

Dedicated versus off-label transcatheter devices for pure native aortic regurgitation via transfemoral access: a meta-analysis of contemporary outcomes



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This paper also includes supplementary data published online at: <https://AsiaIntervention.pronline.com/doi/10.4244/AIJ-D-26-00011>

ABSTRACT

BACKGROUND: Pure native aortic regurgitation (PNAR) poses unique technical challenges for transcatheter aortic valve implantation (TAVI), including annular dilatation and absent calcification for anchoring. Whilst dedicated aortic regurgitation (AR) devices have been developed, their comparative performance against off-label devices specifically via transfemoral access – the contemporary standard approach – remains incompletely defined.

AIMS: We aimed to compare the outcomes of dedicated versus off-label transcatheter devices for PNAR via transfemoral access in contemporary practice.

METHODS: We systematically searched PubMed (MEDLINE) and Cochrane CENTRAL (January 2020–November 2025) for studies reporting transfemoral TAVI outcomes in PNAR. The primary outcome was 30-day mortality. Random-effects meta-analysis with meta-regression was performed.

RESULTS: Twenty-four studies (2,956 patients) were included comprising 25 cohorts: 4 cohorts (537 patients) evaluated dedicated devices, and 21 cohorts (2,419 patients) assessed off-label devices. Overall, 30-day mortality was 3.3% (95% confidence interval [CI]: 2.3–4.8%). Dedicated devices showed a trend towards lower mortality (1.9% vs 4.1%, odds ratio [OR] 0.45, 95% CI: 0.20–1.00; $p=0.051$; risk ratio 0.40, 95% CI: 0.19–0.83). Dedicated devices achieved higher device success (95.8% vs 85.7%, OR 3.64; $p=0.012$), lower rates of residual AR $\geq$ moderate (0.6% vs 6.2%, OR 0.11; $p=0.048$), reduced valve embolisation (2.0% vs 7.3%, OR 0.26; $p=0.048$), and fewer reinterventions (2.0% vs 7.9%, OR 0.22; $p=0.010$). Permanent pacemaker implantation (20.8%), stroke (2.6%), and major bleeding (3.0%) were similar between groups.

CONCLUSIONS: In contemporary transfemoral TAVI for PNAR, dedicated devices demonstrated superior procedural outcomes compared with off-label devices. These findings support the preferential use of dedicated devices in this population, though randomised trials are needed to establish definite treatment recommendations.

KEYWORDS: aortic regurgitation; aortic valve insufficiency; dedicated devices; structural heart disease; transcatheter aortic valve implantation; transfemoral access

Aortic regurgitation (AR) represents one of the most common valvular heart diseases, with moderate or greater disease found in 2.5-2.8% of adults; its prevalence and severity increase with advancing age.¹⁻³ Unlike aortic stenosis (AS), which is characterised by leaflet calcification and restriction, pure AR results from either primary leaflet pathology (bicuspid valve, prolapse, endocarditis, rheumatic disease) or aortic root dilatation, which leads to incomplete coaptation and diastolic backflow into the left ventricle.^{4,5} Chronic volume overload leads to progressive left ventricular dilatation and dysfunction, with surgical aortic valve replacement remaining the definitive treatment for symptomatic severe disease or left ventricular decompensation.⁶

Transcatheter aortic valve implantation (TAVI) has transformed the management of AS across all surgical risk categories, yet its application in pure AR has progressed more cautiously. The absence of annular or leaflet calcification – which normally provides anchoring for transcatheter valves – combined with a dilated aortic annulus and root creates challenges for device stability and positioning. Early TAVI experience in AR relied predominantly on transapical access to enable precise device deployment, though this approach carries higher morbidity than transfemoral delivery. Off-label use of devices designed for AS yielded variable results, with higher rates of device embolisation, permanent pacemaker implantation, paravalvular leak, and procedural failure than standard use in AS.⁷⁻⁹

Recognition of these anatomical and procedural challenges prompted the development of dedicated AR devices incorporating specific design features: enlarged anchoring skirts, repositionability, and mechanisms to engage the native leaflets or aortic root rather than relying solely on radial force against calcium. Early clinical series demonstrated technical feasibility,¹⁰ though limited patient numbers and heterogeneous access approaches (transapical, transfemoral, transaortic) precluded definitive conclusions regarding comparative effectiveness.

Contemporary TAVI practice has evolved markedly towards transfemoral access as the default approach, driven by the reduced morbidity, shorter recovery, and increasing operator experience.¹¹ This evolution reflects broader technical advances including improved valve designs and refined imaging guidance. Recent meta-analyses have compared dedicated versus off-label devices in pure AR but included heterogeneous access cohorts or historical data from earlier device generations,¹² limiting the applicability to current practice patterns. Whether dedicated devices confer meaningful clinical advantages over contemporary off-label devices when delivered via the transfemoral route, now the predominant access strategy, remains incompletely defined. We therefore conducted a systematic review and meta-analysis comparing dedicated versus off-label TAVI devices for pure

Impact on daily practice

For Heart Teams evaluating patients with pure aortic regurgitation who are at elevated surgical risk, our data support the preferential selection of dedicated aortic regurgitation platforms for transfemoral transcatheter aortic valve implantation, given their higher procedural success, lower embolisation rates, and reduced residual regurgitation. Permanent pacemaker implantation remains frequent regardless of device type and should be discussed during the consent process. Patient selection should integrate age and left ventricular function, both identified as predictors of 30-day mortality in meta-regression.

native aortic regurgitation (PNAR), restricting analysis to transfemoral access and contemporary studies to inform current clinical decision-making.

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Methods

PROTOCOL AND REGISTRATION

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (<https://www.prisma-statement.org/>). The protocol was prospectively registered on the International Prospective Register of Systematic Reviews (PROSPERO: CRD420251135422).

SEARCH STRATEGY

We conducted systematic searches of PubMed (MEDLINE) and the Cochrane Central Register of Controlled Trials (CENTRAL) from 1 January 2020 to 2 November 2025. The search strategy incorporated terms for transcatheter aortic valve implantation, aortic regurgitation, and transfemoral access. We limited searches to English language publications. Reference lists of included studies and relevant systematic reviews were manually searched for additional eligible studies.

Given substantial device iterations and improvements in operator experience over time, we restricted our analysis to contemporary studies published from 2020 onwards. This approach captures current device generations and contemporary practice patterns whilst minimising heterogeneity from historical data with earlier-generation devices.

ELIGIBILITY CRITERIA

We included studies of adults (≥18 years) with moderate-to-severe or severe PNAR undergoing transfemoral TAVI. Eligible devices included dedicated AR devices (JenaValve Trilogy [JenaValve], J-Valve [JC Medical], Hanchor Valve [Healing Medical]) and off-label devices designed for aortic

Abbreviations

AR aortic regurgitation

AS aortic stenosis

LVEF left ventricular ejection fraction

PNAR pure native aortic regurgitation

PPI permanent pacemaker implantation

STS Society of Thoracic Surgeons

TAVI transcatheter aortic valve implantation

VARC Valve Academic Research Consortium

stenosis (SAPIEN [Edwards Lifesciences], CoreValve/Evolut [Medtronic], ACURATE [Boston Scientific], Portico/Navitor [Abbott], Myval [Meril], and other commercially available transcatheter heart valves).

