# GID-HTE10027 Late stage assessment - Transcatheter aortic valve implantation (TAVI) in people with aortic stenosis: Addendum 2

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The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

None of the information included in this report is considered academic in confidence or commercial in confidence.

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# Abbreviations

| Term | Definition |
|---|---|
| AKI | Acute kidney injury |
| AR | Aortic regurgitation |
| BEV | Balloon-expanding valve |
| CI | Confidence Interval |
| EAG | External Assessment Group |
| EuroSCORE | European System for Cardiac Operative Risk Evaluation Score |
| HR | Hazard ratio |
| ITT | Intention to treat |
| LSA | Late stage assessment |
| MA | Meta-analysis |
| MEDLINE | Medical Literature, Analysis, and Retrieval System Online |
| MI | Myocardial infarction |
| NICE | National Institute for Health and Care Excellence |
| NR | Not reported |
| PP | Per protocol |
| PPI | Permanent pacemaker implantation |
| PSM | Propensity scored matching |
| PVL | Paravalvular leak |
| RCT | Randomised controlled trial |
| SAVR | Surgical aortic valve replacement |
| SD | Standard deviation |
| SEV | Self-expanding valve |
| SR | Systematic review |
| STS-PROM | Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM) |
| TAVI | Transcatheter aortic valve implantation |
| TIA | Transient ischaemic attack |
| VARC | Valve Academic Research Consortium |

# 1. Aim

During the NICE resolution process for the late stage assessment on transcatheter aortic valve implantation (TAVI) devices, the panel recommended that the committee should review the approach to searching for and selecting evidence. The aim of this addendum is to support the committee in this discussion by conducting a systematic search of published literature directly inter-comparing the clinical effectiveness of TAVI devices used in the treatment of aortic stenosis, and to summarise any new relevant evidence that has been published since the original External Assessment Group (EAG) report was submitted.

# 2. Methods

The EAG has written this addendum guided by the PRISMA guideline for reporting of systematic reviews (Page et al. 2021). This systematic search and analyses were not prospectively registered.

## 2.1 Literature search

The EAG applied three systematic search approaches to identify relevant evidence describing the inter-comparison of TAVI devices. For each approach a set of terms related to the condition (aortic stenosis) was combined (using the Boolean operator 'AND') with a set of terms related to the intervention (generic terms for TAVI devices as well as specific device/manufacturer related terms).

1) Firstly, the EAG systematically searched for any systematic reviews of randomised controlled trials published since 01 January 2022 (based on the date of the last search for the systematic review by Yang et al. 2023 which was included in the original EAG report) up to the most recent available records on the date the searches were performed (11 April 2025). The sources searched included the Medical Literature, Analysis, and Retrieval System Online (MEDLINE), Embase, the Cochrane Database of Systematic Reviews, and Epistemonikos, Appendix A1. Randomised primary evidence of systematic reviews deemed relevant to the decision problem was also reviewed to determine eligibility.

2) The EAG systematically searched for relevant randomised controlled trials (RCTs) comparing TAVI devices that were published from 01 January 2022 up to 11 April 2025. Searches were conducted in MEDLINE, Embase, and CENTRAL, with the Cochrane RCT filter (Lefebvre, last updated September 2024) applied in MEDLINE and Embase (most records in CENTRAL are RCTs and so no RCT filter is required), Appendix A2.

3) For devices without any RCT evidence available after approaches 1 and 2 described above, the EAG conducted targeted searches for evidence published from 01 January 2022 up to 8 May 2025, Appendix A3. The searches used the device name, with case reports, letters and editorials removed (no study design filters were applied). The aim was to identify the highest-level evidence available for these devices.

The EAG did not explicitly search for ongoing studies as only relevant studies with results available are within the scope of this addendum.

## 2.2 Eligibility criteria

The EAG applied the following eligibility criteria.

*Inclusions*:

- Studies inter-comparing TAVI devices listed in the Final Scope:
  - ACURATE neo2 (Boston Scientific)
  - Allegra (Biosensors)
  - Evolut R, Evolut Pro+, Evolut FX (Medtronic)
  - Hydra (SMT)
  - Myval Octacor (Meril)
  - Navitor (Abbott)
  - Sapien 3, Sapien 3 Ultra (Edwards Lifesciences)
  - Trilogy (JenaValve).
- Published in English language.
- In line with the approach taken by the late stage assessment for drug-eluting coronary stents for treating coronary artery disease (GID-HTE10039, 2024),

where multiple publications associated with the same study were identified, the most recent publication with the longest follow-up period was selected for inclusion.

- Where no RCT was identified comparing two devices in scope, the EAG conducted targeted searches for the named technologies across any study design.

*Exclusions*:

- Indirect comparisons (TAVI compared with TAVI indirectly through SAVR trials) or direct comparisons involving SAVR.
- Evidence using exclusively *older* versions of the devices that are not named in the Final Scope (with the exception of systematic reviews comparing multiple TAVI devices including those in scope):
    - ACURATE neo (Boston Scientific)
    - CoreValve, Evolut Pro (Medtronic)
    - Portico (Abbott)
    - Sapien or Sapien XT (Edwards Lifesciences).

  Note: for technical differences between valves, please see Table 3 in the original EAG report (July 2024).
- Evidence using exclusively *newer* versions of the devices that are not named in the Final Scope (mentioned in the original EAG report as updates expected in the next 12 months):
    - ACURATE Prime aortic valve system (Boston Scientific)
    - IMPERIA delivery system for Allegra valve (Biosensors)
    - Evolut FX+ (Medtronic)
    - Sapien 3 Ultra RESILIA (Edwards).
- Evidence including a device which is not listed in the Final Scope which has been withdrawn from market, for example: Lotus, Direct Flow Medical (except for systematic reviews comparing multiple TAVI devices including those in scope).
- In-vitro, lab-based, bench tests or animal studies.

- Abstracts, posters, letters, commentary, protocols, narrative reviews, non-comparative studies, and non-peer reviewed results.
- Economic evidence (as the focus of this addendum is on clinical effectiveness).

No restriction on setting was applied. No restriction was applied in terms of surgical risk group.

*Evidence hierarchy:*
The EAG applied a hierarchy to newly identified evidence considered in scope for the decision problem. To do this the EAG reviewed all relevant studies against the original EAG report and Addendum 1; detail of studies previously reported are in the original EAG report (July 2024; Appendix B1) or Addendum 1 (October 2024; Section 3.1). In terms of prioritisation applied to evidence (highest to lowest):

- Study design:
    - Systematic reviews comparing TAVI valves with no mixture or combination of valves in the arms were highest priority.
    - RCT evidence where one device was used exclusively in an arm was prioritised; where this was lacking, evidence describing a combination of devices was considered.
    - Other comparative designs (with observational studies adjusting for confounders prioritised over those not adjusting for confounding).
- Largest sample size.
- Longest duration of follow-up.

## 2.3 Study selection

Titles and abstracts were reviewed by a single reviewer, and a 10% random sample by a second reviewer. Following review of title and abstract full papers were retrieved and reviewed by a single reviewer. All included studies were checked by a second reviewer. The flow of studies through all three levels of screening are recorded and displayed on a PRISMA diagram (Appendix B). Studies excluded after full paper review had the reason for exclusion documented and tabulated (see

Appendix C. The EAG also reported the number of included studies which were published after the date of the original EAG searches.

When considering secondary evidence (systematic reviews with meta-analysis) the EAG also cross-checked the primary evidence that contributed to each and extracted the study design and technologies used in each from the systematic review (where reported) and against the original EAG report. The EAG conducted quality assurance, extracting the source information directly only where the study design or technology name differed across the secondary evidence sources. A narrative summary of the key findings and limitations of each included systematic review has been provided.

## 2.4 Critical appraisal

All included papers deemed relevant to the decision problem were formally critically appraised using an appropriate checklist for the study design, for example the Cochrane Collaboration's tool for assessing risk of bias in randomised trials (Higgins et al. 2011), and the Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies (Joanna Briggs Institute, 2017).

The EAG provided a narrative summary of the quality of the evidence, noting those studies already considered in the previous EAG report or Addendum 1 (to avoid repetition).

## 2.5 Data extraction

Key study characteristics (study design, setting, population, intervention, comparator, outcomes, key limitations) were extracted for each included study and summarised in a table. Results were extracted from included clinical studies for mortality, stroke, readmission for heart failure, reintervention, paravalvular leak or aortic regurgitation, permanent pacemaker implantation outcomes by a single reviewer and checked by a second reviewer. Data tables from the original EAG report or Addendum 1 acted as the data extraction table template for this Addendum 2.

A narrative summary of the key findings and limitations was reported for each included systematic review. For the primary evidence, the EAG developed a narrative summary considering the relevance of the identified evidence on a per technology basis and considered the impact of this evidence on previous conclusions drawn.

## 3. Technology updates

The EAG searched NHS Supply Chain (16 April 2025) and note that all 11 TAVI devices in scope for this late stage assessment remain available for purchase in the NHS.

The EAG made the following incidental observations when reviewing company webpages to confirm device characteristics:

- According to a press release in May 2025, Boston Scientific is discontinuing worldwide sales of ACURATE neo2.
- According to a press release in July 2024, Edwards LifeSciences had entered into an agreement to acquire JenaValve Technology. However, the EAG has not found any further updates to confirm the status of this acquisition, and the Trilogy valve is still available on the NHS supply chain (as of 16 April 2025).
- At the time of the original EAG report Medtronic had informed the EAG of their intent to discontinue sales of the Evolut R towards the end of 2024. However, this device remains advertised on the manufacture's website and is still available on the NHS supply chain.

The EAG did not request updated information or regulatory information from each company.

# 4. Results

## 4.1 Study selection

The search for systematic reviews retrieved a total of 466 records after removal of duplicates. These were reviewed by title and abstract and 398 were excluded by a single reviewer (PL), with 10% sample reviewed by a second reviewer (KK). The remaining 68 records had full papers reviewed of which 5 were considered relevant to the scope and 63 were excluded by a single reviewer (PL). The remaining 5 systematic reviews described different combinations of TAVI valves (including combinations in some arms), all included Evolut R or Evolut Pro+ combined with either Evolut Pro (earlier version of Evolut Pro+; not in scope) or CoreValve (earlier version of Evolut R; not in scope), therefore all 5 secondary evidence papers were included for narrative summary only due to lack of direct relevance to the decision problem. Two of these systematic reviews were previously identified and summarised in the original EAG report or Addendum 1 and are included in this report for completeness and context.

The search for RCTs retrieved a total of 1,824 records after removal of duplicates. These were reviewed by title and abstract and 1,771 were excluded by a single reviewer (KB); with a 10% sample QA by a single reviewer (PL, KK). The remaining 53 records had full papers reviewed (KB), of which 15 were considered in scope and 38 excluded (KB, KK).

Following these searches, there remained no randomised evidence for ACURATE neo2, Allegra, Hydra, Navitor, Trilogy; therefore, targeted searches were conducted to find the next highest-level evidence for those specific valves. This retrieved a total of 78 records after removal of duplicates. Of these 69 were excluded by a single reviewer (KB) with 10% sample reviewed by a second reviewer (PL). A total of 9 full papers were retrieved, of which 5 were considered relevant to the scope.

Thirty-three additional primary evidence studies were identified (via reference trawling included evidence) and reviewed by the EAG; of which 6 were considered relevant to the decision problem.

A total of 31 pieces of evidence (N=5 systematic reviews and N=26 primary sources) were considered against the evidence hierarchy and evidence already considered in the original EAG report and Addendum 1. Of these 31 studies, 21 were excluded due to them being duplicates or were deprioritised based on the evidence hierarchy applied. Therefore, across all searches, in total:

- 10 studies were included (detailed study characteristics of the 5 primary sources are described in Appendix E),
- 18 studies were deprioritised (study summary in Appendix D) and
- 124 studies were excluded (reasons for exclusion in Appendix C).

## 4.2 Study characteristics

A summary of 10 included studies (5 systematic reviews, 3 RCTs, and 2 observational studies with propensity score matching) is provided in Table 1.

Evidence across devices included:

- 1 study using Myval Octacor
- 9 studies Sapien 3
- 4 studies Sapien 3 Ultra
- 0 studies Navitor
- 0 studies Allegra
- 2 studies ACURATE neo2
- 0 studies Trilogy
- 7 studies Evolut R
- 2 studies Evolut Pro+
- 0 studies Evolut FX
- 0 studies Hydra.

**Table 1: Summary of included studies (N=10) [†indicating studies which were considered in the original EAG report, and 1st addendum]**

| # | Author (year) | Country (N centres) | Study design | Maximum duration of follow-up (*SR as reported) | Total no. of patients | Myval Octacor (Meril) | Sapien 3 (Edwards Lifesciences) | Sapien 3 Ultra (Edwards Lifesciences) | Navitor (Abbott Medical) | Allegra (Biosensors Int) | ACURATE neo2 (Boston Scientific) | Trilogy (JenaValve) | Evolut R (Medtronic) | Evolut Pro+ (Medtronic) | Evolut FX (Medtronic) | Hydra (SMT) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | †Lerman (IJC, 2023; 100-108) | Cyprus, France, Germany, Israel, Italy, Japan, Spain, US, International (N=NR) | SR and MA (N=19; 2 papers from 1 RCT, 7 papers from 6 PSM studies) | *3.8 years | 35,248 | - | Sapien 3 (n=19,897 of which RCT: n=219 from the SOLVE-TAVI trial) | - | - | - | - | - | R / Pro combination (n=15,351) | - | - | - |
| 2 | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | France, Germany, Greece, India, Israel, Italy, Netherlands, North America, Switzerland, US, Europe (N=NR) | SR and MA (N=16; 2 RCTs, 14 observational; of which 14 PSM) | *5 years | 10,174 | - | Sapien 3 / Sapien 3 Ultra combination (n=5753 of which RCT: n=104) | Sapien 3 / Sapien 3 Ultra combination (n=5753 of which RCT: n=104) | - | - | - | - | - | Pro / Pro+ combination (n=4421 of which RCT: n=101) | - | - |
| 3 | Wang (BMC Cardiovasc Disord, 2023; 382) | NR (N=NR) | SR and MA (4 RCTs, 14 observational; of which 14 PSM) | *3 years | 9,641 (some implanted with Accurate neo) | - | Sapien 3 / Sapien 3 Ultra combination (n=NR) | Sapien 3 / Sapien 3 Ultra combination (n=NR) | - | - | - | - | Evolut R / Pro combination (n=NR) | - | - | - |
| 4 | †Yang (Int J Surg, 2023; 2414-2426) | NR (N=NR) | SR and NMA (5 RCTs, 74 observational; of which 14 PSM) | *30 day | 99,725 | - | 54,691 (includes comparisons of 'out of scope' valve types) | - | - | - | - | - | Evolut R 31872; of which 2441 are combined Evolut R/Pro | - | - | - |
| 5 | Zhang (J Cardiol, 2022; 204-210) | NR (N=NR) | SR and MA (3 RCTs, 12 observational; of which 12 PSM) | *1 year | 23,665 from relevant subgroup analysis | - | Sapien 3 (n=11,817 in subgroup analysis) | - | - | - | - | - | Evolut R (n=11,848 in subgroup analysis) | - | - | - |
| 6 | Feistritzer (J Am Coll Cardiol, 2025; 74-82) | Germany (N=7) | RCT (SOLVE-TAVI) | 5 years | 447 randomised [PP] | - | 219 | - | - | - | - | - | 219 | - | - | - |
| 7 | Nuche (JACC Cardiovasc Interv, 2023; 2999-3012) | International (N=11) Canada, US, Europe | RCT (LYTEN trial) | 1 year outcomes for Rodes-Cabau (2022) | 102 ITT<br>98 PP<br>(Valve-in-valve) | - | 49 ITT<br>46 PP<br>[Combined Sapien 3 (n=40/46) | 49 ITT<br>46 PP<br>[Combined Sapien 3 (n=40/46) | - | - | - | - | 53 ITT<br>52 PP<br>[Combined Evolut R (n=20/52) | 53 ITT<br>52 PP<br>[Combined Evolut R (n=20/52) | - | - |

| # | Author (year) | Country (N centres) | Study design | Maximum duration of follow-up (*SR as reported) | Total no. of patients | Myval Octacor (Meril) | Sapien 3 (Edwards Lifesciences) | Sapien 3 Ultra (Edwards Lifesciences) | Navitor (Abbott Medical) | Allegra (Biosensors Int) | ACURATE neo2 (Boston Scientific) | Trilogy (JenaValve) | Evolut R (Medtronic) | Evolut Pro+ (Medtronic) | Evolut FX (Medtronic) | Hydra (SMT) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | LYTEN trial | | | with Sapien3 Ultra (n=6)] | with Sapien3 Ultra (n=6)] | | | | | with Evolut Pro (n=31/52) with Evolut Pro+ (n=1/52)] | with Evolut Pro (n=31/52) with Evolut Pro+ (n=1/52)] | | |
| 8 | Terkelsen et al. (Lancet, 2025; 1362-1372 | Denmark (N=3) initially aimed at including all-comer patients at eligible Scandinavian and European centres) | RCT (non-inferiority) | 1 year | 1031 (ITT cohort B)<br><br>1346 planned (for Cohort A) | 514 ITT 507 PP [Combined Myval and (n=183) Myval Octacor (n=324)] | Sapien 3 / Sapien 3 Ultra combination (n=517 ITT, 516 PP) | Sapien 3 / Sapien 3 Ultra combination (n=517 ITT, 516 PP) | - | - | - | - | - | - | - | - |
| 9 | Kim (JACC, 2025, 32-40) | Germany (N=3) | Retrospective cohort with PSM | 1 year | 2106 (ITT), 1404 matched | - | - | 702 | - | - | 702 | - | - | - | - | - |
| 1 | Loewenstein (Cardiovas Revascul Med, 2024; 17-22) | Israel (N=5) | 2 Retrospective cohorts; with PSM | 30 days | 3208 (ITT); 338 matched | - | 169 | - | - | - | 169 | - | - | - | - | - |

Abbreviations: ITT, intention to treat; MA, meta-analysis; NMA, network meta-analysis; NR, not reported; PP, per-protocol; PSM, propensity score matched; RCT, randomised controlled trial; SR, systematic review;

## 4.3 Critical appraisal

None of the 5 systematic reviews were directly relevant to the decision problem, as all included combinations of valves or an earlier version of the valve in at least one arm. All systematic reviews included a mixture of experimental and non-experimental study designs. Summary details of the systematic reviews, focusing on the results reported for the devices in scope, are in Table 2. Due to lack of direct relevance to the decision problem, the EAG did not critically appraise the systematic reviews.

None of the identified primary evidence (N=5) was conducted in an UK NHS setting; all were published after the EAG original searches were conducted and all had at least 1 domain which was considered high risk of bias (for critical appraisal checklists see Appendix G). Across the 5 included primary evidence the median age was considered consistent (between 79 and 82 years) however the proportion of male patients varied across studies (between 27.8% and 61%) as did Society of Thoracic Surgeon mortality risk scores (between 2.3% and 5.9%). This demonstrates that patient characteristics differed between studies, thus limiting the ability to draw conclusions between different studies where different TAVI valves were compared.

## 4.4 Summary of results from systematic reviews

The 5 systematic reviews included a total of 103 unique studies; which were considered against the primary evidence incorporated in the original EAG report (see Appendix F). All systematic reviews included both RCTs and observational studies. Of the 5 systematic reviews, that by Yang et al. 2023 was the largest with 79 papers and 99,725 patients:

- Of the 19 papers included in Lerman et al. 2023, 16 were included in Yang et al. 2023.
- Of the 18 studies included in Wang et al. 2023, 9 were included in Yang et al. 2023.
- Of the 16 papers included in Siddiqui et al. 2024, 1 was included in Yang et al. 2023.
- Of the 15 studies included in Zhang et al. 2022, 9 were included in Yang et al. 2023.

