018, Liu 2018, Seiffert 2014, Toggweiler 2018, Zhu 2016) used only NGDs and 3 studies (Testa 2014, Roy 2013, Frerker 2015) used only EGDs.	
4	Liu 2024 China	31 observational studies (n=1,851 people with severe AR and surgery not suitable)	Systematic review and meta-analysis Databases searched: MEDLINE, Embase, Cochrane Library,	RCTs and observational studies including cohort studies, case-controlled studies, and case series with at least 10 cases were included. Studies not reporting the outcomes or from which summary data	**TAVI with NGDs** **Compared 'on-label' and 'off-label' valves.** On-label valves (20 studies, n=1067): J-valve, 15 studies, n=949	Varied across studies. 30 days to 1 year

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
			and Scopus; until April 2023.	could not be extracted were excluded.	JenaValve, 5 studies, n=307 Off-label valves (11 studies, n=784): Evolut, n=284 SAPIEN 3, n=61 Direct Flow, n=90 ACURATE, n=76 Lotus, n=34 Engager, n=26 Portico, n=9 Symetis, n=15 Valve size: 27mm valves mostly used. Access route: 70% TA access 30% TF access	
5	Poletti, 2023, 16 centres across Europe and USA	n=201 people with pure severe native AR. Median age: 79 years (IQR: 73–83 years)	Retrospective analysis (of procedures between 2014 and 2022) NCT05319171	People who underwent TAVI for pure severe native valve AR and whose condition was considered inoperable or for whom surgery	**TAVI with NGDs (including both on-label and off-label valves)** SE valves (n=132; Evolut R 76,	30 days and 1 year. Median follow-up duration was 377 days (IQR: 138-915 days) in 181 people.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Sex: 55.2% male (47.7% in the SE group versus 69.6% in the BE group). Median STS risk score of 5.1% (SE 5.2, BE 4.8, p=0.005). Rate of NYHA functional class III or IV was 76.2%.	PANTHEON international registry	was high risk were included. People with concomitant moderate-to-severe AS, who had treatment with older THVs no longer commercially available and people who had treatment via transapical access were excluded.	Accurate Neo 25, JenaValve 21, Navitor Portico 10**)** and BE valves (n=69; Myval 40, Sapien S3 29**).** Access route: TF approach: n=192 Trans-subclavian approach n=8. SE valves were oversized and 80% people needed rapid pacing. 10% SE valves were dedicated valves (JenaValve for n=21).	
6	Vahl TP 2024 USA	ALIGN-AR IDE trial (NCT 04415047) n=180 people with pure AR. Mean age: 75.5 years	Prospective case series (at 20 centres in USA).	Inclusion criteria: symptomatic people with NYHA functional class II or higher, aged 18 years or over with moderate-to-severe or	**TAVI with on-label NGD JenaValve** Access route: TF Valve size: 23 mm (40 [23%] people),	At 30 days, 6 months and 1 year.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Sex: 53% (95/180) male 73% (131/180) were White. mean STS-PROM score 4.1% (SD 3.4). 89% (161/180) people were deemed to be at high risk on the basis of comorbidities; 34% (61/180) patients were assessed as frail. AR severity: moderate-to-severe in 32% (57/180); severe in 64% (116/180) people. NYHA class III–IV 68% (122/180)		severe native AR (according to the ASE criteria), deemed at high risk for mortality and complications after SAVR by the heart team and independent screening committee assessments. Exclusion criteria: congenital unicuspid or bicuspid valve morphology, previous prosthetic aortic valve implant, straight ascending aorta length less than 55 mm, aortic annulus angulation less than 70°, and severely reduced LVEF (less than 25%).	25 mm (35 [20%]), and 27 mm (102 [58%]). Mean oversizing was 12.6% for the 27-mm valve, 15.4% for the 25-mm valve, and 17.7% for the 23-mm valve. General anaesthesia in 164 (91%) and monitored anaesthesia care in 16 (9%).	

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
7	Li F 2024 China	n=36 people with pure native aortic regurgitation (PNAR) Mean age: 75 years Sex: 64% (23/36) male STS score: 7.14 plus or minus 2.11 NYHA class III or IV 94% (34/36).	Retrospective cohort study (2 centres)	People with PNAR who had TAVI for AR between 2014 and 2018 at 1 centre and between 2018 and 2019 in 1 centre.	**TAVI with dedicated on-label J-valve** under fluoroscopic guidance and general anaesthesia.	Median 5.26 years
8	Da-Wei, 2024, China	n=75 people with pure severe AR. Categorised into 2 groups: low-risk group (STS score less than 4), n=38; intermediate and high-risk group (STS score 4 or more), n=37. Age: low-risk group 73.1 years, high-risk group	Retrospective analysis compared the outcomes of TAVI between low-risk and intermediate or high-risk people with severe AR.	People with pure severe AR eligible for TAVI and who have had no contraindications for the procedure.	**TAVI with off-label NGD** (Venus-A and VitaFlow valves) in people with low risk (STS less than 4) and people with intermediate and high risk with severe AR (STS more than 4). Low risk, n=38 (Venus n=16, VitaFlow n=22)	30 days.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		76.4 years, p=0.028. Sex: n=46 male People in the lower risk group were younger, had a lower BMI, lower prevalence of hypertension, COPD, and previous percutaneous coronary intervention compared to high-risk group (p<0.05). There was no significant difference between the 2 groups for prevalence of hyperlipidaemia, diabetes, and AF.			Intermediate and high risk, n=37 (Venus n=17, VitaFlow n=20) Access route: TF access Size of valve: no significant difference between low-risk and high-risk groups (0.73)	
9	Elkasaby MH 2024	n=6 retrospective cohort studies	Systematic review and meta-analysis	Included RCTs or cohort studies including patients with pure AR, comparing TAVI with	**TAVI versus SAVR in pure AR** Various types of valves (both on-	Varied across studies (from in-hospital to 1 year).

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		33,484 people with pure or isolated AR. (5,633 people in the TAVI group and 27,851 people in the SAVR group). 3 studies in USA, 1 in China and 2 in Germany. Age: TAVI group ranged from 67 to 77 years, versus 60.0 to 75.6 years in the SAVR group. People in the TAVI group were older and had higher comorbidity scores.	Databases searched: PubMed, Embase, Web of Science (WOS), Scopus, and the Cochrane Library Central Register of Controlled Trials (CENTRAL) until June 2023.	SAVR, reporting in-hospital mortality or stroke. Excluded single-arm studies, studies with more than one publication, studies including people with AS or people with mixed AR and AS, case reports, reviews, abstracts, and animal studies.	label and off-label valves) were included in studies.	
10	Ullah W 2024 USA	Unmatched sample n=185,703 (AI 3,873, 181,830) people with AS. Matched sample of 7,929 people (AI 3,873, AS 4,056).	Retrospective study propensity score-matched (PSM) analysis NRD claims data (from 2015 to 2019) were used.	All US adults (over 18 years) who underwent TAVI for pure AS or AI were included, indicating that people were either symptomatic or had a compelling	**TAVI for treatment of AI versus TAVI for treatment of AS** Details of valves used were not	In hospital, 30 days and 180 days.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Mean age: TAVI for AI (mean 76.8 years), TAVI for AS (76.9 years). Women in AI versus AS groups was 38% versus 37%. The Elixhauser comorbidity index (to predict in-hospital mortality) for TAVI in AI versus TAVI in AS (2.63 versus 2.78, p=0.51).		indication for valvular replacement. People who underwent SAVR, had mixed AS and AI, or had the unspecified aortic valvular disease were excluded from the analysis.	available in the article	

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Samimi 2025	**Device success at 30 days (31 studies, n=1,527/1,777)**	**30 days outcomes** **Overall mortality (31 studies, n=1,802)**

First author, date	Efficacy outcomes	Safety outcomes
	The overall pooled device success rate was 90% at 30 days follow up (95% CI 86 to 93%; I^2=77%). **30-day success rate in TAVI group with dedicated valves versus TAVI group with off-label valves** The pooled device success rate in TAVI group with dedicated valves (JenaValve or J-valves) was higher at 93%[1,009/1,077] (95% CI: 90-95%; I^2=54%) compared with off-label valves (82% [518/700]; 95% CI 72-89%; I^2=77%; p<0.01). **Subgroup analysis as per access site (transfemoral versus transapical)** Device success rate was comparable between the 2 subgroups (p=0.17).	The overall pooled all-cause mortality rate at 30 days was 4% (116 events, 95% CI 3% to 7%; I^2=0%). **TAVI group with dedicated valves (18 studies, n=1,019) versus TAVI group with off-label valves (13 studies, n=783)** The pooled all-cause mortality rate in the TAVI group with dedicated valves (JenaValve, J-valve) was much lower compared with the TAVI group with off-label valves (3% [33 events], 95% CI 2% to 6%, I^2=56%) versus 9% [83 events], 95% CI 6% to 14%, I^2=0%; p<0.01). **All-cause mortality at 1 year (23 studies, n=1,217)** The overall pooled all-cause mortality rate at 1 year was 13% (95% CI 8% to 19%; I^2=88%), **TAVI group with dedicated valves (11 studies, n=618) versus TAVI group with off-label valves (12 studies, n=649)** The pooled all-cause mortality rate in the TAVI group with dedicated valves was lower (6% [33 events], 95% CI 5% to 9%; I^2=24%) compared to the TAVI group with off-label valves (24% [219 events], 95% CI: 15% to 34%; I^2=81%; p<0.01). **Moderate or severe residual AR (32 studies, n=2,041)** The overall pooled moderate or severe residual AR rate was 2%, (95% CI 1% to 4%; I^2=47%. **TAVI group with dedicated valves (19 studies, n=1,107) versus TAVI group with off-label valves (13 studies, n=934)** The pooled moderate or severe residual AR rate in the TAVI group with dedicated valves (JenaValve or J-valves) was lower compared with the TAVI group with off-label valves (4% [18 events]; 95% CI 3% to 5%; I^2=0% versus 5% [82 events], 95% CI 2% to 11%; I^2=79%; p=0.03).

First author, date	Efficacy outcomes	Safety outcomes
		Reintervention (31 studies, n=1,990) The overall pooled reintervention rate was 6% (95% CI 4% to 8%; I^2=47%). **TAVI group with dedicated valves (18 studies, n=1,039) versus TAVI group with off-label valves (13 studies, n=951)** The pooled reintervention rate was lower for the TAVI group with dedicated valves (JenaValve, J-valves) compared with the TAVI group with off-label valves 4% [38 events]; 95% CI 3% to 5%; I^2=0% versus 10% [101 events], (95% CI 8% to 14%; I^2=20%, p<0.01). **PPM implantation (33 studies, n=1,797)** The overall pooled PPM implantation rate was 14% (95% CI 10% to 18%; I^2=3%). **TAVI group with dedicated valves (18 studies, n=1,097) versus TAVI group with off-label valves (13 studies, n=700)** The pooled PPM implantation rate in the TAVI group with dedicated valves was lower 11% [147 events], (95% CI 7% to 15%; I^2=68%) compared with the off-label valve group 20% [118 events], (95% CI 15% to 26%; I^2=51%; p<0.01). **TVEM (29 studies, n=1,644)** The pooled TVEM rate was 3% (95% CI 2% to 5%; I^2=53%). **TAVI group with dedicated valves (18 studies, n=1,039) versus TAVI group with off-label valves (11 studies, n=605)**

First author, date	Efficacy outcomes	Safety outcomes
		The TVEM rate in the TAVI group with dedicated valves was significantly lower (2% [17 events], (95% CI: 1% to 3%; I^2=0%) compared with TAVI group off-label valves 8% [52 events], (95% CI 4% to 13%; I^2=52%; p<0.01). **Major bleeding (28 studies, n=1,514)** The pooled major bleeding rate was 3% (95% CI 2% to 6%; I^2=12%). **TAVI group with dedicated valves (17 studies, n=975) versus TAVI group with off-label valves (11 studies, n=539)**The pooled major bleeding rate in the TAVI group with dedicated valves was lower (3% [31 events]; 95% CI: 1 to 5%; I^2=0%) compared to TAVI group with off-label valves (7% [47 events]; 95% CI: 4 to 13%; I^2=0%; p<0.01). **Stroke** The overall pooled stroke rate was 1% (95% CI 1% to 3%; I^2=0%), with no significant differences between the 2 subgroups, TAVI with dedicated valves and TAVI with off-label valves (p=0.09). **Major vascular complications** The rate of major vascular complications was comparable between subgroups, TAVI with dedicated valves and TAVI with off-label valves (2%; 95% CI 1% to 4%; I^2=1%; p=0.12) . **Subgroup analysis as per access site (transfemoral versus transapical)** At 30 days, all outcomes were comparable between the 2 subgroups, except for PPM implantation (27 studies, n=1,439), which was higher in the transfemoral group compared with the transapical group (21% versus 6%; p<0.01).

First author, date	Efficacy outcomes	Safety outcomes
		Subgroup analysis of dedicated valves (JenaValve versus J-valve) At 30 days, PPM implantation (19 studies, n=1,111) was higher in the JenaValve group compared with the J-Valve group (21% versus 6%; p<0.01), and residual AR more than moderate (19 studies, n=1,111) was lower in the JenaValve group compared with the J-Valve group (1% versus 3%; p<0.01). All other outcomes were comparable between the 2 types of valves. **Subgroup analysis excluding studies published before 2016 (time sensitivity analysis): dedicated valves (7 studies, n=578) versus off-label valves (12 studies, n=293)** At 30-days, all-cause mortality rate (2 versus 7%; p<p0.01); reintervention rate (3 versus 13%; p<0.01); and TVEM rates (2 versus 6%; p=0.04) were significantly better in the dedicated valves group compared with the off-label group. At 1 year, all-cause mortality was comparable between the 2 subgroups. **Subgroup analysis as per access site (transfemoral versus transapical)** All-cause mortality rate at 1 year (19 studies, n=1,165) was higher in the transfemoral access group compared with the transapical access group (14% versus 6%; p=0.03). **Subgroup analysis of dedicated valves (JenaValve versus J-valve)** All-cause mortality rate at 1 year (in 11 studies, n=641) was comparable between the 2 types of valves (9% versus 5%, p=0.20).
Rawasi 2019	**NGDs versus EGDs** **Device success** (14 studies, n=524/659 events)	**NGDs versus EGDs**

First author, date	Efficacy outcomes	Safety outcomes
	ES 0.862 (95% CI 0.788 to 0.922), I^2=81.01%, p<0.001. Device success was higher with purpose-specific valves (96.3%, 95% CI 92.2% to 98.9%; I^2=0%) compared with non-purpose-specific valves (84.4% [95% CI 75% to 91.9%]; I^2=46%; p=0.02). Device success did not differ significantly (p=0.32) between the transfemoral (82.1% [95% CI 68%–92.8%]; I^2=78%) and transapical subgroups (90.3% [95% CI 79.2%–97.4%]; I^2=87%).	**Mortality** **30-day** (19 studies, n=122/998) ES 0.119 (95% CI 0.094 to 0.147), I^2=27.99%, p=0.110 There was no statistically significant difference in the rate of 30-day mortality between those purpose-specific (8.2%; 95% CI 4.3 to 13.1%; I^2=0%) and non-purpose-specific valves (13.0%; 95% CI 8.2 to 18.6%; I^2=25%); p=0.13). Also, there was no significant difference in 30-day mortality (p=0.41) between the subgroup (n=475) with primarily transapical access (10% [95% CI 7.4%– 12.8%]; I^2=0%), and the subgroup (n=173) with primarily femoral access (12.6% [95% CI 7.3%–19.0%]; I^2=0%). **1 year** (6 studies, n=155/618) ES 0.247 (95% CI 0.213 to 0.281), I^2=0%, p=0.481. **PPM implantation** (14 studies, n=92/63) ES 0.131 (95% CI 0.093 to 0.175), I^2=44.1%, p=0.034) There was no statistically significant difference in the rate of PPM implantation between purpose-specific (6.8% [95% CI 3.2% to 11.7%; I^2=0%]) and non-purpose-specific valves (19.8% [95% CI 6.7% to 37.5%; I^2=76%; p=0.06). Also, there was no statistically significant difference in the rate of PPM implantation between studies using transfemoral access (13% [95% CI 5.4% to 23.3%]; I^2=58%), and those using transapical access (12%, [95% CI 8.9% to 15.6%]; I^2=8%); p=0.84). **Major bleeding** (11 studies, n=69/582)

First author, date	Efficacy outcomes	Safety outcomes
		ES 0.124 (95% CI 0.061 to 0.204), I^2=82.13%, p<0.001 **Residual moderate-to-severe AR** (18 studies, n=99/966) ES 0.092 (95% CI 0.055 to 0.137), I^2=75%, p<0.001. moderate-to-severe AR was significantly lower (p=0.002) with the use of purpose-specific valves (3.1% [95% CI 0.9% to 6.4%]; I^2=0%) compared with non-purpose-specific valves (14.4% [95% CI 7.6% to 22.9%)]; I^2=54%). There was no significant difference (p=0.18) in the risk of residual moderate-to-severe AR between studies using transapical access (5.2% [95% CI 2.0% to 9.6%]; I^2=57%), and studies using transfemoral access (12.9% [95% CI 4.4% to 25%]; I^2=75%). **Stroke** (14 studies, n=20/648) ES 0.036 (95% CI 0.023 to 0.051), I^2=0%, p=0.967 Myocardial infarction at 30 days (11 studies): no cases
Takagi H 2020	**NGDs versus EGDs** **Device success** Overall, 80.4% (95% CI 72.2% to 88.6%, I^2=92.36%, p=0.000) EGDs (5 studies) 67.2% (95% CI 54.4% to 79.9%, I^2=81.95%, p=0.000); NGDs (7 studies) 90.2% (95% CI 84.0% to 96.3%, I^2=81.63%, p=0.000); p<0.001 between groups.	**NGDs versus EGDs** **Conversion to open surgery** Overall, 3.0% (95% CI 1.5% to 4.4%) EGDs 2.8% (95% CI 0.4% to 5.1%); NGDs 3.1% (95% CI 1.3% to 4.9%); p=0.840 between groups. **Coronary obstruction** Overall, 0.7% (95% CI 0.1% to 1.4%) EGDs 0.4% (95% CI 0.0% to 1.3%)

First author, date	Efficacy outcomes	Safety outcomes
		NGDs 1.2% (95% CI 0.2% to 2.2%); p=0.243 between groups. **Valve-in-valve deployment** Overall, 10.5% (95% CI 4.9% to 16.2%, I^2=86.21%, p=0.000) EGDs (3 studies) 22.1% (95% CI 16.2% to 28.0%, I^2=0, p=0.665) NGDs (5 studies) 4.7% (95% CI 0% to 9.7%, I^2=78.52%, p=0.001); p<0.001 between groups. **Annulus rupture** Overall, 1.5% (95% CI 0.3% to 2.6%) EGDs 1.7% (95% CI 0.0% to 4.0%) NGDs 1.4% (95% CI 0.1% to 2.7%); p=0.834 between groups. **Reintervention** Overall, 3.9% (95% CI 2.5% to 5.3%) EGDs 4.3% (95% CI 1.7% to 6.9%) NGDs 4.0% (95% CI 2.1% to 5.9%), p=0.868 between groups. **PPM implantation** Overall, 11.6% (95% CI 6.8% to 16.4%, I^2=81.68, p=0.000) EGDs (4 studies) 15.6% (95% CI 9.4% to 21.8%, I^2=72.07%, p=0.013) NGDs (6 studies) 8.3% (95% CI 2.0% to 14.5%, I^2=75.78%, p=0.001), p=0.085 between groups.