Studies were required to enrol patients with pure native aortic valve regurgitation without haemodynamically significant concurrent aortic stenosis. We accepted each study's own definition of "pure" AR, which typically required the absence of moderate or greater aortic stenosis on echocardiography.

Studies were excluded if they (1) included predominantly non-transfemoral access ($\geq 90\%$ transfemoral required), (2) enrolled patients with aortic stenosis, (3) reported prosthetic valve regurgitation or valve-in-valve procedures, (4) included fewer than 10 patients, (5) lacked extractable outcome data, or (6) were published before 2020.

STUDY SELECTION AND DATA EXTRACTION

Two reviewers independently screened titles and abstracts, followed by full-text review. Data extraction was performed using a standardised form. Extracted data included study characteristics, patient demographics, clinical characteristics, procedural details, and outcomes. Disagreements were resolved through discussion.

OUTCOMES

The primary outcome was 30-day (or in-hospital) all-cause mortality. Secondary outcomes included device success, residual AR $\geq$ moderate, valve embolisation or migration, permanent pacemaker implantation (PPI), reintervention, stroke, major bleeding, and acute kidney injury (stage 2-3).

Device success and major bleeding were assessed according to Valve Academic Research Consortium (VARC)-2 or VARC-3 criteria as reported by each study (Table 1). To assess the impact of definition heterogeneity, sensitivity analyses were performed, restricting device success to cohorts reporting VARC-3 criteria only.

QUALITY ASSESSMENT

Two reviewers independently assessed the risk of bias using the Newcastle-Ottawa scale (NOS) for non-randomised cohort studies. Individual scores are reported in Supplementary Table 1.

STATISTICAL ANALYSIS

Meta-analyses were performed using R, version 4.3.1 (R Foundation for Statistical Computing) with the meta and metafor packages. Event rates were pooled using random-effects models with restricted maximum likelihood (REML) estimation and logit transformation with 0.5 continuity correction. Heterogeneity was quantified using Cochran's Q , I^2 , and τ^2 . Subgroup differences were assessed using the Q test for subgroup differences.

SUBGROUP ANALYSES AND META-REGRESSION

The primary subgroup comparison evaluated outcomes between dedicated AR devices and off-label devices. This represented an indirect comparison of predominantly single-arm studies. One study (Poletti et al, 2024¹³) reporting data for both device types was treated as two separate cohorts.

Odds ratios (OR) with 95% confidence intervals (CI) were calculated for each outcome using mixed-effects meta-regression with the device category (dedicated vs off-label) as the moderator variable and REML estimation. Risk ratios (RR) with 95% CI were computed from pooled event rates per group.

Univariable meta-regression examined associations between 30-day mortality and mean age, Society of Thoracic Surgeons (STS) score, left ventricular ejection fraction, aortic annulus diameter, year of publication, and valve oversizing percentage using mixed-effects models with REML estimation.

SENSITIVITY ANALYSES

Prespecified sensitivity analyses assessed robustness by excluding studies with < 20 patients, restricting analyses to cohorts with 100% transfemoral access, and limiting the publication year to 2022 or later.

PUBLICATION BIAS

Publication bias was evaluated for outcomes with ≥ 10 studies using funnel plots and Egger's regression test.

Results

STUDY SELECTION AND CHARACTERISTICS

The search identified 994 records after duplicate removal (Figure 1). Following title, abstract, and full-text review, 24 contemporary studies (2020-2025) met the eligibility criteria, contributing 25 cohorts. Fifty-seven studies were excluded for wrong study design ($n=26$), wrong patient population ($n=10$), incorrect route of administration ($n=15$), or other reasons ($n=7$).

The 24 studies enrolled 2,956 patients (median per study: 77 [interquartile range {IQR} 61-128]) encompassing 25 cohorts, due to one study reporting data for both dedicated and off-label devices. Sixteen were retrospective cohorts, seven were prospective, and two were both. Four cohorts (537 patients, 18.2%) evaluated dedicated devices: JenaValve Trilogy ($n=409$) and Hanchor Valve ($n=128$). Twenty-one cohorts (2,419 patients, 81.8%) assessed off-label devices: self-expanding (14 cohorts), balloon-expandable (3 cohorts), and mixed (4 cohorts).

PATIENT AND PROCEDURAL CHARACTERISTICS

Patient characteristics are summarised in Table 1. The mean age was 75.2 ± 3.7 years (range 68.0-81.0), 37.9% were female, and the mean left ventricular ejection fraction (LVEF) was $49.8 \pm 4.8\%$. The mean STS score was $5.1 \pm 2.1\%$, indicating predominantly intermediate surgical risk. Ten studies enrolled high-risk patients, whilst the remainder enrolled intermediate-to low-risk populations. The mean aortic annulus diameter was 25.8 ± 1.1 mm. All cohorts included only pure AR patients.

Transfemoral access was 100% in 20 cohorts and $\geq 90\%$ in 5 cohorts. General anaesthesia was used in 12 cohorts, with mixed approaches in 8 cohorts. The mean valve size was 29.1 ± 0.8 mm.

QUALITY ASSESSMENT

Using the Newcastle-Ottawa scale, 21 cohorts (84.0%) were rated as good quality (NOS ≥ 7) and 4 (16.0%) as fair (NOS 5-6); none were rated as poor (Supplementary Table 1). The

Table 1. Characteristics of included studies.