**Table 2: Summary of identified systematic reviews (N=5)**

| Study | Key findings | Key limitations |
|---|---|---|
| Yang et al. 2023 included 79 papers (n=99,725 patients) and compared ACURATE, DFM, **Evolut R**/Pro, Lotus, Portico and **Sapien 3** valves. | **Sapien 3** was associated with lower mortality, stroke, and PPI than **Evolut R**/Pro from network meta-analysis.<br>Device success rates were comparable for in-hospital and/or 30-day outcomes, among these new-generation valves except the DFM device which is out of scope. Different valves ranked highest for different outcomes (mortality, stroke, major and life-threatening bleeding, acute kidney injury, permanent pacemaker implantation, paravalvular leak, and mean aortic valve gradients). | The network meta-analysis was based mainly on observational studies with numerous confounding factors including patient specific factors and operator learning curve. The observational nature limited the level of evidence to a low or very low level. The range of anatomical differences and surgeon experience may have influenced results, with numbers too small for subgroup analysis. Inclusion criteria stipulated reporting of in-hospital and/or 30-day outcomes; follow-up duration was limited. |
| Lerman et al. 2023 included 19 studies (n=35,248 patients) and **compared Evolut R**/Pro with **Sapien 3** valves. | **Sapien 3** when compared to **Evolut R**/Pro was associated with a lower risk of short-term all-cause mortality, significant AR, PPI and a higher risk of bleeding, major vascular complication, and a higher trans-valvular gradient. There was no significant difference between the valve systems regarding the long-term mortality, risk of stroke, AKI, or device success. | Meta-analysis was based mainly on observational data with only one RCT. There were no data on the institutional TAVI volumes which may affect procedure learning curves and patients' outcomes. The meta-regression analysis was based on aggregate data and there were no statistically significant predictors of mortality, including patients' characteristics or procedure complications. Missing anatomical information in the meta-regression analysis which might have affected outcomes. |
| Siddiqui et al. 2024 included 16 studies (n=10,174 patients) and compared **Evolut** Pro/**Pro+/**FX and **Sapien 3/3 Ultra** valves. | The **Sapien 3/3 Ultra** valves were associated with a lower risk of TIA and stroke, moderate or severe PVL, and PPI in-hospital/30 day. **Sapien 3/3 Ultra** valves were associated with a higher risk of moderate or severe patient-prosthesis mismatch, higher mean gradient, and smaller effective orifice area, compared with the **Evolut** Pro/**Pro+/FX** valves within hospital or at 30 days. No significant differences in all-cause mortality in-hospital/30 day or at 1 year, and no significant difference in heart failure hospitalizations at 1 year. | Meta-analysis was predominantly based on observational studies and is subject to limitations of observational data including selection bias and unmeasured confounding. Different approval timelines for the third-generation balloon-expanding (BEV) and self-expanding valves (SEV) may have influenced the patient profile across studies. Individual patient characteristics may affect outcomes and were not included in the analyses. Follow-up duration was between 1 and 5 years in 6 studies and in-hospital or 30 days in 10 studies. There was no long-term data analysis. |
| Wang et al. 2023 included 18 studies (n=9,641 patients) and compared **ACURATE** neo/**neo2**, Evolut **R**/Pro (SEV) and **Sapien 3/3 Ultra** (BEV) valves. | Compared to **Sapien 3/3 Ultra**, **ACURATE** neo/**neo2** had a lower, and **Evolut R**/Pro a higher risk of PPI at 30 days. BEV and SEV were comparable for 30-day and 1-year mortality, stroke, major bleeding, major vascular complications, AKI, and coronary artery obstruction. SEV were associated with better hemodynamic outcomes, except for a higher incidence of PVL. | The predominant use of observational studies despite propensity score matching includes potential flaws and unidentified biases. There was a high degree of heterogeneity in some of the outcomes. The maximum follow-up period was 1 year, and no data on valve durability and long-term outcomes was available. Differences were found in postoperative outcomes between different self-expanding valves, but a comparison between different valves was not done. Patient characteristics or anatomy were not considered for this meta-analysis. |
| Zhang et al. 2022 included 15 studies (n=37,958 patients) and compared ACURATE neo, **Evolut R**, CoreValve, Portico (SEV) and Sapien, **Sapien 3**/XT (BEV) valves. | Subgroup analysis where **Sapien 3** was compared to **Evolut R** was associated with lower risk of PPI at 30 days, lower all-cause mortality at 30 days, and lower risk estimates of stroke at 30 days. No statistical difference in 30-day major bleeding was found between Sapien 3 and Evolut R.<br>The remaining comparisons were BEV versus SEV by different manufacturers, or new versus older generation valves. | Meta-analysis was based mainly on observational data with 3 underpowered RCTs. Lack of patient characteristic data limited in-depth subgroup analyses. Overall, the SEV group contained different systems (design, deployment mechanism, and radial strength) but subgroup analysis based on SEV types showed largely similar results. Follow-up duration was limited. |

Abbreviations: AKI, acute kidney injury; AR, aortic regurgitation; BEV, balloon-expanding valve; PPI, permanent pacemaker implantation; PSM, propensity score matched; PVL, paravalvular leak; SEV, self-expanding valve; STS–PROM, Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM); TIA, transient ischaemic attack

## 4.5 Summary of results from additional primary evidence

### 4.5.1 Myval Octacor (Meril)

No RCT evidence was identified using Myval Octacor exclusively. However, one non-inferiority RCT (COMPARE-TAVI 1) was published after the EAG report and Addendum 1 (Terkelsen et al. 2025). This study included a mixed intervention group with a higher proportion of participants who received Myval Octacor (64% Myval Octacor, 36% Myval) than the previously identified LANDMARK RCT by Baumbach et al. 2024 (which used 8% Myval Octacor, 92% Myval); the latter was de-prioritised.

One additional paper reported a subset of results of the LANDMARK trial (Van Royen et al. 2024); however, this was similarly de-prioritised because of its mixed intervention arm and lower proportion of patients receiving the TAVI technology in scope (8% Myval Octacor).

The prioritised evidence non-inferiority RCT by Terkelsen et al. 2025 compared Myval valves against Sapien 3 (Table 3) and reported that the Myval valves were non-inferior in terms of the 1-year composite endpoint (death, stroke, moderate or severe aortic regurgitation, moderate or severe haemodynamic transcatheter heart valve deterioration) for which the trial was statistically powered. The authors reported secondary exploratory outcomes, but only a limited number had Bonferroni correction applied. This provides longer-term non-inferiority evidence for Myval Octacor than was reported in the original EAG report and Addendum 1; however it does not change the conclusions.

**Table 3: Summary of results for Myval Octacor (Terkelsen et al. 2025)**

| Study; study design (n, patients)<br>Location | Demographics | Primary outcome | Secondary <u>exploratory</u> outcomes (with Bonferroni correction applied) |
|---|---|---|---|
| Terkelsen et al. 2025 [COMPARE-TAVI 1]<br>Non-inferiority RCT (n=1,031 enrolled)<br><br>Denmark | Sapien 3 (n=517 randomised):<br>Age, median: 81.1 years<br>Male: 60%<br>STS-PROM, median: 2.4%<br><br>Myval (n=514 randomised, including 324 Myval Octacor):<br>Age, median: 81.9 years<br>Male: 60%<br>STS-PROM, median: 2.3% | <u>1 year</u><br>Primary composite endpoint (death, stroke, moderate or severe aortic regurgitation, or moderate or severe haemodynamic THV deterioration), $p_{non\text{-}inferiority}$=0.019 (non-inferiority; one-sided)<br>- Sapien 3 (n=517): 13%<br>- Myval (n=514): 14% | <u>Procedural and in-hospital</u><br>TAVI related complications, p=0.59:<br>- Sapien 3 (n=516): 3%<br>- Myval (n=514): 3%<br><br>Successful implantation, p=0.80<br>- Sapien 3 (n=516): 98%<br>- Myval (n=514): 99%<br><br><u>1 year</u><br>First-time pacemaker implantation, p=0.00024:<br>- Sapien 3 (n=468): 12%<br>- Myval (n=455): 21%<br>(with Myval Octacor only: 23%) |

Abbreviations: NYHA, New York Heart Association functional class; PPI, permanent pacemaker implantation; RCT, randomised controlled trial; STS-PROM, Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM); TAVI, transcatheter aortic valve implantation;

### 4.5.2 Sapien 3 (Edwards Lifesciences)

A total of 8 RCTs were identified that reported on Sapien 3 exclusively in one arm (Elnaggar et al. 2023, Farhan et al. 2022, Feistritzer et al. 2025, Kim et al. 2021, Lanz et al. 2019, Makkar et al. 2020, Terkelsen et al. 2025, Thiele et al. 2020). Of these 3, (Lanz et al. 2019, Makkar et al. 2020, and Thiele et al. 2020) were described in EAG Addendum 1 (Oct, 2024). Two of the 8 were identified from reference trawling of the systematic reviews were also excluded as they compared Sapien 3 with older versions of TAVI valves which were not in scope: ACURATE neo (Kim et al. 2021), Evolut Pro (Elnaggar et al. 2023), Appendix C. Of the remaining 3 RCTs, 2 were prioritised as they were larger with longer-follow-up (Feistritzer et al. 2025, Terkelsen et al. 2025). The EAG note that Feistritzer et al. 2025 reported 5-year outcomes for the SOLVE-TAVI trial; 30-day outcomes were reported previously in Thiele et al. 2020a.

The prioritized evidence RCT (SOLVE-TAVI) compared Sapien 3 and Evolut R with 5-year results reported by Feistritzer et al. 2025 (Table 4). The study showed that Evolut R was superior in terms of myocardial infarction and 5-year stroke rates but when stratified by annular dimensions stroke rate differed between Evolut R and Sapien 3 only in patients with a small aortic annulus (≤430 mm2) and not in those with an annulus >430 mm2 (small annulus 1.0% vs 12.7%; p=0.002; non-small annulus 4.1% vs 6.4%; p=0.36). All other outcomes showed no statistically significant differences (composite endpoint, all-cause mortality, moderate/severe PVL, PPI, clinical efficacy (VARC-2), quality of life measured via EQ5D). The EAG note that 30-day outcomes from the same trial were reported by Farhan et al. 2022, which was considered but de-prioritised (Appendix D).

**Table 4: Summary of results for Sapien 3 (Feistritzer et al. 2025)**

| Study; study design (n, patients)<br>Location | Demographics | Individual outcomes with statistically significant differences reported between comparator(s);<br>(at specified timepoint) | Outcomes where no statistically significant differences were found between comparator(s)<br>(at specified timepoint) |
|---|---|---|---|
| Feistritzer et al. 2025 [SOLVE-TAVI]<br>RCT (n=447 enrolled)<br><br>Germany | Sapien 3 (n=222 randomised):<br>Age, median: 81.5 years<br>Male: 49.8%<br>STS-PROM, median: 4.7%<br><br>Evolut R (n=225 randomised):<br>Age, median: 81.7 years<br>Male: 47.9%<br>STS-PROM, median: 4.9% | <u>5 years</u><br>Stroke (overall), p=0.002:<br>- Sapien 3: 9.6%<br>- Evolut R: 2.2%<br>HR: 4.84 (95% CI: 1.65, 14.18)<br><br>Stroke (small aortic annulus ≤430mm2), p=0.002<br>- Sapien 3: 12.7%<br>- Evolut R: 1%<br>HR: 12.7 (95% CI: 1.62, 100)<br><br>Myocardial infarction, p=0.02:<br>- Sapien 3: 2.5%<br>- Evolut R: 0.0%<br><br>Mean aortic valve gradient, mmHg, median [Q1,Q3], p=0.005:<br>- Sapien 3 (n=19): 11 [9, 13]<br>- Evolut R (n=19): 7 [6, 10] | <u>5 years</u>: Valve-related composite endpoint (all-cause mortality, stroke, moderate or severe paravalvular leakage (PVL), and permanent pacemaker implantation (PPI)).<br><br>All-cause mortality, moderate/severe PVL, PPI, clinical efficacy (VARC-2), quality of life (EQ5D)<br><br>Stroke (aortic annulus >430mm2), p=0.36<br>- Sapien 3: 6.4%<br>- Evolut R: 4.1%<br>HR: 1.89 (95% CI: 0.47-7.66) |

Abbreviations: CI, confidence interval; HR, hazard ratio; PPI, permanent pacemaker implantation; PVL, paravalvular leak; STS-PROM; Society of Thoracic Surgeons Predicted Risk of Mortality;

### 4.5.3 Sapien 3 Ultra (Edwards Lifesciences)

No RCT identified Sapien 3 Ultra exclusively. Two RCTs with mixed intervention groups were identified for a specific clinical group: valve-in-valve replacement after failed small stented *surgical* aortic bioprostheses (#23-mm and #21-mm inner diameter): Nuche et al. (2023) is a 1-year follow-up of the LYTEN trial (Rodes-Cabau et al. 2022). The prioritised new evidence, the RCT by Nuche et al. (2023), compared mixed Sapien 3 (87%, 40/46) and Sapien 3 Ultra (13%, 6/46) versus mixed Evolut R (38%, 20/52), Evolut Pro (60%, 31/52), and Pro+ (2%, 1/52) (Table 5) and reported that the Sapien arm showed higher transvalvular gradients, a lower indexed orifice effective area, and a lower rate of intended valve performance as evaluated by Doppler echocardiography at 1-year follow-up. Clinical outcomes showed no statistically significant differences (composite (death, heart failure hospitalisation, or stroke), all-cause mortality, heart failure hospitalisation, stroke, myocardial infarction, major or life-threatening bleed, and permanent pacemaker implantation), functional status (NYHA), quality of life (KCCQ). Hemodynamic performance outcomes with no statistically significant difference were LVEF and aortic regurgitation. The EAG note that 30-day outcomes from the same trial were reported by Rodes-Cabau et al. 2022, which was considered but de-prioritised (Appendix D). Whilst both Sapien and Evolut TAVI devices are both indicated for TAVI-in-SAVR procedures (see EAG report July, 2024); the EAG note that for context TAVI-in-SAVR was conducted in 3.8% of TAVI procedures reported in the UK TAVI Registry (see Section 5.3.2 of the original EAG report July, 2024). Therefore, this additional evidence is limited in generalisability to a general population.

For evidence of TAVI inserted into a *native* aortic valve, the EAG identified and previously reported RCTs with mixed comparator groups which were Baumbach et al. 2024 (Sapien 3 Ultra n=87, mixed with Sapien 3 n=103, Evolut R n=71, Evolut Pro n=116, Evolut Pro+ n=10, Evolut FX n=5 as a combined comparator group) and Herrmann et al. 2024 (Sapien 3 Ultra n=295 combined with Sapien 3 n=70 as a combined comparator arm, compared with Evolut valves); see original EAG report (July, 2024). Within the systematic search of this addendum, the EAG also identified a retrospective cohort with propensity score matching (Kim et al. 2025) which

compared outcomes up to 1 year in patients treated with Sapien 3 Ultra (n=702) or ACURATE neo2 (n=702 matched); see results in section 4.5.6.

**Table 5: Summary of results for Sapien 3 Ultra (Nuche et al. 2023)**

| Study; study design (n, patients)<br>Location | Demographics | Individual outcomes with statistically significant differences reported between comparator(s);<br>(at specified timepoint) | Outcomes where no statistically significant differences were found between comparator(s)<br>(at specified timepoint) |
|---|---|---|---|
| Nuche et al. 2023 [LYTEN]<br>RCT (n=102 enrolled)<br><br>Canada, Europe, US | **Valve-in-valve**<br>Sapien 3/3 Ultra (n=46 randomised):<br>Age, median: 79 years<br>Male: 46%<br>STS, median: 5.9%<br>(Patients received smaller prostheses and underwent more frequent surgical ring fracture (30% vs Evolut 13%; p=0.041)<br><br>Evolut R/Pro/Pro+ (n=52 randomised):<br>Age, median: 80 years<br>Male: 61%<br>STS, median: 4.9% | <u>1-year haemodynamic performance</u><br>Intended valve performance, p<0.001:<br>- Sapien 3/3 Ultra (n=33): 30%<br>- Evolut R/Pro/Pro+ (n=34): 76%<br><br>Mean aortic gradient, mmHg, mean (±SD), p<0.001:<br>- Sapien 3/3 Ultra (n=33): 22 (±8)<br>- Evolut R/Pro/Pro+ (n=38): 14 (±7)<br><br>Peak aortic gradient, mmHg, mean (±SD), p<0.001:<br>- Sapien 3/3 Ultra (n=33): 42 (±15)<br>- Evolut R/Pro/Pro+ (n=38): 27 (±14)<br><br>Effective orifice area, cm2, mean (±SD), p=0.003:<br>- Sapien 3/3 Ultra (n=33): 1.27 (±0.51)<br>- Evolut R/Pro/Pro+ (n=38): 1.61 (±0.52)<br><br>Doppler velocity index, mean (±SD), p<0.001:<br>- Sapien 3/3 Ultra (n=33): 0.33 (±0.12)<br>- Evolut R/Pro/Pro+ (n=38): 0.46 ((±0.16)<br><br>Peak velocity ≥3 m/s, mean p<0.001:<br>- Sapien 3/3 Ultra (n=33): 61%<br>- Evolut R/Pro/Pro+ (n=36): 19% | <u>1 year</u>: composite (death, heart failure, hospitalisation, or stroke), all-cause mortality, heart failure hospitalisation, stroke, myocardial infarction, major or life-threatening bleed, permanent pacemaker implantation, functional status (NYHA), quality of life (KCCQ).<br><br><u>1-year hemodynamic performance</u>:<br>LVEF, aortic regurgitation. |

Abbreviations: KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class; SD, standard deviation; STS-PROM; Society of Thoracic Surgeons Predicted Risk of Mortality;

### 4.5.4 Navitor (Abbott Medical)

No RCTs using Navitor were identified by the EAG. From targeted searching, no comparative full peer-reviewed publications were identified which compared Navitor to the other TAVI devices in scope. The EAG previously identified the retrospective non-randomised study by Eckel et al. 2023 which reported 30-day outcomes when comparing Navitor (n=137 patients) with its predecessor, Portico (n=139). This study was summarised in the original EAG report (July, 2024). The EAG did identify a sub-analysis of 232 pacemaker naïve patients from the NAVITOR IDE study by Sultan et al. 2024 which investigated predictors of new permanent pacemaker implantation. However, this single arm study of Navitor lacks relevance to the decision problem. The longest follow-up available remains 1 year as reported by Sondergaard et al. 2023 (PORTICO NG study), which was single arm and included 120 patients, as summarised in the original EAG report (July 2024).

### 4.5.5 Allegra (Biosensors Int)

No RCTs using Allegra were identified by the EAG. The two ongoing studies mentioned in the original EAG report (July 2024) are still in progress and not due to complete recruitment until August and November 2025. From additional targeted searching, no comparative full peer-reviewed publications were identified which compared Allegra to the other TAVI devices in scope. The EAG previously identified the retrospective non-randomised study of the European TAVI registry reported by Santos-Martinez et al. (2022) which compared Myval to alternative balloon expanding (Sapien 3) and self-expanding (Allegra, Evolut R/Pro, ACURATE neo, Sapien 3 and Portico) TAVI valves. This study was summarised in the original EAG Report and remains the highest quality comparative evidence for Allegra.

The EAG did identify a larger single arm cohort for Allegra (n=1,002 consecutive patients), described by Gonzalez et al. 2024; however, this only reported in-hospital outcomes and was excluded due to being available in abstract form only (no full paper publication was identified). An additional slightly larger (n=137 patients) pre-market study with 30-day follow-up was described by Antonio Baz et al. (2025) where the Allegra device was used alongside a new IMPERIA delivery system in patients with either severe calcific aortic stenosis or degenerated surgical prothesis. However, as this is non-comparative the EAG consider this not directly relevant to

the decision problem. The longest follow-up available remains that reported by Wolfrum et al. 2023, which was single arm and included 103 patients from the Swiss TAVI registry, reporting mortality up to 3 years, and other clinical outcomes up to 1 year, as summarised in the original EAG report (July 2024).