First author, date	Efficacy outcomes	Safety outcomes
		Moderate or higher paravalvular AR Overall, 7.4% (95% CI 4.0% to 10.9%, I^2=78.02%, p=0.000) EGDs (4 studies) 17.3% (95% CI 6.7% to 27.9%, I^2=83.17%, p=0.000) NGDs (7 studies) 3.4% (95% CI 1.8% to 5.0%, I^2=0, p=0.908); p<0.001 between groups. **30-day mortality** **All-cause** Overall, 9.5% (95% CI 6.4% to 12.6%, I^2=61.25%, p=0.003) EGDs (5 studies) 14.7% (95% CI 10.8% to 18.6%, I^2=0%, p=0.417) NGDs (7 studies) 6.1% (95% CI 3.2% to 8.9%, I^2=40.31%, p=0.122); p<0.001 between groups. **Cardiovascular related** Overall, 6.6% (95% CI 4.4% to 8.8%) EGDs 9.5% (95% CI 3.2% to 15.7%) NGDs 5.8% (95% CI 3.7% to 7.9%); p=0.193. **Mid-term all-cause mortality** (between 6 to 12 months) Overall, 18.8% (95% CI 10.9% to 26.7%, I^2=84.85%, p=0.000) EGDs (4 studies) 32.2% (95% CI 25.7% to 38.8%, I^2=0%, p=0.454) NGDs (6 studies) 11.8% (95% CI 4.5% to 19.0%, I^2=77.79%, p=0.000); p<0.001 between groups. **Stroke**

First author, date	Efficacy outcomes	Safety outcomes
		Overall, 2.7% (95% CI 1.7% to 3.8%) EGDs 2.3% (95% CI 0.6% to 3.9%) NGDs 2.9% (95% CI 1.5% to 4.4%); p=0.541 between groups. **Life-threatening or major bleeding complications** Overall, 5.7% (95% CI 2.8% to 8.6%, I^2=0%, p=0.480) EGDs (5 studies) 12.4% (95% CI 4.9% to 19.9%, I^2=0%, p=0.950) NGDs (6 studies) 3.5% (95% CI 0.4% to 6.7%, I^2=0%, p=0.458); p=0.015 between groups. **Acute kidney injury** (stage 1 to 3): Overall, 10.5% (95% CI 2.6% to 18.3%) EGDs 18.2% (95% CI 2.1% to 34.3%) NGDs 9.1% (95% CI 0.9% to 17.33%); p=0.309 between groups. **Major vascular complications:** Overall, 3.9 (95% CI 2.7% to 5.2%) EGDs 6.2% (95% CI 3.5% to 8.8%) NGDs 3.0% (95% CI 1.5% to 4.5%); p=0.041 between groups. **Stepwise random-effects meta-regression** Meta-regression showed that none of the covariates or factors assessed were associated with 30-day all-cause mortality.

First author, date	Efficacy outcomes	Safety outcomes
Liu 2024	**Device success at 30 days (as per VARC-2 criteria)** NGDs: ES 0.945 (95% CI 0.913 to 0.971), I^2=76.8%, p=0.000. On-label valves: ES 0.978 (95% CI 0.964 to 0.989), I^2=8.2, p=0.358. Off-label valves (6 studies, n=258): ES 0.899 (95% CI 0.848 to 0.941), I^2=10.3, p=0.350; (p<0.001 between on and off-label valves) Access route: TF (8 studies, n=340): ES 0.925 (95% CI 0.875 to 0.964), I^2=35.6, p=0.144. TA (16 studies, n=873): ES 0.961 (95% CI 0.939 to 0.979), I^2=50.4, p=0.003. (p=0.000 between routes).	**NGDs; on-label versus off-label** **Mortality** 30 days NGDs: ES 0.042 (95% CI 0.027 to 0.059), I^2=43.8, p=0.008 On-label valves: ES 0.026 (95% CI 0.013 to 0.043), I^2=22.1, p=0.192 Off-label valves: ES 0.051 (95% CI 0.016 to 0.102), I^2=30.4, p=0.219 (p=0.006 between on and off-label valves) Access route: TF: ES 0.040 (95% CI 0.012 to 0.078), I^2=28.9, p=0.208 TA: ES 0.029 (95% CI 0.014 to 0.047), I^2=30.7, p=0.117 (p=0.052 between routes) 1 year NGDs: ES 0.081 (95% CI 0.051 to 0.117), I^2=67.3, P=0.001 On-label valves: ES 0.059 (95% CI 0.035 to 0.087), I^2=23.3, p=0.251 Off-label valves: N/A **Permanent pacemaker implantation** NGDs: ES 0.088 (95% CI 0.061 to 0.119), I^2=57, p=0.000 On-label valves: ES 0.069 (95% CI 0.046 to 0.095), I^2=40, p=0.041 Off-label valves: ES 0.184 (95% CI 0.132 to 0.242), I^2=0, p=0.928 (p<0.001 between on and off-label valves) Access route: TF: ES 0.194 (95% CI 0.148 to 0.244), I^2=0, p=0.814 TA: ES 0.060 (95% CI 0.043 to 0.078), I^2=0, P=0.787 (p=0.000 between routes)

First author, date	Efficacy outcomes	Safety outcomes
		Conversion to SAVR NGDs: ES 0.022 (95% CI 0.009 to 0.038), I^2=0, p=0.981 On-label valves: ES 0.025 (95% CI 0.012 to 0.042), I^2=0, p=0.957 Off-label valves: N/A **Annulus rupture** NGDs: ES 0.002 (95% CI 0.000 to 0.017), I^2=0, P=0.941 On-label valves: N/A Off-label valves: N/A **Reintervention** NGDs: ES 0.023 (95% CI 0.007 to 0.045), I^2=13.9, p=0.324 On-label valves: N/A Off-label valves: ES 0.028 (95% CI 0.000 to 0.114), I^2=54.6, p=0.111 **Greater-than-mild PVL** NGDs: ES 0.012 (95% CI 0.004 to 0.022), I^2=0, p=0.713 On-label valves: ES 0.009 (95% CI 0.002 to 0.019), I^2=0, p=0.942 Off-label valves: ES 0.038 (95% CI 0.012 to 0.074), I^2=0, p=0.611 (p=0.003 between on- and off-label valves) Access route: TF ES 0.034 (95% CI 0.012 to 0.063), I^2=0.0, p=0.791 TA ES 0.008 (95% CI 0.001 to 0.018), I^2=0.0, p=0.960 (p=0.002 between routes) **Mild PVL** NGDs: ES 0.209 (95% CI 0.176 to 0.244), I^2=12.8, p=0.304 On-label valves: ES 0.203 (95% CI 0.165 to 0.243), I^2=19, p=0.241

First author, date	Efficacy outcomes	Safety outcomes
		Off-label valves: N/A Access route: TF ES 0.184 (95% CI 0.115 to 0.263), I^2=29.5, p=0.235 TA ES 0.216 (95% CI 0.117 to 0.259), I^2=13.1, p=0.314 (p=0.314 between routes) **None/trace PVL** NGDs: ES 0.774 (95% CI 0.708 to 0.835), I^2=71.3, p=0 On-label valves: ES 0.780 (95% CI 0.705 to 0.847), I^2=73.4, p=0 Off-label valves: N/A Access route: TF ES 0.781 (95% CI 0.685 to 0.866), I2=42.9, p=0.154 TA ES 0.769 (95% CI 0.683 to 0.846), I^2=76.2, p=0.000 (p=0.897 between routes)
Poletti, 2023 NCT05319171 PANTHEON international registry	**Technical success** (according to the VARC-3 criteria, included freedom from mortality, successful delivery of the device, retrieval of the delivery system, correct positioning of the valve and freedom from surgery or intervention related to the device, access or cardiac structural complication at the time of exit from the procedure room): Overall: 83.6% (168/201)	**In-hospital events** **All-cause death** Overall, 5% (10/201) SE group 5.3% (7/132) versus BE group 4.4% (3/69), p=0.767 **Cardiovascular Death:** Overall: 4.0% (8/201) SE group 3.8% (5/132) versus BE group 4.4% (3/69), p=0.847 **Stroke/TIA:**

First author, date	Efficacy outcomes	Safety outcomes
	SE: 80.3% (106/132) versus BE: 89.9% (62/69); p=0.108. **Device Success at 1 month** (defined as technical success at 30 days along with satisfactory valve performance [mean gradient less than 20 mmHg, and less than moderate regurgitation]): Overall: 76.1% (153/201) SE: 75.8% (100/132) versus BE: 76.8% (53/69); p=0.868.	Overall: 1.5% (3/201) SE group 2.3% (3/132) versus BE group 0% (0/69), p=0.553 **Transcatheter valve embolisation or migration** (TVEM defined according to the VARC-3 definition and included valve migration, embolisation and ectopic valve deployment). The causes of TVEM were malpositioning [32%], oversizing [20%], valve failure to anchor [20%], manipulation [8%] and unknown causes [12%] Overall, 12.4% (25/201) SE group 13.6% (18/132) versus BE group 10.1% (7/69), p=0.476. Post-dilation was the single independent variable associated with TVEM on multivariate analysis. **Residual moderate or greater AR (in-hospital echocardiography):** Overall, 9.5% (19/201) SE group 9.2% (12/132) versus BE group 10.1% (7/69), p=0.835. **New PPM implantation:** Overall: 22.3% (36/201) SE group 22.6% (24/132) versus BE: 21.8% (12/69), p=0.918 **Major vascular complications:** Overall: 7.5% (13/201) SE group 8.1% (9/201) versus BE group 6.5% (4/69), p=0.532. **Major bleeding:**

First author, date	Efficacy outcomes	Safety outcomes
		Overall: 10.6% (20/201) SE: 12.6% (16/132) versus BE group 6.5% (4/69), p=0.197 **Conversion to surgery:** Overall: 2.0% (4/201) SE group 1.5% (2/132) versus BE group 2.9% (2/69), p=0.612 **AKI (network classification 2 or more):** Overall: 10.5% (18/201) SE group 10.9% (12/201) versus BE group 9.8% (6/69), p=0.827 **Second valve needed:** Overall: 10.5% (21/201; THV implantation in 10, snaring in 5, repositioning in 2, procedure aborted in 4). SE group 11.4% (15/132) versus BE group 8.7% (6/69), p=0.557 **Postprocedural mean gradient (mm Hg):** Overall: 6.7 (SD 3.9) SE group 6.3 (SD 2.7) versus BE: 7.5 (SD 5.3), p=0.049 **Final transvalvular gradient:** BE group (7.5 SD 5.3 mm Hg) versus SE group (6.3 SD 2.7 mm Hg); p=0.049.

First author, date	Efficacy outcomes	Safety outcomes
		Composite endpoint at 1 year (composite of all-cause mortality and heart failure rehospitalisation), in 90% (181/201): Overall incidence 17.1% (95% CI: 10.4% to 23.4%), SE group 18.1% (95% CI: 9.1% to 26.2%) BE group 15.1% (95% CI: 4.7% to 24.4%; log-rank p=0.52). Incidence of composite endpoint in people with TVEM: 25.7% (95% CI: 5.6% to 41.5%) versus people without TVEM: 15.8% (95% CI 10.4% to 23.4%); p=0.05. There was no significant difference in the incidence of TVEM between the SE and BE valve groups (14.6% for SE and 16.1% for BE, p=0.835). After adjusting for propensity score, there was no significant difference between the SE or BE valves in terms of technical failure (aOR: 0.48; 95% CI: 0.18 to 1.18; p=0.127), device failure (aOR: 1.04; 95% CI 0.49 to 2.13; p=0.923), TVEM (aOR: 0.71; 95% CI 0.25 to 1.81; p=0.486), or the rate of residual moderate or severe AR (aOR: 1.07; 95% CI 0.36 to 2.98; p=0.894). Even after propensity matching, TVEM led to a higher 1-year incidence of the composite endpoint (HR: 2.45; 95% CI 1.00 to 6.18; p=0.05) and all-cause mortality (HR: 4.06; 95% CI 1.50 to 11.0; p=0.006).
Vahl 2024 NCT 04415047	**NGD with on-label (JenaValve)** **Technical success** 95% (171/180). Mean total procedure time was 71.8 min (SD 24.9). **All-cause mortality at 1-year** (primary efficacy point): achieved, in 7.8% (14/180 [97.5% CI 3.3% to	**NGD with on-label (JenaValve)** **The 30-day composite primary safety endpoint*** was achieved in 27% (48/180; 97.5% CI 19.2 to 34.0) people ($p^{non\text{-}inferiority}$<0.0001), when compared with the pre-specified safety performance goal of 40.5%. *(a non-hierarchical composite consisting of all-cause mortality, any stroke, life-threatening or major bleeding, AKI stage 2 to 3 or dialysis [7-day endpoint], major vascular complications, surgery or intervention related to

First author, date	Efficacy outcomes	Safety outcomes
	12.3%]) people (p<0.0001) when compared for non-inferiority with a performance goal of 25%. <u>In a pre-specified group who had successful valve implantation</u>: primary efficacy was achieved in 16.2% (11/177; [97.5% CI 2.2% to 10.3%)]; $p^{non\text{-}inferiority}$<0.0001) people at 1 year. **Haemodynamic outcomes** Data are mean (SD) **Mean aortic gradient, mmHg** Baseline (n=180) 8.7 (6.6) 30 days (n=172) 3.9 (1.6) 6 months (n=154) 4.3 (2.0) 12 months (n=141) 4.3 (1.8). **Effective orifice area, cm²** 30 days (n=172) 2.9 (0.6) 6 months (n=154) 2.7 (0.6) 12 months (n=141) 2.8 (0.6).	the device [including coronary intervention], new permanent pacemaker implantation, and moderate or severe total AR at 30 days after the procedure according to VARC-2 definitions). **Total adverse events 27% (48/180)** Death 2% (4/180) Any stroke 2% (4/180) • disabling stroke 1% (1/180) • non-disabling stroke 1% (1/180). Major or life-threatening bleeding 4% (8/180) Major vascular complication 4% (7/180) AKI (stage 2 or 3) or dialysis (7 days) 1% (2/180) Surgery or intervention related to the valve 3% (5/180) • SAVR for valve embolisation 1 • commercial THV for valve embolisation 1 • aortic endograft and commercial THV for catheter induced aortic dissection 1 • second Trilogy THV for valve embolisation in 2. New PPM implantation in 24% (36/150; 30 people had a previous pacemaker) **Paravalvular AR at 1 year** • moderate or greater paravalvular AR 1 • mild or mild-to-moderate PAR reduced from 19% (n=31) at 30 days to 8% (n=11)

First author, date	Efficacy outcomes	Safety outcomes
	Effective orifice area index, cm^2/m^2 30 days (n=172) 1.7 (0.4) 6 months (n=154) 1.5 (0.4) 12 months (n=141) 1.6 (0.3). **LVEF, %** Baseline (n=180) 53.8 (11.4) 30 days (n=172) 49.7(12.6) 6 months (n=154) 51.9 (12.0) 12 months (n=141) 55.0 (11.6). **LV remodelling/ dimensions** (by echocardiography) Mean LV mass declined from 323.7 g (SD 123.4) at baseline to 219.5 g (SD 101.4; p<0.0001) at 1 year Mean LVESd decreased from 39.6 mm (SD 10.2) at baseline to 34.2 mm (SD 9.0; p<0.0001) at 1 year. **Functional status (NYHA classification)** Baseline	• none or trace in 92% (n=130)

First author, date	Efficacy outcomes	Safety outcomes
	Class II 32% Class III 63% Class IV 5% <u>At 30 days</u> Class I 51% (91/180) Class II 34% (62/180) Class III 9% (17/180). <u>At 1 year</u> Class I 50% (90/180) Class II 27% (48/180) NYHA functional class improved by at least one category in 125 (83%) people. **Quality of life (assessed using KCCQ scoring)** From baseline to 1-year, the mean KCCQ overall score increased by 20.6 points (SD 24.3) from a mean of 55.3 (27.1) to 77.6 (22.7; p<0·0001; Large improvement (20-point or more increase) 41% (63/152)	

First author, date	Efficacy outcomes	Safety outcomes
	Moderate improvement (increase between 10 and <20 points 16% (24/152) Small improvement (increase between 5 and <10 points) 7% (11/152) No change (change between -5 and less than 5 points) 18% (27/152) Worse (more than 5-point decrease from baseline) 11% (16/152) Dead 7% (11/152). **6-minute walk test** An increase in 6-min walk test distance was found and 48% (62/180) people had an improvement of at least 15 m from baseline to 1 year.	
Li F 2024	**Implantation procedure success** 94.4% (34/36) **NYHA** **Functional class I or II** Baseline 5.5% (2/36)	**Perioperative adverse events** Conversion to surgery 5.5% (2/36) • LV perforation in 1 person (valve embolised in LV, needed immediate surgery to remove the prosthesis followed by replacement of the ascending aorta and aortic valve). • THV mispositioning in 1 person (embolisation of the valve into the ascending aorta, the displaced valve was subsequently repositioned

First author, date	Efficacy outcomes	Safety outcomes
	Follow up: 79% (23/29) **Survival** The cumulative survival rate at 5 years was 74%. **Haemodynamic outcomes** **Peak velocity, m/s** Baseline (n=36): 1.78 plus or minus 0.40 Discharge (n=31): 1.94 plus or minus 0.34, p value NS Follow up (n=26): 1.82 plus or minus 0.45, p value NS **Peak pressure gradient, mmHg** Baseline (n=36): 13.85 plus or minus 4.44 Discharge (n=31): 16.26 plus or minus 4.95, p value, NS Follow up (n=26): 14.78 plus or minus 6.31, p value NS **LVEF, %**	within the aortic arch, distal to the left subclavian artery and a second valve was implanted in the anatomically correct position). Cardiac failure in 1 Acute renal insufficiency in 1 person Massive cerebral infarction in 1 person Mild paravalvular leakage in 7/34 (20.6%) people. **Adverse events at follow up** Mortality 19.4% (7/36) Causes: • 1 from MI 8.9 years after TAVI, • 1 from pulmonary infection 6 months after TAVI • 2 from COVID-19 at 3.7 and 4.5 years • 1 from lung cancer at 3.8 years • 2 because of sudden cardiac death at 2.4 and 4.7 years. Paravalvular regurgitation • none or trivial: discharge 80.6% (25/36); follow up 76.9% (20/26) • mild: discharge 16.1% (5/36); follow up 23.0% (6/36) • moderate: discharge 3.2% (1/31) **Intra-prosthetic AR** • None or trivial: baseline 0; discharge 87.1% (27/36); follow up 69.2% (18/26)

First author, date	Efficacy outcomes	Safety outcomes
	Baseline (n=36): 55.46 plus or minus 9.98 Discharge (n=31): 51.93 plus or minus 9.86, p value NS Follow up (n=26): 54.65 plus or minus 9.54, p value NS **LVEDd, mm** Baseline (n=36): 60.60 plus or minus 8.50 Discharge (n=31): 56.23 plus or minus 7.76, p value, NS Follow up (n=26): 50.77 plus or minus 7.49 (p<0.01 between baseline and follow up). **Effective orifice area, cm^2** Baseline 2.56 plus or minus 0.23 Discharge 2.12 plus or minus 0.22 (p<0.01) Follow up 2.06 plus or minus 0.20 (p<0.01).	• Mild: baseline 20.5% (7/36) discharge 12.9 (4/31); follow up 30.7% (8/26) • Moderate or severe: none. **Valve durability** Prosthetic valve thrombosis: none reported Morphological SVD (defined according to the standardised criteria set by the EAPCI/ESC/EACTS: none reported.
Da-Wei, 2024	**Echocardiography outcomes** Low-risk group: LVEDd and LVESd significantly decreased at 1 month from	**All-cause mortality (postoperative and at 30 days):** Low-risk group 0% (0/38) versus intermediate and high-risk group: 0% (0/37) **Cardiovascular mortality (postoperative and at 30 days):**