Study	Country	N	Device category	Specific device(s)	TF, %	FU, days	Age, years	Female, %	STS-PROM score, %	NYHA III/IV, %	LVEF, %	Annulus diameter, mm	VARC
Pan 2025 ¹⁶	China	128	Dedicated	Hancho Valve ^a	100	30	74.0	23.4	4.8	84.4	54.0	26.4	Custom
Wienemann 2025 ¹⁸	Multiple (Germany+UK)	141	Dedicated	JenaValve Trilogy ^b	100	30	81.0±4.4	41.0	ES-II 3.6	70.2	NR	26.7	NR
Poletti 2024 ¹³	Multicentre	256	Both	JenaValve Trilogy ^b ; SAPIEN ^c ; Evolut ^d ; ACURATE ^e ; Portico ^f	100	364	80.0	44.5	3.1	76.2	47.4	25.4	VARC-3
Vahl 2024 ¹⁷	USA	180	Dedicated	JenaValve Trilogy ^b	100	365	75.5±10.8	47.2	4.1±3.4	67.8	53.8±11.4	24.8	VARC-2
Ju 2025 ²⁹	China	69	Off-label	VitaFlow Liberty ^g	100	180	73.6±7.7	40.6	4.0	NR	56.1±11.6	NR	NR
Poletti 2025 ³³	Multiple (Europe+USA)	144	Off-label	Myval ^h ; SAPIEN 3/Ultra ^c	99.3	365	79.7	33.3	2.7	69.4	40.0	28.3	VARC-3
Xia 2025 ³⁴	China	121	Off-label	TaurusElite ⁱ	100	30	72.7±8.0	45.5	4.6±3.8	67.7	53.4±11.8	24.5±2.0	VARC-3
Yang 2025 ³⁵	China	87	Off-label	VitaFlow ^c ; VenusA-Valve ^j	100	30	72.1±8.5	52.9	3.3±2.1	43.7	55.7±11.6	25.6±2.0	VARC-3
Yu 2025 ³⁷	China	100	Off-label	VitaFlow ^g	98.4	365	72.7±7.2	37.0	9.1±5.8	64.0	53.0±10.7	25.6±1.7	VARC-3
Hu 2024 ⁴⁰	China	70	Off-label	VitaFlow ^c ; VenusA-Valve ^j	100	30	73.7±7.6	44.3	4.1±3.4	72.9	49.9	24.4	VARC-2
Kong 2024 ⁴²	China	62	Off-label	VitaFlow ^g	100	365	71.6±7.3	41.9	5.4±3.2	61.3	54.0±10.8	25.0±2.2	VARC-3
Le Ruz 2024 ²³	France	227	Off-label	Evolut R/PRO ^d ; SAPIEN 3 ^c	91.6	480	81.0	35.7	ES-II 6.0	77.3	46.0	26.0	VARC-3
Lin 2024 ²⁴	China	75	Off-label	VenusA-Valve ^j ; VitaFlow ^g	100	30	74.7	38.7	4.2	72.0	48.5	25.8	VARC-3
Orzalkiewicz 2024 ²⁶	Italy	13	Off-label	SAPIEN 3 ^c	100	300	80.8±5.6	30.8	4.0±1.7	NR	44.8±12.0	26.1	VARC-3
Yu 2024 ³⁶	China	30	Off-label	VenusA-Valve ^j	100	NR	70.4±8.4	26.7	NR	53.3	53.2±14.4	25.8±2.6	NR
Zhang 2024 ⁴⁰	China	68	Off-label	VitaFlow Liberty ^g	100	30	74.5±8.2	48.5	7.9±1.5	NR	52.9±9.6	24.5±2.5	VARC-3
Chen 2023 ³²	China	37	Off-label	VitaFlow ^c ; VenusA-Valve ^j	97.3	365	73.1±8.7	37.8	8.6±2.1	45.9	53.1±12.1	26.0±2.2	NR
Koch 2023 ²¹	United States	34	Off-label	SAPIEN 3 ^c ; Evolut ^d	100	30	68.0±12.2	26.5	4.0	88.2	50.2±13.7	26.3±2.3	VARC-3
Oettinger 2023 ²⁵	Germany	786	Off-label	NR	100	30	76.8±8.7	34.2	NR	54.6	NR	NR	NR
Sanchez-Luna 2023 ²⁷	Multiple (Europe+USA+Asia-Pacific region)	113	Off-label	Myval ^h	100	365	78.4±7.5	35.4	2.7±1.7	62.8	43.4±14.7	28.2±2.6	VARC-3
Zheng 2023 ³⁸	China	45	Off-label	VenusA-Valve ^j	100	365	73.5±5.5	26.7	NR	95.6	41.5±4.6	NR	VARC-2
Chen 2022 ¹⁹	China	32	Off-label	VenusA-Valve ^j ; VitaFlow ^g	100	30	71.9±8.0	22.1	8.6±1.7	71.9	48.1±9.5	26.4±2.0	VARC-3
Chen 2022 (CT Indexes) ³¹	China	77	Off-label	VenusA-Valve ^j ; VitaFlow ^g	100	NR	78.1±12.5	52.0	7.7±5.9	68.0	43.9±13.9	25.8±2.7	VARC-2
Wang 2022 ²⁸	China	61	Off-label	VenusA-Valve/ VenusA-Plus ^j	98.4	30	72.8±6.7	37.7	5.8±1.8	82.0	54.3±12.4	24.6±2.2	VARC-3

Data are n, %, or mean±standard deviation. ^aPoletti 2024¹³ reported data for both dedicated and off-label device cohorts and was treated as two separate cohorts in the analysis. ^bBy Healing Medical; ^cby Edwards Lifesciences; ^dby Medtronic; ^eby Boston Scientific; ^fby Abbott; ^gby MicroPort; ^hby Meril; ⁱby Peijia Medical; ^jby Venus Medtech; ES-II: European System for Cardiac Operative Risk Evaluation II; FU: follow-up; LVEF: left ventricular ejection fraction; N: number of patients; NR: not reported; NYHA: New York Heart Association; STS-PROM: Society of Thoracic Surgeons Predicted Risk of Mortality; TF: transfemoral access; VARC: Valve Academic Research Consortium

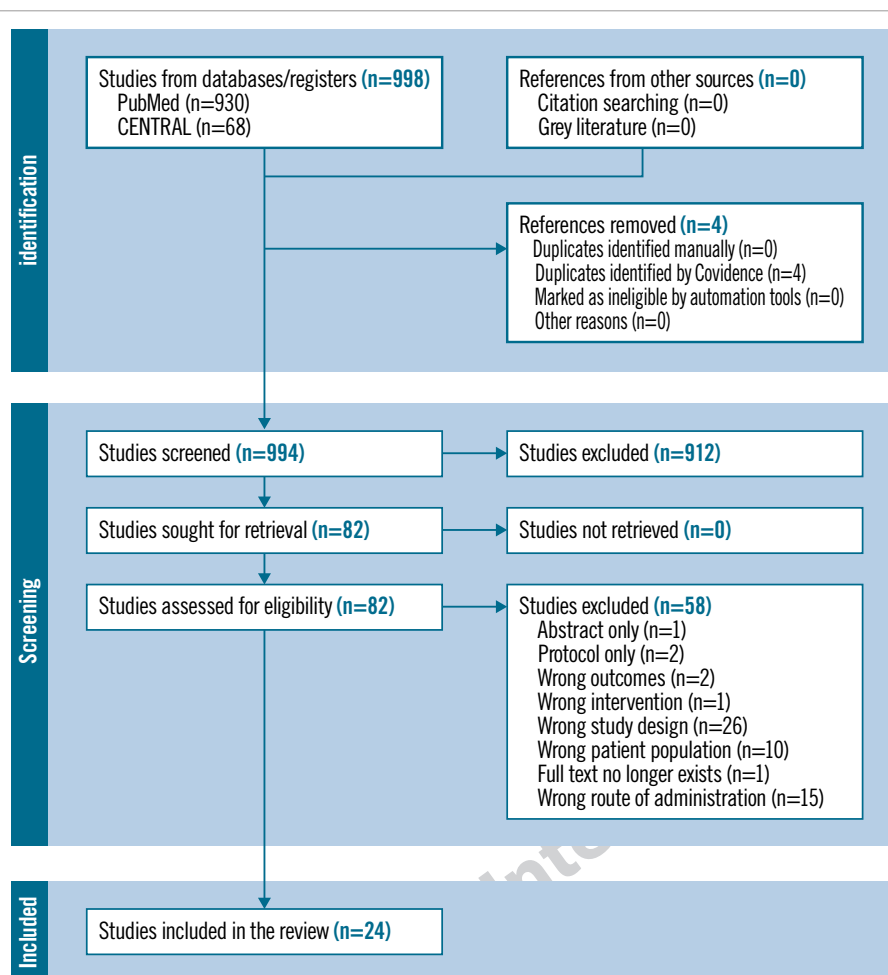


Figure 1. PRISMA 2020 flow diagram for study selection. Studies were excluded for wrong access route (non-transfemoral), wrong patient population (aortic stenosis or prosthetic valve), or insufficient patient numbers (<10). One study (Poletti 2024¹³) contributed two separate cohorts (dedicated and off-label devices).

median NOS score was 7 (IQR 7-8). All four dedicated device cohorts were rated as good quality.