### 4.5.6 ACURATE neo2 (Boston Scientific)

No RCTs using ACURATE neo2 were identified by the EAG. Two retrospective cohorts reporting the use of ACURATE neo2 exclusively with propensity score matching comparing with different TAVI valves were prioritized (Table 6). Kim et al. 2025 which reported 1-year outcomes from 702 matched pairs treated with ACURATE neo2 or Sapien 3 Ultra, and Loewenstein et al. 2024 which reported results from 169 matched pairs treated with ACURATE neo2 or Sapien 3 where in-hospital outcomes and mortality at 30 days was reported. These demonstrated no statistical difference across a number of in-hospital outcomes, however there was limited reporting of outcomes post-discharge. Where statistical differences were observed in some clinical outcomes (when compared to Sapien 3 Ultra and Sapien 3), the clinical significance of these is unclear, and there were limitations inherent to their study design (not prospectively powered to detect differences, risk of confounding by other factors). Neither of these studies were conducted in a UK setting.

**Table 6: Summary of results for ACURATE neo2 (Kim et al. 2025; Loewenstein et al. 2024)**

| Study; study design (n, patients)<br>Location | Demographics | Individual outcomes with statistically significant differences reported between comparator(s);<br>(at specified timepoint) | Outcomes where no statistically significant differences were found between comparator(s)<br>(at specified timepoint) |
|---|---|---|---|
| Kim et al. 2025<br><br>Retrospective cohort with PSM (n=2,106 enrolled)<br><br>Germany | ACURATE neo2 (n=702 matched):<br>Age, median: 82 years<br>Male: 51.7%<br>EuroSCORE II, median: 3.1%<br><br>Sapien 3 Ultra (n=702 matched):<br>Age, median: 81 years<br>Male: 51.7%<br>EuroSCORE II, median: 3.3% | <u>In-hospital</u><br>Paravalvular leak, p<0.001:<br>- ACURATE neo2: 67.9% none/trace, 30.1% mild, 2.0% moderate<br>- Sapien 3 Ultra: 82.1% none/trace, 17.2% mild, 0.7% moderate<br><br>Mean transaortic gradient post-intervention, mmHg, p<0.001:<br>- ACURATE neo2: 8 (6,11)<br>- Sapien 3 Ultra: 13 (10,15)<br><br>Aortic valve area post-intervention, cm2, p<0.001<br>- ACURATE neo2: 1.8 (1.5,2.1)<br>- Sapien 3 Ultra: 1.6 (1.4,1.8)<br><br>Valve embolisation, p=0.033<br>- ACURATE neo2: 1.3%<br>- Sapien 3 Ultra: 0.3%<br><br>Major cardiac structural complications, p=0.044<br>- ACURATE neo2: 0.6%<br>- Sapien 3 Ultra: 1.7%<br><br>Major vascular complication, p=0.006<br>- ACURATE neo2: 6.7%<br>- Sapien 3 Ultra: 10.8%<br><br><u>30 days</u><br>Device success, p=0.007:<br>- ACURATE neo2: 87.5%,<br>- Sapien 3 Ultra: 82.3% | <u>In-hospital</u><br>Technical success, coronary obstruction, conversion to sternotomy, multiple valves, bleeding, AKI stage II-IV, pacemaker implantation, stroke.<br><br><u>1 year</u><br>Primary endpoint (composite of all-cause mortality, any stroke or hospitalisation); mortality, stroke, hospitalisation |
| Loewenstein et al. 2024<br><br>Retrospective cohort with PSM<br>n=3,208 enrolled<br><br>Israel | ACURATE neo2 (n=169 matched):<br>Age, mean: 80.9 years<br>Male: 28.6%<br>STS, mean: 2.74%<br><br>Sapien 3 (n=169 matched):<br>Age, mean: 81.0 years<br>Male: 27.8%<br>STS, mean: 2.82% | <u>Procedural outcomes</u><br>Perivalvular leak by echo (mild and above), p<0.001<br>- ACURATE neo2: 2.3%<br>- Sapien 3: 34.7%<br><br>Any conduction disturbance, p<0.001<br>- ACURATE neo2: 15.8%<br>- Sapien 3: 37.5% | <u>Procedural outcomes</u><br>New permanent pacemaker implantation, need for second valve, conversion to open surgery, tamponade, cardiopulmonary bypass, rupture, embolisation or migration, cardiopulmonary resuscitation, ventricular tachycardia/fibrillation, valve thrombosis, peri-procedural or spontaneous MI, major or life-threatening bleeding, major vascular complications, AKI stage II/III, perivalvular leak by angiography (above mild) or by echo (above mild), in-hospital death, aortic valve area (<0.6 cm2), mean aortic valve pressure, systolic pulmonary artery pressure, device success (VARC-2 criteria).<br><br><u>30 days</u><br>Death |

Abbreviations: AKI, acute kidney injury; MI, myocardial infarction; STS, Society of Thoracic Surgeons score; VARC, Valve Academic Research Consortium

### 4.5.7 Trilogy (JenaValve)

No RCTs using Trilogy were identified by the EAG. From targeted searching, no comparative full peer-reviewed publications were identified which compared Trilogy to the other TAVI devices in scope. The EAG did not identify any larger single arm cohort using Trilogy in an aortic stenosis population than those previously reported in the original EAG report or Addendum 1. The longest follow-up available remains 1 year as reported by Silaschi et al. 2016 which was single arm and included 180 patients with aortic stenosis undergoing transapical TAVI, as summarised in the original EAG report (July 2024).

### 4.5.8 Evolut R (Medtronic)

A total of 3 RCTs were identified that reported Evolut R exclusively in one arm (Farhan et al. 2022, Feistritzer et al. 2025, Thiele et al. 2020a). Thiele et al. 2020a was described in EAG Addendum 1 (Oct, 2024). Of the remaining 2 RCTs, 1 was prioritised as it was larger with longer-follow-up (Feistritzer et al. 2025). The results from this study are shown above in Section 4.5.2 and Table 4.

### 4.5.9 Evolut Pro+ (Medtronic)

No RCTs identified on Evolut Pro+ exclusively. Two RCTs (Nuche et al. 2023; Rodes-Cabau et al. 2022) with mixed intervention groups were identified for a specific clinical group of patients undergoing valve-in-valve replacement after failed small stented surgical aortic bioprostheses (23-mm and 21-mm inner diameter). Nuche et al. (2023) is a 1 year follow-up of the LYTEN trial and the detail of this study is reported above in Section 4.5.3 and Table 5. The EAG note that 30-day outcomes from the same trial were reported by Rodes-Cabau et al. 2022, which was considered but de-prioritised (Appendix D).

Previously reported RCTs with mixed comparator groups were Baumbach (2024, Evolut Pro+ n=10/192 ITT) and Herrmann (2024, Evolut Pro+ n=273/350 ITT), see original EAG report (July 2024).

### 4.5.10 Evolut FX (Medtronic)

No RCT identified on Evolut FX exclusively. Previously reported RCTs with mixed comparator groups were Baumbach (2024, Evolut FX n=5) and Herrmann (2024, Evolut FX n=15), see original EAG report (July 2024).

### 4.5.11 Hydra (SMT)

No RCTs using Hydra were identified by the EAG. From targeted searching, no comparative full peer-reviewed publications were identified which compared Hydra to the other TAVI devices in scope. The EAG did not identify any larger single arm cohort using Hydra than those previously reported in the original EAG report or Addendum 1. The longest follow-up available remains 1 year as reported by Aidietis et al. 2022 which was single arm and included 157 patients across 18 European centres, as summarised in the original EAG report (July 2024).

## 5. Summary of newly identified evidence

From an updated systematic search, the EAG identified 5 new pieces of evidence relevant to the decision problem which reported inter-comparisons of TAVI devices. This included:

- 3 RCTs:
    - Terkelsen et al. 2025 showed that the primary clinical efficacy composite outcome (death, stroke, moderate/severe aortic regurgitation, or moderate to severe haemodynamic deterioration; defined by VARC3) for MyVal/MyVal Octacor (n=514) was not inferior to Sapien 3/Sapien 3 Ultra (n=517) at 1 year.
    - Feistritzer et al. 2025 showed fewer myocardial infarctions and lower mean aortic gradient with Evolut R (n=219) when compared to Sapien 3 (n=219) at 5 years. Significantly fewer strokes at 5 years were also found with Evolut R compared to Sapien 3 but when stratified by annular dimension; this finding only held for those with an annular diameter less than or equal to 430 $mm^2$ (defined as small annulus) which applied to approximately 50% of the study population. The EAG note that this trial was powered for equivalence of the primary composite endpoint (all-cause mortality, stroke, moderate to severe prosthetic valve regurgitation, and permanent pacemaker implant) at 30 days.

    - Nuche et al. 2023 showed higher proportion of patients achieving intended valve performance, lower mean aortic gradient, lower peak aortic gradient and larger effective orifice area at 1 year for patients undergoing TAVI in a failed surgical aortic valve bioprosthesis (TAVI-in-SAVR) treated with Evolut R/Pro/Pro+ (n=38) compared to Sapien 3/3Ultra (n=33). The clinical significance of these findings remain uncertain. The EAG note the small sample size and that the primary outcome of this LYTEN trial was haemodynamic performance (residual maximal and mean transvalvular gradient, severe patient prosthesis mismatch, or moderate to severe aortic regurgitation as evaluated by Doppler) at 30 days.
- 2 additional retrospective observational studies with propensity score matching (Kim et al. 2025; Loewenstein et al. 2024) which exclusively used ACURATE neo2 in the intervention arm (previously available evidence was mixed with or exclusively on the ACURATE neo predecessor). The EAG note that ACURATE neo2 TAVI device has been discontinued from sale globally.

No new comparative evidence for Navitor, Allegra, Trilogy, Evolut FX or Hydra compared against TAVI devices in scope was identified from the updated search.

A summary of the TAVI comparisons described within the published primary identified within this Addendum 2 and those which were possible in the data analysis of the UK TAVI Registry within the original EAG report is shown in Figure 1.

**Figure 1: Summary of inter-comparisons of TAVI from newly identified primary comparative evidence (top right, blue) and from the previously reported UK TAVI registry (bottom left, green) [Key: *denotes a mixed device intervention or comparator arm]**

| Devices | Myval Octacor | Sapien 3 | Sapien 3 Ultra | Navitor | Allegra | ACURATE neo2 | Trilogy | Evolut R | Evolut Pro+ | Evolut FX | Hydra |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Myval Octacor** | | * (Terkelsen et al. 2025) | * (Terkelsen et al. 2025) | - | - | - | - | - | - | - | - |
| **Sapien 3** | - | | - | - | - | ✓ (Loewenstein et al. 2024) | - | * (Nuche et al. 2023) ✓ (Feistritzer et al. 2025) | * (Nuche et al. 2023) | - | - |
| **Sapien 3 Ultra** | - | ✓ | | - | - | ✓ (Kim et al. 2025) | - | * (Nuche et al. 2023) | * (Nuche et al. 2023) | - | - |
| **Navitor** | - | ✓ | ✓ | | - | - | - | - | - | - | - |
| **Allegra** | - | - | - | - | | - | - | - | - | - | - |
| **ACURATE neo2** | - | ✓ | ✓ | ✓ | - | | - | - | - | - | - |
| **Trilogy** | - | - | - | - | - | - | | - | - | - | - |
| **Evolut R** | - | ✓ | ✓ | ✓ | - | ✓ | - | | - | - | - |
| **Evolut Pro+** | - | ✓ | ✓ | ✓ | - | ✓ | - | ✓ | | - | - |
| **Evolut FX** | - | - | - | - | - | - | - | - | - | | - |
| **Hydra** | - | - | - | - | - | - | - | - | - | - | |

## 6. Conclusions

From a systematic search the EAG identified 5 additional (primary evidence) studies which were considered relevant to the decision problem; all were published after the original searches conducted by the EAG, none were conducted in a UK setting.

The key limitations described in the original EAG report for the published evidence describing inter-comparisons of TAVI devices (described across the original EAG report, Addendum 1 and Addendum 2) remain, including:

- no randomised evidence was generated from a UK NHS setting,
- majority of randomised evidence was powered for non-inferiority or equivalence on short-term outcomes,
- differences in patient characteristics (proportion male sex and STS score) were noted between studies indicating a lack of transitivity across the studies, limiting their use for indirect comparisons of TAVI devices,
- potential for high risk of bias (including potential conflicts of interest by companies) and,
- lack of comparative evidence for some valves (Navitor, Trilogy, Hydra).

The key limitations described in the original report which reported an analysis of the UK TAVI registry also remain, including:

- potential for high risk of bias due to inability to adjust for key confounders (for example annular calcification, bicuspid valves),
- device model required verification of serial numbers with companies due to limited capture of the specific valve model used in the registry.
- self-reported unvalidated in-hospital outcomes and longer-term outcomes were derived through linkage to Hospital Episode Statistics and mortality databases which lack clinical detail (for example no long-term haemodynamic performance is captured).
- lack of comparative evidence for newer generation valves (Myval Octacor, Trilogy, Evolut FX, Hydra).

Economic models comparing different TAVI valves requires consideration of relevant clinical outcomes (as defined by the Valve Academic Research Consortium, VARC) including: death, stroke, major or severe paravalvular leak, pacemaker implantation, subsequent TAVI or SAVR intervention, all of which can occur in-hospital or longer-term. Due to limited reporting of all these outcomes across the published trials, data from different studies would have to be synthesised to populate an economic model. An added difficulty is that the trials have population differences (such as age mean and range, eligibility criteria, comorbidities), study differences (powered for different outcomes, different duration of follow-up) and differences in definition of outcomes and timepoints at which they were measured. Distributional information on patient characteristics is not always reported in the published trials limiting the ability to estimate effect sizes for modelled patients (for example 80-year-old females with no comorbidities), and intervention or comparator arms often have mixed valve types. These limitations combined, limit the generalisability of an economic model derived from the existing published trial data.

An alternative approach to understanding differences between real-world outcomes and trial outcomes is to use information from a national registry to identify populations which replicate those recruited to trials, and thus enable comparison of real-world outcomes with trial outcomes. However, the UK registry as it stands is not suitable for this purpose due to lack of recorded data (including known confounders and capturing newer TAVI models). This could, and should, be addressed and improved going forwards. The UK registry would also align the health care environment much more closely to the NHS than trials done in other countries and health care systems. Taking into account both sources of information, the EAG consider that univariable analysis of 6,267 patients (multivariable analysis conducted in a subset of 3,917 patients with complete data) from the UK TAVI Registry has more suitable data generalisable to a UK population (with coverage across England reflecting current clinical pathways in the NHS) and to the decision problem of investigating whether pricing differences between the valves are justified.

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# 8. Appendix

## Appendix A – Literature search

### Appendix A1: Systematic reviews of RCTs

For both the systematic searches for systematic reviews of RCTs in MEDLINE databases and Embase (all in Ovid) the Ovid search filters for systematic reviews 'Expert Searches' were applied. (Postscript 19 May 2025 - please note – after these searches were performed Ovid revised this webpage and these filters are no longer currently publicly available.)

The date of search for all the searches was 11 April 2025.

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions** 1946 to April 10, 2025
https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=6fjdusgFfdiiR1NBO1TUSvROTWqcpb21heV901KDE430Cb2HvLHXeK8xqhQVurRVe

Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | Transcatheter Aortic Valve Replacement/ or Heart Valve Prosthesis Implantation/ or Heart Valve prosthesis/ | 67033 |
| 2 | ("Transcatheter Aortic Valve Implantation" or "Transcatheter Aortic Valve Replacement" or "Percutaneous Aortic Valve Implantation" or "Percutaneous Aortic Valve Replacement").ti,ab,kf. | 17604 |
| 3 | (TAVI or TAVR or PAVR).ti,ab,kf. | 14428 |
| 4 | ((transapical or transventricular or percutaneous or transcatheter*) adj3 (valve* or prosthe* or bioprosthe* or valv* or flap* or leaflet* implant* or repair* or replace* or balloon-expand* or self-expand* or balloon expand* or self expand*)).ti,ab,kf. | 28330 |
| 5 | or/1-4 | 77927 |

| # | Searches | Results |
|---|---|---|
| 6 | ("Myval Octacor" or "Sapien 3" or "Sapien 3 Ultra" or "ACURATE neo2" or "Allegra" or "Evolut R" or "Evolut Pro" or "Evolut FX" or "Hydra" or "Navitor" or "Trilogy").ti,ab,kf. | 4685 |
| 7 | ("JenaValve" or "Abbott Medical" or "SMT" or "Medtronic" or "Biosensors" or "Boston Scientific" or "Edwards Lifesciences" or "Meril" or TAVI).ab,in,go,ci. | 76387 |
| 8 | 6 and 7 | 833 |
| 9 | 5 or 8 | 77942 |
| 10 | exp Aortic Valve Stenosis/ | 55123 |
| 11 | (aortic adj3 stenos*).ti,ab,kf. | 30639 |
| 12 | (aortic valv* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 6610 |
| 13 | (aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 1 |
| 14 | (aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 0 |
| 15 | or/10-14 | 68727 |
| 16 | 9 and 15 | 24985 |
| 17 | systematic review.ti. or meta-analysis.pt. or meta-analysis.ti. or systematic literature review.ti. or this systematic review.tw,kf,hw. or pooling project.tw,kf,hw. or (systematic review.ti,ab. and review.pt.) or meta synthesis.ti. or meta-analy*.ti. or integrative review.tw,kf,hw. or integrative research review.tw,kf,hw. or rapid review.tw,kf,hw. or umbrella review.tw,kf,hw. or consensus development conference.pt. or practice guideline.pt. or drug class reviews.ti. or (1469-493X or 1361-6137).is. or (1539-8560 or 1056-8751).is. or (2046-4924 or 1366-5278).is. or 1530-440X.is. or 2202-4433.is. | 546673 |
| 18 | (clinical guideline and management).tw,kf,hw. or ((evidence based.ti. or exp evidence-based medicine/ or best practice*.ti. or evidence synthesis.ti,ab.) and (review.pt. or exp diseases non mesh/ or exp "behavior and behavior mechanisms"/ or exp therapeutics/ or evaluation studies.pt. or validation studies.pt. or guideline.pt. or pmcbook.af.)) | 71265 |

| # | Searches | Results |
|---|---|---|
| 19 | (systematic or systematically).tw,kf,hw. or critical.ti,ab. or study selection.tw,kf,hw. or ((predetermined or inclusion) and criteri*).tw,kf,hw. or exclusion criteri*.tw,kf,hw. or main outcome measures.tw,kf,hw. or standard of care.tw,kf,hw. or standards of care.tw,kf,hw. | 2165842 |
| 20 | (survey or surveys).ti,ab. or overview*.tw,kf,hw. or review.ti,ab. or reviews.ti,ab. or search*.tw,kf,hw. or handsearch.tw,kf,hw. or analysis.ti. or critique.ti,ab. or appraisal.tw,kf,hw. or (reduction.tw,kf,hw. and (exp risk/ or risk.tw,kf,hw.) and (exp "death"/ or "death".af. or (exp "recurrence"/ or "recurrence".af.))) | 4991278 |
| 21 | (literature or articles or publications or publication or bibliography or bibliographies or published).ti,ab. or pooled data.tw,kf,hw. or unpublished.tw,kf,hw. or citation.tw,kf,hw. or citations.tw,kf,hw. or database.ti,ab. or internet.ti,ab. or textbooks.ti,ab. or references.tw,kf,hw. or scales.tw,kf,hw. or papers.tw,kf,hw. or datasets.tw,kf,hw. or trials.ti,ab. or meta-analy*.tw,kf,hw. or (clinical and studies).ti,ab. or exp treatment outcome/ or treatment outcome.tw,kf,hw. or pmcbook.af. | 5171599 |
| 22 | (letter or newspaper article).pt. | 1309155 |
| 23 | 17 or 18 | 605595 |
| 24 | 19 and 20 and 21 | 582992 |
| 25 | 23 or 24 | 794702 |
| 26 | 25 not 22 | 781806 |
| 27 | 16 and 26 | 1220 |
| 28 | Randomized controlled trial/ or (random* or quasi* or RCT).ab. | 1793687 |
| 29 | 27 and 28 | 524 |
| 30 | limit 29 to yr="2022-Current" | 192 |