First author, date	Efficacy outcomes	Safety outcomes
	baseline (LVEDd: 54.3 [SD 6.2] versus 50.4 [SD 6.4], p=0.017; LVESd: 40.2 [8.4] versus 35.9 [SD 7.3], p=0.037). There was no significant difference in LVEF 50.9 [10.2] versus 51.8 [SD 11.0], p=0.73). There was no significant difference in LVEF, moderate-to-severe MR, and moderate-to-severe TR. <u>Intermediate and high-risk group:</u> LVEDd decreased significantly at 1 month from baseline (57.6 [SD 6.2] versus 53.3 [SD 8.1], p=0.035) The rate of moderate-to-severe MR was also significant (p=0.036) but the difference in LVESd, LVEF, and moderate-to-severe TR, was not significant. **NYHA functional class** Changes in NYHA functional class in low, intermediate and high-risk groups significantly improved from	Low-risk group 0% (0/38) versus intermediate and high-risk group: 0% (0/37) **Bleeding Events (postoperative and at 30 days):** Low-risk group 2.6% (1/38) versus intermediate and high-risk group: 0% (0/37), p=0.32 **Major vascular complications:** **Postoperative** Low-risk group 2.6% (1/38) versus intermediate and high-risk group: 2.7% (1/37), p=0.98 **30 days** Low-risk group 0 versus intermediate and high-risk group 0 **Acute renal failure (postoperative and at 30 days):** Low-risk group 0 versus intermediate and high-risk group 0 **Stroke (postoperative and at 30 days):** Low-risk group 0 versus intermediate and high-risk group: 2.7% (1/37), p=0.31 **Myocardial infarction (postoperative and at 30 days):** Low-risk group 0 versus intermediate and high-risk group 0 **Degree of AR**

First author, date	Efficacy outcomes	Safety outcomes
	baseline at both 1 and 30 days after TAVI (both p<0.001).	Changes in AR degree in low, intermediate and high-risk groups significantly improved from baseline at both 1 and 30 days after TAVI (both p<0.001). none had severe AR after TAVI. **New-onset AF:** **Postoperative** Low-risk group 13.2% (5/38) versus intermediate and high-risk group: 8.1% (3/37), p=0.48. **30 days** Low-risk group 0 versus intermediate and high-risk group 0 **New left bundle branch block (LBBB):** **Postoperative** Low-risk group 13.2% (5/38) versus intermediate and high-risk group: 21.6% (8/37), p=0.33. **30 days** Low-risk group 0 versus intermediate and high-risk group: 2.7% (1/37), p=0.31. **New atrioventricular block (AVB):** **Postoperative** Low-risk group 18.4% (7/38) versus intermediate and high-risk group: 18.9% (7/37), p=0.96. **30 days** Low-risk group 0 versus intermediate and high-risk group 0

First author, date	Efficacy outcomes	Safety outcomes
		New complete AVB (postoperative and at 30 days): Low-risk group 0 versus intermediate and high-risk group 0 **New PPM implantation:** **Postoperative** Low-risk group 18.4% (7/38) versus intermediate and high-risk group: 13.5% (5/37), p=0.56. **30 days** Low-risk group 2.6% (1/38) versus intermediate and high-risk group: 5.4% (2/37), p=0.54. **Endocarditis (postoperative and at 30 days):** Low-risk group 0 versus intermediate and high-risk group 0 **Readmission for heart failure (30 days)** Low-risk group 2.6% (1/38) versus intermediate and high-risk group: 2.7% (1/37), p=0.98. **Valve in valve** Low-risk group 13.2% (5/38) versus intermediate and high-risk group 10.8% (4/37)
Elkasaby 2024	**TAVI versus SAVR**	**TAVI versus SAVR** **In-hospital mortality** (5 studies)

First author, date	Efficacy outcomes	Safety outcomes
	Length of hospital stay (4 studies) TAVI (n=4,718) versus SAVR (n=17,115); (MD=−4.76 days; 95% CI: −5.27 to −4.25, p<0.001; I^2=88%, p<0.001).	TAVI (174/5442) versus SAVR (1027/27643; RR=0.89, 95% CI 0.56 to 1.42, p=0.63; I^2=86%, p<0.001). In-hospital mortality (4 studies, excluding Stachon 2020) (RR=0.72; 95% CI: 0.59 to 0.89, p=0.003). Subgroup analysis according to access route: TA TAVI versus SAVR (RR=1.53; 95% CI 1.02% to 2.31%, p=0.04; I^2=0%, p=0.47). TF TAVI versus SAVR (RR=0.99; 95% CI 0.48% to 2.04%, p=0.97; I^2=91%, p<0.001). Undefined TAVI approach versus SAVR: (RR=0.60; 95% CI 0.41% to 0.87%, p=0.008; I^2=9%, p=0.30). Subgroup analysis according to country TAVI was favoured over SAVR in studies conducted in China (RR=0.67; CI: 0.45 to 0.1, p=0.05). There were no differences between TAVI and SAVR in the USA (p=0.29) and Germany (p=0.88) subgroups. **30-day mortality** (1 study Mentias 2023) TAVI (25/1147) versus SAVR (267/9880; RR=0.81, 95% CI 0.54 to 1.21, p=0.30). **1 year mortality** (1 study Mentias 2023) TAVI (79/1147) versus SAVR (563/9880; RR=1.21, 95% CI 0.96 to 1.52, p=0.10). **In-hospital stroke** (4 studies)

First author, date	Efficacy outcomes	Safety outcomes
		TAVI (80/4295) versus SAVR (735/17763; RR=0.50; 95% CI 0.39 to 0.66, p<0.001; I^2=11%, p=0.34). **30-day stroke** (1 study Mentias 2023) TAVI (29/1147) versus SAVR (198/9880; RR=1.26, 95% CI 0.86 to 1.85, p=0.24). **Postoperative new-onset AF** (2 studies) TAVI (436/2062) versus SAVR (3681/11270; RR=0.26, 95% CI 0.02 to 3.80, p=0.33; I^2=100%, p<0.0001). **Post-operative AKI** (4 studies) TAVI (630/3987) versus SAVR (2711/13140; RR=0.56; 95% CI: 0.41 to 0.76, p=0.0002; I^2=91%, p<0.00001). **Postoperative major bleeding** (5 studies) TAVI (276/5442) versus SAVR (5597/27643; RR=0.23; 95% CI: 0.17 to 0.32, p<0.001; I^2=85%, p<0.001). **Pacemaker implantation** (3 studies) TAVI (507/3882) versus SAVR (945/13090; RR=1.68; 95% CI: 1.50 to 1.88, p<0.001; I^2=0% p=0.83). **Delirium (2 studies)** TAVI (100/1560) versus SAVR (1216/14553; RR 0.68, 95% CI 0.25 to 1.88, p=0.46; I^2=96%, p<0.0001)

First author, date	Efficacy outcomes	Safety outcomes
		Pneumonia (2 studies) TAVI (74/2735) versus SAVR (161/3210; RR 0.53, 95% CI 0.40 to 0.70, p<0.0001; I^2=0%, p=0.54) **Sepsis (2 studies)** TAVI (42/2735) versus SAVR (127/3210; RR 0.15, 95% CI 0.01 to 2.23, p=0.17; I^2=74%, p=0.05).
Ullah W 2024	**The mean length of stay (days)** TAVI in AI=6.18 (SD 7.5) TAVI in AS=5.18 (SD 6.3).	**Pooled outcomes between TAVI for treatment of AI and TAVI for treatment of AS** **In-hospital outcomes** **NACE** TAVI in AI (5.6%, n=217) versus TAVI in AS (2.9%, n=117); (aOR 2.0, 95% CI 1.59 to 2.51) **All-cause mortality** TAVI in AI (2.5%, n=98) versus TAVI in AS (0.7%, n=29); (aOR 3.1, 95% CI 2.4 to 5.5) **Stroke** TAVI in AI (0.8%, n=29) versus TAVI in AS (0.6%, n=24); (aOR 1.3, 95% CI 0.7 to 2.2) **Major bleeding** TAVI in AI (2.8%, n=107) versus TAVI in AS (1.8%, n=74); (aOR 1.53, 95% CI 1.1 to 2.1) **Cardiac tamponade** TAVI in AI (n=fewer than 11 events) versus TAVI in AS (0.4%, n=16); (aOR 1.9, 95% CI 1.0 to 3.5)

First author, date	Efficacy outcomes	Safety outcomes
		Cardiogenic shock TAVI in AI (0.8%, n=29) versus TAVI in AS (n=16); (aOR 0.5, 95% CI 0.2 to 1.2) **Valvular complications** (aOR 9.48, 95% CI 6.73 to 13.38) **Adjusted analysis** **30 days** **NACE** TAVI in AI (5.9%, n=25) versus TAVI in AS (6.1%, n=26); (aOR 0.9, 95% CI 0.5 to 1.7) **Mortality** TAVI in AI (3.2%, n=14) versus TAVI in AS (3.3%, n=14); (aOR 1.0, 95% CI 0.5 to 2.1) **Major bleeding** TAVI in AI (n<11 events) versus TAVI in AS (3.1%, n=13); (aOR 0.8, 95% CI 0.3 to 1.7) **PPM implantation** TAVI in AI (9.7%, n=42) versus TAVI in AS (13.8%, n=59); (aOR 0.7, 95% CI 0.4 to 1.0) **180 days** **NACE** TAVI in AI (7.3%, n=30) versus TAVI in AS (7.7%, n=33); (aOR 0.9, 95% CI 0.6 to 1.6)

First author, date	Efficacy outcomes	Safety outcomes
		Mortality TAVI in AI (4.9%, n=20) versus TAVI in AS (3.7%, n=16); (aOR 1.3, 95% CI 0.7 to 2.6) **Stroke** TAVI in AI (n=<11 events) versus TAVI in AS (n=<11 events); (aOR 0.5, 95% CI 0.1 to 1.7) **Major bleeding** TAVI in AI (n=<11 events) versus TAVI in AS (n=<11 events); (aOR 0.6, 95% CI 0.2 to 1.7) **PPM implantation** TAVI in AI (12.4%, n=51) versus TAVI in AS (10.5, n=45); (aOR 1.2, 95% CI 0.8 to 1.8) **Impact of age and sex on outcomes of TAVI for AI compared to AS.** A sensitivity analysis based on age (under 80 years, and 80 years and over) and sex (male and female) mirrored the findings of the pooled analysis. On unadjusted analysis, TAVI in AI was associated with significantly higher odds of NACE, mortality, major bleeding, and post-procedure complications.

Procedure technique

There were variations in the valves used across studies. Existing old and new-generation TAVI valves have been used on an off-label basis in some studies. Dedicated on-label valves have been used in some studies. Both TA and TF access routes have been primarily used in studies. In limited cases (n=8) a trans-subclavian approach was used.

Efficacy

Technical success

NGD with on-label

In a prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), technical success (defined as absence of procedural mortality, successful access, delivery, and retrieval of transcatheter delivery system, deployment and correct positioning of a single THV, freedom from reintervention related to the device or access procedure) was achieved in 95% (171/180) people (Vahl 2024).

A retrospective cohort study of 36 people with pure native AR who had TAVI with an on-label dedicated valve reported that the device was successfully implanted during the procedure in 95% (34/36) people (Li 2024).

NGDs off-label (SE versus BE valves)

In an international PANTHEON registry analysis of 201 people who had TAVI with NGDs (including only 10% dedicated valves) for pure severe native AR, the overall technical success rate according to the VARC-3 criteria (defined as freedom from mortality, successful delivery of the device, retrieval of the delivery system, correct positioning of the valve and freedom from surgery or intervention related to the device, access or cardiac structural complication at the time of exit from the procedure room) was 84%, with no statistically significant difference in

technical success rates between people who had treatment with SE and BE valves (80% versus 90%, p=0.108; Poletti, 2023).

Device success

NGDs: on-label versus off-label valves

A systematic review and meta-analysis of 31 studies on TAVI with NGDs for pure AR, compared on-label (2 valve prosthesis systems) and off-label valves. A pooled analysis reported that the total device success rate (defined by the VARC-3 criteria) at 30 days was 95% (95% CI 91.3% to 97.1%, I^2=76.8%). A subgroup pooled analysis showed that the device success rate was higher for TAVI with on-label valves than TAVI with off-label valves (98% versus 90%; p<0.001). When TA and TF access routes were compared, the TA approach showed a significantly higher device success rate than the TF approach (96% versus 93%, p<0.001; Liu 2024).

The systematic review and meta-analysis of 34 studies comparing dedicated on-label valves with off-label valves among high surgical risk people with pure native AR reported that the pooled device success rate in the TAVI group with dedicated on-label valves was higher compared with off-label valves (93% versus 82%; p<0.01). Subgroup analyses according to access site reported that device success rate was comparable between the transfemoral and transapical access groups (p=0.17; Samimi 2024).

NGDs off-label (SE versus BE valves)

In the PANTHEON international registry analysis of 201 people who had TAVI with NGDs (including only 10% dedicated valves) for pure severe native AR, the overall device success rate at 1 month (defined as technical success at 30 days along with satisfactory valve performance [mean gradient less than 20 mmHg, and less than moderate regurgitation]) was 76%, with no statistically significant difference in device success rates between people who had treatment with SE and BE valves (76% versus 77%, p=0.868; Poletti, 2023).

NGDs versus EGDs

In a meta-analysis of 19 studies on TAVI for pure AR, a pooled analysis of 14 studies reported that the rate of device success (as per VARC-2 criteria, defined as a composite of absence of procedural mortality, correct positioning of valve prosthesis, and intended performance of the prosthetic valve) was 86% (524/659, 95% CI 78.8 to 92.2%, I^2=81.01%, p<0.001). A subgroup analysis showed that the use of NGDs was associated with higher device success compared with EGDs (p=0.009). Device success was higher with new-generation purpose-specific dedicated valves (96%, 95% CI 92.2% to 98.9%; I^2=0%) compared with non-purpose-specific valves (85% [95% CI 75% to 91.9%]; I^2=46%; p=0.02; Rawasi 2019).

A meta-analysis of 11 studies (including 911 people with pure AR who had TAVI), reported 81% device success. A subgroup pooled analysis reported significantly higher device success rates after TAVI using NGDs when compared with TAVI using EGDs (90% versus 67%; p<0.001; Takagi 2020).

Left ventricular remodelling (echocardiography findings)

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), mean LV mass declined from 323.7 g at baseline to 219.5 g (p<0.001) at 1 year and mean LVESd significantly decreased from 39.6 cm at baseline to 34.2 cm (p<0.0001) at 1 year (Vahl 2024).

In the retrospective cohort study of 36 people with pure native AR who had TAVI with an on-label dedicated valve, a statistically significant reduction in LVEDd was observed at follow-up assessment compared to pre-operative values (60.6 to 50.7, p<0.01). Whereas, no significant difference was reported between the pre-operative and discharge values (60.6 to 56.2, p=0.086). The effective orifice area measurements at both discharge and follow up were significantly lower compared

to pre-operative levels (p<0.01).There were no statistically significant differences in peak velocity, peak pressure gradient, or LVEF at pre-operative, discharge, and follow-up assessments (Li 2024).

NGDs off-label (low-risk [STS below 4] versus intermediate and high-risk groups [STS 4 and above])

A retrospective analysis of 75 people who had TAVI with off-label valves for pure severe AR reported that people in the low-risk group reported a statistically significant decrease in mean LVEDd (p=0.017) and LVESd (p=0.037) from baseline at 1 month follow up. People in the intermediate and high-risk group reported a statistically significant decrease in LVEDd (p=0.035) but not LVESd (p=0.23; Da-Wei 2024).

Functional status (NYHA classification)

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), 68% (122/180) people had NYHA functional class III to IV disease at baseline. At 30 days, NYHA functional class status was class I in 51% (91/180), class II in 34% (62/180), and class III in 9% (17/180) of people. At 1 year, 50% (90/180) of people had class I and 27% (48/180) had class II. NYHA functional class improved by at least 1 category in 83% (125/180) of people (Vahl 2024).

In the retrospective cohort study of 36 people with pure native AR who had TAVI with an on-label dedicated valve, 79% (23/29) people were classed as NYHA functional class I or II during the follow-up period compared to only 6% (2/36) people at baseline (Li 2024).

NGDs off-label (low-risk [STS below 4] versus intermediate and high-risk groups [STS 4 and above])

The retrospective analysis of 75 people who had TAVI with off-label valves for pure severe AR reported that compared to people in the low-risk group (n=38), people in the intermediate and high-risk groups (n=37) had a statistically significant improvement in NYHA functional class from baseline at both 1- and 30-days after TAVI (both p<0.001; Da-Wei 2024).

Quality of life

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), the mean KCCQ overall score increased by 20.6 points at 1 year (from baseline mean 55.3 to 77.6; p<0.0001). Of 152 people who responded, the number of people with a KCCQ overall score of at least 75 was 63% (88/152) and 11% (16/152) of people had a 5 point or more decrease from baseline (felt worse; Vahl 2024).

6-minute walk test

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), an increase in 6-min walk test distance (from baseline 262.7 m to 312.5 m at 1 year) was reported and 48% (62/180) people had an improvement of at least 15 m at 1 year (p values were not reported; Vahl 2024).

Length of hospital stay (LOS)

TAVI versus SAVR

In a systematic review and meta-analysis of 6 studies comparing TAVI with SAVR for pure AR, a pooled analysis of 4 studies showed that the LOS was shorter with TAVI compared to SAVR (MD=−4.76 days; 95% CI −5.27 to −4.25, p<0.001). A subgroup pooled analysis showed that TF TAVI was associated with shorter LOS compared to SAVR (MD=−4.33 days, 95% CI −4.42 to −4.23, p<0.001) but TA TAVI was not associated with shorter LOS compared to SAVR (MD=−1.98 days, 95% CI −4.33 to 0.93, p=0.21). The undefined TAVI approach subgroup was also associated with shorter LOS compared to SAVR (MD=−4.66days, 95% CI −5.35 to −3.98, p<0.0001; Elkasaby 2024).

Survival (NGD with on-label)

In the retrospective cohort study of 36 people with pure native AR who had TAVI with an on-label dedicated valve, the cumulative survival rate at 5 years was 74% (Li 2024).

Safety

Composite primary safety endpoint

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), the 30-day composite primary safety endpoint (all-cause mortality, major bleeding, stroke, acute kidney injury, new pacemaker implantation or valve dysfunction requiring surgical or percutaneous intervention) was achieved in 27% (48/180, 97.5% CI 19.2 to 34.0) people ($p^{\text{non-inferiority}}$<0·0001), when compared with the pre-specified safety performance goal of 40.5% (Vahl 2024).