PRIMARY OUTCOME: 30-DAY MORTALITY

Thirty-day mortality data were available from 19 cohorts (2,554 patients, 83 deaths). Overall pooled mortality was 3.3% (95% CI: 2.3-4.8%, $I^2=45.7\%$; $p=0.016$). Dedicated devices achieved lower mortality (1.9%, 95% CI: 1.0-3.6%; 4 cohorts, 537 patients) than off-label devices (4.1%, 95% CI: 2.8-5.9%; 15 cohorts, 2,017 patients; OR 0.45, 95% CI: 0.20-1.00; $p=0.051$; RR 0.40, 95% CI: 0.19-0.83) (**Figure 2**). Heterogeneity was absent in the dedicated subgroup ($I^2=0\%$) and moderate in the off-label subgroup ($I^2=42.8\%$).

SECONDARY OUTCOMES

Device success (19 cohorts, 1,635 patients) was 87.7% overall (95% CI: 83.0-91.2%). Dedicated devices achieved higher success (95.8%, 95% CI: 92.2-97.8%) than off-label devices (85.7%, 95% CI: 81.0-89.4%; OR 3.64, 95% CI: 1.33-9.95; $p=0.012$).

Residual AR $\geq$ moderate (16 cohorts, 1,540 patients) occurred in 3.7% overall (95% CI: 1.7-7.9%), with markedly

lower rates for dedicated devices (0.6%, 95% CI: 0.2-1.9%) than for off-label devices (6.2%, 95% CI: 2.9-12.6%; OR 0.11, 95% CI: 0.02-0.52; $p=0.006$).

Valve embolisation or migration (20 cohorts, 1,811 patients) occurred in 5.8% overall (95% CI: 3.4-9.9%), with lower rates for dedicated devices (2.1%, 95% CI: 1.1-4.1%) than for off-label devices (7.3%, 95% CI: 4.1-12.4%; OR 0.26, 95% CI: 0.07-0.99; $p=0.048$).

Permanent pacemaker implantation (23 cohorts, 1,998 patients) was required in 20.8% (95% CI: 17.5-24.6%), with no difference between groups (OR 0.99, 95% CI: 0.58-1.69; $p=0.963$). Stroke (15 cohorts, 1,975 patients) occurred in 2.6% (95% CI: 2.0-3.5%; OR 0.59, 95% CI: 0.25-1.38; $p=0.223$), and major bleeding (16 cohorts, 2,176 patients) in 3.0% (95% CI: 1.9-4.9%; OR 0.80, 95% CI: 0.27-2.41; $p=0.692$), with no device-related differences. Reintervention (15 cohorts, 1,616 patients) was required in 5.1% (95% CI: 2.6-9.7%), with lower rates for dedicated devices (2.0%) than for off-label devices (7.9%; OR 0.22, 95% CI: 0.07-0.69; $p=0.010$). Conversion to surgery (20 cohorts, 3,039 patients) occurred in 1.6% (95% CI: 1.0-2.5%), with a trend favouring dedicated devices (OR 0.41, 95% CI: 0.14-1.22; $p=0.108$).

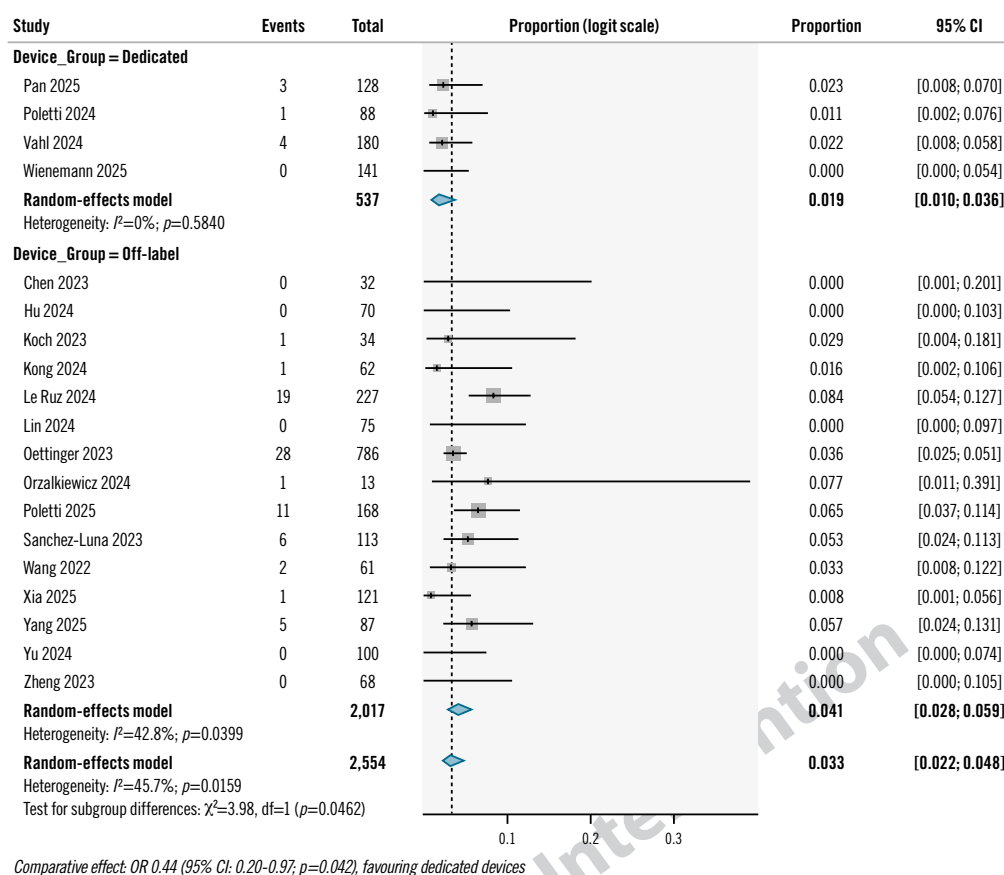


Figure 2. Forest plot showing pooled 30-day all-cause mortality for dedicated AR devices and off-label devices. Pooling used random-effects models with REML estimation and logit transformation. The diamonds represent the pooled estimates. The study references are listed in Table 1. AR: aortic regurgitation; CI: confidence interval; I^2 : heterogeneity statistic; OR: odds ratio; REML: restricted maximum likelihood

Acute kidney injury stage 2-3 (10 cohorts, 947 patients) occurred in 2.2% (95% CI: 1.2-4.0%), with no difference between groups (OR 0.48, 95% CI: 0.14-1.60; $p=0.229$).

Forest plots for outcomes with significant subgroup differences are presented in Figure 3-Figure 6, with those not reaching significance reported in Supplementary Figure 1. Comparative odds ratios for all outcomes are summarised in Figure 7.