Database(s): **Embase** 1974 to 2025 April 10

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=3qhrO5icG7qmxU8VDHfVDnKN9tn1CFIFpyCO7KtLWVft3a6EYfixn4b9TIeeF

znGE

Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | transcatheter aortic valve implantation/ | 37901 |
| 2 | heart valve prosthesis/ | 22576 |
| 3 | ("Transcatheter Aortic Valve Implantation" or "Transcatheter Aortic Valve Replacement" or "Percutaneous Aortic Valve Implantation" or "Percutaneous Aortic Valve Replacement").ti,ab,kf. | 29769 |
| 4 | (TAVI or TAVR or PAVR).ti,ab,kf. | 28772 |
| 5 | ((transapical or transventricular or percutaneous or transcatheter*) adj3 (valve* or prosthe* or bioprosthe* or valv* or flap* or leaflet* implant* or repair* or replace* or balloon-expand* or self-expand* or balloon expand* or self expand*)).ti,ab,kf. | 46637 |
| 6 | or/1-5 | 77002 |
| 7 | ("Myval Octacor" or "Sapien 3" or "Sapien 3 Ultra" or "ACURATE neo2" or "Allegra" or "Evolut R" or "Evolut Pro" or "Evolut FX" or "Hydra" or "Navitor" or "Trilogy").ti,ab,kf,dv. | 11009 |
| 8 | ("JenaValve" or "Abbott Medical" or "SMT" or "Medtronic" or "Biosensors" or "Boston Scientific" or "Edwards Lifesciences" or "Meril" or TAVI).ab,mf,my,mv,dm,dv,in,tn,so,dc,de,ct. | 152439 |
| 9 | 7 and 8 | 4219 |
| 10 | 6 or 9 | 77202 |
| 11 | exp aortic valve stenosis/ | 18450 |
| 12 | (aortic adj3 stenos*).ti,ab,kf. | 48284 |
| 13 | (aortic valv* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 9038 |
| 14 | (aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 1 |
| 15 | (aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 0 |
| 16 | or/11-15 | 60558 |
| 17 | 10 and 16 | 23941 |
| 18 | exp Meta Analysis/ | 352288 |

| # | Searches | Results |
|---|---|---|
| 19 | ((meta adj analy$) or metaanalys$).tw. | 425124 |
| 20 | (systematic adj (review$1 or overview$1)).tw. | 441100 |
| 21 | or/18-20 | 686973 |
| 22 | cancerlit.ab. | 748 |
| 23 | cochrane.ab. | 207887 |
| 24 | embase.ab. | 238745 |
| 25 | (psychlit or psyclit).ab. | 1009 |
| 26 | (psychinfo or psycinfo).ab. | 67625 |
| 27 | (cinahl or cinhal).ab. | 66184 |
| 28 | science citation index.ab. | 4692 |
| 29 | bids.ab. | 963 |
| 30 | or/22-29 | 360810 |
| 31 | reference lists.ab. | 25548 |
| 32 | bibliograph$.ab. | 31850 |
| 33 | hand-search$.ab. | 11327 |
| 34 | manual search$.ab. | 8101 |
| 35 | relevant journals.ab. | 1692 |
| 36 | or/31-35 | 71005 |
| 37 | data extraction.ab. | 49265 |
| 38 | selection criteria.ab. | 49290 |
| 39 | 37 or 38 | 95628 |
| 40 | review.pt. | 3340548 |
| 41 | 39 and 40 | 42483 |
| 42 | letter.pt. | 1354180 |
| 43 | editorial.pt. | 832378 |
| 44 | animal/ | 1695659 |
| 45 | human/ | 27653706 |
| 46 | 44 not (44 and 45) | 1242489 |
| 47 | or/42-43,46 | 3410221 |

| # | Searches | Results |
|---|---|---|
| 48 | 21 or 30 or 36 or 41 | 806958 |
| 49 | 48 not 47 | 787619 |
| 50 | 17 and 49 | 1103 |
| 51 | Randomized controlled trial/ or (random* or quasi* or RCT).ab. | 2365608 |
| 52 | 50 and 51 | 608 |
| 53 | limit 52 to yr="2022-Current" | 241 |

Cochrane Library (CDSR) Issue 3, 2025

https://www.cochranelibrary.com/advanced-search/search-manager?search=7673246

| # | Searches | Results |
|---|---|---|
| 1 | MeSH descriptor: [Transcatheter Aortic Valve Replacement] this term only | 517 |
| 2 | MeSH descriptor: [Heart Valve Prosthesis Implantation] explode all trees | 1455 |
| 3 | MeSH descriptor: [Heart Valve Prosthesis] this term only | 846 |
| 4 | ("Transcatheter Aortic Valve Implantation" or "Transcatheter Aortic Valve Replacement" or "Percutaneous Aortic Valve Implantation" OR "Percutaneous Aortic Valve Replacement"):ti,ab,kw | 1331 |
| 5 | (TAVI OR TAVR OR PAVR):ti,ab,kw | 1282 |
| 6 | ((transapical or transventricular or percutaneous or transcatheter*) NEAR/3 (valve* or prosthe* or bioprosthe* or valv* or flap* or leaflet* implant* or repair* or replace* or balloon-expand* or self-expand* or balloon expand* or self expand*)):ti,ab,kw | 2336 |
| 7 | {OR #1-#6} | 3603 |
| 8 | (("Myval Octacor" or "Sapien 3" or "Sapien 3 Ultra" or "ACURATE neo2" or "Allegra" or "Evolut R" or "Evolut Pro" or "Evolut FX" or "Hydra" or "Navitor" or "Trilogy")):ti,ab,kw | 366 |
| 9 | (("JenaValve" or "Abbott Medical" or "SMT" or "Medtronic" or "Biosensors" or "Boston Scientific" or "Edwards Lifesciences" or "Meril" orTAVI)) | 4889 |
| 10 | #8 AND #9 | 97 |

| # | Searches | Results |
|---|---|---|
| 11 | #7 OR #10 | 3607 |
| 12 | MeSH descriptor: [Aortic Valve Stenosis] explode all trees | 1609 |
| 13 | ((aortic NEAR/3 stenos*)):ti,ab,kw | 2093 |
| 14 | ((aortic valv* NEAR (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*))):ti,ab,kw | 1434 |
| 15 | ((aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*))):ti,ab,kw | 0 |
| 16 | ((aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*))):ti,ab,kw | 0 |
| 17 | {OR #12-#16} | 3292 |
| 18 | #11 AND #17 with Cochrane Library publication date Between Jan 2022 and Apr 2025, in Cochrane Reviews | 0 |

Epistemonikos 2025

| Search | Results |
|---|---|
| (advanced_title_en:(((aortic valv* OR flap* OR leaflet*) AND (stenosis OR disease* OR disorder* OR fail* OR dysfunction* OR insufficien* OR damage* OR leak*)) AND ((("Myval Octacor" OR "Sapien 3" OR "Sapien 3 Ultra" OR "ACURATE neo2" OR "Allegra" OR "Evolut R" OR "Evolut Pro" OR "Evolut FX" OR "Hydra" OR "Navitor" OR "Trilogy") AND ("JenaValve" OR "Abbott Medical" OR "SMT" OR "Medtronic" OR "Biosensors" OR "Boston Scientific" OR "Edwards Lifesciences" OR "Meril" OR TAVI)) OR "Transcatheter Aortic Valve Implantation" OR "Transcatheter Aortic Valve Replacement" OR "Percutaneous Aortic Valve Implantation" OR "Percutaneous Aortic Valve Replacement" OR TAVI OR TAVR OR PAVR OR ((transapical OR transventricular OR percutaneous OR transcatheter*) AND (valve* OR prosthe* OR bioprosthe* OR valv* OR flap* OR leaflet* implant* OR repair* OR replace* OR balloon-expand* OR self-expand* OR balloon expand* OR self expand*)))) OR advanced_abstract_en:(((aortic valv* OR flap* OR leaflet*) AND (stenosis OR disease* OR disorder* OR fail* OR dysfunction* OR insufficien* OR damage* OR leak*)) AND ((("Myval Octacor" OR "Sapien 3" OR "Sapien 3 Ultra" OR "ACURATE neo2" OR "Allegra" OR "Evolut R" OR "Evolut Pro" OR "Evolut FX" OR "Hydra" OR "Navitor" OR "Trilogy") AND ("JenaValve" OR "Abbott Medical" OR "SMT" OR "Medtronic" OR "Biosensors" OR "Boston Scientific" OR "Edwards Lifesciences" OR "Meril" OR TAVI)) OR "Transcatheter Aortic Valve Implantation" OR "Transcatheter Aortic Valve Replacement" OR "Percutaneous Aortic Valve Implantation" OR "Percutaneous Aortic Valve Replacement" OR TAVI OR TAVR OR PAVR OR ((transapical OR transventricular OR percutaneous OR transcatheter*) AND (valve* OR prosthe* OR | 258 |

| | |
|---|---|
| bioprosthe* OR valv* OR flap* OR leaflet* implant* OR repair* OR replace* OR balloon-expand* OR self-expand* OR balloon expand* OR self expand*))))) [Filters: classification=systematic-review, protocol=no, min_year=2022, max_year=2025] | |

## Appendix A2: RCTs

For both the systematic searches for RCTs in MEDLINE databases and Embase (all in Ovid) the Cochrane search filters for RCTs were applied (for MEDLINE the sensitivity- and precision-maximising version was used which is available in the Technical Supplement to the Cochrane Handbook; (Lefebvre, last updated September 2024).

The date of search for all the searches was 11 April 2025.

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions** 1946 to April 10, 2025
https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=1M0suqoLLXoSmfxIenOvYbWx3VHf2S5xhw6zXOcLn1pLWlE2NjFq7YEfWNSpNX3ID

Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | Transcatheter Aortic Valve Replacement/ or Heart Valve Prosthesis Implantation/ or Heart Valve prosthesis/ | 67033 |
| 2 | ("Transcatheter Aortic Valve Implantation" or "Transcatheter Aortic Valve Replacement" or "Percutaneous Aortic Valve Implantation" or "Percutaneous Aortic Valve Replacement").ti,ab,kf. | 17604 |
| 3 | (TAVI or TAVR or PAVR).ti,ab,kf. | 14428 |
| 4 | ((transapical or transventricular or percutaneous or transcatheter*) adj3 (valve* or prosthe* or bioprosthe* or valv* or flap* or leaflet* implant* or repair* or replace* or balloon-expand* or self-expand* or balloon expand* or self expand*)).ti,ab,kf. | 28330 |
| 5 | or/1-4 | 77927 |
| 6 | ("Myval Octacor" or "Sapien 3" or "Sapien 3 Ultra" or "ACURATE neo2" or "Allegra" or "Evolut R" or "Evolut Pro" or "Evolut FX" or "Hydra" or "Navitor" or "Trilogy").ti,ab,kf. | 4685 |

| # | Searches | Results |
|---|---|---|
| 7 | ("JenaValve" or "Abbott Medical" or "SMT" or "Medtronic" or "Biosensors" or "Boston Scientific" or "Edwards Lifesciences" or "Meril" or TAVI).ab,in,go,ci. | 76387 |
| 8 | 6 and 7 | 833 |
| 9 | 5 or 8 | 77942 |
| 10 | exp Aortic Valve Stenosis/ | 55123 |
| 11 | (aortic adj3 stenos*).ti,ab,kf. | 30639 |
| 12 | (aortic valv* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 6610 |
| 13 | (aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 1 |
| 14 | (aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 0 |
| 15 | or/10-14 | 68727 |
| 16 | 9 and 15 | 24985 |
| 17 | exp randomized controlled trial/ | 637378 |
| 18 | controlled clinical trial.pt. | 95690 |
| 19 | randomized.ab. | 686367 |
| 20 | placebo.ab. | 257366 |
| 21 | clinical trials as topic/ | 204757 |
| 22 | randomly.ab. | 456944 |
| 23 | trial.ti. | 332790 |
| 24 | or/17-23 | 1674066 |
| 25 | exp animals/ not humans/ | 5326259 |
| 26 | 24 not 25 | 1543436 |
| 27 | 16 and 26 | 1660 |
| 28 | limit 27 to yr="2022-Current" | 461 |
| 29 | limit 28 to english language | 453 |

Database(s): **Embase** 1974 to 2025 April 10

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=4XbrDXiijliaHl6gs26Tsv0zEurIcYRjNIrAKidR6IsZSK291LLON2waxC1AaLr7c

Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | transcatheter aortic valve implantation/ | 37901 |
| 2 | heart valve prosthesis/ | 22576 |
| 3 | ("Transcatheter Aortic Valve Implantation" or "Transcatheter Aortic Valve Replacement" or "Percutaneous Aortic Valve Implantation" or "Percutaneous Aortic Valve Replacement").ti,ab,kf. | 29769 |
| 4 | (TAVI or TAVR or PAVR).ti,ab,kf. | 28772 |
| 5 | ((transapical or transventricular or percutaneous or transcatheter*) adj3 (valve* or prosthe* or bioprosthe* or valv* or flap* or leaflet* implant* or repair* or replace* or balloon-expand* or self-expand* or balloon expand* or self expand*)).ti,ab,kf. | 46637 |
| 6 | or/1-5 | 77002 |
| 7 | ("Myval Octacor" or "Sapien 3" or "Sapien 3 Ultra" or "ACURATE neo2" or "Allegra" or "Evolut R" or "Evolut Pro" or "Evolut FX" or "Hydra" or "Navitor" or "Trilogy").ti,ab,kf,dv. | 11009 |
| 8 | ("JenaValve" or "Abbott Medical" or "SMT" or "Medtronic" or "Biosensors" or "Boston Scientific" or "Edwards Lifesciences" or "Meril" or TAVI).ab,mf,my,mv,dm,dv,in,tn,so,dc,de,ct. | 152439 |
| 9 | 7 and 8 | 4219 |
| 10 | 6 or 9 | 77202 |
| 11 | exp aortic valve stenosis/ | 18450 |
| 12 | (aortic adj3 stenos*).ti,ab,kf. | 48284 |
| 13 | (aortic valv* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 9038 |
| 14 | (aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 1 |
| 15 | (aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 0 |
| 16 | or/11-15 | 60558 |

| # | Searches | Results |
|---|---|---|
| 17 | 10 and 16 | 23941 |
| 18 | exp randomized controlled trial/ | 878612 |
| 19 | Controlled clinical trial/ | 445307 |
| 20 | random$.ti,ab. | 2192374 |
| 21 | randomization/ | 100555 |
| 22 | intermethod comparison/ | 313485 |
| 23 | placebo.ti,ab. | 391365 |
| 24 | (compare or compared or comparison).ti. | 648346 |
| 25 | ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. | 3115469 |
| 26 | (open adj label).ti,ab. | 123129 |
| 27 | ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. | 293155 |
| 28 | double blind procedure/ | 230782 |
| 29 | parallel group$1.ti,ab. | 35283 |
| 30 | (crossover or cross over).ti,ab. | 133329 |
| 31 | ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. | 456483 |
| 32 | (assigned or allocated).ti,ab. | 539855 |
| 33 | (controlled adj7 (study or design or trial)).ti,ab. | 500518 |
| 34 | (volunteer or volunteers).ti,ab. | 297176 |
| 35 | human experiment/ | 688037 |
| 36 | trial.ti. | 453947 |
| 37 | or/18-36 | 6943251 |
| 38 | (random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) | 10384 |
| 39 | Cross-sectional study/ not (exp randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.) | 436123 |

| # | Searches | Results |
|---|---|---|
| 40 | (((case adj control$) and random$) not randomi?ed controlled).ti,ab. | 23443 |
| 41 | Systematic review.ti,ab. not (trial or study).ti. | 396734 |
| 42 | (nonrandom$ not random$).ti,ab. | 20111 |
| 43 | "random field$".ti,ab. | 3141 |
| 44 | (random cluster adj3 sampl$).ti,ab. | 1743 |
| 45 | (review.ab. and review.pt.) not trial.ti. | 1273817 |
| 46 | "we searched".ab. and (review.ti. or review.pt.) | 57496 |
| 47 | "update review".ab. | 153 |
| 48 | (databases adj4 searched).ab. | 75399 |
| 49 | (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/ | 1295594 |
| 50 | Animal experiment/ not (human experiment/ or human/) | 2730695 |
| 51 | or/38-50 | 4829916 |
| 52 | 37 not 51 | 6081699 |
| 53 | 17 and 52 | 6030 |
| 54 | limit 53 to yr="2022-Current" | 1522 |
| 55 | limit 54 to english language | 1496 |

Cochrane Library (CENTRAL) Issue 3, 2025
https://www.cochranelibrary.com/advanced-search/search-manager?search=7673246

| # | Searches | Results |
|---|---|---|
| 1 | MeSH descriptor: [Transcatheter Aortic Valve Replacement] this term only | 517 |
| 2 | MeSH descriptor: [Heart Valve Prosthesis Implantation] explode all trees | 1455 |
| 3 | MeSH descriptor: [Heart Valve Prosthesis] this term only | 846 |
| 4 | ("Transcatheter Aortic Valve Implantation" or "Transcatheter Aortic Valve Replacement" or "Percutaneous Aortic Valve Implantation" OR "Percutaneous Aortic Valve Replacement"):ti,ab,kw | 1331 |
| 5 | (TAVI OR TAVR OR PAVR):ti,ab,kw | 1282 |
| 6 | ((transapical or transventricular or percutaneous or transcatheter*) NEAR/3 (valve* or prosthe* or bioprosthe* or valv* or flap* or leaflet* implant* or repair* or replace* or balloon-expand* or self-expand* or balloon expand* or self expand*)):ti,ab,kw | 2336 |
| 7 | {OR #1-#6} | 3603 |
| 8 | (("Myval Octacor" or "Sapien 3" or "Sapien 3 Ultra" or "ACURATE neo2" or "Allegra" or "Evolut R" or "Evolut Pro" or "Evolut FX" or "Hydra" or "Navitor" or "Trilogy")):ti,ab,kw | 366 |
| 9 | (("JenaValve" or "Abbott Medical" or "SMT" or "Medtronic" or "Biosensors" or "Boston Scientific" or "Edwards Lifesciences" or "Meril" or TAVI)) | 4889 |
| 10 | #8 AND #9 | 97 |
| 11 | #7 OR #10 | 3607 |
| 12 | MeSH descriptor: [Aortic Valve Stenosis] explode all trees | 1609 |
| 13 | ((aortic NEAR/3 stenos*)):ti,ab,kw | 2093 |
| 14 | ((aortic valv* NEAR (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*))):ti,ab,kw | 1434 |
| 15 | ((aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*))):ti,ab,kw | 0 |
| 16 | ((aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*))):ti,ab,kw | 0 |
| 17 | {OR #12-#16} | 3292 |

| # | Searches | Results |
|---|---|---|
| 18 | #11 AND #17 with Cochrane Library publication date Between Jan 2022 and Apr 2025, in Trials | 397 |

## Appendix A3: Non-RCTs for ACURATE neo2, Allegra, Hydra, Navitor, and Trilogy

For the systematic searches (in MEDLINE and Embase) for non-RCTs no study design filters were applied.

All searches were performed on 9 May 2025.