Composite endpoint (all-cause mortality and heart failure rehospitalisation at 1 year)

NGDs off-label (SE versus BE valves)

The PANTHEON international registry analysis of 201 people who had TAVI with NGDs (including only 10% dedicated valves) for pure severe native AR reported that the overall incidence of the composite endpoint (all-cause mortality and heart failure rehospitalisation) at 1 year (in 181 people) was 17% (95% CI 10.4% to 23.4%). There was no statistically significant difference in the incidence in people treated with SE and BE valves (18% [95% CI 9.1% to 26.2%] versus 15% [95% CI 4.7% to 24.4%]; p=0.52). People who had TVEM had a higher incidence of the composite endpoint compared to people in the non-TVEM group (25.7% [95% CI 5.6% to 41.5%] versus 15.8% [95% CI 8.5% to 22.5%]. log-rank p=0.05). After adjusting for propensity scores, TVEM was associated with a higher 1-year incidence of the composite endpoint (HR: 2.45; 95% CI: 1.00 to 6.18; p=0.05) and increased all-cause mortality (HR: 4.06; 95% CI: 1.50 to 11.0; p=0.006; Poletti, 2023).

NACE (a composite of all-cause in-hospital mortality, stroke, and major bleeding)

TAVI for AR versus TAVI for AS

In a retrospective propensity score-matched analysis of NRD data (n=7,929) comparing people who had TAVI for AI (n=3,873) with poeple who had TAVI for AS (n=4,056), in-hospital NACE was statistically significantly higher in the AI group compared with the AS group (TAVI in AI [5.6%, n=217] versus TAVI in AS [2.9%, n=117]; aOR 2.0, 95% CI 1.6 to 2.5). But there was no statistically significant difference in NACE at 30 days (TAVI in AI [5.9%, n=25] versus TAVI in AS [6.1%, n=26]; aOR 0.9, 95% CI 0.5 to 1.7) and 180 days (TAVI in AI [7.3%, n=30] versus TAVI in AS [7.7%, n=33]; aOR 0.9, 95% CI 0.6 to 1.6), respectively (Ullah 2024).

In-hospital mortality

NGD off-label (SE versus BE valves)

The PANTHEON international registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (including only 10% dedicated valves) reported that the incidence of in-hospital all-cause mortality was 5.0% (10/201), with no statistically significant difference in rates between people treated with SE and BE valves (5.3% [7/132] versus 4.4% [3/69], p=0.767; Poletti, 2023).

TAVI for AR versus TAVI for AS

In the retrospective propensity score-matched analysis of NRD data (n=7,929) comparing people who had TAVI for AI (n=3,873) with people who had TAVI for AS (n=4,056), in-hospital mortality was statistically significantly higher in the AI group compared with the AS group (TAVI in AI [2.5%, n=98] versus TAVI in AS [0.7%, n=29]; aOR 3.01, 95% CI 2.4 to 5.5; Ullah 2024).

TAVI versus SAVR

In the systematic review and meta-analysis of 6 studies comparing TAVI with SAVR, a pooled analysis of 6 studies showed that in-hospital mortality rate was comparable between the 2 procedures (RR=0.89, 95% CI 0.56 to 1.42, p=0.63; I^2=86%). A pooled analysis after excluding 1 study (Stachon 2020, the source of heterogeneity) suggests that TAVI may be associated with a decreased mortality rate than SAVR (RR=0.72; 95% CI 0.59 to 0.89, p=0.003).

A subgroup analysis on the approach of TAVI (TA and TF) showed that TA TAVI was associated with an increased in-hospital mortality rate compared to SAVR (RR=1.53; 95% CI 1.02 to 2.31, p=0.04; I^2=0%). TF TAVI was associated with a similar in-hospital mortality rate compared to SAVR (RR=0.99; 95% CI 0.48 to 2.04, p=0.97; I^2=91%). Pooled results of undefined TAVI approaches showed a lower rate of in-hospital mortality compared to SAVR (RR=0.60; 95% CI 0.41 to 0.87, p=0.008; I^2=9%). Subgroup analysis according to the country of origin

showed that TAVI was favoured over SAVR in studies done in China (RR=0.67; CI 0.45 to 0.1, p=0.05). There were no differences between TAVI and SAVR in the USA (p=0.29) and Germany (p=0.88) subgroups (Elkasaby 2024).

Mortality at 30 days

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial) mortality at 30 days was 2% (4/180; Vahl 2024).

NGD off-label (low-risk [STS below 4] versus intermediate and high-risk groups [STS above 4])

A retrospective analysis of 75 people who had TAVI with off-label valves for pure severe AR reported that in both the low, intermediate and high-risk groups, there were no recorded cases of all-cause mortality following the procedure and at 30 days follow up (Da-Wei 2024).

NGDs: on-label versus off-label valves

The systematic review and meta-analysis of 31 studies on new-generation TAVI valves for pure AR reported that the 30-day all-cause mortality was 4% (95% CI 2.7% to 5.9%, I^2=43.8%). A subgroup analysis comparing on-label (2 valve prosthesis systems) and off-label valves showed a statistically significantly lower 30-day mortality rate for TAVI using on-label valves than off-label valves (3% versus 5%; p=0.006). When comparing TA and TF access routes, 30-day mortality was lower for the TA group than the TF group (3% versus 4%, p=0.052; Liu 2024).

The systematic review and meta-analysis of 34 studies comparing dedicated on-label valves with off-label valves among people with high surgical risk with pure native AR reported that the pooled all-cause mortality rate at 30 days in the TAVI group with dedicated on-label valves was much lower compared with the TAVI

group with off-label valves (3% versus 9%; p<0.01). Subgroup analyses according to access site reported that the 30-day mortality rate was comparable between the transfemoral and transapical access groups (Samimi 2024).

NGDs versus EGDs

In the systematic review and meta-analysis of 19 studies, a pooled analysis reported that the rate of 30-day mortality was 12% (122/998, 95% CI 9.4% to 14.7%, I^2=28%, p=0.110). A subgroup analysis showed the use of NGDs was associated with a lower 30-day mortality compared to EGDs (p=0.02). There was no statistically significant difference in the rate of 30-day mortality between new-generation purpose-specific dedicated valves (8.2%; 95% CI 4.3% to 13.1%; I^2=0%) and non-purpose-specific valves (13.0%; 95% CI 8.2% to 18.6%; I^2=25%; p=0.13; Rawasi 2019).

In the meta-analysis of 11 studies (n=911), a pooled analysis reported a 30-day all-cause mortality rate of 9.5% and a 30-day cardiovascular mortality rate of 6.6%. A subgroup analysis reported a statistically significantly lower incidence of 30-day all-cause mortality in the NGD group compared to the EGD group (6% versus 15%; p<0.001). There were no statistically significant differences in the incidence of 30-day cardiovascular mortality between the 2 groups (6% versus 10%; p=0.193; Takagi 2020).

TAVI for AR versus TAVI for AS

In the retrospective propensity score-matched analysis of NRD data (n=7,929) comparing people who had TAVI for AI (n=3,873) with people who had TAVI for AS (n=4,056), there was no statistically significant difference in mortality at 30 days (TAVI in AI [3.2%, n=14] versus TAVI in AS [3.3%, n=14]; aOR 1.0, 95% CI 0.5 to 2.1) and 180 days (TAVI in AI [4.9%, n=20] versus TAVI in AS [3.7%, n=16]; aOR 1.3, 95% CI 0.7 to 2.6) between the groups (Ullah 2024).

TAVI versus SAVR

In the systematic review and meta-analysis of 6 studies comparing TAVI with SAVR, 1 included study (Mentias 2023) reported that the mortality rates were comparable between the 2 procedures at 30-day follow up (RR=0.81; 95% CI 0.54 to 1.21, p=0.30; Elkasaby 2024).

Mortality at 1 year

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial) all-cause mortality at 1-year (primary efficacy endpoint) was achieved, in 8% (14/180 [97.5% CI 3.3 to 12.3]) of people (p<0·0001) when compared for non-inferiority with a performance goal of 25%. In the pre-specified group who had successful valve implantation (n=177), primary efficacy was achieved in 16% (11/177; [97.5% CI 2.2 to 10.3)]; $p^{non\text{-}inferiority}$<0.0001) people at 1 year (Vahl 2024).

NGDs versus EGDs

The systematic review and meta-analysis of 31 studies on new-generation TAVI valves for pure AR reported that the estimated 1-year mortality was 8% (95% CI 5.1% to 11.7%, I^2=67.3%). A subgroup analysis reported that the estimated 1-year mortality was 6% for TAVI using NGDs with on-label valves (Liu 2024).

In the systematic review and meta-analysis of 34 studies, the pooled all-cause mortality rate at 1 year in the TAVI group with dedicated on-label valves was lower compared to TAVI group with off-label valves (6% versus 24%; p< 0.01). A subgroup analysis according to access site showed that the rate was higher in the transfemoral access group compared with the transapical access group (14% versus 6%; p=0.03; Samimi 2024).

In the meta-analysis of 11 studies (n=911), a pooled analysis reported an all-cause mortality of 19% at mid-term (4 months to 1 year). A subgroup analysis reported a significantly lower incidence of mid-term all-cause mortality in the NGD group compared to EGD group (12% versus 32%; p<0.001; Takagi 2020).

In the systematic review and meta-analysis of 19 studies, 6 studies reported that the incidence of 1-year mortality ranged from 20% to 31%, with a pooled incidence of 25% (155/618, 95% CI 21.3% to 28.1%; I^2=0%, p=0.481; Rawasi 2019).

TAVI versus SAVR

In the systematic review and meta-analysis of 6 studies comparing TAVI with SAVR, only 1 included study (Mentias 2023) reported that the mortality rates were comparable between the 2 procedures at 1-year follow up (RR=1.21; 95% CI 0.98 to 1.52, p=0.1; Elkasaby 2024).

Mortality at 5 years (NGD with on-label)

In the retrospective cohort study of 36 people with pure native AR who had TAVI with an on-label dedicated valve, all-cause mortality rate of 19.5% (7/36) was reported at a median follow up of 5.26 years (Li 2024).

PPM implantation

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), new PPM implantation was reported in 24% (36/150) of people without a PPM before the procedure. A pre-existing PPM was present in 30 people (Vahl 2024).

NGD off-label (SE versus BE valves)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (including only 10% dedicated valves), new

PPM implantation was reported in 22% (36/201) people, with no statistically significant difference in rates between people who had treatment with SE and BE valves (23% [24/132) versus 22% [12/69], p=0.918; Poletti, 2023).

NGD off-label (low-risk [STS below 4] versus intermediate and high-risk groups [STS above 4])

The retrospective analysis of 75 people who had TAVI with off-label valves for pure severe AR reported no statistically significant difference in rates of PPM implantation in low, intermediate and high-risk patient groups at 30 days after TAVI (2.6% [1/38] versus 5.4% [2/37], p=0.54; Da-Wei 2024).

NGDs: on-label versus off-label valves

The systematic review and meta-analysis of 31 studies on new-generation TAVI valves for pure AR reported that the PPM implantation rate at 30 days was 9% (95% CI 6.1% to 11.9%, I^2=57.0%). A subgroup analysis reported that PPM implantation using on-label valves was statistically significantly lower in the TAVI group using on-label valves than in the group using off-label valves (7% versus 19%; p<0.001). When comparing access routes, PPM implantation was lower for the TA group than the TF group (6% versus 20%, p<0.001; Liu 2024).

In the systematic review and meta-analysis of 34 studies, the pooled PPM implantation rate in the TAVI group with dedicated on-label valves was lower compared with the off-label valve group (11% versus 20%; p<0.01). A subgroup analysis according to access site reported that PPM implantation rate was higher in the transfemoral group compared with the transapical group (21% versus 6%; p<0.01; Samimi 2024).

NGDs versus EGDs

In the systematic review and meta-analysis of 19 studies, a pooled analysis of 14 studies reported that the rate of post-procedural PPM implantation ranged from 0% to 44%, with a pooled estimate of 13% (95% CI 9.3% to 17.5%; I^2=44%,

p=0.034). A subgroup analysis reported that there was no statistically significant difference in the rate of PPM implantation between the studies using NGDs (10.4% [95% CI 6.6 to 15.0%]; I^2=15%), and those using EGDs (17.7% [95% CI 10.6 to 26.1%]; I^2=62%; p=0.09). There was no statistically significant difference in the rate of PPM implantation between new-generation purpose-specific dedicated valves (6.8% [3.2% to 11.7%]; I^2=0%) and non-purpose-specific valves (19.8% [95% CI 6.7% to 37.5%]; I^2=76%; p=0.06). Also, there was no statistically significant difference in the rate of PPM implantation between studies using TF access (13% [95% CI 5.4% to 23.3%]; I^2=58%), and those using TA access (12%, [95% CI 8.9% to 15.6%]; I^2=8%; p=0.84). A meta-regression revealed a statistically significant positive association between average age and rate of PPM implantation after the procedure (p<0.001). Rate of PPM implantation was not associated with mean annulus size (p=0.55), proportion of people with moderate-to-severe MR (p=0.89), or logistic EUROSCORE (p=0.72; Rawasi 2019).

In the meta-analysis of 11 studies (n=911), PPM implantation rate was 12% (95% CI 6.8% to 16.4%). A subgroup analysis revealed that there was no statistically significant difference in the incidence of PPM implantation between the NGD and EGD groups (8% versus 16%; p=0.085; Takagi 2020).

TAVI for AR versus TAVI for AS

In the retrospective propensity score-matched analysis of NRD data (n=7,929) comparing people who had TAVI for AI (n=3,873) with people who had TAVI for AS (n=4,056), there was no statistically significant difference in PPM implantation post procedure between the 2 groups (TAVI in AI [8.5%, n=328] versus TAVI in AS [7.5%, n=306]; aOR 1.1, 95% CI 1.0 to 1.3). The need for PPM was similar between the groups at 30 days (TAVI in AI [9.7%, n=42] versus TAVI in AS [13.8%, n=59]; aOR 0.7, 95% CI 0.4 to 1.0) and 180 days (TAVI in AI [12.4%, n=51] versus TAVI in AS [10.5%, n=45]; aOR 1.2, 95% CI 0.8 to 1.8). respectively (Ullah 2024).

TAVI versus SAVR

In the systematic review and meta-analysis of 6 studies comparing TAVI versus SAVR, a pooled analysis of 4 studies showed that TAVI was associated with a higher rate of PPM implantation than SAVR (RR=1.68; 95% CI 1.50 to 1.88, p<0.001; Elkasaby 2024).

Residual or post-procedure AR

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), moderate paravalvular AR was present in 1 patient at 30 days and it was mild at 1 year. Mild or mild-to-moderate paravalvular AR decreased from 19% (31/180) at 30 days to 8% (11/180) at 1 year. Paravalvular AR was none or trace in 92% (130/180) people at 1 year (Vahl 2024).

In the retrospective cohort study of 36 people with pure native AR who had TAVI with a dedicated valve, only 1 person experienced moderate paravalvular leakage at discharge, which required SAVR 4 years after TAVI. Additionally, no instances of moderate or severe intra-prosthetic regurgitation were detected at discharge or follow up (Li 2024).

NGD off-label (SE versus BE valves)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (including only 10% dedicated valves), residual moderate or severe AR was reported in 10% (19/201) people, with no statistically significant difference in rates between people who had treatment with SE and BE valves (9% [12/132] versus 10% [7/69], p=0.835; Poletti, 2023).

NGD off-label (low-risk [STS below 4] versus intermediate and high-risk groups [STS above 4])

The retrospective analysis of 75 people who had TAVI off-label valves for pure severe AR reported that AR degree in low-risk and intermediate and high-risk groups significantly improved from baseline at both 1 and 30 days after TAVI (both $p<0.001$). No one had severe AR after TAVI. Trivial AR was observed in 3 cases on the first day post procedure. By 30 days 7 people showed mild residual AR (Da-Wei 2024).

NGDs on-label versus off-label

The systematic review and meta-analysis of 31 studies on new-generation TAVI valves for pure AR reported that the rate of greater-than-mild PVL at 30 days was 1.2% (95% CI: 0.4% to 2.2%, $I^2=0.0\%$). A subgroup analysis reported that the rate of greater-than-mild PVL was statistically significantly higher in the TAVI group using on-label valves compared with those using off-label valves (0.9% versus 3.8%; $p=0.003$). When comparing access routes, procedures with the TA route had slightly higher PVL than the TF route (22% versus 19%, $p=0.314$) but greater-than-mild PVL rates were higher in the TF group than TA group (0.8% versus 4%, (Liu 2024).

In the systematic review and meta-analysis of 34 studies, the pooled moderate or severe residual AR rate in TAVI group with dedicated on-label valves was lower compared with the TAVI group with off-label valves (4% versus 5%; $p=0.03$). Subgroup analyses according to access site reported that moderate or severe residual AR rate was comparable between the transfemoral and transapical access groups (Samimi 2024).

NGDs versus EGDs

In the systematic review and meta-analysis of 19 studies, a pooled analysis of 18 studies reported that the occurrence of residual moderate-to-severe AR ranged from 0% to 29%, with a pooled estimate of 9% (95% CI 5.5% to 13.7%;

I^2=75%). A subgroup analysis reported that the residual moderate-to-severe AR after the procedure was statistically significantly lower in studies with NGDs (3% [95% CI 1.8% to 4.8%; I^2=0%) when compared with EGDs (20% [95% CI 11.5% to 28.6%; I^2=73%; p<0.001). Also, it was statistically significantly lower in those that had new-generation purpose-specific dedicated valves (3% [95% CI 0.9 to 6.4%]; I^2=0%) compared with people who had non-purpose-specific valves (15% [95% CI 7.6 to 22.9%]; I^2=54%; p=0.002). There was no statistically significant difference in the outcome between studies using TA access (5%, 95% CI 2.0% to 9.6%; I^2=57%), and studies using TF access (13%, 95% CI 4.4% to 25%; I^2=75%; p=0.18). A meta-regression revealed that moderate-to-severe AR was not associated with average age (p=0.53), mean annulus size (p=0.28), proportion of people with moderate-to-severe MR (p=0.76), or logistic EUROSCORE (p=0.97; Rawasi 2019).

In the meta-analysis of 11 studies (including 911 people who had TAVI for AR), moderate or higher paravalvular AR rate was 8%. A subgroup pooled analysis revealed a significantly lower incidence of moderate or higher paravalvular AR in the NGD group than in the EGD group (4% versus 17%; p<0.001; Takagi 2020).

Major bleeding

NGD on-label versus off-label

In the systematic review and meta-analysis of 34 studies, the pooled major bleeding rate in the TAVI group with dedicated valves was lower compared to TAVI group with off-label valves (3% versus 7%; p<0.01). Subgroup analyses according to access site reported that bleeding rate was comparable between the transfemoral and transapical access groups (Samimi 2024).

NGD off-label (SE versus BE valves)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (including only 10% dedicated valves), the incidence of major bleeding was reported in 11% (20/201) people, with no

statistically significant difference in rates between people treated with SE and BE valves (13% [16/132] versus 7% [4/69], p=0.197; Poletti, 2023).

NGD off-label (low-risk [STS below 4] versus intermediate and high-risk groups [STS above 4])

The retrospective analysis of 75 people who had TAVI off-label valves for pure severe AR reported no statistically significant difference in rates of bleeding complications in low, and intermediate and high-risk patient groups postoperatively and at 30 days after TAVI (2.6%, 1/38 versus 0, p=0.32; Da-Wei 2024).

NGDs versus EGDs

In the systematic review and meta-analysis of 19 studies, a pooled analysis of 11 studies (n=69/582) reported the incidence of major bleeding after the procedure ranged from 0% to 15%, with a pooled estimate of 13% [95% CI 6.1% to 20.4%, I^2=82%, p<0.001; Rawasi 2019).