META-REGRESSION

Univariable meta-regression for 30-day mortality identified two significant predictors of 30-day mortality. Increasing age was associated with higher mortality (coefficient 0.10 per year, 95% CI: 0.02-0.18; $p=0.016$; $R^2=81.2\%$), whilst higher LVEF was associated with lower mortality (coefficient -0.08 per percentage point, 95% CI: -0.16 to -0.01; $p=0.030$; $R^2=72.6\%$). The mean STS score ($p=0.12$) and aortic annulus diameter ($p=0.27$) were not significantly associated with mortality.

SENSITIVITY ANALYSES

Sensitivity analyses confirmed the robustness of the primary mortality finding. Excluding studies with <20 patients (17 cohorts, 2,420 patients) yielded similar results (dedicated 1.9% vs off-label 4.3%; $p=0.031$). Restricting analysis

to studies with 100% transfemoral access (15 cohorts, 2,045 patients) maintained the observed difference (dedicated 1.9% vs off-label 4.2%; $p=0.032$).

Restricting device success to the 14 cohorts using VARC-3 criteria confirmed an overall rate of 87.4% (95% CI: 82.4-91.2), and the subgroup difference between device types remained significant (dedicated 95.5% vs off-label 86.4%; $p=0.028$), though only one dedicated device cohort used VARC-3 criteria. Too few VARC-2 cohorts ($n=2$) were available for formal subgroup analysis. When restricted to VARC-3 cohorts (10 cohorts), residual AR $\geq$ moderate showed an overall rate of 5.4% (95% CI: 2.6-11.3%), with a numerically lower rate for dedicated devices versus off-label devices (1.1% vs 6.3%) that did not reach significance ($p=0.102$).

PUBLICATION BIAS

Funnel plot asymmetry was detected for 30-day mortality, device success, and PPI, suggesting potential small-study effects or selective reporting.

Discussion

This systematic review of contemporary transfemoral TAVI for PNAR demonstrates pooled 30-day mortality of 3.3%,

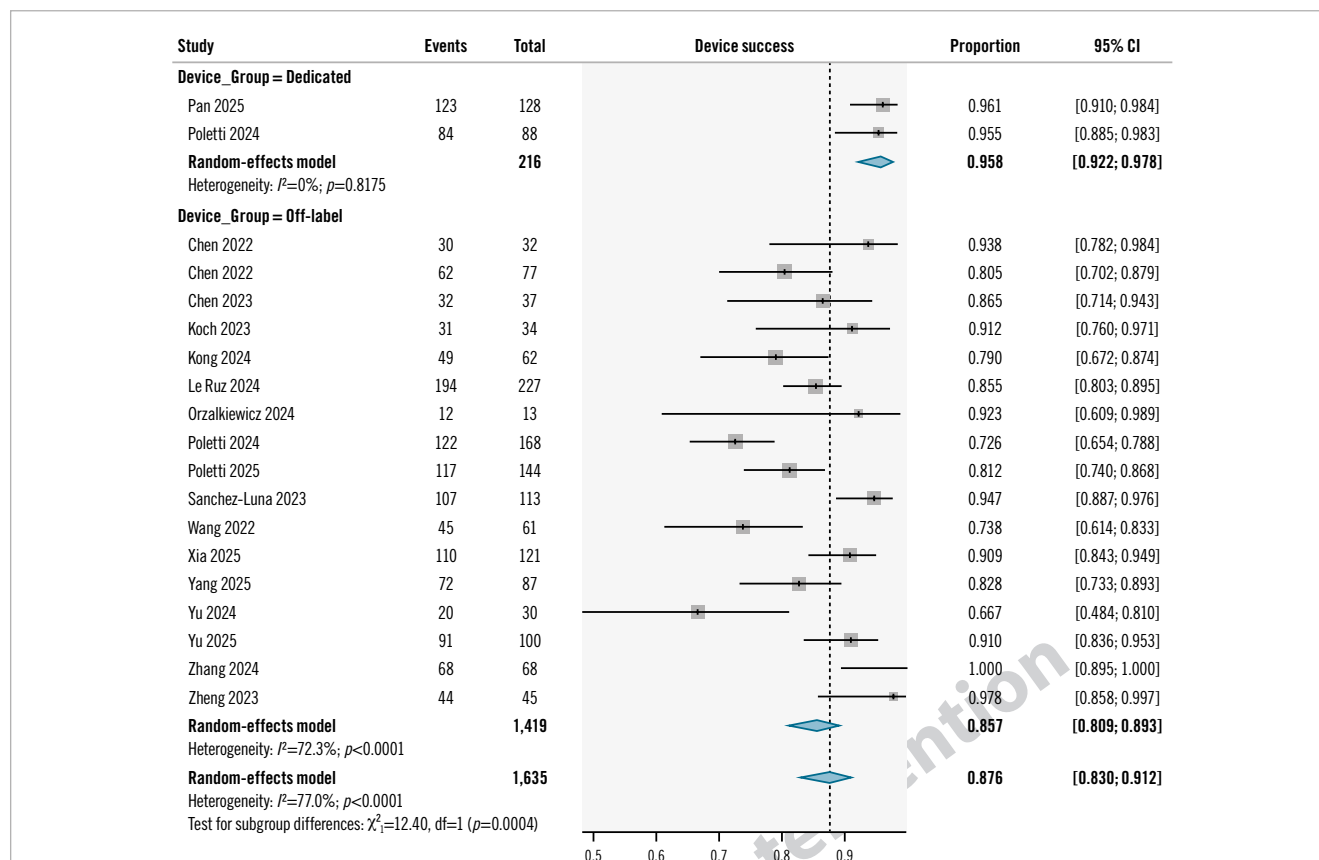


Figure 3. Forest plot of pooled key outcomes with significant subgroup differences between dedicated and off-label devices – device success. VARC-2 or VARC-3 criteria as reported per study. All analyses used random-effects models with REML estimation. The diamonds represent the pooled estimates. The study references are listed in Table 1. CI: confidence interval; I^2 : heterogeneity statistic; REML: restricted maximum likelihood; VARC: Valve Academic Research Consortium

device success of 87.7%, and stroke rates of 2.6%. Dedicated devices achieved superior outcomes compared with off-label devices: lower mortality, higher device success, reduced residual AR $\geq$ moderate, fewer valve embolisations, and lower reintervention rates. PPI, stroke, and bleeding rates were similar across device types. Meta-regression identified increasing age and reduced LVEF as mortality predictors, whilst surgical risk scores showed no association. Findings remained robust across all sensitivity analyses.

PNAR presents unique anatomical and haemodynamic challenges for transcatheter valve replacement. Off-label devices, designed for aortic stenosis, have historically had lower device success rates, as they rely on annular and leaflet calcification for mechanical fixation and fluoroscopic landmarks.¹⁴ In PNAR, the annulus is often elliptical, dilated, and non-calcified, removing anchoring points and visual landmarks, which results in difficulties with device stability and positioning. Consequently, this contributes to higher levels of embolisation, paravalvular leakage, and overall lower device success.