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions** 1946 to May 08, 2025
https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=3WWbiEONZ7yngKfLQQXsoNR1DCXUZfAEBIzBsqc1334Zv5dy6gW2CJmNdPB6LftUn

Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | ("ACURATE neo2" or "Allegra" or "Hydra" or "Navitor" or "Trilogy").af. | 7140 |
| 2 | ("JenaValve" or "Abbott Medical" or "SMT" or "Biosensors" or "Boston Scientific").ab,in,go,ci. | 49325 |
| 3 | 1 and 2 | 86 |
| 4 | exp Aortic Valve Stenosis/ | 55366 |
| 5 | (aortic adj3 stenos*).ti,ab,kf. | 30865 |
| 6 | (aortic valv* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 6650 |
| 7 | (aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 1 |
| 8 | (aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 0 |
| 9 | or/4-8 | 69094 |
| 10 | 3 and 9 | 55 |
| 11 | exp animals/ not humans/ | 5342279 |

| | | |
|---|---|---|
| 12 | (letter or newspaper article or editorial or case report or case study).pt. | 2035720 |
| 13 | 10 not (11 or 12) | 54 |
| 14 | limit 13 to yr="2022-Current" | 48 |
| 15 | limit 14 to english language | 48 |

Database(s): **Embase** 1974 to 2025 May 08

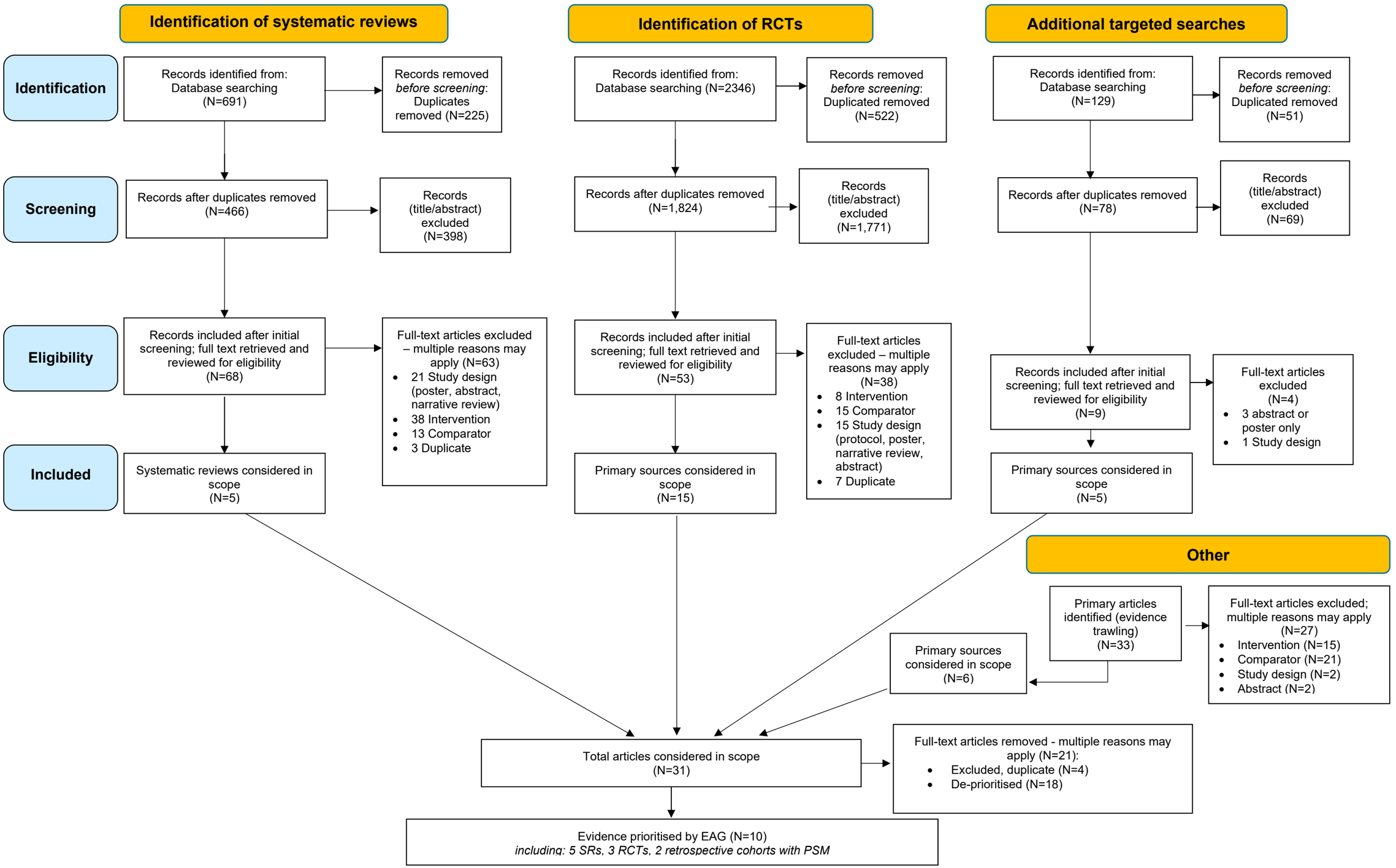
https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=6Z23UHO2uVVD8P9W0RsVGjO5qVC5Q0yTVOBR9XKQmwNovUlDLYxSIUUstGUOsEYNI

Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | ("ACURATE neo2" or "Allegra" or "Hydra" or "Navitor" or "Trilogy").af. | 11330 |
| 2 | ("JenaValve" or "Abbott Medical" or "SMT" or "Biosensors" or "Boston Scientific").ab,mf,my,mv,dm,dv,in,tn,so,dc,de,ct. | 79999 |
| 3 | 1 and 2 | 305 |
| 4 | exp aortic valve stenosis/ | 18546 |
| 5 | (aortic adj3 stenos*).ti,ab,kf. | 48607 |
| 6 | (aortic valv* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 9082 |
| 7 | (aortic leaflet* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 1 |
| 8 | (aortic flap* adj (disease* or disorder* or fail* or dysfunction* or insufficien* or damage* or leak*)).ti,ab,kf. | 0 |
| 9 | or/4-8 | 60929 |
| 10 | 3 and 9 | 109 |
| 11 | exp animal/ not human/ | 5904647 |
| 12 | (letter or newspaper article or editorial or case report or case study).pt. | 2193577 |

| | | |
|---|---|---|
| 13 | 10 not (11 or 12) | 103 |
| 14 | limit 13 to yr="2022-Current" | 82 |
| 15 | limit 14 to english language | 81 |

## Appendix B – PRISMA diagram



## Appendix C – Excluded studies (N=124)

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| **1.** | Abdel-Wahab (JACC Cardiovasc Interv, 2020; 1071-1082) | RCT (CHOICE) | Intervention: Sapien XT (earlier version of TAVI device made by Edwards)<br>Comparator: CoreValve (earlier version of TAVI device made by Medtronic) |
| **2.** | Abdel-Wahab (JAMA, 2014; 1503-1514) | RCT (CHOICE) | Intervention: Sapien XT (earlier version of TAVI device made by Edwards)<br>Comparator: CoreValve (earlier version of TAVI device made by Medtronic) |
| **3.** | Abdulelah (Circulation, 2024; Supp1_4146666) | | Abstract |
| **4.** | Abu Rmilah (Heart Rhythm O2, 2022; 385-392) | SR and MA | Intervention/Comparator: Included CoreValve, Sapien, Lotus (valve out of scope) |
| **5.** | Adnan (JACC, 2024; B394) | | Abstract |
| **6.** | Aggarwal (Cardiovasc Revascul Med, 2023; S105) | Meta analysis | Abstract<br>Comparator: ACURATE neo (earlier version of TAVI device made by Boston Scientific) |
| **7.** | Ahmed (Int J Cardiol Heart Vasc, 2024; 101542) | SR | Intervention: Included valves out of scope (e.g. Sapien XT, Symetis, CoreValve) |
| **8.** | Akkawi (JACC, 2024; B396) | | Abstract |
| **9.** | Albalbissi (JACC, 2025; Supp 12_1124) | | Poster |
| **10.** | Antonio-Baz (Structural Heart, 2025; 100391) | Pre-market prospective study<br>(EMPIRE I) | Study design: single arm |
| **11.** | Asch (Circulation, 2018: 2557-2567) | RCT (REPRISE III) | Intervention: Lotus<br>Comparator: CoreValve (earlier version of TAVI device made by Medtronic) |
| **12.** | Balda (JACC, 2025; Supp 12_2309) | | Poster |
| **13.** | Bansal (Am J Cardiol, 2023; 88-97) | SR and MA | Intervention: Evolut |
| **14.** | Baudo (Cardiovasc Interv Ther, 2025; online) | SR and MA | Intervention: BEV (included: Sapien XT/3/3 Ultra)<br>Comparator: SEV (included: CoreValve, Evolut R/Pro/Pro+/FX/ACURATE neo/neo2/Portico) |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| **15.** | Baudo (Am J Cardiol, 2024; 9-18) | Retrospective observational with PSM | Intervention: SEV (included Evolut Pro 46.8%; older version) |
| **16.** | Baumbach (Lancet, 2024; 2695–708) addendum | Addendum (correction of spelling author name) | Duplicate |
| **17.** | Bhogal (Int J Cardiology, 2024) | Combined RCTs | Comparator: Mixture of CoreValve, Evolut R, Evolut Pro |
| **18.** | Boissonnet (Value Health Reg Issues, 2022; 148-160) | SR and MA | Intervention: Valves not specified |
| **19.** | Carabetta (Int J Cardiol, 2024; 131572) | SR | Comparator: Valves out of scope (e.g. ACURATE neo) |
| **20.** | Castro-Mejia (Int J Cardiol, 2022; 128-136) | Non-randomised (registry) | Comparator: Portico, Evolut R/Pro, ACURATE neo included old versions or mixture with old versions. Could consider as single arm (Allegra n=60), however larger single arm evidence available (Gonzalez et al. 2024). |
| **21.** | De Michele (Eu Heart J, 2023; Supp D_D157)_abstract | | Abstract |
| **22.** | Demir (J Invasive Cardiol, 2022; E226-E236) | SR and MA | Intervention: Valves not specified<br>Comparator: SAVR |
| **23.** | Di Pietro (Am J Cardiol, 2024; 1-12) | SR and MA | Intervention/Comparator: SEV vs BEV; includes older versions (CoreValve, Sapien XT, Evolut Pro, ACURATE neo, Portico, Engager) |
| **24.** | Diaz (Cardiovasc Interv Ther, 2022; 167-181) | SR and MA | Intervention: Valves not specified |
| **25.** | Diegoli (Arq Bras Cardiol, 2023; e20220701) | SR and MA | Comparator: SAVR |
| **26.** | Dogosh (J Clin Med, 2022; 5299) | SR and MA | Comparator: SAVR |
| **27.** | Eckel (J. Clin. Med., 2023; 3999) | Retrospective observational | Comparator: Portico |
| **28.** | Eikelboom (Current Opinion in Cardiology, 2022; 173-179) | Review | Study design: Narrative review |
| **29.** | El Amrawy (JACC: Cardiovascular Inter, 2025; S96) | Cohort [Abstract only] | Available as abstract only (limited information)<br>Comparator: no comparison of TAVI devices (mixed intervention arm |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| | | | including Evolut R and ACURATE neo2) |
| **30.** | Elkholy (JACC, 2024; B396) | SR | Abstract |
| **31.** | Elnaggar (REC Interv Cardiol. 2023; 5(2):94–101) | RCT | Comparator: Evolut Pro (out of scope) |
| **32.** | Elseidy (JACC, 2024; B393), supplement | Meta-analysis (Abstract only) | Abstract: Available as abstract only (limited information) |
| **33.** | Feldman (JAMA, 2018; 27-37) | RCT (REPRISE III) | Intervention: Lotus<br>Comparator: CoreValve/Evolut R mixture (that is including earlier version of TAVI device made by Medtronic) |
| **34.** | Fernades (Cardiol Rev, 2022; 318-323) | SR | Comparator: Combined single arm |
| **35.** | Fundación EPIC (NCT, 2025; NCT06049654) | | Trial Protocol |
| **36.** | Gallo (Eur J Cardiothorac Surg, 2022; 967-976) | SR | Intervention: Not comparison of valves (combining case reports, series to determine outcome of TAVI-in-TAVI procedures) |
| **37.** | Généreux (AHJ, 2024; 94-104) | RCT (EARLY TAVR) | Comparator: Clinical surveillance (Intervention was: Sapien 3/Sapien 3 Ultra) |
| **38.** | Giacobbe (Eur Heart J Qual Care Clin Outcomes, 2025; 1-15) | SR and MA | Intervention: Included valves out of scope (Sapien XT, ACURATE neo, Evolut Pro, CoreValve) |
| **39.** | Gonzalez (J Am Coll Cardiol, 2024; B373) | European registry (ALLOW) | Abstract: limited information |
| **40.** | Goulden (Cardiol Rev, 2024; online) | SR | Intervention: Device unspecified |
| **41.** | Gozdek (J Clin Med, 2020; 397) | SR and MA | Intervention: ACURATE neo (predecessor to ACURATE neo2) |
| **42.** | Gozdek (Int J Environ Res Public Health, 2023; 3439) | SR and MA | Comparator: Evolut Pro |
| **43.** | Groberio (Eu Heart J, 2024; Supp 1) | | Abstract<br>Comparator: SAVR |
| **44.** | Grubb (Eurointervention, 2023) | N/A | Study design: Virtual implantation of Sapien 3 using CT scans of patients having Evolut TAVI. |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| **45.** | Hiltner (medRxiv, 2022; no page) | | Comparator: Indirect comparison via SAVR [note: already considered in original EAG report (July, 2024) |
| **46.** | Hiltner(JACC, 2022; Supp S_61)_abstract | | Abstract |
| **47.** | Hori (Journal of Artifcial Organs, 2024; 23–31) | Retrospective cohort | Comparator: Inspiris, Intuity, Perceval, Evolut |
| **48.** | Hosseinpour (Am J Cardiol, 2023; 257-267) | SR and MA | Intervention: Device unspecified (searches included Sapien XT/Sapien 3/CoreValve/Evolut R/Pro/Pro+/Portico/Engager/ACURATE) |
| **49.** | Ivanov (Perfusion, 2023, 115-123) | Retrospective cohort, Propensity score matched | Intervention: CoreValve<br>Comparator: ACURATE neo (earlier version of TAVI device made by Boston Scientific) |
| **50.** | Jacquemyn (Cardiol Clin, 2024; 373-387) | SR and MA | Intervention/Comparator: SEV vs BEV; Includes older versions (Sapien XT, CoreValve, Evolut Pro, ACURATE neo, Portico) |
| **51.** | Jain (Circulation, 2024; Supp1_A4136704) | | Abstract |
| **52.** | Jammoul (American Heart Journal, 2024; 13-22) | RCT (DIRCTAVI) | Comparator: Sapien 3 with or without prior balloon aortic valvuloplasty |
| **53.** | Khalefa (Cardiol Rev, 2024; online) | SR and MA | Intervention: included valves out of scope (e.g. Sapien XT, CoreValve, Portico, ACURATE neo, Evolut Pro, Engager) |
| **54.** | Khan (Ann Med Surg (Lond), 2024; 4060-4074) | SR and MA | Intervention/Comparator: Devices not named |
| **55.** | Kim (Circulation. 2021;143(12):1267–9) | RCT [SCOPEI] | Comparator: ACURATE neo (out of scope) |
| **56.** | Kooistra (Neth Heart J, 2020; 253-265) | RCT (ELECT) | Comparator: CoreValve (earlier version of TAVI device made by Medtronic) |
| **57.** | Kornyeva (Front Cardiovasc Med, 2023; 1175246) | Retrospective cohort, database with propensity score matching | Intervention: SEV included Evolut R, Evolut Pro, Portico, ACURATE neo2.<br>Comparator: BEV not explicitly reported. |
| **58.** | Ktenopoulos (Eu Heart J, 2024; Supp 1_no page)_abstract | | Abstract<br>Intervention: Device unspecified |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| **59.** | Kühne (Open Heart, 2025; e003110) | SR and MA | Intervention: Device unspecified |
| **60.** | Lanz (Lancet, 2019; 1619-1628) | RCT (SCOPE I) | Intervention: ACURATE neo (earlier version of TAVI device made by Boston Scientific) |
| **61.** | Lanz (Circulation Cardiovascular Interventions, 2023) | RCT | Intervention: ACURATE neo (earlier version of TAVI device made by Boston Scientific) |
| **62.** | Linke (Catheter Cardiovasc Interv, 2017; 1016-1026) | RCT (BRAVO-3) | Intervention: mixture of Sapien XT (earlier version of TAVI device made by Edwards) and Sapien 3<br>Comparator: mixture of CoreValve (earlier version of TAVI device made by Medtronic), Evolut R, Portico, Lotus, Symetis ACURATE neo, Direct Flow |
| **63.** | Liu (ESC Heart Fail, 2024; 3488-3500) | SR and MA | Population: Aortic regurgitation (not aortic stenosis) |
| **64.** | Magro (Interactive Cardiovas Thora Surgery, 2022) | SR | Comparator: SAVR |
| **65.** | Makkar (Lancet, 2020; 669-683) | RCT (PORTICO IDE) | Intervention: Portico (earlier version of TAVI device made by Abbott)<br>Comparator: Mixture and includes devices in Final Scope and older generation of TAVI devices made by Edwards and Medtronic (intra-annular balloon-expandable SAPIEN, SAPIEN XT, or SAPIEN 3 valve; or a supra-annular self-expanding CoreValve, Evolut-R, or Evolut-PRO valve) |
| **66.** | Montenegro-Palacios (J Cardiovasc Dev Dis, 2025; 90) | SR and MA | Intervention: Includes CoreValve, Sapien, Sapien XT, Not specified. |
| **67.** | Moroni (J Am Heart Assoc, 2022; e024707) | SR and MA | Intervention: Includes Lotus, Evolut Pro, Portico |
| **68.** | Munguti (Cardiovasc revasc med, 2024; 8-13) | SR, Observational | Intervention/comparator: Not comparison of TAVI devices/ transcarotid versus transthoracic TAVI |
| **69.** | Musallam et al. 2022; Cardiovasc Revasc Med; 1-7 | Retrospective cohort | Intervention/Comparator: Not comparison of TAVI devices |
| **70.** | Nuche (JACC, 2024; B228) | | Abstract/Poster: limited information |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| **71.** | Nuche (JACC, 2024; B384) | | Abstract/Poster: limited information |
| **72.** | O'Hair (JAMA Cardiol, 2023; 111-119) | RCT (pooled data from SURTAVI and CoreValve US High Risk Pivotal trial) | Intervention: CoreValve/ Evolut R<br>Comparator: SAVR |
| **73.** | Olivas Medina (Eur Heart J, 2024; Suppl1) | Prospective cohort | Abstract/Poster: limited information |
| **74.** | Oliveira (Circulation, 2024; Supp1_4147118)_abstract | | Abstract |
| **75.** | Parker (Annals of translational medicine, 2025; 6) | SR | Study Design: not comparison of TAVI devices, but reporting outcomes in patients with hypertropic cardiomyopathy undergoing TAVI<br>Intervention: included older valves (Sapien, CoreValve) and valve type not reported in 4 cases. |
| **76.** | Passos (Circulation, 2024; Supp1_4147872)_abstract | | Abstract |
| **77.** | Pellegrini (EuroIntervention, 2023, e1077-e1087) | RCT (SCOPE 2) | Intervention: ACURATE neo (earlier version of TAVI device made by Boston Scientific)<br>Comparator: CoreValve Evolut (earlier version of TAVI device made by Medtronic) |
| **78.** | Pollock (J Cardiovasc Nurs, 2024; E126-E135) | SR | Study Design: not comparison of TAVI devices, but reporting changes in quality of life<br>Intervention: Device unspecified |
| **79.** | Portilho (JACC, 2025; Supp 12_1138) | | Poster |
| **80.** | Radhakrishnan (Can J Diabetes, 2023; S19-S20) | Combination of RCTs | Abstract<br>Comparator: SAVR |
| **81.** | Rao, (Struct Heart, 2024; 100392) | SR and MA | Intervention: Device unspecified; however included mechanically-expandable valves (MEV) |
| **82.** | Reardon (JACC Cardiovasc Intervent, 2023; 681-689) | Prospective observational (single arm) (PORTICO-NG) | Comparator: none (single arm)<br>[Note 30-day outcomes reported, longer outcomes reported by Sondergaard et al. 2023] |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| **83.** | Reardon (JAMA Cardiol, 2019; 223-229) | RCT (REPRISE III) | Intervention: Lotus<br>Comparator: CoreValve (earlier version of TAVI device made by Medtronic) |
| **84.** | Rivera (Rev Cardiovasc Med, 2023; 79) | SR and MA | Study design: Not comparison of valves.<br>Intervention: included Sapien XT, Sapien, CoreValve, Lotus, J-Valve, Venus A, TaurusOne, VitaFlow, ACURATE neo, |
| **85.** | Robert (Catheter Cardiovasc Interv, 2024; 97-104) | RCT | Intervention: Not comparison of TAVI devices/ comparison of balloon predilation and no balloon predilation |
| **86.** | Sá (Am J Cardiol, 2023; 120-127) | SR and MA | Intervention: Included Sapien, Sapien XT<br>Comparator: Included CoreValve, Evolut |
| **87.** | Sá (Trends Cardiovasc Med, 2023; 458-467) | SR and MA | Study design: Not comparison of valves (late outcomes in bicuspid versus tricuspid) |
| **88.** | Saeed Al-Asad (Am J Cardiol, 2023; 105-112) | SR and MA | Study design: Not comparison of valves (late outcomes in bicuspid versus tricuspid) |
| **89.** | Salah (Curr Probl Cardiol, 2023; 101155) | SR and MA | Intervention: Device unspecified |
| **90.** | Samimi (JACC, 2025; Supp 12_2290) | | Poster |
| **91.** | Sattar (Curr Probl Cardiol, 2023; 101467) | SR and MA | Study design: Comparison of newer versus older generation<br>Intervention/Comparator: Includes Lotus, CoreValve, Sapien/Sapien XT, Symetis, ACURATE neo, ACURATE, DFM, Portico |
| **92.** | Scardini (Circulation, 2024; Supp1_4145313)_abstract | | Abstract |
| **93.** | Senguttuvan (Front Cardiovasc Med, 2023; 1130354) | SR and MA | Intervention: Included Sapien, Sapien XT, CoreValve, Evolut Pro, Portico (comparison of BEV and SEV) |
| **94.** | Serruys (JACC, 2025; S87) | | Abstract |
| **95.** | Sherbini (JACC, 2025; Supp A_1095)_poster | | Poster |
| **96.** | Shi (Front Cardiovasc Med, 2023; 1170979) | SR and MA | Study design: Not comparison of valves<br>Intervention: Included Sapien, Sapien |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| | | | XT, CoreValve, Venus A, VitaFlow, Taurus One, Lotus, Lotus Edge, ACURATE neo, Portico, Centera, Evolut Pro, JenaValve, Engager, Symetis, |
| **97.** | Siddiqui (Circulation, 2024; Supp1_4139940)_abstract | | Abstract |
| **98.** | Smiths (JACC, 2024; B33) | | Abstract |
| **99.** | Smiths (JACC, 2024; B386) | | Abstract |
| **100.** | Stachel (Int J Cardiovascular Imaging, 2022, 2469) | RCT (SOLVE-TAVI) | Comparator: not comparison of TAVI devices/ looking for predictors of paravalvular leak (using data from SOLVE-TAVI trial) |
| **101.** | Sondergaard (EuroIntervention. 2023; 248-255) | Prospective observational, single arm (PORTICO-NG) | Comparator: none (single arm)<br>[Note: 1-year outcomes reported] |
| **102.** | Sultan (Structural Heart, 2024; 100293) | Cohort, single arm (NAVITOR-IDE) | Comparator: none (single arm) |
| **103.** | Tamburino (Circulation, 2020: 2431-2442) | RCT (SCOPE 2) | Intervention: ACURATE neo (earlier version of TAVI device made by Boston Scientific)<br>Comparator: CoreValve Evolut (earlier version of TAVI device made by Medtronic) |
| **104.** | Tamm (JACC Cardiovasc Interv, 2025; 60-68) | Retrospective observational (single arm) | Comparator: none (single arm) |
| **105.** | Tchétché (Jama Cardiol, 2024) | RCT | Comparator: SAVR |
| **106.** | Thiele (Circulation, 2020b; 1437-1447) | RCT (SOLVE-TAVI) | Intervention/Comparator: Comparison of anaesthesia type: conscious sedation vs. general anaesthesia (no focus on comparison of devices) |
| **107.** | Thyregod (Eur Heart J, 2024; 1116-1124) | RCT | Intervention: CoreValve (not in scope)<br>Comparator: SAVR |
| **108.** | Tobe (JACC, 2023; B294) | | Abstract |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| **109.** | Tobe (JACC: Cardiovascular Interventions, 2025; S88) | | Abstract |
| **110.** | Tobe (JACC: Cardiovascular Interventions, 2025; S95) | | Abstract |
| **111.** | Tobe (Struct Heart J, 2024; 100277) | Narrative review | Study design: narrative review |
| **112.** | Tobe (JACC, 2023; 17_supplement) | Narrative review [Abstract only] | Abstract |
| **113.** | Samimi (JACC, 2025) | SR | Conference Poster (no full manuscript available) |
| **114.** | Waksman (JACC Cardiovasc Intervention, 2025) | Editorial comment | Study design: Editorial |
| **115.** | Wang (Front Cardiovasc Med, 2025; 1479200) | SR and MA | Comparator: SAVR |
| **116.** | Wei (AsiaIntervention, 2024; 110-118) | SR | Intervention: Included Venus A-Valve, VitaFlow, Taurus One. |
| **117.** | Wenz et al. (JACC, 2025; 893) | Retrospective cohort | Intervention: Sapien 3 Ultra Resilia |
| **118.** | Wienemann (Hellenic Journal of Cardiology, 2023; 1) | Propensity score matched | Comparator: three-armed comparison of Evolut R, Evolut Pro and ACURATE neo (older version). |
| **119.** | Wilczek (Adv Interv Cardiol, 2023; 359–366) | Retrospective cohort | Comparator: Comparison for valve size |
| **120.** | Yakubov (JACC, 2025, 1419-1430) | RCT (pooled data from SURTAVI and CoreValve US High Risk Pivotal trial) | Intervention: CoreValve/Evolut R<br>Comparator: SAVR |
| **121.** | Yasmin (Curr Probl Cardiol, 2023; 101428) | SR and MA | Intervention: Device unspecified |
| **122.** | Yokoyama (J Cardiol, 2023; 1-7) | SR and MA | Study design: not comparison of TAVI devices<br>Intervention: Device unspecified |
| **123.** | Zhang (Front Cardiovasc Med, 2022; 794850) | SR and MA | Intervention: Device unspecified but included Sapien, Sapien XT, CoreValve, Venus A-Valve, Lotus, Evolut Pro, Portico, ACURATE neo |