In the meta-analysis of 11 studies (including 911 people), the rate of life-threatening or major bleeding complications was 6% (95% CI 2.8% to 8.6%). A subgroup analysis reported a statistically significantly lower incidence of major bleeding complications in the NGD group compared with the EGD group (4% versus 13%; p=0.015; Takagi 2020).

TAVI for AR versus TAVI for AS

In the retrospective propensity score-matched analysis of NRD data (n=7,929) comparing people who had TAVI for AI (n=3,873) with people who had TAVI for AS (n=4,056), major bleeding after the procedure was statistically significantly higher in people who had TAVI for AI compared with people who had TAVI for AS (TAVI in AI [2.8%, n=107] versus TAVI in AS [1.8%, n=74]; aOR 1.5, 95% CI 1.1 to 2.1). But there was no statistically significant difference between the groups at 30 days (TAVI in AI [n<11] versus TAVI in AS [n=13]; aOR 0.8, 95% CI 0.3 to

1.7) and 180 days (TAVI in AI [n<11] versus TAVI in AS [n<11]; aOR 0.6, 95% CI 0.2 to 1.7) respectively (Ullah 2024).

TAVI versus SAVR

In the systematic review and meta-analysis of 6 studies comparing TAVI with SAVR, a pooled analysis of 5 studies showed that TAVI was associated with a statistically significantly lower risk of major bleeding than SAVR (RR 0.23, 95% CI 0.17 to 0.32, p<0.001). A subgroup analysis according to TAVI approach (TF or TA) reported that TA TAVI, TF TAVI and undefined TAVI approaches were favoured over SAVR, (RR=0.41; 95% CI 0.28 to 0.59, p<0.001; I^2=0%); (RR=0.19; 95% CI 0.11 to 0.34, p<0.001; I^2=87%) and (RR=0.26; 95% CI 0.20 to 0.34, p<0.001; I^2=55%, p=0.14; Elkasaby 2024).

Cardiovascular outcomes (including stroke and MI)

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), 2 (1%) disabling and 2 (1%) non-disabling strokes were reported at 30 days (Vahl 2024).

In the systematic review and meta-analysis of 34 studies comparing TAVI with dedicated on-label valves to TAVI with off-label valves, there were no significant differences in the rate of strokes between the 2 subgroups (p=0.09; Samimi 2024).

NGD off-label (SE versus BE valves)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (including only 10% dedicated valves), cardiovascular death was reported in 4% (8/201) people, with no statistically significant difference in rates between people treated with SE and BE valves (3.8% [5/132] versus 4.4% [3/69], p=0.847). The overall rate of stroke and TIAs

was 1.5% (3/201), with no statistically significant difference in rates between people treated with SE and BE valves (2.3% [3/132] versus 0 [0/69], p=0.553; Poletti, 2023).

NGD off-label (low-risk [STS below 4] versus intermediate and high-risk groups [STS above 4])

The retrospective analysis of 75 people who had TAVI off-label valves for pure severe AR reported no significant difference in rates of strokes in people in low, intermediate and high-risk groups postoperatively and at 30-days after TAVI (0 versus 2.7% [1/37] versus 5.4% [2/37], p=0.31). There were no cases of MI reported in both groups (Da-Wei 2024).

NGDs versus EGDs

In the systematic review and meta-analysis of 19 studies, 11 studies reported no cases of MI at 30 days. Thirteen studies reported that the incidence of stroke ranged from 0% to 6%, with a pooled estimate of 3.6% [20/648, 95% CI 2.3% to 5.1%; I^2=0%, p=0.967; Rawasi 2019).

In the meta-analysis of 11 studies (including 911 people), the rate of stroke was 2.7%. There were no statistically significant difference in the incidence of stroke between the NGD and EGD subgroups (2.9% versus 2.3%; p=0.541; Takagi 2020).

TAVI for AR versus TAVI for AS

In the retrospective propensity score-matched analysis of NRD data (n=7,929) comparing people who had TAVI for AI (n=3,873) with people who had TAVI for AS (n=4,056), the incidence of stroke after the procedure was similar between the groups at 30 days (TAVI in AI [0.8%, n=29] versus TAVI in AS [0.6%, n=24]; aOR 1.3, 95% CI 0.7 to 2.2) and at 180 days (TAVI in AI [n<11] versus TAVI in AS [n<11]; aOR 0.5, 95% CI 0.1 to 1.7) respectively (Ullah 2024).

TAVI versus SAVR

In the systematic review and meta-analysis of 6 studies comparing TAVI with SAVR, a pooled analysis of 4 studies showed that in-hospital stroke was lower in the TAVI group compared with the SAVR group (RR=0.50; 95% CI 0.39 to 0.66, p<0.001, I^2=11%, p=0.34). A subgroup analysis on the approach of TAVI (TA and TF) found that TA TAVI was not protective against stroke compared to SAVR (RR=0.64; 95% CI 0.31 to 1.35, p=0.24; I^2=1%, p=0.31), while TF TAVI approach was protective compared to SAVR (RR=0.39; 95% CI 0.26 to 0.59, p<0.001; I^2=0%, p=0.85). Also, the undefined TAVI approach was associated with a lower rate of in-hospital stroke (RR=0.60; CI 0.41 to 0.87, p=0.008; I^2=9%, p=0.30). A subgroup analysis according to the country of origin reported that there was no statistically significant difference between TAVI and SAVR in the USA (RR=0.84; CI 0.40 to 1.74, p=0.63), while TAVI was protective in Germany (RR=0.42; CI 0.30 to 0.60, p<0.001; I^2=0%) and China (RR=0.54; 95% CI 0.36 to 0.80, p=0.002). One included study (Mentias 2023) reported that 30-day stroke was similar in the TAVI and SAVR groups (RR=1.26; 95% CI 0.86 to 1.85, p=0.24). (Elkasaby 2024).

In the systematic review and meta-analysis of 6 studies comparing TAVI with SAVR, MI was reported in only 1 included study (Alharbi 2020), which showed no difference between TAVI and SAVR groups (RR=0.79; [95% CI 0.59 to 1.05], p=0.11; Elkasaby 2024)

In the systematic review and meta-analysis of 6 studies comparing TAVI with SAVR, MACCE was reported in only 1 included study (Rali 2022), which favoured TAVI over SAVR (RR=0.48; 95% CI 0.25 to 0.90, p=0.02).

Conversion to open surgery

NGD with on-label

In the retrospective cohort study of 36 people with pure native AR who had TAVI, the rate of conversion to surgery was 6% (2/36). In 1 person the valve embolised

into the left ventricle (needed immediate surgery to remove the prosthesis followed by replacement of the ascending aorta and aortic valve). In another person the valve embolised into the ascending aorta (displaced valve was subsequently repositioned within the aortic arch, distal to the left subclavian artery and a second valve was implanted in the anatomically correct position; Li 2024).

NGD off-label (SE versus BE valves)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (including only 10% dedicated valves), cardiovascular death was reported in 2% (4/201) people, with no statistically significant difference in rates between peeple who had SE and BE valves (1.5% [2/132] versus 2.9% [2/69], p=0.612; Poletti 2023).

NGDs on-label versus off-label

The systematic review and meta-analysis of 31 studies on new-generation TAVI valves for pure AR reported that the rate of conversion to SAVR at 30 days was 2.2% (95% CI 0.9% to 3.8%, I^2=0.0%); and in the on-label group it was 2.5% (95% CI 1.2% to 4.2%, I^2=0.0%; Liu 2024).

NGDs versus EGDs

In the meta-analysis of 11 studies (including 911 people), a conversion to open surgery rate was 3.0%. There was no statistically significant difference in the incidence of conversion to open surgery between the NGD and the EGD subgroups (3.1% versus 2.8%; p=0.840; Takagi 2020).

Major vascular complications

NGD with on-label

In the prospective study of 180 symptomatic people with moderate-to-severe or severe AR who had TF TAVI with an on-label dedicated valve (ALIGN-AR trial), 4 valve embolisations occurred. In 2 people, the embolised valves were placed in

the descending aorta and a second THV was implanted, 1 was treated with a commercial THV and another with SAVR (Vahl 2024).

NGDs on-label versus off-label

In the systematic review and meta-analysis of 34 studies, the TVEM rate in the TAVI group with dedicated on-label valves was significantly lower compared with TAVI group off-label valves (2% versus 8%; p<0.01). The rate of other major vascular complications was comparable between the 2 groups (p=0.12; Samimi 2024).

NGD off-label (SE versus BE valves)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (including only 10% dedicated valves), major vascular complications were reported in 7.5% (13/201) people, with no statistically significant difference in rates between people treated with SE and BE valves (8.1% [9/132) versus 6.5% [4/69], p=0.532). In the same study, TVEM (defined according to the VARC-3 and included valve migration and embolisation as well as ectopic valve deployment) was reported in 12.4% (25/201) people, with no statistically significant difference in rates between treatment with SE and BE valves (13.6% [18/132) versus 10.1% [7/69], p=0.476; Poletti, 2023).

NGDs versus EGDs

In the meta-analysis of 11 studies (including 911 people), major vascular complications rate was 3.9%. Subgroup pooled analysis revealed a significantly lower incidence of major vascular complications in the NGD subgroup than in the EGD subgroup (3.0% versus 6.2%; p=0.041; Takagi 2020).

TAVI for AR versus TAVI for AS

In the retrospective propensity score-matched analysis of NRD data (n=7,929) comparing people who had TAVI for AI (n=3873) with people who had TAVI for AS (N=4,056), valvular complications (paravalvular leak, embolisation and

thrombosis) were statistically significantly higher in people who had TAVI for AI compared with people who had TAVI for AS (aOR 9.48, 95% CI 6.73 to 13.38; Ullah 2024).

Re-intervention

NGD off-label (SE versus BE valve)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (only 10% dedicated valves), reintervention (second valve) was needed in 10.5% (21/201) people, with no statistically significant difference in rates between people who had treatment with SE and BE valves (11.4% [15/132) versus 8.7% [6/69], p=0.557). All these were done for management of TVEM, in 10 cases a second valve was implanted, snaring of the embolised valve was done in 5, repositioning of the valve was done in 2, 4 needed surgical conversion (Poletti, 2023).

NGD on-label versus off-label

The systematic review and meta-analysis of 31 studies on new-generation TAVI valves for pure AR reported that the rate of reintervention (repeat procedure for second prosthetic heart valve at 30 days) was 2.3% (95% CI: 0.7 to 4.5%, I^2=13.9%) and in the on-label valves group the estimated rate was 2.8% (95% CI 0.0 to 11.4%, I^2=54.6%; Liu 2024).

In the systematic review and meta-analysis of 34 studies, the pooled reintervention rate was lower in the TAVI group with dedicated on-label valves compared with TAVI group with off-label valves 4% versus 10%; p<0.01). Subgroup analyses according to access site reported that reintervention rate was comparable between the transfemoral and transapical access groups (Samimi 2024).

NGDs versus EGDs

The meta-analysis of 11 studies (including 911 people) reported reintervention rate of 3.9%. There were no statistically significant differences in the incidence of reintervention rates between the NGD and EGD subgroups (4.0% versus 4.3%; p=0.868; Takagi 2020). Valve-in-valve deployment rate was around 10.5%. Subgroup pooled analysis revealed a statistically significantly lower incidence of valve-in-valve deployment (4.7% versus 22.1%; p<0.001) in the NGD subgroup than in the EGD subgroup (Takagi 2020).

Annulus rupture

NGD on-label versus off-label

The systematic review and meta-analysis of 31 studies on new-generation TAVI valves for pure AR reported that the rate of annulus rupture in procedure was 0.2% (95% CI 0.0 to 1.7%, I^2=0.0%; Liu 2024).

NGDs versus EGDs

The meta-analysis of 11 studies (including 911 people), reported annulus rupture rate of 1.5%. There were no statistically significant differences in the incidence of annulus rupture (1.4% versus 1.7%; p=0.834), between the NGD and EGD subgroups (Takagi 2020).

Acute kidney injury

NGD off-label (SE versus BE valves)

In the retrospective PANTHEON registry analysis of 201 people with pure severe native AR who had TAVI with NGDs (only 10% dedicated valves), AKI was reported in 10.5% (18/201) people, with no statistically significant difference in rates between people who had treatment with SE and BE valves (10.9% [12/132]) versus 9.8% [6/69], p=0.827; Poletti, 2023).

NGDs versus EGDs

The meta-analysis of 11 studies (including 911 people), reported AKI (stage 1 to 3) rate of 10.5%. There were no statistically significant differences in the incidence of any AKI (9.1% versus 18.2%; p=0.309) between the NGD and EGD subgroups (Takagi 2020).

TAVI versus SAVR

In the meta-analysis of 6 studies comparing TAVI with SAVR, pooled analysis of 4 studies showed that in-hospital AKI was lower in TAVI than SAVR (RR=0.56; 95% CI: [0.41, 0.76], p<0.001). A subgroup pooled analysis according to the approach of TAVI showed that the result favoured TF TAVI over SAVR (RR=0.36; 95% CI: [0.29, 0.45], p<0.001), and the undefined approach over SAVR (RR=0.66; 95% CI: [0.56, 0.78], p<0.001; Elkasaby 2024).

Coronary obstruction

NGDs versus EGDs

The meta-analysis of 11 studies (including 911 people), reported coronary obstruction rate of 0.7%. There were no significant differences in the incidence of coronary obstruction (1.2% versus 0.4%; p=0.243), between the NGD and EGD subgroups (Takagi 2020).

Cardiac tamponade

TAVI for AR versus TAVI for AS

In the retrospective propensity score-matched analysis of NRD data (n=7929) comparing people who had TAVI for AI (n=3873) with people who had TAVI for AS (N=4056), cardiac tamponade was significantly higher in people undergoing TAVI for AI compared with people who had TAVI for AS (TAVI in AI [0.8%, n=29] versus TAVI in AS [0.4%, n=16]; (aOR 1.91, 95% CI 1.0 to 3.5; Ullah 2024).

Valve durability

In the retrospective cohort study of 36 people with pure native AR who had TAVI with a dedicated valve, there were no instances of prosthetic valve thrombosis or morphological SVD (defined according to the standardised criteria set by the EAPCI/ESC/EACTS; Li 2024).

Other adverse events

TAVI versus SAVR

In the meta-analysis of 6 studies comparing TAVI with SAVR, pooled analysis showed that the overall effect estimates for delirium and sepsis did not favour either of the 2 procedures (RR=0.68; 95% CI 0.25, 1.88, p=0.46); and (RR=0.15; 95% CI 0.01, 2.23, p=0.17) but TAVI was associated with an decreased risk of pneumonia (RR=0.53; 95% CI 0.40, 0.70, p<0.001; Elkasaby 2024).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical). This advice was generalised across on and off-label TAVI usage for AR.

They listed the following anecdotal or theoretical adverse event:

- Left ventricular migration or embolisation leading to severe aortic incompetence.

Seven professional expert questionnaires and British Cardiovascular Society support statement were submitted for this procedure. Find full details of what the

professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- There are no RCTs assessing the outcomes of TAVI in pure native AR.
- Studies included in the systematic reviews were mainly small observational or registry studies reporting short-term outcomes in patients with surgical risks.
- There is no data on long-term outcomes.
- There was significant heterogeneity across the available studies in terms of valves used, access site, and outcomes reported.
- There is very limited data on haemodynamic outcomes and valve durability.
- Most evidence is on TAVI with non-dedicated valves for AR. The evidence on one dedicated TAVI valve for AR has been analysed in one prospective study in people with severe AR and high surgical risk (Vahl 2024).

Any ongoing trials

NCT04864145: Transcatheter self-expandable valve implantation for the treatment of severe native aortic regurgitation a prospective, multicentre, randomised study; RCT (SEASON-AR), n=210 patients with severe native AR and high surgical risk, intervention: transfemoral TAVI (with VitaFlow™ system) plus medical therapy versus medical therapy alone; follow up at 1, 6, and 12 months and annually until 5 years; location: China; completion date May 2031; status recruiting.

NCT05536310: Trilogy heart valve system for management of patients with aortic valve disease: patient registry and post-market clinical follow-up study (TAVIS Registry). n=600 patients with aortic valve disease (symptomatic severe AR or symptomatic, severe AS, who are at high risk for SAVR), intervention: TAVI with JenaValve; primary outcome: all-cause mortality at 30 days; location Germany, follow up 5 years, completion date October 2027; status not yet recruiting.

NCT06381271: Transcatheter aortic valve replacement for pure severe aortic valve regurgitation (TRUST TAVR registry); prospective cohort study, n=500 patients with native AR undergoing TAVI, follow up 10 years, location: China, completion date October 2034; status: recruiting.

NCT06379386: Long-term prognosis and valve durability of TAVR (TRACE TAVR registry); prospective single centre observational study; n=1000 patients with aortic valve disease (AR, AS); intervention: TAVI; primary outcome: all-cause mortality, valve related long-term efficacy; follow-up 5 years; location: China, completion date December 2030; status: recruiting.

NCT05737264: Safety and effectiveness of transcatheter treatment of severe native aortic regurgitation with self-expandable valve implantation: a multicentre, observational, prospective cohort study (SENSE-AR). N=76, primary outcome: all-cause mortality; follow up 12 months; location: China, completion date December 2023; status recruiting.

NCT06034028: J-Valve TF Early Feasibility Study; prospective, single-arm, multi-centre, interventional study, n=25 patients with symptomatic severe native AR treated with J-Valve, primary outcome: freedom from death or disabling stroke at 30 days, clinical efficacy 5 years after the procedure; location: USA, Canada, completion date June 2029; status active.

NCT05580952: Efficacy and safety of the J-Valve transcatheter aortic valve replacement system in patients with aortic regurgitation disease. Prospective multicentre study; n=120 patients with symptomatic severe native AR treated with J-Valve, primary outcome: all-cause mortality at 12 months; location: China, completion date May 2024; status unknown.

NCT02732704: THE ALIGN-AR TRIAL: Safety and effectiveness/performance of the transfemoral JenaValve pericardial TAVR system in the treatment of patients with symptomatic severe aortic regurgitation (AR). n=100, primary outcome: all-cause mortality at 30 days; location: USA, completion date September 2027; status active.

NCT04671758: Transcatheter aortic valve implantation with Sapien 3 transcatheter heart valve for pure aortic regurgitation. Cohort study, n=50, primary outcome: feasibility and 30-day safety; location: France, completion date March 2022; status unknown.

NCT05424653: To evaluate safety and effectiveness of transcatheter aortic valve system in patients with severe aortic insufficiency. Observational study, n=10, primary outcomes: device success rate, procedure success rate, rate of no residual AR, incidence of MACCE, rate of all-cause mortality at 30 days; Location: China; completion date: August 2023; status unknown.

Neo2 registry: European multicentre registry on the use of ACURATE neo2 in native AR (ongoing study).

Existing assessments of this procedure

The European Society of Cardiology and European Association for Cardio-Thoracic Surgery Guidelines for the management of valvular heart disease 2025 state that 'TAVI may be considered for the treatment of severe AR in symptomatic patients ineligible for surgery according to the Heart Team, if the anatomy is suitable.' They also state that 'current transcatheter options for AR are limited' and 'more evidence is required on transcatheter treatment options for AR, in particular using dedicated devices' (Praz et al. 2025).

The American College of Cardiology/American Heart/Association clinical practice guideline (ACC/AHA 2020), recommends that 'in patients with isolated severe AR who have indications for SAVR and are candidates for surgery, TAVI should not be performed'.