Dedicated devices for PNAR circumvent some of these issues through various anchoring mechanisms including the use of leaflet-engaging locators and enhanced sealing skirts.¹⁵ The ability to anchor the device onto a non-calcified, dilated aortic root helps maintain commissural alignment and provide

an effective seal to minimise paravalvular leakage and reduce embolisation even in the presence of a large stroke volume and regurgitant backflow.⁸

Our findings align with a previous meta-analysis which reported 30-day mortality of 3% for dedicated devices versus 9% for off-label devices.¹² Three methodological differences are worth highlighting. Samimi and colleagues included mixed-access approaches (transfemoral, transapical, transcarotid, and transsubclavian) and extended their search to 2014, incorporating earlier device generations; their analysis also included the J-Valve, delivered via transapical access in published studies. By contrast, our exclusive focus on transfemoral access and restriction to studies from 2020 onwards eliminates confounding from higher-morbidity access routes and earlier-generation devices. The lower off-label mortality in our analysis (4.1% vs their 9%) likely reflects these methodological distinctions. Both analyses converge on the central finding that dedicated devices confer superior procedural success and lower short-term mortality, and our provision of direct comparative effect sizes (OR 0.45, 95% CI: 0.20-1.00 for mortality) quantified this advantage in a contemporary transfemoral-only context.

Patient selection should prioritise high-risk surgical candidates where TAVI offers mortality rates comparable to aortic stenosis outcomes. Results support cautious expansion

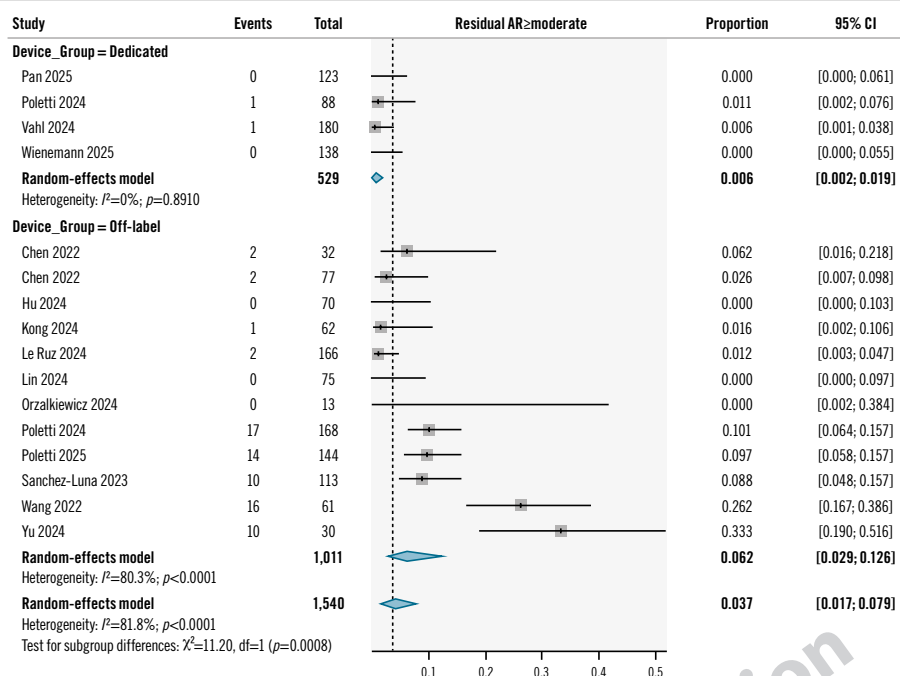


Figure 4. Forest plot of pooled key outcomes with significant subgroup differences between dedicated and off-label devices – residual aortic regurgitation $\geq$ moderate. Residual aortic regurgitation $\geq$ moderate on postprocedural echocardiography. All analyses used random-effects models with REML estimation. The diamonds represent the pooled estimates. The study references are listed in Table 1. AR: aortic regurgitation; CI: confidence interval; I^2 : heterogeneity statistic; REML: restricted maximum likelihood