| # | Study | Study design (study name) | Reason(s) for exclusion |
|---|---|---|---|
| | | | (included comparison of BEV versus SEV, older versus newer generation). |
| **124.** | Zreigh (JACC, 2025; Supp 12_931) | | Poster |

Abbreviations: MA, meta-analysis; N/A, not applicable; RCT, randomised controlled trial; SAVR, surgical aortic valve replacement; SR, systematic review

## Appendix D – In scope but not prioritised (N=18)

| # | Study | Study design (study name) | TAVI device (n, patients) | Reason(s) for lower prioritisation |
|---|---|---|---|---|
| **1.** | Abdelghani (JACC Cardiovasc Interv, 2018; 2507-2518) | Prospective cohort; no matching (CHOICE-Extend registry) | Evolut R (n=44)<br>Sapien 3 (n=78)<br>In small aortic annulus population | Herrmann et al. is an RCT comparing Sapien and Evolut families in small aortic annulus population (n=715); considered in the original report. |
| **2.** | Baumbach (Lancet, 2024: 2695-2708) [NCT04275726] | RCT (non-inferiority) [LANDMARK] | Myval (n=384 randomised, included 336 Myval and 32 Myval octacor)<br>Contemporary valves (n=384 randomised, included 108 Sapien 3 / 87 Sapien 3 Ultra / 71 Evolut R / 10 Evolut Pro+ / 5 Evolut FX | Larger RCT with higher proportion of Myval Octacor (valve in scope) included (Terkelsen et al. 2024). |
| **3.** | Chiabrando (Minerva Cardiology and Angiology, 2024; 435-444) | Retrospective case review | Accurate neo2 (n=65); Evolut R/Pro/Sapien/ Myval combined (n=49) | De-prioritised, other studies with propensity score matching included, and non-mixed comparator group have been included. |
| **4.** | Costa (EuroIntervention, 2024; 95-103) | Retrospective observational with PSM | Sapien 3 Ultra (n=587)<br>Evolut R/Pro combined (n=587) | Randomised evidence is available comparing Sapien 3/3 Ultra and Evolut R/Pro/Pro+ (Nuche et al. 2023; Rodes-Cabau et al. 2022) |
| **5.** | Eckel (Circ Cardiov Interv, 2024; e013608) | Retrospective cohort with PSM | Sapien 3 Ultra (n=219); ACURATE neo2 (n=219) | Number of patients lower and shorter follow up than Kim (JACC, 2025, 32-40) |
| **6.** | Eckel (Cathet Cardio Intervent, 2024; 591-599) | Retrospective cohort with PSM | Sapien 3 Ultra (n=246 matched)<br>ACURATE neo2 (n=246 matched) | Number of patients lower than Kim (JACC, 2025; 32-40) |
| **7.** | Farhan (EuroIntervention, 2022; 759) [NCT02737150] | RCT [SOLVE-TAVI] | Sapien 3 (n=208)<br>Evolut R (n=208) | Short follow-up 30-days, longer follow-up from same trial reported in Feistritzer et al. 2025 |
| **8.** | Feistritzer (J Am Coll Cardiol, 2021; 2204-2215) [NCT02737150] | RCT 2x2 factorial design (SOLVE-TAVI) | Sapien 3 (n=219)<br>Evolut R (n=219) | Longer follow-up reported in Feistritzer et al. 2025; 5-years] |
| **9.** | Hase (Catheter Cardiovasc Interv, 2021; E875-86) | Propensity score matched (OCEAN-TAVI registry) | Evolut R (n=69),<br>Sapien 3 (n=69) in small aortic annulus population. | Herrmann et al. is an RCT comparing Sapien and Evolut families in small aortic annulus population (n=715); considered in the original report. |
| **10.** | Herrmann (NEJM, 2024) | RCT (non-inferiority) | Evolut R/Pro/Pro+/FX<br>Sapien 3/3 Ultra | Considered in the original report; both intervention and comparator arms are mixed (difficult to attribute outcomes to specific model). |

| # | Study | Study design (study name) | TAVI device (n, patients) | Reason(s) for lower prioritisation |
|---|---|---|---|---|
| **11.** | Kalogeras (J Am Heart Assoc, 2023; e028038) | Retrospective cohort | Sapien 3/3 Ultra combined (n=756, 139 propensity score matched)<br>Evolut R/Pro combined (n=917; 139 propensity score matched) | Randomised evidence available comparing Sapien 3 and Evolut R |
| **12.** | Moscarella et al. 2022; Int J Cardiol. 2022; 31–38 | Retrospective cohort | Sapien 3 (n=203);<br>Evolut R/Pro combined (n=88) | Randomised evidence is available comparing Sapien 3 and Evolut R which did not have a mixed comparator group (e.g. Feistritzer et al. 2025) |
| **13.** | Ochiai (JACC Cardiovasc Interv, 2023; 1192-1204) | Observational | Sapien 3 (n=258); Evolut R/Pro/Pro+ (n=160) | Randomised evidence is available comparing Sapien 3 and Evolut R which did not have a mixed comparator group (e.g. Feistritzer et al. 2025) |
| **14.** | Pellegrini et al. 2023, EuroIntervention; 987-995 | Retrospective with PSM | ACURATE neo2 (n=472 matched)<br>Sapien 3 Ultra (n=472 matched) | Number of patients lower and length of follow-up shorter than that reported by Kim et al. 2025. |
| **15.** | Rodes-Cabau (JACC, 2022, 681-693) [NCT03520101] | RCT | Sapien 3/3 Ultra (n=49); Evolut R/Pro/Pro+ (n=53) | Short follow-up 30-days, longer follow-up from same trial reported in Nuche et al. 2023 |
| **16.** | Santos-Martinez (Int J Cardiol, 2022; 25-31) | Non-randomised comparative analysis of the European TAVI Registry | Myval (n=135),<br>Allegra (n=103)<br>Evolut R/Pro (n=298)<br>ACURATE neo (n=180)<br>Sapien 3 (n=290)<br>Portico (n=125) | Considered in the original report; |
| **17.** | Scotti (JACC Cardiovasc Interv, 2024; 681-692) | Propensity score matched | Sapien Ultra; assumed to be Sapien 3 Ultra (n=251);<br>Evolut Pro/Pro+ (n=251; 16.3% pro+) | Number of patients lower than Costa et al. 2024; 95-103 |
| **18.** | Van Royen (EuroIntervention, 2024; e1-e14) [NCT04275726] | Substudy of RCT (non-inferiority) [LANDMARK] | Myval (n=384 randomised, included 336 Myval and 32 Myval Octacor)<br>Contemporary valves (n=384 randomised, included Sapien 3/Sapien 3 Ultra/Evolut R/Evolut Pro+/Evolut FX) | Larger RCT with higher proportion of Myval Octacor (valve in scope) included (Terkelsen et al. 2024).<br><br>Substudy of LANDMARK (see Baumbach et al. 2024) |

Abbreviations: PSM, propensity score matched; RCT, randomised controlled trial

## Appendix E – Study characteristics of included primary evidence (N=5)

| # | Author (year); Funding | Design and intervention(s) | Participants and Setting | Outcomes | EAG comments |
|---|---|---|---|---|---|
| **1.** | Feistritzer (JACC, 2025)<br><br>*Funding:* German Heart Research Foundation and Helios Health Institute,<br><br>*Declaration of interests:* None | RCT (Follow up of SOLVE-TAVI after 5 years) open-label; 2 x 2 factorial design (SEV or BEV as well as conscious sedation or general anaesthesia).<br><br>*Intervention:* Sapien 3 (n=219)<br><br>*Comparator*: Evolut R (n=219) | *Inclusion:*<br>Patients with severe symptomatic aortic valve stenosis, age ≥75 years, and at intermediate- to high risk for conventional surgical aortic valve replacement were eligible for enrolment (i.e. logistic European System for Cardiac Operative Risk Evaluation ≥20% or Society of Thoracic Surgeons risk score ≥10% or other high-risk criteria by heart team consensus). A native aortic valve annulus appropriate for the available valve sizes and suitability for transfemoral vascular access were also required.<br><br>*Exclusion*:<br>Contraindication for a specific mode of anaesthesia or the TAVR procedure; clear patient-specific clinical reasons to prefer one form of anaesthesia over the other; cardiogenic shock or hemodynamic instability; history of or active endocarditis; active infection requiring antibiotic treatment; life expectancy <12 months; active peptic ulcer or upper gastrointestinal bleeding <3 months; hypersensitivity or contraindication to aspirin, heparin, or clopidogrel; and participation in another trial.<br><br>*Setting:* Germany (N=7)<br><br>*Recruitment period:* NR (April 2016 and April 2018?)<br><br>*Follow-up:* 5 years | *Primary outcomes:*<br>- For valve-related comparison, a combination of all-cause mortality, stroke, moderate or severe paravalvular leakage (PVL), and permanent pacemaker implantation (PPI).<br>- For anesthesia comparison, a combined endpoint including all-cause mortality, stroke, myocardial infarction, and acute kidney injury was used.<br><br>*Secondary outcomes:*<br>- Individual components of the combined endpoints, myocardial infarction, valve-related long-term clinical efficacy according to the predefined Valve Academic Research Consortium (VARC)-2 criteria, and quality of life using the EuroQol-5 questionnaire. Grading of PVL was done semi-quantitatively by estimating the jet size in relation to the circumference of the valve stent (<10% mild, 10%-20% moderate, >20% severe) | Authors state a number of limitations:<br>-Trial was a priori powered for equivalence of the primary composite endpoint (all-cause mortality, stroke, moderate to severe prosthetic valve regurgitation, and permanent pacemaker implant) at 30 days.<br>-Echocardiographic data at 5 years were available in only a small proportion of patients limiting the analysis of structural valve deterioration.<br>-The use of cerebral embolic protection devices was not systematically assessed in the SOLVE-TAVI trial. Therefore, it could not be analyzed whether differences in stroke rates between the SEV and BEV groups were related to different use of cerebral embolic protection devices.<br>-Differences in valve-related outcomes could have been affected by learning curve.<br><br>Additional study characteristics reported in Thiele et al. 2020a, Thiele et al. 2020b and Farhan et al. 2022 |
| **2.** | Kim (JACC, 2025, 32-40)<br><br>*Funding/ Declaration of interests:* Authors report relations with Abbott, Boston Scientific, Edwards Lifesciences, Meril Life Sciences, Shockwave, HID Imaging, CytoSorbents, Getinge, AstraZeneca, SIS Medical, Translumina, Eli Lilly, Biotronik, OrbusNeich. | Retrospective non-randomised cohort with PSM<br><br>*Intervention:* Sapien 3 Ultra (n=702)<br><br>*Comparator*: Accurate neo2 (n=702) | *Inclusion:*<br>Patients undergoing transfemoral TAVR for severe, native aortic stenosis<br><br>*Exclusion*:<br>Procedures for bicuspid aortic valve, pure aortic regurgitation, failed surgical bioprosthesis<br>or failed TAVR prosthesis, Patients without 1-year<br>follow-up<br><br>*Setting:* Germany (N=3)<br><br>*Recruitment period:*<br>March 2019 and June 2022<br><br>*Follow-up:* 1 year | *Primary outcomes:*<br>- Composite of all-cause mortality, stroke, and rehospitalization at 1 year.<br><br>*Secondary outcomes:*<br>- Individual components of the primary endpoint at 1 year. | Authors acknowledged limitations: a lack of independent event adjudication, health status information, core laboratory adjudication of echocardiographic and computed tomographic measurements, and echocardiographic data through 1-year follow-up |
| **3.** | Loewenstein (Cardiovas Revascul Med, 2024; 17-22)<br><br>*Funding: NR*<br><br>*Declaration of interests:* Authors report relationship with Abbott, Boston Scientific, Edwards Lifesciences, and Medtronic | 2 Retrospective cohorts; with PSM<br><br>*Intervention:*<br>• ACURATE neo2 (n=169)<br><br>*Comparators:*<br>• Evolut PRO (n=169)<br>• Sapien 3 (n=169) | *Inclusion:*<br>Patients with symptomatic aortic stenosis who underwent strictly femoral approach TAVR using ACURATE neo2, Edwards Sapien 3 and Evolut PRO valves<br><br>*Exclusion*:<br>Missing documentation of valve-type implanted with older-generation valves, or valves used in small numbers, rendering adequate comparisons unfeasible<br>TAVR using a non-femoral route<br><br>*Setting:* Isreal (N=5)<br><br>*Recruitment period:* Data from the Israeli TAVR registry between 2014 and 03/2023. *Follow-up:* in-hospital but mortality reported at 30 days | *Primary outcomes:*<br>- Post-procedural atrio-ventricular block (2nd or 3rd degree)<br>- New left bundle branch block<br>- New permanent pacemaker implantation<br>- Composite of the above listed conduction disorders<br><br>*Secondary outcomes:*<br>measures included paravalvular leak of different severities, and technical success and safety outcomes (defined according to the Valve Academic Research Consortium 2 consensus definitions) | - Mixed follow-up time for echocardiographic tests (data not available to researchers)<br>- Propensity score matching based on society of thoracic surgeon scores,, however, those scores differed between arms despite PSM |
| **4.** | Nuche (JACC Cardiovasc Interv, 2023; | RCT (LYTEN trial) | *Inclusion:*<br>Patients with surgical aortic bioprosthetic dysfunction defined as | *Primary outcomes*:<br>- Rate of severe patient-prosthesis mismatch or | Authors acknowledge several limitations: |