'TAVI for isolated chronic AR is challenging because of dilation of the aortic annulus and aortic root and, in many patients, lack of sufficient leaflet calcification. Risks of TAVI for treatment of AR include transcatheter valve migration and significant paravalvular leak. TAVI is rarely feasible, and then only in carefully selected patients with severe AR and HF who have a prohibitive surgical risk and in whom valvular calcification and annular size are appropriate for a transcatheter approach' (Oto 2021).

These assessments were done based on evidence available for off-label TAVI devices.

Related NICE guidance

Interventional procedures

Valve-in-valve TAVI for aortic bioprosthetic valve dysfunction (2019) NICE interventional procedures guidance 653. (Recommendation: standard arrangement).

Transcatheter aortic valve implantation for aortic stenosis (2017) NICE interventional procedures guidance 586. (Recommendation: standard arrangement).

NICE guidelines

Heart valve disease presenting in adults: investigation and management (2021) NICE guideline NG208.

Professional societies

- Society of Cardiothoracic Surgery of Great Britain and Ireland
- British Cardiovascular Intervention Society
- British Society of Echocardiography.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 2 completed submissions. These were considered by the interventional procedures technical team and any relevant points have been taken into consideration when preparing this overview.

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Appendix A: Methods and literature search strategy

NICE has identified studies and reviews relevant to transcatheter aortic valve implantation for native aortic valve regurgitation from the medical literature.

Search strategy design and peer review

This search report is informed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses literature search extension (PRISMA-S).

A NICE information specialist ran the literature searches on 09/08/2024 and updated them on 10/02/2025. See the search strategy history for the full search strategy for each database. Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The principal search strategy was developed in MEDLINE ALL (Ovid interface). It was adapted for use in each of the databases listed in table 4a, taking into account the database's size, search functionality and subject coverage. The MEDLINE ALL strategy was quality assured by a NICE senior information specialist. All translated search strategies were peer reviewed to ensure their accuracy. The quality assurance and peer review procedures were adapted from the Peer Review of Electronic Search Strategies (PRESS) 2015 evidence-based checklist.

Review management

The search results were managed in EPPI-Reviewer version 5 (EPPI-R5). Duplicates were removed in EPPI-R5 using a 2-step process. First, automated deduplication was done using a high-value algorithm. Second, manual deduplication was used to assess low-probability matches. All decisions about inclusion, exclusion and deduplication were recorded and stored.

Limits and restrictions

The CENTRAL database search removed trial registry records and conference material. The Embase search excluded conference material.

English language limits were applied to the search when possible in the database due to the volume of results.

The limit to remove animal studies in the searches is standard NICE practice, which has been adapted from Dickersin K, Scherer R, Lefebvre C (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. BMJ 309(6964): 1286.

Main search

Table 4a Main search results

Database	Date searched	Database platform	Database segment or version	Number of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	09/08/2024	Wiley	Issue 7 of 12, July 2024	121
Cochrane Database of Systematic Reviews (CDSR)	09/08/2024	Wiley	Issue 8 of 12, August 2024	3 Reviews 1 Protocol
Embase	09/08/2024	Ovid	1974 to 2024 August 08	3345
INAHTA International HTA Database	09/08/2024	https://database.inahta.org/	-	16
MEDLINE ALL	09/08/2024	Ovid	1946 to 2024 August 08	2253

Update search

Table 4b Update search results

Database	Date searched	Database platform	Database segment or version	Number of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	10/02/2025	Wiley	Issue 12 of 12, December 2024	7
Cochrane Database of Systematic Reviews (CDSR)	10/02/2025	Wiley	Issue 12 of 12, December 2024	0
Embase	10/02/2025	Ovid	1974 to February 07 2025	151
INAHTA International HTA Database	10/02/2025	https://database.inahta.org/	-	0
MEDLINE ALL	10/02/2025	Ovid	1946 to February 07 2025	108

Search strategy history

For the updated searches there was no change to the strategy apart from the date limit from 09 August 2024 to 10 February 2025. So, the rerun strategies have not been included.

MEDLINE ALL search strategy

1 Transcatheter Aortic Valve Replacement/ 12187

2 ((Transcatheter or Transapical or transventricular) adj4 (Aortic or "heart valve") adj4 (Replacement* or transplant* or implant* or prosthes*)).tw. 16125

3 (PAVR or TAVI or TAVR).ti,ab. 12434

4 or/1-3 19632

5 Aortic Valve Insufficiency/ 16282

6 (Aortic adj4 (Insufficienc* or Regurgitation or incompetence or degeneration)).tw. 17007

7 (AR or NPAR).ti,ab. 66009

8 or/5-7 88364

9 4 and 8 2276

10 animals/ not humans/ 5212304

11 9 not 10 2252

12 J-Valve.tw. 56

13 CoreValve.tw. 1236

14 "ACURATE neo".tw. 173

15 "Sapien 3".tw. 852

16 Lotus.tw. 4675

17 or/12-16 6779

18 8 and 17 565

19 11 or 18 2312

20 limit 19 to English language 2252

Embase search strategy

1 transcatheter aortic valve implantation/ 35141

2 ((Transcatheter or Transapical or transventricular) adj4 (Aortic or "heart valve") adj4 (Replacement* or transplant* or implant* or prosthes*)).tw. 27802

3 (PAVR or TAVI or TAVR).ti,ab. 25722

4 or/1-3 39674

5 aortic regurgitation/ 13817

6 (Aortic adj4 (Insufficienc* or Regurgitation or incompetence or degeneration)).tw. 25302

7 (AR or NPAR).ti,ab. 89890

8 5 or 6 or 7 118058

9 4 and 8 5634

10 Nonhuman/ not Human/ 5506959

11 9 not 10 5578

12 J-Valve.tw,dv,dm. 128

13 CoreValve.tw,dv,dm. 5830

14 "ACURATE neo".tw,dv,dm. 543

15 "Sapien 3".tw,dv,dm. 3474

16 Lotus.tw,dv,dm. 5750

17 or/12-16 13725

18 8 and 17 2118

19 11 or 18 5688

20 limit 19 to english language 5583

21 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5997612

22 20 not 21 3344

Cochrane Library (CDSR and CENTRAL) search strategy

Search Hits

#1 MeSH descriptor: [Transcatheter Aortic Valve Replacement] this term only 495

#2 ((Transcatheter or Transapical or transventricular) NEAR/4 (Aortic or "heart valve") NEAR/4 (Replacement* or transplant* or implant* or prosthes*)) 1331

#3 PAVR or TAVI or TAVR 1237

#4 #1 or #2 or #3 1471

#5 MeSH descriptor: [Aortic Valve Insufficiency] this term only 197

#6 Aortic NEAR/4 (Insufficienc* or Regurgitation or incompetence or degeneration) 616

#7 (AR or NPAR) 20782

#8 {OR #5-#7} 21321

#9 #4 AND #8 188

#10 J-Valve 4

#11 CoreValve 173

#12 "ACURATE neo" 19

#13 "Sapien 3" 117

#14 Lotus 225

#15 {OR #10-#14} 480

#16 #8 AND #15 86

#17 #9 or #16 199

#18 "conference":pt or (clinicaltrials or trialsearch):so 770307

#19 #17 NOT #18 in Cochrane Reviews, Cochrane Protocols 4

#20 #17 NOT #18 in Trials 121

INAHTA HTA Database search strategy

Line Query Hits

1 (Transcatheter Aortic Valve Replacement)[mh] 34

2 ((Transcatheter or Transapical or transventricular) AND (Aortic or "heart valve") AND (Replacement* or transplant* or implant* or prosthes*))62

3 PAVR or TAVI or TAVR 58

4 #3 OR #2 OR #1 74

5 (Aortic Valve Insufficiency)[mh] 5

6 (Aortic AND (Insufficienc* or Regurgitation or incompetence or degeneration)) 14

7	(AR or NPAR)	0
8	#7 OR #6 OR #5	19
9	#8 AND #4	12
10	J-Valve	186
11	CoreValve	5
12	"ACURATE neo"	0
13	"Sapien 3"	0
14	Lotus	0
15	#14 OR #13 OR #12 OR #11 OR #10	186
16	#15 AND #8	16

Inclusion criteria

The following inclusion criteria were applied to the abstracts identified by the literature search.

Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events not available in the published literature.

People with aortic regurgitation or aortic incompetence.

Intervention or test: Transcatheter aortic valve implantation.

Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in Appendix B: Other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Appendix B: Other relevant studies

Other potentially relevant studies that were not included in the main evidence summary (tables 2 and 3) are listed in table 5 below. Studies with fewer than 10 people were excluded.

Table 5 additional studies identified

Study	Number of people and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Al Ahmad J, Danson E. (2024) Transcatheter Aortic Valve Implantation for Severe Chronic Aortic Regurgitation. J Clin Med. 13(10): 2997.	Review	This review article describes the current evidence for the off-label use of TAVI in pure AR and the various clinical syndromes associated with AR where there may be specific challenges in the application of TAVI.	Review
Alharbi AA, Khan MZ, Osman M et al. (2020) Transcatheter Aortic Valve Replacement vs Surgical Replacement in Patients With Pure Aortic Insufficiency. Mayo Clin Proc.95 (12): 2655–2664.	Propensity-matched retrospective cohort study (NIS database) Patients with pure AI. TAVI, n=915 versus SAVR, n=1390 TAVI used as an off-label procedure in some cases.	There was no evidence of a significant statistical difference in in-hospital mortality between patients with pure AI treated by either SAVR or TAVR, both in unmatched and propensity-	Study already included in systematic review added to summary of evidence.

		matched cohorts. TAVR could be considered for patients with pure AI who are not candidates for surgery.	
Adam M, Tamm AR, Wienemann H et al. (2023) Transcatheter Aortic Valve Replacement for Isolated Aortic Regurgitation Using a New Self-Expanding TAVR System. JACC Cardiovasc Interv. 16(16): 1965–1973.	Case series (German registry) n=58 people for isolated severe and symptomatic AR underwent TAVR with the JenaValve Trilogy system (new generation). Follow up 30 days.	Treatment of patients with severe symptomatic AR using the transfemoral JV system is safe and effective. This system may offer a new treatment option for patients with AR not suitable for surgery.	Larger studies with longer follow up included in the summary of evidence.
Anwaruddin S, Desai ND, Szeto WY et al. (2019) Self-Expanding Valve System for Treatment of Native Aortic Regurgitation by Transcatheter Aortic Valve Implantation (from the STS/ACC TVT Registry). Am J Cardiol.124(5): 781–788.	Retrospective case series N=230 patients in the TVT Registry underwent transfemoral TAVI for primary severe native AR with early generation self-expanding valves (n=81, CoreValve; n=149, Evolut R). Follow up 30 days.	Despite higher 30-day all-cause mortality, self-expanding TAVI may be an option in selected patients with AR who have no surgical options.	Study already included in systematic review added to summary of evidence.
Baumbach A, Patel KP, Kennon S et al. (2023) A heart valve dedicated for aortic regurgitation: Review of technology and early clinical experience with the transfemoral Trilogy system. Catheter Cardiovasc Interv.102 (4): 766–771.	Review and case series of 12 patients with severe AR had TAVI with JenaValve Trilogy.	Expert review on the technical aspects of the Trilogy system, provides a guide for implantation, discuss the available evidence for the technology and provide illustrative case examples.	Large studies with longer follow up were included in the summary of evidence.

Belkin MN, Imamura T, Fujino T et al. (2020) Transcatheter Aortic Valve Replacement in Left Ventricular Assist Device Patients with Aortic Regurgitation STRUCTURAL HEART, 4, 2, 107–112	Retrospective analysis N=7 LVAD patients underwent 9 TAVR procedures. Median follow up of 9 months.	Two patients died of paravalvular complications following device deployment. Procedural success was achieved in 67% of attempts, with significant improvement in RF from 44.8% pre-procedurally to 28.1% at six-month follow up. Qualitatively moderate paravalvular leak was noted. There was significant improvement in right ventricular function at 6-month follow up.	More comprehensive studies included in the summary of evidence.
Bob-Manuel T, Kadire S, Heckle MR et al. (2018) Outcomes following transcatheter aortic valve replacement in patients with native aortic valve regurgitation. Ann Transl Med. 6(1): 8, 1–9.	Systematic review 30 studies describing 182 patients were identified.	TAVR is associated with favourable pacemaker implantation and 1-year mortality rates with a high 30-day mortality among selected patients with NAVR.	More recent comprehensive studies included in summary of evidence.
Costanzo P, Bamborough P, Peterson M (2022) Transcatheter Aortic Valve Implantation for Severe Pure Aortic Regurgitation With Dedicated Devices. Interv Cardiol. 17: e11.	Review	TAVI for patients with pure severe AR and at surgical risk is occasionally performed with 2 dedicated transcatheter valves (J-Valve and JenaValve). Both devices have been used successfully via the transapical approach. The	Review

		transfemoral experience is limited.	
Chen S, Zheng F, Li M, Hou S et al. (2022) A study on correlation between preprocedural CT indexes and procedural success rate of transfemoral transcatheter aortic valve replacement with different self-expanding valves (VitaFlow or VenusA-Valve) in patients with pure native aortic regurgitation. Ann Transl Med. 10(11): 643	Retrospective comparative study N=77 symptomatic patients with severe pure native AR (STS score 7.7), who had TF TAVI using a VenusA-Valve (n=47) or a VitaFlow valve (n=30). 2 kinds of self-expanding valves with different shaped frameworks were compared.	Patients with severe pure native AR with a smaller aortic annulus (AA), left ventricular outflow tract (LVOT), sinotubular junction (STJ), and leaflet thickening might have a higher success rate in TF TAVI using a self-expanding valve. The self-expanding valve with a non-A-shaped framework might be a better choice for improved procedural outcomes.	Larger studies included in the summary of evidence.
De Backer O, Pilgrim T, Simonato M, Mackensen GB et al. (2018) Usefulness of transcatheter aortic valve implantation for treatment of pure native aortic valve regurgitation. Am J Cardiol, 122: 1028–1035.	Retrospective case series N=254 patients with pure NAVR had transapical, transfemoral TAVI (devices: Evolut, ACURATE, Portico, SAPIEN 3, Lotus, Direct Flow, JenaValve, Engager) N=109 old-generation devices 145 new-generation devices.	TAVI is a feasible treatment in high-risk people with NAVR but is associated with a considerable risk of valve malpositioning and residual AR.	Study already included in systematic review added to summary of evidence.
De Backer O, Pilgrim T, Sondergaard L et al. (2017) TCT-448 Transcatheter aortic valve replacement for isolated severe native	Retrospective case series n=187 patients had transapical, transfemoral TAVI	TAVR for pure native aortic valve regurgitation is challenging and associated with high rates of post-	Study already included in systematic review added

aortic valve regurgitation—Results from the TAVR-NAVR registry. J Am Coll Cardiol 70: B184.	for severe native AR. 69 had early generation devices (65 CoreValve, 4 Sapien/XT) and 118 had new-generation devices (33 JenaValve, 23 Evolut R, 18 Direct Flow, 15 Symetis, 10 Lotus, 9 Engager, 7 Sapien 3, 3 Portico). Follow up 1 year	procedural aortic regurgitation and a need for a second device in addition to high mortality. New-generation devices had better clinical outcomes than early generation implants.	to summary of evidence.
Delhomme C, M. Urena-Alcazar, O. Zouaghi et al. (2024) Transcatheter aortic valve implantation using the SAPIEN 3 valve to treat aortic regurgitation: The French multicentre S3AR study. Archives of Cardiovascular Diseases. 117, 1, 93–105.	Retrospective and prospective multicentre observational study. N=37 patients with symptomatic, severe, pure AR on native, non-calcified valves, contraindicated to, or at high-risk for surgical valve replacement. TAVI using the balloon-expandable SAPIEN 3 THV.	TAVI using SAPIEN 3 THV seems technically feasible in carefully selected, high-risk people with pure AR on native and non-calcified valves, who are contraindicated for surgery. It remains an off-label and compassionate use with no mention in current international guidelines.	Larger studies included in the summary of evidence.
Deng Md, Wei X, Zhang Xl et al. (2019) Changes in left ventricular function in patients with aortic regurgitation 12 months after transapical transcatheter aortic valve implantation. *Int J Cardiovasc Imaging* **35**, 99–105.	Case series n=30 patients with AR had transapical TAVI Follow up 12 months.	Our results indicate that LV function was improved in terms of myocardial deformation but worsened in terms of apical rotation 12 months after TAVI in patients with AR.	Larger studies included in the summary of evidence.
El-Gamel A. (2021) Transcatheter Aortic Valve Replacement in Pure Native Aortic Valve Regurgitation:	Review	Currently, off-label indication for TAVR in pure native AR could be a feasible and	Review

Challenging Pathology Awaiting Specialized Devices. Aorta (Stamford). 9(2): 56–59.		reasonable option, as a compassionate treatment is limited to inoperable patients and agreed on by the heart team.	
Franzone A, Piccolo R, Siontis GCM et al. (2016) Transcatheter Aortic Valve Replacement for the Treatment of Pure Native Aortic Valve Regurgitation: A Systematic Review. JACC Cardiovasc Interv.28; 9(22): 2308–2317.	Systematic review N=13 studies including 237 patients	Among selected patients with native pure AR deemed at high risk for SAVR, TAVR is technically feasible and associated with an acceptable risk of early mortality.	More recent comprehensive studies included in summary of evidence.
Gera P, Wasserstein DH, Frishman WH et al (2024) Transcatheter Aortic Valve Implantation for Aortic Regurgitation: A Comprehensive Review. Cardiol Rev.	Review	This article synthesizes current knowledge on AR management, emphasizing advancements in transcatheter aortic valve implantation (TAVI).	Review
Garcia S, Ye J, Webb J, Reardon M, Kleiman N et al. (2023) Transcatheter Treatment of Native Aortic Valve Regurgitation: The North American Experience With a Novel Device. JACC Cardiovasc Interv. 16(16): 1953–1960.	Case series N=27 patients at high surgical risk, with native valve AR had TAVI with the J-Valve. Follow up 30 days.	The J-Valve provides a safe and effective alternative to surgery in patients with pure AR and elevated or prohibitive surgical risk.	More recent comprehensive studies included in summary of evidence.
Haddad A, Arwani R, Altayar O, Sawas T, Murad MH, de Marchena E. Transcatheter aortic valve replacement in patients with pure native	Systematic review and meta-analysis. N=638 patients across 12 studies were included.	AVR appears to be a feasible treatment choice for NAVR patients at high risk for surgical valve replacement.	More recent comprehensive studies included in summary of evidence.

aortic valve regurgitation: A systematic review and meta-analysis. Clin Cardiol. 2019 Jan;42(1): 159–166.		Second-generation valves show promising results in terms of short-term outcomes.	
Hinkov H, Lee CB, Pitts L et al. (2024) Transcatheter management of pure native aortic valve regurgitation in patients with left ventricular assist device. Eur J Cardiothorac Surg. 65(3), ezae028	Retrospective analysis of TAVI for AR in patients with LVAD. N=27	TAVI yields promising procedural outcomes and early survival rates in LVAD patients with AR. Tailored TAVI devices and pre-stenting techniques enhance procedural success. Continued research into these strategies is essential.	
Huded CP, Allen KB, Chhatriwalla AK. (2021) Counterpoint: challenges and limitations of transcatheter aortic valve implantation for aortic regurgitation. Heart. 107(24): 1942–1945.	Review	Reviews the challenges, evidence and future directions of TAVI for isolated AR. There are no RCTs or mid-term data. Observational studies have shown that outcomes of TAVI for AR are worse than outcomes of TAVI for AS. Two emerging valves have shown promise for AR and data are limited.	Review
Isogai T, Saad AM, Ahuja KR et al. (2021) Short-term outcomes of transcatheter aortic valve replacement for pure native aortic	Retrospective database analysis TAVR for pure AR and TAVR for AS. pure AR (n=1,222, 1.50%), pure AS	TAVR for pure AR was significantly associated with a higher risk of acute kidney injury, cardiac tamponade	More recent comprehensive studies included in summary of evidence.