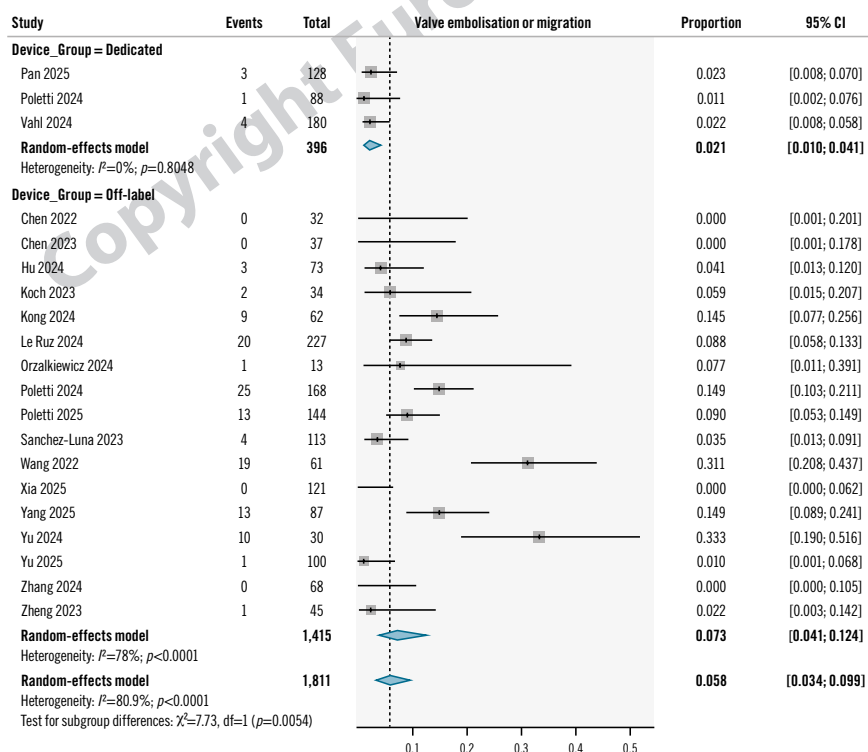
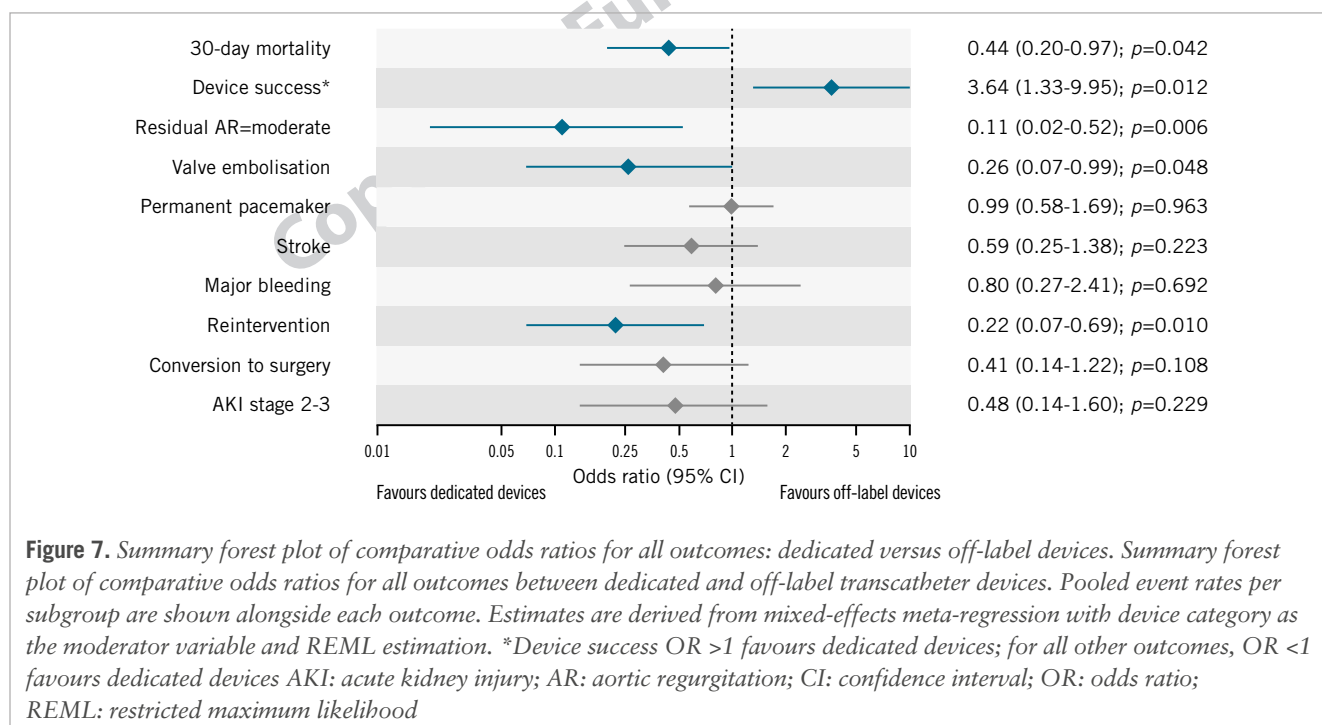
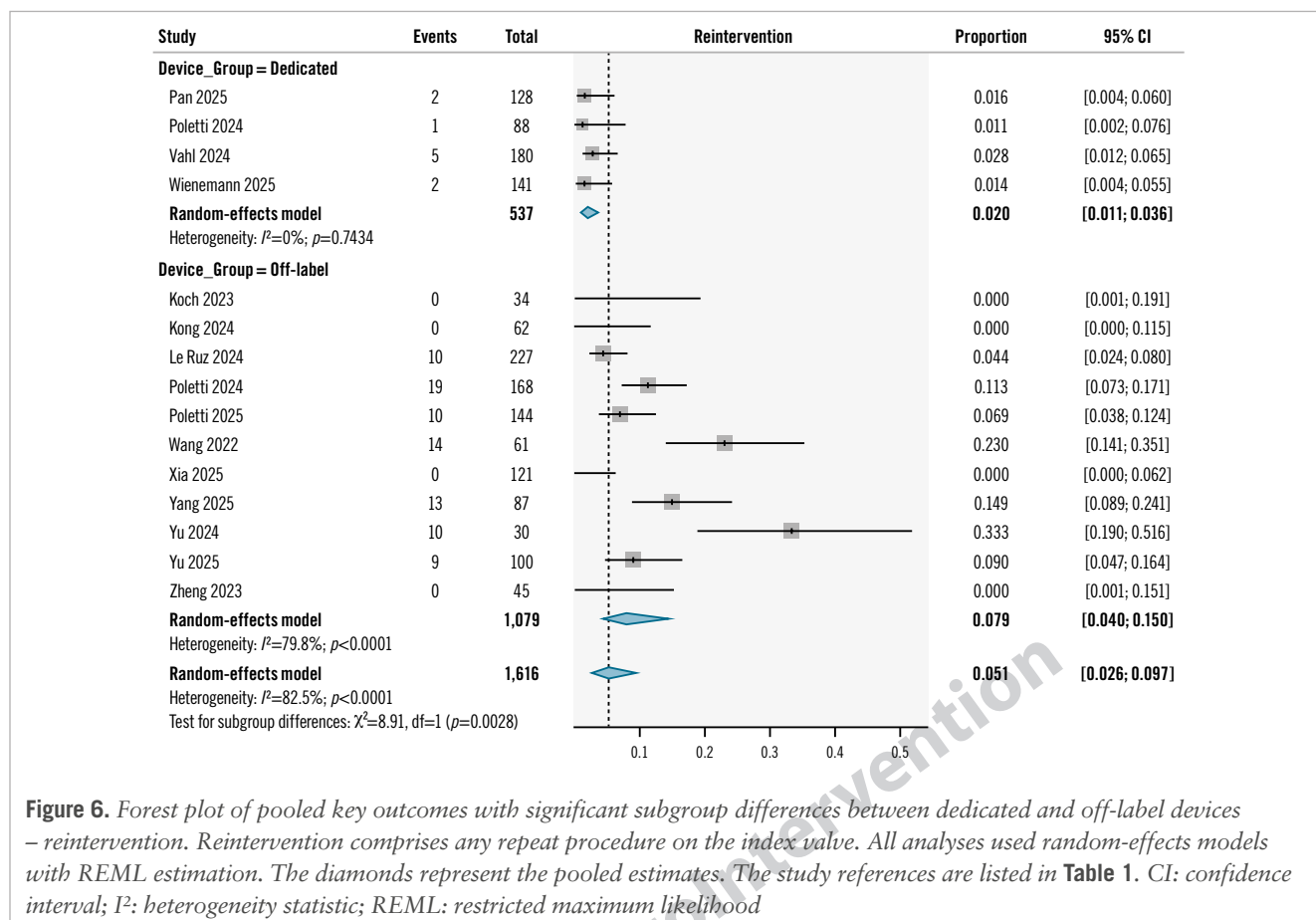


Figure 5. Forest plot of pooled key outcomes with significant subgroup differences between dedicated and off-label devices – valve embolisation or migration. Valve embolisation or migration. All analyses used random-effects models with REML estimation. The diamonds represent the pooled estimates. The study references are listed in Table 1. CI: confidence interval; I^2 : heterogeneity statistic; REML: restricted maximum likelihood



to intermediate-risk patients, though randomised trials remain ongoing. Device selection should favour dedicated platforms given the superior procedural success and lower embolisation rates. Valve sizing requires 10-20% oversizing in non-calcified

anatomy to ensure adequate anchoring whilst minimising conduction disturbances. Integration of these considerations into multidisciplinary Heart Team decision-making ensures appropriate patient selection, device choice, and expectations.

The association between increasing age and mortality likely reflects frailty and diminished physiological reserve. A preserved LVEF exerted protective effects, suggesting better adaptation to acute afterload changes post-implantation. The absence of an association with the STS score highlights the potential limitations of surgical risk models developed for open heart surgery when applied to transcatheter treatment of pure AR. These findings underscore the need for TAVI-specific risk tools that incorporate anatomical parameters – such as annular diameter, calcification degree, and root geometry – which influence procedural success.

Consistency across the sensitivity analyses strengthens confidence in our findings. Excluding studies with <20 patients yielded identical results, whilst restriction to 100% transfemoral access maintained dedicated device superiority. Funnel plot asymmetry suggests potential small-study effects or selective reporting, though the magnitude and direction of treatment effects remained robust. The biological plausibility of dedicated device superiority provides mechanistic support to statistical associations, and consistent findings across independent registries mitigate concerns.