| # | Author (year); Funding | Design and intervention(s) | Participants and Setting | Outcomes | EAG comments |
|---|---|---|---|---|---|
| | 2999-3012). [NCT03520101]<br><br>*Funding:* Authors report fees and grants from various sources including Fundación Alfonso Martín Escudero (Spain), Fondation Famille Jacques Larivière, Edwards Lifesciences, Spanish Ministry of Science and Innovation (Instituto de Salud Carlos III), Medtronic, Abbott, JenaValve, Neovase, Boston Scientific, New Valve Technology, MicroInterventions, Pi-Cardia, Cardiac Success, Roche Diagnostics.<br><br>*Declaration of interests:* One author reports speaker fees from Edwards Lifesciences and Medtronic | *Intervention (n=46):* including mixture<br>• Sapien 3 (n=40)<br>• Sapien 3 Ultra (n=6)<br><br>*Comparator (n=52):* including mixture<br>• Evolut R (n=20)<br>• Evolut Pro (n=31)<br>• Evolut Pro+ (n=1) | severe aortic stenosis and/or regurgitation approved for a ViV procedure by the Heart Team, stented surgical valves, small (≤23mm) surgical valve<br><br>*Exclusion*:<br>Stentless or sutureless surgical valves<br><br>*Setting:* International (N=11) Canada, US, Europe<br><br>*Recruitment period:* May 2017 and January 2022<br><br>*Follow-up:* 1 year | moderate-severe AR at 30 days<br><br>*Secondary outcomes:*<br>-1-year Doppler echocardiography-based assessment of the valve performance (transvalvular gradient, intended valve performance, significant AR, hemodynamic valve degeneration);<br>-clinical outcomes (death, stroke, bleeding, pacemaker implantation, myocardial infarction, heart failure hospitalization).<br>-Functional status (NYHA functional class) and quality of life (Kansas City Cardiomyopathy questionnaire [KCCQ] overall summary score) at 30-day and 1-year | -primary outcome of the LYTNE trial) was valve haemodynamic (residual maximal and mean transvalvular gradient, severe patient prosthesis mismatch, or moderate to severe aortic regurgitation as evaluated by Doppler) at 30 days.<br>- missing echocardiography data at 1-year follow-up accounted for 22% of patients at risk (i.e., those included in the study and alive at 1 year), which may have partially biased the results.<br>-The performance of bioprosthetic ring fracture was left to the operator's discretion |
| **5.** | Terkelsen et al. (Lancet, 2025; 1-11)<br><br>*Funding:* Meril Life Sciences, Vingmed Denmark, the Danish Heart Foundation, and the Central Denmark Region.<br><br>*Declaration of interests*: Authors received fees from Abbott, Meril Life Sciences; Edwards Lifesciences, Terumo, Chiesi, and Medtronic. | RCT; non-inferiority; randomisation (1:1) COMPARE-TAVI trial<br><br>*Intervention*: Myval, n=514 (ITT, 507 PP) [combined group] included Myval n=183, Octacor n=324}<br><br>*Comparator:* Sapien 3/Sapien 3 Ultra n=517 (ITT, 516 PP) [combined group] | *Inclusion:*<br>>18 years of age, eligible for at least 2 valves being implanted routinely at the participating centre, according to a TAVI heart team conference, the centre experience for each of the valves considered should be more than 15 cases a year, and the treating physician should have implanted at least 15 of each valves used in the trial, the centre volume =/> 75 cases a year. The patient has given signed informed consent, TAVI is performed via the femoral artery.<br><br>Additional inclusion/exclusion criteria may apply to new cohorts, if one or both valves being compared are not eligible for all-comer use.<br><br>*Setting:* Denmark (N=3)<br><br>*Recruitment period:* June 15, 2020, and Nov 3, 2023 (paused from Feb 17, 2021, to March 28, 2021, and from Aug 31, 2021, to Aug 22, 2022)<br><br>*Follow-up:* 1 year (but planned up to 10 years) | *Primary outcomes:*<br>Composite of death, stroke, moderate or severe aortic regurgitation, or moderate or severe haemodynamic THV deterioration at 1 year according to VARC-3 criteria<br><br>*Secondary outcomes (non-powered):*<br>-The proportion of patients with successful implantation of the chosen valve (defined as no need for more than one THV, no change to an unplanned THV during the procedure, and no conversion to surgery or procedure-related death),<br>- Pacemaker implantation (defined as first-time pacemaker implantation within 1 year after TAVI in patients without a previous pacemaker)<br>- TAVI-related complications (defined as conversion to open surgery during implantation, unplanned use of cardiopulmonary support, coronary artery obstruction, ventricular septal perforation, mitral valve apparatus damage or dysfunction, cardiac tamponade, valve embolisation, valve migration or need for TAVI-in-TAVI deployment, annulus rupture, aortic rupture or perforation, aortic dissection, or shunts other than ventricular septum defects).<br><br>*Exploratory secondary endpoint*s: Endocarditis according to VARC-3 criteria at 30 days and 1 year, reoperation (TAVI, surgical aortic valve replacement, or balloon aortic valvuloplasty) at 30 days and 1 year, readmission for congestive heart failure according to VARC-3 criteria at 30 days and 1 year, readmission for | Seven participant crossovers from Myval to Sapien arm.<br>Powered for non-inferiority of primary composite endpoints. Authors stated that "The non-inferiority margin used in this trial is the smallest to date in any head-to-head comparison of THVs (i.e. 5·3% for the observed event rate of 13%)"; however also stated that one-sided α of 5% in the non-inferiority analysis might be too high because it increases the risk of falsely claiming non-inferiority). The authors noted that the margin was altered due to higher than expected blinded event rate.<br><br>Statistical difference in pre-dilatation performed between arms: 21% Sapien 3, 45% Myval, p<0.0001. |

| # | Author (year); Funding | Design and intervention(s) | Participants and Setting | Outcomes | EAG comments |
|---|---|---|---|---|---|
| | | | | acute myocardial infarction according to VARC-3 criteria at 30 days and 1-year, percutaneous coronary intervention or coronary artery bypass grafting (not scheduled before TAVI) at 30 days and 1 year, newly diagnosed atrial fibrillation or flutter at 30 days and 1 year, 6-min walk test at 30 days and 1 year, VARC-3 bleeding type 2, 3, or 4 at 30 days, major vascular access site and access-related complications resulting in endovascular or open surgery at 30 days, acute kidney injury of stage 2 or worse (increase in renal creatinine level ≥200% or dialysis) at 30 days, and moderate or severe patient–prosthesis mismatch at 30 days. | |

**Abbreviations:** BE THV, balloon-expandable transcatheter heart valve; BVD, bioprosthetic valve dysfunction; BVF, bioprosthetic valve failure; LBBB, left bundle branch block, MI, myocardial infarction; NYHA, New York Heart Association; NR, not reported; PPI, permanent pacemaker; PVL, paravalvular; SE THV, self-expanding transcatheter heart valve; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; VARC, Valve Academic Research Consortium