regurgitation in the United States. Catheter Cardiovasc Interv. 97(3): 477–485	(n=72,690, 89.1%), and AS + AR (n=7,630, 9.36%). the severity of valve disease, and calcification of aortic valve leaflets and annulus), and details of TAVR procedures not reported. In-hospital and 30-day outcomes reported.	and prolonged hospital stay compared with TAVR for pure AS, whereas it was not significantly associated with in-hospital mortality and other outcomes.	
Jin M, Zhang H, Zhou Q et al. (2024) Transcatheter aortic valve implantation for severe aortic regurgitation using the J-Valve system: A midterm follow-up study. Catheter Cardiovasc Interv. 104(5): 1052–1059.	Retrospective cohort study N=36 high-risk AR patients treated with the J-Valve system. Follow up 3 years.	The J-Valve system has shown positive therapeutic outcomes in treating AR, with effectiveness in managing the condition and significant improvements in heart failure symptoms and cardiac remodelling. However, due to the limited sample size and partial follow-up data, it is important to emphasize the need for further research with comprehensive long-term follow-up, to fully validate these results.	More comprehensive studies included in the summary of evidence.
Jin M, Zhou Q, Li S, Zhang H, Wang D. Image-based analysis of correlation between valve stent deformation and valve function in transcatheter aortic	Retrospective study N=39 AR patients treated with the J-Valve transcatheter heart valve system during TAVR.	During the TAVR procedure, ensuring sufficient expansion in the mid and transition level of the stent, maintaining the	More comprehensive studies included in the summary of evidence.

valve replacement. Catheter Cardiovasc Interv. 2025 Jan 26. doi: 10.1002/ccd.31421. Epub ahead of print.	Postoperative CT angiography data used to explore correlation.	stent in a rectangular configuration, and avoiding tilting of the commissural posts contribute to achieving favourable postoperative hemodynamics.	
Jiang J, Liu X, He Y et al. (2018) Transcatheter Aortic Valve Replacement for Pure Native Aortic Valve Regurgitation: A Systematic Review. Cardiology. 141(3): 132-140.	Systematic Review n=10 studies on TAVR in 266 patients with pure NAVR were included.	Aortic regurgitation remains a challenging pathology for TAVR. TAVR is a feasible and reasonable option for carefully selected patients with pure aortic regurgitation.	More recent comprehensive studies included in summary of evidence.
Koliastasis L, Doundoulakis I, Kokkinidis DG, et al. (2022) TAVI with the ACURATE neo transcatheter heart valve in special populations: A systematic review. Hellenic J Cardiol. 66: 67–71.	Systematic Review TAVI with ACURATE neo in special populations (in bicuspid aortic valve, in patients with small aortic annulus, pure aortic regurgitation and valve-in-valve procedures)	ACURATE neo valve may be a feasible and safe option for patients with bicuspid anatomy, small aortic annulus, previously implanted bioprosthetic aortic valve and pure aortic regurgitation.	More recent comprehensive studies included in summary of evidence.
Koch R, Inci E, Grubb K et al. (2023) A comparison of thirty-day clinical and echocardiographic outcomes of patients undergoing transcatheter vs. surgical aortic valve replacement for native aortic insufficiency. Cardiovasc Revasc Med; 46: 85–9.	Comparative cohort study (retrospective) 125 people at high risk with native AI 91 receiving SAVR and 34 receiving TAVR (CoreValve, Evolut R, and Evolut Pro)- femoral and caval route Follow up 30 days.	Patients who received TAVR had a significantly higher STS predictive risk of mortality (STS-PROM) score than people in the SAVR group (3.96% versus 1.25%). But the in-hospital mortality and 30-day	Similar comparative study included in the summary of evidence.

		outcomes (including mortality, stroke, myocardial infarction, residual AR, or repeat valve intervention) did not differ between groups. The results indicated a significantly higher rate of complete heart block requiring PPI in the TAVR group (20.9% versus 2.2%).	
Kong M, Hong Z, Liu X et al. (2022) 30-day outcomes after surgical or transapical aortic valve replacement in symptomatic aortic regurgitation. J Cardiovasc Dev Dis; 9:9, 224, 1–10.	Comparative study (retrospective) N=69 transapical TAVI with J-valve versus n=42 SAVR in patients with symptomatic AR. Follow up 30 days.	The TA-TAVR approach is safe and reliable, with similar clinical efficacy to SAVR, and has advantages in bleeding rate and speed of recovery.	Study already included in systematic review added to summary of evidence.
Kong XQ, Zhang J, Gao XF et al. (2024) Single-center experience with self-expanding transcatheter aortic valve system for symptomatic high-risk patients with severe aortic regurgitation: One-year outcomes. Catheter Cardiovasc Interv. 104(6): 1275–1280.	Retrospective cohort study N=62 patients who underwent transfemoral TAVI procedure for pure, symptomatic severe AR with the VitaFlow system. Follow up 1 year.	Transfemoral TAVI procedure shows efficacy in treating patients with severe pure native AR. The safety is improved with the development of the VitaFlow system.	More comprehensive studies included in the summary of evidence.
Kirtchuk D, Williams T, Cockburn J et al. (2020) Transcatheter Aortic Valve Implantation in Patients With Symptomatic Severe Aortic Regurgitation Using the Self-Expanding Acurate neo	Case series N=4 patients with isolated AR treated using the Acurate Neo valve.	Three of the patients had significant symptomatic improvement, one had limited symptomatic improvement despite resolution	Large studies included in the summary of evidence.

Valve. Cardiovasc Revasc Med. 21(11S): 14–17.		of her AR on aortogram post TAVI.	
Le Ruz R, Leroux L, Lhermusier T et al. (2024) Outcomes of transcatheter aortic valve implantation for native aortic valve regurgitation. EuroIntervention. 20(17): e1076–e1085	Prospective study (FRANCE-TAVI Registry) N=227 patients with grade III or IV pure aortic valve regurgitation (PAVR) had TAVI with NGD (CoreValve Evolut PRO, Corevalve Evolut R, Sapien 3). Follow up 4 years	TAVI with NGD in PAVR patients is efficient and reasonably safe. Preventing the need for a second valve implantation embodies the major technical challenge. Larger implanted valves may have limited this complication, outweighing the increased risk of permanent pacemaker implantation. Despite successful TAVI, PAVR patients experience frequent clinical events at long-term follow up.	More comprehensive studies included in the summary of evidence.
Lin DW, Weng ZL, Fan JN et al. (2024) Outcome of transcatheter aortic valve replacement for pure native aortic regurgitation in patients with pulmonary hypertension. Rev Cardiovasc Med. 25(8):307. doi: 10.31083/j.rcm2508307.	Retrospective cohort study N=103 patients with PNAR undergoing TAVR (48 with pulmonary hypertension and 55 without pulmonary hypertension). Follow up 6 months.	We found TAVR to be a safe and effective treatment for patients with pure native aortic regurgitation (PNAR) and pulmonary hypertension (PH), reducing the degree of aortic regurgitation and PH without increasing the risk of postoperative adverse events.	More comprehensive studies included in the summary of evidence.
Liu R, Fu Z and Yao J et al. (2023) Transcatheter Aortic Valve Replacement for Aortic	Review	This review examines current evidence and clinical practice,	Review

Regurgitation – A Review. *CVIA.* 8(1).		and presents technological advancements in devices for AR.	
Liu H, Yang Y, Wang W et al (2018). Transapical transcatheter aortic valve replacement for aortic regurgitation with a second-generation heart valve. J Thorac Cardiovasc Surg. 156: 106–116.	Case series (prospective) ChiCTR-OPC-15006354 N=43 patients with high-risk severe pure native AR had transapical TAVI with the J-Valve.	This multicentre study shows that the J-Valve transcatheter heart valve system is a reasonable option for patients with predominant AR.	Study already included in systematic review added to summary of evidence.
Liu L, Zhang J, Peng Y et al. (2020) Learning curve for transcatheter aortic valve replacement for native aortic regurgitation: Safety and technical performance study. Clin Cardiol. 43(5): 475–482.	Retrospective case series (reviewed a prospective database) N=134 patients with pure native AR who had TAVI with the J-valve. Patients were divided as early (group 1: first 52 cases) and skilled (group 2: the next 82 cases).	For a surgeon without previous TAVR experience, 52 cases of performance is the minimal requirement to gain the proficiency of TAVR for native AR. The skilled surgeons have been observed with reduced procedural time, fluoroscopy times, radiation exposure dose, and contrast volume usage. However, the overall prognosis was not significantly different between the 2 groups.	More comprehensive studies included in the summary of evidence.
Liu H, Liu S, Lu Y, et al. (2020) Transapical transcatheter aortic valve implantation for predominant aortic regurgitation with a self-expandable valve. J	Case series N=47 patients with predominant AR had transapical TAVI with J-Valve. Follow up 4 years.	This study revealed that, transapical TAVI with J-Valve for treating AR has encouraging mid-term outcomes, and the advantages at 1	Study already included in systematic review added to summary of evidence.

Thorac Dis. 12 (3): 538–549.		year demonstrated in previous study can be maintained through 4 years.	
Liu L, Chen S, Shi J et al. (2020) Transcatheter Aortic Valve Replacement in Aortic Regurgitation. Ann Thorac Surg. 110 (6): 1959–1965.	Case series N=134 patients with severe AR and high surgical risk had transapical TAVI with the J-Valve Follow up 6 months.	Transcatheter aortic valve replacement with the J-Valve proved to have acceptable early and midterm clinical outcomes for patients with aortic regurgitation.	Study already included in systematic review added to summary of evidence.
Liu L, Peng Y, Shi J, et al. (2022) Initial experience with repositionable J-Valve for severe aortic regurgitation: A single-center experience. J Cardiovasc Surg (Torino); 63: 521–528	Case series n=290 (161 people had severe AR and 129 people had severe AS) had transapical TAVI with J-Valve.	Prognosis of patients with AR is comparable to that of patients with AS after TAVI with J-valve. Pace- maker rate in the AR group was higher, but structural valve deterioration was more common in AS patients.	Study already included in systematic review added to summary of evidence.
Liu L, Yao X, Peng Y, et al. (2022) One-year outcome after transcatheter aortic valve replacement for aortic regurgitation: A single-center study. J Card Surg; 37: 882–892	Case series N=134 high-risk patients with pure, symptomatic severe AR had TA TAVI Follow up 1 year.	In high-risk patients undergoing transapical-TAVR for AR, the use of the J-Valve is safe and effective TAVR should be considered as a reasonable option for high-risk patients with pure AR.	Study already included in systematic review added to summary of evidence.
Li F, Wang X, Wang Y et al. (2020) Structural Valve Deterioration after Transcatheter Aortic Valve Implantation Using J-Valve: A Long-Term Follow-Up. Ann Thorac Cardiovasc Surg. 26(3): 158–165.	Prospective case series N=4 patients with AS and 4 patients with pure AR who had TAVI using J-valve. 4-year follow up.	The limited number of cases provides a preliminary indication of the long-term efficacy of TAVI using J-Valve in patients with PAR. None of the hemodynamic SVD occurred in	More comprehensive studies included in the summary of evidence.

		patients with PAR. In patients with AS, although the higher rate of SVD was observed, the overall transcatheter heart valve (THV) hemodynamic remained stable over time after prosthetic valve implantation and the long-term durability of J-Valve was convincing.	
Lu Y, Yang Y, Liu H et al. (2022) Short-Term Outcomes After Transcatheter Aortic Valve Replacement in Predominant Aortic Regurgitation with Left Ventricular Dysfunction. Int Heart J.63(1): 30–35.	Case series n=27 symptomatic patients with AR and ejection fraction < 50% underwent TAVI using the J-Valve™ system. Follow up median 369 days.	TAVI using the J-Valve™ system is a reasonable alternative for patients with AR and left ventricular dysfunction regarding promising short-term outcomes.	More comprehensive studies included in the evidence summary.
Luo X, Wang X, Li X et al. (2017) Transapical transcatheter aortic valve implantation using the J-Valve system: A 1-year follow-up study. J Thorac Cardiovasc Surg.154 (1): 46–55.	Case series n=21 people with AS (n=17) or AR (n=4) at high risk for open surgery received transapical TAVI using the J-Valve system. Follow up 1 year.	Study showed excellent performance regarding echocardiographic parameters, improvement in NYHA class after a 12-month follow up.	More comprehensive studies included in the evidence summary.
Mao Y, Liu Y, Zhai M et al. (2024) Transapical transcatheter aortic valve replacement under 3-dimensional guidance to treat pure aortic regurgitation in patients with a large aortic annulus. Rev Cardiovasc Med. 25(9):319, 1–11.	Prospective cohort study N=125 patients with non-calcified AR with a large annulus (annular diameter >29 mm) who underwent transapical TAVR (43 in 3D printing simulation group	Based on 3D printing guidance, transapical TAVR using extra oversizing was safe and feasible for patients with noncalcified AR with a large annulus. Extra oversizing and	More comprehensive studies included in the summary of evidence.

	versus 82 in non-simulation 3D printing group). Follow up 2 years.	coaxial angle were predictors of postprocedural transcatheter heart valve displacement and more than mild paravalvular leakage in such patients.	
Mentias A, Saad M, Menon V et al. (2023) Transcatheter vs Surgical Aortic Valve Replacement in Pure Native Aortic Regurgitation. Ann Thorac Surg. 115(4): 870–876	Propensity-matched retrospective cohort study n=11,027 patients with pure AR underwent elective AVR (TAVR, n=1,147; SAVR, n=9,880). Median follow up of 31 months	In Medicare patients with pure native AR, TAVR with the current commercially available transcatheter valves has comparable short-term outcomes. Although long-term outcomes were inferior to SAVR, the possibility of residual confounding, biasing long-term outcomes, given older and frailer TAVR patients, cannot be excluded	Study already included in systematic review added to summary of evidence.
Narayan P. Native aortic valve regurgitation: TAVR's place in the PANTHEON. Indian J Thorac Cardiovasc Surg. 2023 Nov;39(6): 643–645.	Appraisal of the PANTHEON study. TAVI in patients with severe pure native aortic valve regurgitation.	The major complications included valve embolisation or migration in 12.4%, moderate-to-severe AR in 9.5% cases and need for PPM in 22.3% cases. Self-expanding and balloon-expandable devices demonstrated similar outcomes. People	More comprehensive study included in the summary of evidence.

		experiencing valve embolisation or migration had higher 1-year adverse event rates.	
Noble S, Mauler-Wittwer S. (2024) TAVR as an Alternative to SAVR for Pure Native Aortic Regurgitation. Can J Cardiol. 40 (2): 316–325.	Review	The first-generation transcatheter valves were associated with a higher mortality rate and lower procedural success. Early studies with the dedicated devices showed safety and promising results and will serve a growing number of patients with native AR at risk for surgery.	Review
Orzalkiewicz M, Foroni M, Chietera F, Bendandi F et al. (2024) Off-Label Use of Balloon-Expandable Transcatheter Valves to Treat Pure Aortic Regurgitation. Am J Cardiol. 222: 20–22.	Case series n=13 tricuspid aortic valve patients who underwent transfemoral TAVIs for pure AR with Sapien ballon expandable valve.	TAVI in pure AR with oversized Sapien BEV showed good procedural and short-term outcomes when ≥20% oversizing was predictably achievable.	Large studies included in the summary of evidence.
Oettinger V, Hilgendorf I, Wolf D et al. (2023) Treatment of pure aortic regurgitation using surgical or transcatheter aortic valve replacement between 2018 and 2020 in Germany. Front Cardiovasc Med.10: 1091983.	Retrospective cohort study database analysis n=4,861 procedures: 4,025 SAVR and 836 TAVR for AR TA TAVI, N=50 TF TAVI, N=329 balloon-expandable valves	TAVR is a viable alternative to SAVR in the treatment of pure aortic regurgitation for selected patients, showing overall low in-hospital mortality and complication rates, especially with regard to self-expanding	Study already included in systematic review added to summary of evidence..

	TF TAVI, n=457, self-expanding valves. In-hospital outcomes reported.	transfemoral TAVR.	
Pesarini G, Lunardi M, Piccoli A et al. (2018) Effectiveness and Safety of Transcatheter Aortic Valve Implantation in Patients With Pure Aortic Regurgitation and Advanced Heart Failure. Am J Cardiol. 121(5): 642–648.	Case series n=13 inoperable patients with non-calcific, pure AR, and advanced heart failure treated with transfemoral TAVI-self-expandable CoreValves. Follow up 30 days.	Implanting self-expandable transcatheter valves in patients pure AR in this small study was safe and effective, and represented an important option for inoperable patients with non-calcific severe AR.	Larger studies included in the summary of evidence.
Phan K, Haswell JM, Xu J et al. (2017) Percutaneous Transcatheter Interventions for Aortic Insufficiency in Continuous-Flow Left Ventricular Assist Device Patients: A Systematic Review and Meta-Analysis. ASAIO J. 63 (2): 117–122.	Systematic review and meta-analysis n=5 published studies and 3 unpublished studies . (n=29 patients) TAVI for AR in LVAD patients.	In the TAVR cohort, 2 people experienced device migration and another had significant postimplant perivalvular leakage. Our results indicate that percutaneous interventions for AI in CF-LVAD patients with TAVR, and closure devices demonstrate similar efficacy in significantly reducing severe AI.	More comprehensive studies included in the summary of evidence.
Poletti E, Adam M, Wienemann H et al. (2024) Performance of Purpose-Built vs Off-Label Transcatheter Devices for Aortic Regurgitation: The PURPOSE Study. JACC Cardiovasc Interv. 17(13): 1597–1606.	Retrospective multicentre registry N=256 inoperable patients with severe AR of the native valve had TAVI with off-label devices in 168 cases (66%), and J-valve was	The J-valve has a better acute performance than other THVs when used off-label for inoperable patients with severe AR. A longer follow up is needed to detect a	Similar comparative study already included in the summary of evidence

	used in 88 cases (34%). Follow up 1 year.	possible impact on prognosis.	
Poletti E, Amat-Santos I, Criscione E et al. (2024) Performance of balloon-expandable transcatheter bioprostheses in inoperable patients with pure aortic regurgitation of a native valve: The BE-PANTHEON international project. Cardiovasc Revasc Med. S1553-8389(24)00630-4.	Retrospective study (PANTHEON registry) N=144 patients with severe pure NAVR (native aortic valve regurgitation) deemed high risk were treated with balloon-expandable (BE) valve TAVR (n=41 had Myval valve and 103 with Sapien valve). Follow up 1 year.	Off-label use of BE devices for pure NAVR represents a potential alternative in high-risk patients in the absence of dedicated devices. However, BE in NAVR is associated with suboptimal outcomes. The availability of larger transcatheter heart valve sizes may introduce TAVR as an effective treatment for patients traditionally deemed unsuitable.	More comprehensive studies included in the summary of evidence.
Purita PAM, Tahoces LS, Fraccaro C et al. (2020) Transcatheter treatment of native aortic valve regurgitation: Results from an international registry using the transfemoral ACURATE *neo* valve. Int J Cardiol Heart Vasc. 27:100480.	Case series n=24 patients with severe NAVR had TAVI with self-expandable ACURATE neo valve. Follow up 30 days.	This multicentre study suggests good feasibility and early safety of transfemoral TAVI with the self-expandable ACURATE neo device in patients with severe NAVR refused for surgery. Rates of moderate PVL, new pacemaker implantation and need for a second valve were higher than those reported for TAVI in AS.	Study already included in systematic review added to summary of evidence.