Limitations

The comparison between dedicated and off-label devices is indirect, derived from predominantly single-arm cohorts, and subject to unmeasured confounding in patient selection and operator experience. Follow-up was predominantly short-term, which is insufficient to assess valve durability – a particularly relevant consideration given that PNAR patients are typically younger than AS populations. Device success definitions varied across studies (VARC-2, VARC-3, or custom criteria); sensitivity analysis restricted to VARC-3 cohorts yielded consistent findings. Funnel plot asymmetry for several outcomes suggests possible small-study effects. The majority of off-label cohorts originated from Asia, which may limit generalisability. The dedicated device evidence is confined to two platforms (JenaValve Trilogy and Hancock Valve), as J-Valve data were exclusively transapical, and limited granular procedural and imaging data precluded subgroup analysis beyond broad device categories.

Conclusions

Contemporary transfemoral TAVI for pure native aortic regurgitation achieves acceptable safety and efficacy. Dedicated devices demonstrated lower mortality, higher device success, less residual regurgitation, fewer valve embolisations, and lower reintervention rates compared with off-label devices. These findings support the preferential use of dedicated platforms in selected patients, though randomised trials with extended follow-up remain essential.

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Conflict of interest statement

J.K.F. Hon reports reception of speaker honoraria from Edwards Lifesciences and Medtronic. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Table 1. Newcastle-Ottawa scale quality assessment.

Supplementary Figure 1. Forest plots of secondary outcomes without significant subgroup differences between dedicated and off-label devices.

Ethics statement.

Patient and public involvement.

The supplementary data are published online at:

<https://AsiaIntervention.pcronline.com/>

doi/10.4244/AIJ-D-26-00011

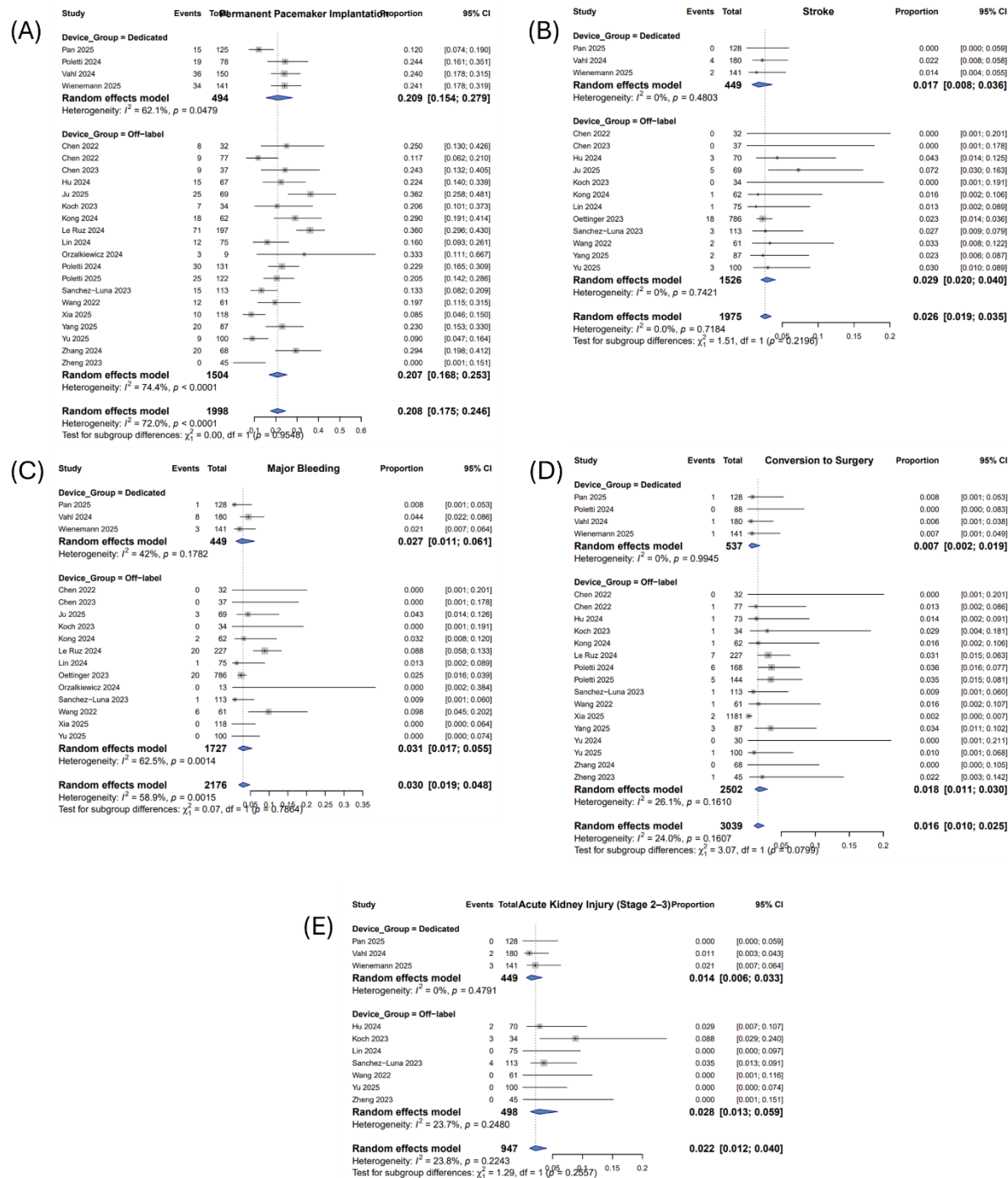


Supplementary data

Supplementary Table 1. Newcastle-Ottawa scale quality assessment.

Study*	NOS Score (Out of 9)	Overall Quality
Wienemann 2025 ¹⁸	7	Good
Pan 2025 ¹⁶	7	Good
Vahl 2024 ¹⁷	7	Good
Poletti 2024 ¹³ (Dedicated)	8	Good
Poletti 2024 ¹³ (Off-label)	8	Good
Xia 2025 ³⁴	8	Good
Yu 2025 ³⁷	9	Good
Yang 2025 ³⁵	9	Good
Ju 2025 ²⁹	9	Good
Poletti 2025 ³³	8	Good
Kong 2024 ²²	6	Good
Le Ruz 2024 ²³	6	Good
Yu 2024 ³⁶	5	Fair
Lin 2024 ²⁴	6	Fair
Orzalkiewicz 2024 ²⁶	6	Fair
Hu 2024 ²⁰	5	Fair
Zhang 2024 ³⁰	8	Good
Sanchez-Luna 2023 ²⁷	7	Good
Zheng 2023 ³⁸	7	Good
Oettinger 2023 ²⁵	8	Good
Chen 2023 ³²	7	Good
Koch 2023 ²¹	7	Good
Wang 2022 ²⁸	7	Good
Chen 2022 ¹⁹	8	Good
Chen 2022 ³¹ (CT indexes)	7	Good

Studies scoring ≥ 7 were classified as good quality; 5–6 as fair; < 5 as poor.



Supplementary Figure 1. Forest plots of secondary outcomes without significant subgroup differences between dedicated and off-label devices.

(A) Permanent pacemaker implantation. (B) Stroke. (C) Major bleeding. (D) Conversion to surgery. (E) Acute kidney injury stage 2-3. See **Supplementary Table 1** for all study references.

Ethics statement.

This study involved human participants however did not require review by an ethics committee given its nature as a systematic review and meta-analysis using published data.

Patient and public involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.