Rali AS, Taduru SS, Tran LE et al. (2022) Transcatheter Aortic Valve Replacement and Surgical Aortic Valve Replacement Outcomes in Left Ventricular Assist Device Patients with Aortic Insufficiency. Card Fail Rev. 8: e30.	Retrospective cohort study (NIS database) N=155 patients with pre-existing continuous-flow LVAD undergoing TAVR (105) or SAVR (50) for AI/pure AR.	In this nationally representative cohort of LVAD patients with post-implant AI, it was observed that TAVR was associated with a lower risk of adverse short-term outcomes compared with SAVR.	Study already included in systematic review added to summary of evidence.
Roy DA, Schaefer U, Guetta V, et al. Transcatheter aortic valve implantation for pure severe native aortic valve regurgitation. J Am Coll Cardiol. 2013;61(15): 1577–1584.	Case series (registry-retrospective and prospective) N=43 patients with pure severe NAVR underwent TAVI with the CoreValve (early generation device). Follow up 12 months.	This registry analysis demonstrates the feasibility and potential procedure difficulties when using TAVI for severe NAVR. Acceptable results may be achieved in carefully selected patients who are deemed too high risk for conventional surgery.	Study already included in systematic review added to summary of evidence.
Sanchez-Luna JP, Martín P, Dager AE et al. (2023) Clinical outcomes of TAVI with the Myval balloon-expandable valve for non-calcified aortic regurgitation. EuroIntervention. 19(7): 580–588.	Retrospective cohort study N=113 patients with non-calcified AR (STS 2.7±1.7%) had TAVI with Myval valve. Follow up 1 year.	Myval is a feasible and safe option for selected non-operable patients with NCAR and demonstrated good midterm outcomes and lack of impact of oversizing on device durability.	Larger studies included in the evidence summary.
Santos-Martínez S, Amat-Santos IJ. (2021) New Challenging Scenarios in Transcatheter Aortic Valve Implantation: Valve-in-valve, Bicuspid and Native Aortic	Review	This review aims to discuss the current evidence available supporting the use of TAVI for VIV, bicuspid and Native AR. Evidence for TAVI	Review

Regurgitation. Eur Cardiol. 2021 Aug 26;16: e29.		in pure AR is still anecdotal because of suboptimal outcomes.	
Sawaya FJ, Deutsch MA, Seiffert M et al. (2017) Safety and efficacy of transcatheter aortic valve replacement in the treatment of pure aortic regurgitation in native valves and failing surgical bioprostheses: Results from an international registry study. JACC Cardiovasc Interv, 10: 1048–1056	Case series (retrospective and prospective) N=78 patients with pure NAVR, 68 patients in the failing SHV group. (Evolut R, JenaValve, Direct Flow, Lotus, SAPIEN 3).	AVR for pure NAVR remains a challenging condition, with old-generation THVs being associated with THV embolisation and migration and significant paravalvular regurgitation. Newer-generation THVs show more promising outcomes. For people with severe AR due to failing SHVs, TAVR is a valuable therapeutic option.	Study already included in systematic review added to summary of evidence.
Schofer J, Nietlispach F, Bijuklic K et al. (2015) Implantation of a Fully Repositionable and Retrievable Transcatheter Valve for Noncalcified Pure Aortic Regurgitation. JACC Cardiovasc Interv. 8 (14): 1842–9.	Case series (retrospective) N=11 patients with severe non-calcific pure AR with transfemoral implantation of a TAVI with DirectFlow valve (new generation). 30-day follow up.	This study reports the feasibility of treating severe non-calcific AR with the Direct Flow prosthesis via the transfemoral route.	Study already included in systematic review added to summary of evidence.
Schlingloff F, Schäfer U, Frerker C et al. (2014) Transcatheter aortic valve implantation of a second-generation valve for pure aortic regurgitation: procedural outcome, haemodynamic data and follow-up. Interact	Case series N=10 transapical TAVI implantations with JenaValve for pure AR. Follow up 12 months.	Intraprocedural success and haemodynamic data were good. The mortality rate highlighted the importance of careful patient selection. This device proved to	Study already included in systematic review added to summary of evidence.

Cardiovasc Thorac Surg.19 (3): 388–93.		be suitable for treatment of AR in surgical high-risk patients.	
Seiffert M, Bader R, Kappert U et al. (2014) Initial German experience with transapical implantation of a second-generation transcatheter heart valve for the treatment of aortic regurgitation. JACC Cardiovasc Interv. 7 (10): 1168–74.	Case series (retrospective) N=31 patients had transapical TAVI with JenaValve for severe pure native AR. Follow up 6 months.	This study revealed this is a reasonable option in this subset of patients. However, a significant early noncardiac mortality related to the high-risk population emphasizes the need for careful patient selection.	Study already included in systematic review added to summary of evidence.
Shi J, Wei L, Chen Y et al. (2021) Transcatheter aortic valve implantation with J-Valve: 2-year outcomes from a multicenter study. Ann Thorac Surg; 111: 1530–1536.	Case series N=107 patients with AR (n=44) or AS (n=63) had transapical TAVI with J-valve Follow up 2 years.	This study demonstrated good midterm outcomes of TAVI with the J-Valve system in the treatment of patients with either AS or AI. It suggests that the J-Valve system is a promising alternative therapy in high-risk patients	Study already included in systematic review added to summary of evidence.
Silaschi M, Conradi L, Wendler O et al. (2018) The JUPITER registry: One-year outcomes of transapical aortic valve implantation using a second-generation transcatheter heart valve for aortic regurgitation. Catheter Cardiovasc Interv. 91(7): 1345–1351.	Case series (JUPITER) Registry n=30 people with pure native AR Follow up 1 year.	Rate of THV embolisation, residual AR and permanent pacemaker implantation was low. One-year results using the JenaValve for AR encourage its use for this indication.	Study already included in systematic review added to summary of evidence.
Siddique, S., Vora, A., & Gada, H. (2020). Transcatheter Approaches to Aortic	Review	Long-term follow up of patients with severe AR has demonstrated	Review

Insufficiency. *Structural Heart*, *5*(1), 55–64.		excess morbidity and mortality, necessitating consideration of early surgical or transcatheter treatment in high-risk patients.	
Spina R, Anthony C, Muller DW et al. (2015) Transcatheter Aortic Valve Replacement for Native Aortic Valve Regurgitation. Interv Cardiol. 10(1): 49–54.	Review	Reviews the clinical context, technical characteristics and outcomes associated with transcatheter treatment of native AR.	Review
Soong EL, Ong YJ, Ho JSY et al. (2021) Transcatheter aortic valve replacement for aortic regurgitation in Asians: TAVR for aortic regurgitation in Asians. Asia Intervention. 7(2): 103–111.	Systematic review N=5 studies (n=274 patients with pure native AR undergoing TAVI) and 8 case reports were included.	TAVR has demonstrated acceptable safety and efficacy in Asian patients with pure AR displaying low mortality rates and few adverse outcomes.	More recent comprehensive studies included in summary of evidence.
Stachon P, Kaier K, Heidt T et al. (2020) Nationwide outcomes of aortic valve replacement for pure aortic regurgitation in Germany 2008–2015. Catheter Cardiovasc Interv. 95: 810–6.	Comparative cohort study (retrospective) SAVR versus TAVI in patients with pure AR. SAVR, n=10,528 TF TAVI, n=476 TA TAVI, n=248.	TAVR is off-label used in AR in clinical practice. TAVR seems to be a safe option for AR with regard to in-hospital outcomes. However, further research evaluating long-term outcomes is required to establish the feasibility of TAVR in pure AR.	Study already included in systematic review added to summary of evidence..
Testa L, Latib A, Rossi ML, et al. CoreValve implantation for severe aortic regurgitation: a multicentre registry.	Case series (prospective) N=26 inoperable patients undergoing CoreValve TAVR for severe pure	TAVR for AR is associated with a significantly higher mortality compared to TAVR for AS. Considering the	Study already included in systematic review added to summary of evidence.

EuroIntervention. 2014; 10(6): 739–745.	native AR compared to patients treated for severe native AS, n=1531. Follow up 12 months.	ominous prognosis of these patients when treated medically, TAVR may be a reasonable choice in selected patients.	
Toggweiler S, Cerillo AG, Kim WK et al. (2018) Transfemoral Implantation of the Acurate neo for the Treatment of Aortic Regurgitation. J Invasive Cardiol. 30 (9): 329–333.	Case series n=20 people with pure native AR undergoing transfemoral TAVR with the Acurate neo prosthesis. Follow up 30 days.	Transfemoral TAVR using the Acurate neo transcatheter heart valve was successful in treating aortic regurgitation, significantly reduced left ventricular dimensions, and improved clinical symptoms.	Large studies included in the summary of evidence.
Tung M, Wang X, Li F et al. (2018) A versatile transapical device for aortic valvular disease: One-year outcomes of a multicenter study on the J-Valve system. J Cardiol. 72(5): 377–384.	Case series N=107 high-risk patients with severe AS (n=64) or AR (n=43) had TA TAVI with J-valve. Follow up 1 year.	Study provides further evidence on the safety and efficacy of the J-Valve in high-risk patients with AS or AR for surgery.	Similar study included in systematic review added to summary of evidence.
Wang Y, Yu S, Qian D, et al. (2022) Anatomic predictor of severe prosthesis malposition following transcatheter aortic valve replacement with self- expandable Venus-A Valve among pure aortic regurgitation: A multicenter retrospective study. Front Cardiovasc Med. 9:1002071.	Retrospective multicentre cohort study. N=62 patients with native AR who underwent TAVI with Venus-A Valve. Outcomes were compared between non-/mild malposition (n=42) and severe malposition groups (n=19).	Larger and higher sinotubular junction (STJ), as well as greater STJ to valve crown diameter ratio, may help identify patients at high risk for severe prosthesis malposition among patients with native AR undergoing TAVI.	Larger studies included in the summary of evidence.
Wernly B, Eder S, Navarese EP et al. (2019) Transcatheter	Review N=12 studies (640 patients)	observational data TAVR for pure AR shows that it is	More comprehensiv e studies

aortic valve replacement for pure aortic valve regurgitation: "on-label" versus "off-label" use of TAVR devices. Clin Res Cardiol.108 (8): 921–930.	208 (33%) patients with pure AR were treated with "on-label" devices: JenaValve and). J-valve	feasible and safe in patients deemed inoperable. First-generation TAVR devices are associated with inferior outcome and should be avoided. The use of “on-label" devices is associated with a significantly higher procedural success rate and might be favourable compared to other second-generation devices.	included in the summary of evidence.
Vahl T, Makkar R, Kodali S, Baldus S, Treede H, Daniels D, et al. 30-day outcomes of transfemoral transcatheter aortic valve replacement for aortic regurgitation with a novel self-expanding prosthesis. J Am Coll Cardiol 2021;77: 919.	ALIGN-AR trial (NCT 04415047) Prospective study N=71 patients with primary symptomatic AR at high surgical risk had transfemoral TAVI with the JenaValve. Follow up 30 days.	This study has reported technical feasibility and promising short-term clinical and hemodynamic outcomes.	Study already included in systematic review added to summary of evidence.
Xue Y, Zhou Q, Li S et al. (2021) Transapical Transcatheter Valve Replacement Using J-Valve for Aortic Valve Diseases. Ann Thorac Surg. 112(4): 1243–1249.	Case series N=23 patients had TAVI using the J-Valve system. 10 had AS, 11 had AR, 2 had VIV.	TAVI with the J-Valve system is effective, even when it is traumatic and requires the transapical route.	Larger studies included in the summary of evidence.
Yang L, Chen S, Zhang X et al. (2024) Comparisons of noncoronary sinus pivot implantation (NCPI) and conventional method for transcatheter aortic valve replacement with	Retrospective case series (NTCVR registry analysis). N=55 patients with pure AR had TF TAVI with self-expanding valves	TAVR with a self-expanding valve using the NCPI method had a higher procedure success rate and dramatically low complications than	Larger studies included in the summary of evidence.

self-expanding valve in pure aortic regurgitation (PAR). Catheter Cardiovasc Interv.103(7): 1093–1100.	(VitaFlow and Venus A valve). Sub-groups: Group A had noncoronary sinus pivot implantation (NCPI method, n=16). Group B had conventional method (n=39)	that using the conventional method (valve was implanted below both the noncoronary sinus and left coronary sinus) in patients with pure AR.	
Yin WH, Lee YT, Tsao TP et al. (2022) Outcomes of transcatheter aortic valve replacement for pure native aortic regurgitation with the use of newer- *vs.* early generation devices. Ann Transl Med.10 (1): 24	Comparative study (retrospective analysis) N=25 TAVI was done with early- (N=15, CoreValve, Lotus and Sapien XT) and newer-generation (N=10, Evolut R in 7 and J-valve in 3) valves in patients with pure native AR at an intermediate-to-high risk for SAVR. Median follow up of 14 months	Early generation TAVR devices are associated with less satisfactory outcomes in the treatment of patients with pure native AR and should be avoided. TAVR using newer-generation THVs has yielded better procedural outcomes and can be a great asset to treat certain patients. Dedicated TAVR devices for pure native AR are preferred to other newer-generation devices.	Larger studies included in the summary of evidence.
Yin M, Lu Y, Chen J et al. (2025) Incremental prognostic value of computed tomography determined mitral annular dilatation in patients with severe aortic regurgitation undergoing transcatheter aortic valve replacement: a retrospective cohort study. Quant Imaging	Retrospective cohort study N=281 patients with symptomatic severe AR who underwent pre-TAVR computed tomography (CT) Median follow up 2 years.	Mitral annular dilatation was an independent predictor of adverse outcomes after TAVR in patients with severe AR, and added incremental prognostic value to a baseline model composed of clinical and	More comprehensive studies included in the summary of evidence.

Med Surg;15(2): 1229–1240.		echocardiographic characteristics.	
Yousef A, MacDonald Z, Simard T et al. (2018) Transcatheter Aortic Valve Implantation (TAVI) for Native Aortic Valve Regurgitation - A Systematic Review. Circ J. 82(3): 895–902.	Systematic review 175 patients were included from 31 studies.	TAVI demonstrates acceptable safety and efficacy in high-risk patients with severe NAVR. Second-generation valves may afford a similar safety profile with improved device success. Dedicated studies are needed to definitively establish the efficacy of TAVI in this population.	More recent comprehensive studies included in summary of evidence.
Yoon SH, Schmidt T, Bleiziffer S et al (2017). Transcatheter aortic valve replacement in pure native aortic valve regurgitation. J Am Coll Cardiol; 70: 2752–2763.	Registry analysis (retrospective and prospective). N=331 patients with pure NAVR underwent TAVI (transfemoral, transapical). The early- and new-generation devices were used in 119 patients (36.0%) and 212 patients (64.0%). (SAPIEN 3, Evolut R, JenaValve, Direct Flow, J-Valve, Engager, Portico, ACURATE, Lotus). Follow up 1 year.	Compared with the early generation devices, TAVR using the new-generation devices was associated with improved procedural outcomes in treating patients with pure native AR. In patients with pure native AR, significant post-procedural AR was independently associated with increased mortality.	Study already included in systematic review added to summary of evidence.
Zheng HJ, Cheng YB, Yan CJ, et al. (2023) Transfemoral transcatheter aortic valve replacement for pure native aortic regurgitation: one-year	Retrospective study N=45 patients with pure native AR had transfemoral Venus A-valve implantation. Follow- up 1 year.	Study reported a 97.8% success rate with 1 patient requiring conversion to SAVR. They observed a	Larger study included in the summary of evidence.

outcomes of a single center study. BMC Cardiovasc Disord. 23:330.		significant increase in LVEF from 42% at baseline to 62% at 1-year. In-hospital mortality rate and 1-year mortality rate were 2.3% and 4.7%, respectively. They concluded that further study is needed to assess the long-term durability of the Venus A-valve	
Zhu D, Chen Y, Guo Y, et al. (2015) Transapical transcatheter aortic valve implantation using a new second-generation TAVI system - J-Valve for high-risk patients with aortic valve diseases: Initial results with 90-day follow-up. Int J Cardiol.199: 155–162	Case series n=20 patients with isolated aortic valve disease (11 with pure/dominant AR and 9 with AS) at high risk for SAVR had TAVI with J-valve. Follow up 3 months.	Trans-apical TAVI using the J-Valve™ prosthesis is potentially an effective treatment option for patients with AS or pure/dominant AR at high risk for open-heart surgery.	Study already included in systematic review added to summary of evidence.
Zhu D, Wei L, Cheung A et al. (2016) Treatment of pure aortic regurgitation using a second-generation transcatheter aortic valve implantation system. J Am Coll Cardiol; 67: 2803–5.	Case series N=33 patients with pure native AR and high surgical risk had TA TAVI with J-valve.	Our results demonstrated that this new valve could become a potentially feasible treatment option in patients with AR who are at high risk for SAVR.	Study already included in systematic review added to summary of evidence.
Zhu L, Guo Y, Wang W et al. (2018) Transapical transcatheter aortic valve replacement with a novel transcatheter aortic valve replacement system in high-risk patients with severe aortic valve diseases. J Thorac Cardiovasc Surg. 155(2): 588–597.	Case series n=107 high-risk people (had TAVI with the J-Valve (63 people with AS and 44 people with pure native AR). Follow up 6 months.	TAVI by the J-Valve is an adequate clinical option to treat high-risk patients with severe aortic stenosis or aortic regurgitation.	Study already included in systematic review added to summary of evidence.

Zhu D, Chen Y, Zhang J et al. (2015) Transapical implantation of a new second-generation transcatheter heart valve in patients with pure aortic regurgitation: a preliminary report. Interact CardioVasc Thorac Surg; 20: 860–2	Case series n=7 high-risk patients with pure native AR treated with a TAVI using the J-Valve™ system.	Patients were successfully treated with the TAVI procedure.	Larger studies were included in the summary of evidence.
Zhou C, Xia Z, Song Y, Lian Z. (2023) Transcatheter versus surgical aortic valve replacement in patients with aortic regurgitation: a propensity-matched analysis. Heliyon. 9(6): e16734.	Propensity score-matched retrospective cohort study n=3640 patients with AR TAVI 1820 versus SAVR 1820 Follow up 6 months	TAVR and SAVR had similar risks of hospital death and lower rates of 30-day and 6-month all-cause and cardiovascular readmission. But TAVR had a higher risk of permanent pacemaker implantation than SAVR in patients with AR, suggesting that TAVR can be performed safely in patients with pure AR.	Study already included in systematic review added to summary of evidence.
Zhang, X., Liang, C., Zha, L. et al. (2024) Predictors for new-onset conduction block in patients with pure native aortic regurgitation after transcatheter aortic valve replacement with a new-generation self-expanding valve (VitaFlow Liberty™): a retrospective cohort study. BMC Cardiovasc Disord 24, 77.	Retrospective cohort study n=68 patients with pure native AR who had TAVI using new-generation self-expanding valves (VitaFlow Liberty™). 20 patients had PPM implanted after TAVI.	Multivariate logistic regression analysis revealed an association between the need for postoperative PPI and preoperative complete right bundle branch block (cRBBB) or first-degree atrioventricular block (AVB), as well as a non-tubular left ventricular outflow tract (LVOT).	More comprehensive studies included in the summary of evidence.