## Appendix F – Cross-referencing the evidence included in 5 systematic reviews and the original EAG report

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **1.** | Abdelghani (JACC Cardiovasc Interv 2018; 11:2507–18) | Observational (n=434) | NR | Evolut R, Sapien 3 | | | | | ✓ | |
| **2.** | Abdelfattah (Am J Cardiol, 2022; 170-172) | SR and MA (n=4,107) | NR | Sapien 3, Sapien 3 Ultra | ✓ | | | | | |
| **3.** | Abdel-Wahab (JAMA 2014; 311: 1503–14) | RCT [CHOICE] (n=241) | NR | CoreValve, Sapien XT | | | | | | ✓ |
| **4.** | Aideitis (JACC Cardiovasc Interv, 2022; 93-104) | Observational, prospective single arm (n=157) | International (N=18 centres) | Hydra | ✓ | | | | | |
| **5.** | Akodad (Am J Cardiol 2018; 121:1225–30) | Observational (n=228) | NR | Evolut R, Sapien 3 | | | | | ✓ | |
| **6.** | Akyüz (Herz, 2022; 449-455) | Observational, prospective single arm (n=25) | Turkey | Myval | * | | | | | |
| **7.** | Ali (Catheter Cardiovasc Interv, 2023; 932-942) | Observational, retrospective, registry (n=214) | UK (N=11 centres) | CoreValve, Sapien/Sapien XT, Portico | ✓ | | | | | |
| **8.** | Al-abcha (Cardiovasc Revasc Med, 2021; 57-62) | SR and MA (n=3,442) | NR | Sapien, Evolut R | * | | | | | |
| **9.** | Amat-Santos (Rev Esp Cardiol (Engl Ed). 2023; 76(11):872–880) | Observational with PSM [TRITON] (n=360) | Europe, India | Myval, Sapien 3, Evolut Pro+ | ✓ | | ✓ [comparison of Sapien 3, Evolut Pro+ only] | | | |
| **10.** | Armijo (Cardiovasc Interv, 2020; 13:e009047) | Observational (n=833) | NR | Evolut R, Sapien 3 | | | | | ✓ | |
| **11.** | Arslan (Anatol J Cardiol 2020; 361-363) | Observational, prospective, single-arm (n=9) | Turkey | Myval | * | | | | | |
| **12.** | Ayhen (J Geriatr Cardiol, 2022; 562-564) | Case study (n=1) | Turkey | Myval | * | | | | | |
| **13.** | Baggio (EuroIntervention, 2023; 977-986) | Non-randomised with PSM (n=904) | International | ACURATE neo2, Evolut Pro/Pro+ | ✓ | | | | | |
| **14.** | Bajwa (JSCAI, 2023; 100652) | Survey (n=539 physicians) | US | Evolut FX | * | | | | | |
| **15.** | Barki (Int J Cardiol, 2023; 131236) | Observational registry (n=407) | Italy | ACURATE neo2, ACURATE neo | * | | | | | |
| **16.** | Barki (J Clin Med, 2022: 959) | Observational retrospective (n=166) | Italy | Myval, Evolut R | * | | | | | |
| **17.** | Barth (EuroIntervention 2019; 15:884–91) | Observational with PSM (n=658) | NR | ACURATE/ACURATE neo, Sapien 3 | | | | ✓ | ✓ | ✓ |
| **18.** | Baumbach (Lancet, 2024; 2695-2708) | RCT, non-inferiority (n=768) | International | Mval/Myval Octacor, Evolut R/Pro/Pro+/FX/Sapien 3/Sapien 3 Ultra | ✓ | | | | | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **19.** | Ben-Shoshan (Am J Cardiol 2017; 119:302–7). | Observational (n=232) | Israel | Sapien 3, †Evolut R | | ✓ | | | ✓ | |
| **20.** | Bieliauskas (JACC Cardiovasc Interv 2021; 14:2097–2108) | Observational with PSM (n=60) | Denmark | Evolut R/Pro, ACURATE neo2, Portico | * | | | | ✓ | |
| **21.** | Bisson (J Am Heart Assoc 2020; 9: e015896) | Observational (n=39,620) | NR | Evolut R, Sapien 3 | | | | | ✓ | |
| **22.** | Brown (Am J Cardiol, 2023; 48-53) | Observational, retrospective (n=560) | US | Evolut Pro+, Sapien 3 Ultra, Portico | ✓ | | | | | |
| **23.** | Buono (JACC Cardiovasc Interv, 2022b, 1101-1110) | Observational with PSM (n=410) | Italy | ACURATE neo2, ACURATE neo | ✓ | | | | | |
| **24.** | Cannata (EuroIntervention, 2023; 1418-1427) | Observational with PSM (n=992) | Italy, the Netherlands, Portugal, Spain | Sapien 3 Ultra, Sapien 3 | ✓ | | | | | |
| **25.** | Castro-Mejia (Int J Cardiol, 2022; 128-136) | Non-randomised (n=344) | Spain | Portico, Allegra, ACURATE neo, Evolut R/Pro | * | | | | | |
| **26.** | Catalano (J Card Surg 2021;36:191–6) | Observational (n=346) | NR | Evolut R/Pro, Sapien 3 | | | | | ✓ | |
| **27.** | Chandra (Catheter Cardiovasc Interv, 2021: 371-379) | Observational, prospective single arm (n=40) | India | Hydra | * | | | | | |
| **28.** | Chetcuti (JACC Cardiovasc Intervn, 2023; S92) Abstract | Survey (n=285 physicians) | US | Evolut FX | * | | | | | |
| **29.** | Chieffo (J Am Coll Cardiol 2013 ;61:830–6) | Observational with PSM (n=408) | NR | CoreValve, Sapien/Sapien XT | | | | | | ✓ |
| **30.** | Corcione (Am J Cardiol 2020;125:1209–15) | Observational (n=233) | NR | Evolut R/Pro, Portico | | | | | ✓ | |
| **31.** | Costa (EuroIntervention, 2024; 95-103) | Observational with PSM [OPERA-TAVI] (n=1,174) | Europe, US | Sapien 3 Ultra, Evolut Pro/Pro+ | * | | | | | |
| **32.** | Costa (JACC Cardiovasc Interv. 2022; 15(23):2398–2407) | Observational with PSM [OPERA-TAVI] (n=1,366) | Europe, US | Sapien 3 Ultra, Evolut Pro/Pro+ | | | ✓ | ✓ | | |
| **33.** | Costa (OBSERVANT II) (Circ Cardiovasc Interv. 2022; 15(12):e012294) | Observational (n=2,728) | Italy | Evolut R, Evolut Pro Sapien 3, ACURATE neo, Portico | ✓ | | ✓ | | | |
| **34.** | Costa (Cardiovasc. Interv. 2020; 95 398–407) | Observational with PSM (n=144) | Italy | ACURATE neo, Sapien 3, Evolut R | | ✓ | | ✓ | | ✓ |
| **35.** | Deharo (Circulation | Observational with PSM (n=20,918) | France | Sapien 3, CoreValve/Evolut R | | ✓ | | | ✓ | ✓ |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2020; 141:260–268) | | | | | | | | | |
| **36.** | Delgado-Arana (Heart, 2022; 725-732) | Observational with PSM (n=206) | Europe | Myval, Sapien 3 | * | | | | | |
| **37.** | Eckel (J Clin Med, 2023: 3999) | Observational, retrospective (n=276) | Germany | Navitor, Portico | ✓ | | | | | |
| **38.** | Edlinge (Front Cardiovasc Med 2021; 8: 671719) | Observational with PSM (n=84) | NR | DFM, Sapien 3 | | | | | ✓ | |
| **39.** | Eftychiou (Hellenic J Cardiol 2021;62:57–64) | Observational (n=235) | Cyprus | Sapien 3, Evolut R/Pro | | ✓ | | | ✓ | |
| **40.** | Eitan (Cardiovasc Interv 2018;92:1374–1379) | Observational (n=92) | Germany | Sapien 3, †Evolut R | | ✓ | | | ✓ | |
| **41.** | Elkoumy (Int J Cardiol, 2024; 131792) | Observational registry (n=499) | Europe | ACURATE neo2 | * | | | | | |
| **42.** | Elkoumy (Int J Cardiol, 2023; 68-75) | Observational, retrospective single arm (n=103) | India | Myval Octacor | ✓ | | | | | |
| **43.** | Elkoumy (J Clin Med, 2022; 443) | Observational, retrospective single arm (n=68) | India, Denmark, Italy, Croatia | Myval | ✓ | | | | | |
| **44.** | Eltchaninoff (EuroIntervention, 2018; e264-e271) | Non-randomised (n=378) | France | Cribier, Sapien, Sapien XT | * | | | | | |
| **45.** | Elnaggar (REC Interv Cardiol. 2023; 5(2):94–101) | RCT (n=110) | Germany | Sapien 3, Evolut Pro | | | ✓ | | | |
| **46.** | Enríquez-Rodríguez (Rev Esp Cardiol (Engl Ed) 2018;71:735–42) | Case-control (n=144) | Spain | Sapien 3, †Evolut R | | ✓ | | | ✓ | |
| **47.** | Feistritzer (J Am Coll Cardiol. 2021; 77(17):2204–15) | RCT [SOLVE-TAVI] (n=438) | Germany | Sapien 3, Evolut R | | | | ✓ | | |
| **48.** | Feldman (JAMA 2018; 319:27–37). | RCT (n=664) | NR | CoreValve/Evolut R, Lotus | | | | | ✓ | |
| **49.** | Ferrara (J Clin Med. 2022; 11(7):1959) | Observational (n=102) | France | Sapien 3, Evolut Pro | | | ✓ | | | |
| **50.** | Finkelstein (Catheter Cardiovasc Interv 2019; 94:E44–e53) | Observational with PSM (n=252) | NR | Evolut R, Sapien 3 | | | | | ✓ | |
| **51.** | Finkelstein (Clin. Res. Cardiol 2019; 108,430–437) | Observational with PSM (n=252) | Israel | Sapien 3, †Evolut R | | ✓ | | ✓ | | |
| **52.** | Fukuda (Value Health 2021; 24: 497–504) | Observational (†n=7,244) | Japan | Sapien 3, CoreValve, Evolut R | | ✓ | | | ✓ | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **53.** | Fukui (Circulation. 2022; 146(6):480–493) | Observational, prospective (n=565) | US | Sapien 3, Evolut Pro | | | ✓ | | | |
| **54.** | Fukui (J Cardiovasc Comput Tomogr 2021; 15:403–11) | Observational (n=447) | NR | Evolut R/Pro, Sapien 3 | | | | | ✓ | |
| **55.** | Gama (Int J Cardiovasc Imaging 2022; 38: 225–35) | Observational (n=81) | NR | ACURATE, Portico | | | | | ✓ | |
| **56.** | Gamal (J Cardiovasc Transl Res 2020; 13:790–5) | Observational (n=167) | NR | DFM, Sapien 3 | | | | | ✓ | |
| **57.** | Garcia-Gomez (Catheter Cardiovasc Interv, 2022; 889-895) | Observational registry, single-arm (n=100) | Europe | Myval | * | | | | | |
| **58.** | Geyer (JACC Case Rep, 2023; 102116) | Case report (n=1) | Germany | Trilogy | ✓ | | | | | |
| **59.** | Giannini (Am. J. Cardiol 2020; 125,441–448) | Observational (n=303) | International | Sapien 3, Evolut R/Pro | | ✓ | | | | |
| **60.** | Giannini (Catheter Cardiovasc Interv 2018; 91:966–74) | Observational (n=175) | NR | Lotus, DFM | | | | | ✓ | |
| **61.** | Giordano (Clin Res Cardiol, 2024b; 86-93) | Observational retrospective, single arm (n=803) | Europe (N=7 centres) | Portico | ✓ | | | | | |
| **62.** | Giordano (Sci Rep 2019;9:17098) | Observational with PSM (n=1,976 unadjusted; unclear how many when adjusted) | Italy | †Evolut, ACURATE, Portico, Lotus, Sapien 3 | | ✓ (subset) | | | ✓ | |
| **63.** | Gonzalez-Bravo (Case Rep Cardiol 2022; 4458109) | Case report (n=1) | Puerto Rico | Evolut Pro+ | * | | | | | |
| **64.** | Gorla (Catheter Cardiovasc Interv 2021; 97:E135–e145) | Observational (n=374) | NR | Evolut R, Portico | | | | | ✓ | |
| **65.** | Gorla (EuroIntervention 2020; 15:e1588–91) | Observational (n=392) | NR | Evolut R, ACURATE neo, Portico | | | | | ✓ | |
| **66.** | Grubb (JACC Cardiovasc Interv, 2024; 1007-1016) | Pooled analysis (RCTs, single arm; n=5,925) | NR | CoreValve, Evolut Pro | * | | | | | |
| **67.** | Habertheuer (Ann Thorac Surg 2021; 111:1968–74). | Observational (n=563) | US | Sapien 3, Evolut R/Pro | | ✓ | | | ✓ | |
| **68.** | Halim (J Clin Med, 2023a; 4213) | Observational with PSM, retrospective (n=182) | The Netherlands | Myval, Evolut R/Pro | * | | | | | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **69.** | Halim (Neth Heart J, 2023; 500-505) | Observational, single-arm (n=120) | The Netherlands | Myval | * | | | | | |
| **70.** | Halim (J Intervn Cardiol, 2022; 3139476) | Observational, prospective single arm (n=60) | The Netherlands | Myval | * | | | | | |
| **71.** | Hase (Catheter Cardiovasc Interv 2021; 97:E875–e886) | Observational with propensity score matching [OCEAN-TAVI] (n=138) | Japan | Sapien 3, Evolut R | | ✓ | | ✓ | ✓ | |
| **72.** | Herrmann (N Engl J Med, 2024; 1959-1971) | RCT, non-inferiority (n=715) | International (N=83 sites in 13 countries) | Evolut R/Pro/Pro+/FX, Sapien 3/3 Ultra | ✓ | | | | | |
| **73.** | Holzamer (Catheter Cardiovasc Interv, 2023; 1364-1375) | Observational, retrospective single-arm (n=10) | Germany, India, Italy, Poland, South Africa, Spain | Myval | * | | | | | |
| **74.** | Husser (JACC Cardiovasc Interv 2017; 10:2078–87) | Observational with PSM (n=933) | NR | ACURATE neo, Sapien 3 | | | | ✓ | ✓ | ✓ |
| **75.** | Husser (JACC Cardiovasc Interv 2019; 12:1781–93) | Observational with PSM (n=130) | NR | ACURATE neo, Sapien 3 | | | | | ✓ | |
| **76.** | Ielasi (JACC Cardiovasc Interv, 2024; 101-103) | Case report (n=1) | Italy | Myval Octacor | ✓ | | | | | |
| **77.** | Ivanov (Perfusion (United Kingdom) 2023; 38:115–23) | Observational with PSM (n=152) | NR | Evolut R, ACURATE neo | | | | | ✓ | |
| **78.** | Jarr (J Invasive Cardiol 2017; 29:30–5) | Observational (n=153) | NR | Lotus, Sapien 3 | | | | | ✓ | |
| **79.** | Jose (Cardiovasc Revasc Med, 2024; 1-7) | Observational, retrospective, registry (n=123) | India | Myval Octacor | ✓ | | | | | |
| **80.** | Kalogeras (J Am Heart Assoc. 2023;12(11): e028038) | Observational (n=1,673) | Greece, UK | Sapien 3/3 Ultra, Evolut Pro/Pro+ | | | ✓ | | | |
| **81.** | Kanso (J Clin Med 2021; 10:1–13) | Observational (n=210) | NR | Evolut R, Sapien 3 | | | | | ✓ | |
| **82.** | Kim (EuroIntervention, 2024; 85-94) | Observational, prospective single arm (n=250) | Europe | ACURATE neo2 | ✓ | | | | | |
| **83.** | Kim (Int J Cardiol, 2022; 77-82) | Observational, retrospective (n=448) | Germany | ACURATE neo2 | * | | | | | |
| **84.** | Kim (J Invasive Cardiol, 2022; E804-E810) | Non-randomised (n=2,865) | Germany | ACURATE neo, ACURATE neo2 | ✓ | | | | | |
| **85.** | Kim (Circulation. 2021; 143(12):1267–9) | RCT [SCOPEI] (n=735) | NR | ACURATE neo, Sapien 3 | | | | ✓ | | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **86.** | Kim (Clin Res Cardiol 2017; 106:995–1004) | Observational (n=948) | NR | Evolut R, ACURATE neo, Portico, Sapien 3 | | | | | ✓ | |
| **87.** | Kooistra (Catheter Cardiovasc Interv 2021; 97:E597–e606) | Observational (n=308) | NR | ACURATE neo, Sapien 3 | | | | | ✓ | |
| **88.** | Lanz (Lancet 2019;394:1619–1628) | RCT [SCOPEI] (n=739) | NR | ACURATE neo, Sapien 3 | | | | ✓ | ✓ | ✓ |
| **89.** | Lee (Korean Circ J 2021; 51:222–231) | Observational (n=70) | NR | Evolut R/Pro, Sapien 3 | | | | | ✓ | |
| **90.** | Leone (EuroIntervention. 2023; 19(3):256–266) | Observational (n=1,036) | Europe | Sapien 3, Evolut Pro | | | ✓ | | | |
| **91.** | Leone (Jacc-Cardiovasc Interv 2021;14:1218–1228) | Observational with PSM (n=445) | NR | Evolut, ACURATE neo, Portico | | | | | ✓ | |
| **92.** | Magyari (Catheter Cardiovasc Interv, 2023; 1317-1330) | Observational single arm (n=100) | Hungary | Myval | * | | | | | |
| **93.** | Makkar (Lancet 2020; 396:669–683) | RCT (n=691) | NR | Evolut R/Pro, Portico, Sapien 3 | | | | | ✓ | |
| **94.** | Mangieri (Circ Cardiovasc Interv. 2020; 13(7): e008714) | Observational with PSM [BEAT] (n=154) | NR | Evolut R/Pro, Sapien 3 | | | | ✓ | | |
| **95.** | Marzahn (J Cardiol 2018; 71:101–8) | Observational (n=315) | NR | Portico, Lotus, DFM, Sapien 3 | | | | | ✓ | |
| **96.** | Mas-Peiro (J Invasive Cardiol 2019;31:E199–e204) | Observational with PSM (n=177) | NR | †Portico, Sapien 3 | | | | | ✓ | ✓ |
| **97.** | Mauri (Open Heart 2020; 7:e001164) | Observational (n=642) | NR | Evolut R, ACURATE neo, Lotus, Sapien 3 | | | | | ✓ | |
| **98.** | Mauri (Circ Cardiovasc Interv 2017; 10:e005013) | Observational with PSM (n=184) | NR | ACURATE neo, Sapien 3 | | | | ✓ | ✓ | ✓ |
| **99.** | Meduri (JACC Cardiovasc Interv, 2023; 670-677) | Observational, prospective, single arm (n=170) | Sweden | ACURATE neo2 | * | | | | | |
| **100.** | Medranda (Am J Cardiol. 2022; 174:101–106) | Observational (n=389) | US | Sapien 3, Evolut Pro/Pro+ | | | ✓ | | | |
| **101.** | Medranda (JACC Cardiovasc Interv 2021;14:1209–15) | Observational (n=841) | NR | Evolut Pro, Sapein 3 | | | | | ✓ | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **102.** | Meguro (Circulation Journal 2021; 85:967) | Observational (n=193) | NR | Evolut R, Sapien 3 | | | | | ✓ | |
| **103.** | Merdler (Cardiovasc Revasc Med, 2023; 1-6) | Non-randomised, retrospective (n=200) | US | Evolut FX, Evolut Pro+ | ✓ | | | | | |
| **104.** | Milan (Cardiol J, 2021; 825-830) | Observational, retrospective single-arm (n=27) | Poland | Allegra | * | | | | | |
| **105.** | Minha (Catheter Cardiovasc Interv 2021; 98:E990–e999) | Observational (n=397) | NR | Evolut R/Pro, Sapien 3 | | | | | ✓ | |
| **106.** | Miura (Eur Heart J, 2019; 1354) | Case report (n=1) | Switzerland | Allegra | * | | | | | |
| **107.** | Miyashita (Cardiovasc Revasc Med, 2023; 62-69) | Observational with PSM (n=188) | Finland | ACURATE neo, ACURATE neo2 | * | | | | | |
| **108.** | Modolo (JACC Cardiovasc Interv 2020; 13:1303–1311) | Observational, retrospective case series (†n=2,258) | Netherlands | CoreValve Evolut R, Evolut Pro, ACURATE, Lotus, Sapien XT, Sapien 3 | | | ✓ (subset) | | ✓ (subset) | |
| **109.** | Möllmann (Clin Res Cardiol, 2021; 1912-1920) | Observational, prospective, single arm (n=120) | Switzerland, Denmark, Germany | ACURATE neo2 | * | | | | | |
| **110.** | Moreno (Catheter Cardiovasc Inter, 2021; 365-370) | Observational registry (n=29) | Spain | Allegra | * | | | | | |
| **111.** | Moriyama (Circ Cardiovasc Interv 2019; 12:e007756) | Observational (n-249) | NR | ACURATE neo, Sapien 3 | | | | | ✓ | |
| **112.** | Moscarella (Int J Cardiol, 2024: 131701) | Non-randomised, retrospective (n=166) | Italy | Myval, Evolut R | ✓ | | | | | |
| **113.** | Mosleh (Am J Cardiol. 2023; 192:31–38) | Observational (n=573) | US | Sapien 3 Ultra, Evolut Pro/Pro+ | | | ✓ | | | |
| **114.** | Mosleh (Am J Cardiol 2019; 124:1621–1629) | Observational (n=581) | US | Sapien 3, Evolut R/Pro | | ✓ | | | ✓ | |
| **115.** | Mosquera (JTCVS Tech, 2023; 150-158) | Observational, single arm (n=40) | Spain | ACURATE neo2 | * | | | | | |
| **116.** | Nai Fovino (J Cardiovasc Med, 2018: 655-63) | Observational with PSM (n=186) | NR | Lotus, Sapien 3 | | | | | ✓ | |
| **117.** | Nazif (Circ Cardiovasc Interv, 2021; e010543) | Observational with PSM, registry (n=2,648) | US | Sapien 3 Ultra, Sapien 3 | ✓ | | | | | |
| **118.** | Neuser (Catheter Cardiovasc Interv, 2022; 1234-1242) | Observational, retrospective, single arm (n=93) | Germany | Allegra | * | | | | | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **119.** | Nicolas (Catheter Cardiovasc Interv 2021; 98:E908–17) | Observational (n=362) | NR | Evolut R, Lotus, DFM, Sapien 3 | | | | | ✓ | |
| **120.** | Nijenhuis (Neth Heart J, 2015; 35-41) | Observational, retrospective single arm (n=24) | The Netherlands | JenaValve | * | | | | | |
| **121.** | Nikolayeyska (Clin Res Cardiol 2024; 18-28) | Non-randomised (n=112) | Germany | Sapien/XT/3, Allegra, CoreValve/Evolut R | * | | | | | |
| **122.** | Okuno (JACC Cardiovasc Interv. 2023; 16(4):429–440) | Observational with PSM (n=342) | Switzerland | Sapien 3/3 Ultra, Evolut Pro/Pro+ | | | ✓ | | | |
| **123.** | Okuno 2020 (JACC Cardiovasc Interv 2020;13:1789–99) | Observational (n=1,018) | NR | Evolut, ACURATE, Portico, Lotus, Sapien 3 | | | | | ✓ | |
| **124.** | Okuyama (Circ J 2020; 84: 2015–22) | Observational (n=46) | NR | Evolut R/Pro, Sapien 3 | | | | | ✓ | |
| **125.** | Olasińska-Wiśniewska (Kardiol Pol, 2021; 207-208) | Case report (n=1) | Poland | ACURATE neo2 | * | | | | | |
| **126.** | Pagnesi (JACC Cardiovasc Interv 2019; 12:433–43) | Observational with PSM (n=502) | NR | Evolut Pro, ACURATE neo | | | | | ✓ | |
| **127.** | Paitazoglou (J Invasive Cardiol 2021; 33:E356–e364) | Observational (†n=253) | Germany | Sapien 3, Evolut R/Pro | | ✓ | | | ✓ | |
| **128.** | Panoulas (Catheter Cardiovasc Interv 2021; 97:516–26) | Observational (n=120) | NR | Evolut R, Lotus, DFM, Sapien 3 | | | | | ✓ | |
| **129.** | Pellegrini (EuroIntervention. 2023; 18(12):987–95) | Observational with PSM (n=944) | Germany | ACURATE neo2, Sapien 3 Ultra | * | | | ✓ | | |
| **130.** | Pellicano (JACC Cardiovasc Interv, 2021; e173-e176) | Case report (n=1) | Italy | ACURATE neo2 | * | | | | | |
| **131.** | Pilgrim (J Am Heart Assoc 2016; 5) | Observational (n=955) | NR | Lotus, Sapien 3 | | | | | ✓ | |
| **132.** | Pollari (J Thorac Cardiovasc Surg 2019; 157:1406–415.e1403) | Observational (n=303) | NR | ACURATE, Sapien 3 | | | | | ✓ | |
| **133.** | Potratz (J Clin Med. 2022; 11(15):4570) | Observational with PSM (n=340) | Germany | Sapien 3, Evout Pro | | | ✓ | ✓ | | |
| **134.** | Rao (Heart Lung Circ, 2023; 1482-1488) | Observational, retrospective single arm (n=10) | Australia | Evolut Pro+ | * | | | | | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **135.** | Regazzoli (JACC Cardiovasc Interv 2020; 13:196–206) | Observational, retrospective case series (n=859) | NR | †Evolut R, Evolut Pro, ACURATE Portico | | | | | ✓ | |
| **136.** | Reuthebuch (Innovations, 2014; 368-374) | Observational, prospective, single-arm (n=27) | Switzerland | JenaValve | * | | | | | |
| **137.** | Rheude (Clin Res Cardiol, 2024; 38-47) | Observational with PSM (n=310) | Germany | ACURATE neo2, Evolut Pro | * | | | | | |
| **138.** | Rheude (Int J Cardiol. 2022; 357:115–120) | Observational with PSM (†n=934) | Germany | Sapien 3 Ultra, †Evolut R/Pro | | | ✓ | ✓ | | |
| **139.** | Rodes-Cabau (LYTEN) (J Am Coll Cardiol. 2022; 80(7): 681–693) | RCT (n=97) | Europe, US | Sapien 3/3Ultra, Evolut Pro/Pro+ | | | ✓ | | | |
| **140.** | Rodríguez-Olivares (Int J Cardiol 2016;216: 9–15) | Observational (n=61) | NR | Lotus, Sapien 3 | | | | | ✓ | |
| **141.** | Rogers (J Interv Cardiol 2017; 30:356–61) | Observational (n=257) | US | Sapien 3, †Evolut R/CoreValve | | ✓ | | | ✓ | |
| **142.** | Rück (J Am Heart Assoc, 2023; e029464) | Registry, single arm | Europe | ACURATE neo2 | * | | | | | |
| **143.** | Rück (J Clin Med, 2021; 4627) | Observational registry (n=228) | Germany, Sweden | ACURATE neo, ACURATE neo2 | * | | | | | |
| **144.** | Rudolph (Clin Res Cardiol, 2024; 75-85) | Observational, registry (n=24,124) | Germany | Sapien 3, Evolut R, ACURATE neo, Portico | ✓ | | | | | |
| **145.** | Russo (J Am Coll Cardiol, 2019; 805-8) | Observational, registry (n=61,949) | US | Sapien, Sapien XT, Sapien 3 | ✓ | | | | | |
| **146.** | Santos-Martinez (Int J Cardiol 2022; 351: 25–31) | Observational (n=1,131) | NR | Myval, Allegra, Evolut R/Pro, ACURATE neo, Sapien 3, Portico | ✓ | | | | ✓ | |
| **147.** | Sathananthan (Catheter Cardiovasc Interv, 2021; E431-E437) | Non-randomised (n=235) | Canada | Cribier, Sapien, CoreValve | * | | | | | |
| **148.** | Sathananthan (Can J Cardiol 2018; 34:1165–73) | Observational (n=208) | NR | Lotus, Sapien 3 | | | | ✓ | ✓ | |
| **149.** | Schafer (EuroIntervention, 2022; 1077-1080) | Observational, prospective single arm (n=30) | Germany | Allegra | * | | | | | |
| **150.** | Schafer (Catheter Cardiovasc Interv, 2018; 1453-1457) | Case report (n=1) | Germany | Allegra | * | | | | | |
| **151.** | Schaefer (Interact Cardiovasc Thorac Surg | Observational with PSM (n=208) | NR | ACURATE neo, Sapien 3 | | | | ✓ | ✓ | ✓ |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2017; 25:905–11) | | | | | | | | | |
| **152.** | Schmidt (Clin. Res. Cardiol. 2022, 111,1336–1347) | Observational, retrospective case series (†n=2,609) | Germany | †Sapien 3,<br>ACURATE neo,<br>Evolut R,<br>Evolut Pro | | | ✓<br>(subset) | | | |
| **153.** | Schofer (J Cardiol 2018; 71:540–6) | Observational (n=273) | NR | Lotus,<br>Sapien 3 | | | | | ✓ | |
| **154.** | Schulz (Int J Cardiol 2017 ;232:186–91) | Observational (n=174) | NR | DFM,<br>Sapien 3 | | | | | ✓ | |
| **155.** | Scotti (EuroIntervention, 2022; 804-811) | Non-randomised registry (n=2,026)0 | International | ACURATE neo2,<br>ACURATE neo | ✓ | | | | | |
| **156.** | Seeger (Circ Cardiovasc Interv 2017; 10: e004670) | Observational with PSM (n=404) | NR | Lotus,<br>Sapien 3 | | | | | ✓ | |
| **157.** | Seeger (Cardiovasc Interv Ther 2018; 33:247–55) | Observational (n=200) | NR | Lotus,<br>Sapien 3 | | | | | ✓ | |
| **158.** | Seiffert (Eur Heart J Cardiovasc Imaging 2016; 576-584) | Non-randomised (n=537) | Germany | Sapien XT,<br>ACURATE neo,<br>JenaValve,<br>Engager/CoreValve | * | | | | | |
| **159.** | Seiffert (Eur J Cardiothorac Surg, 2015; 39-45) | Non-randomised, retrospective (n=200) | Germany | Engager,<br>JenaValve,<br>Symetis ACURATE | ✓ | | | | | |
| **160.** | Sharma (EuroIntervention, 2020; 421-429) | Non-randomised, prospective, single arm (n=30) | India | Myval | * | | | | | |
| **161.** | Silaschi (Eur J Cardiothorac Surg, 2016; 874-881) | Observational, retrospective single arm (n=180) | Europe | JenaValve | ✓ | | | | | |
| **162.** | Siqueira (Catheter Cardiovasc Interv, 2021; 167-174) | Observational, prospective single-arm (n=104) | Brazil | ACURATE neo | ✓ | | | | | |
| **163.** | Soliman (Eur Heart J Cardiovasc Imaging 2018; 19:157–67) | Observational (n=162) | NR | Lotus,<br>Sapien 3 | | | | | ✓ | |
| **164.** | Sondergaard (EuroIntervention, 2023; 248-255) | Observational, prospective single arm (n=120) | International | Navitor | ✓ | | | | | |
| **165.** | Stolte (Struct Heart, 2023; 100229) | Case report (n=1) | Switzerland | Evolut Pro+ | * | | | | | |
| **166.** | Stundl (PLoS One 2019; 14:e0217544) | Observational (n=357) | NR | Evolut R,<br>Lotus,<br>DFM,<br>Sapien 3 | | | | | ✓ | |
| **167.** | Tamburino (Circulation 2020; 142:2431–42) | RCT (796) | NR | Evolut,<br>ACURATE neo | | | | | ✓ | |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **168.** | Tamm (J Clin Med 2021; 10:3102) | Observational (n=359) | Germany | Sapien 3,<br>Evolut R | ✓ | ✓ | | | ✓ | |
| **169.** | Tang (JACC Cardiovasc Interv, 2021; 964-976) | Non-randomised (n=32,542) | US | Evolut Pro/Pro+,<br>Evolut R | ✓ | | | | | |
| **170.** | Tang (Am J Cardiol, 2019; 1091-1098) | Observational with PSM, registry (n=3,626) | US | CoreValve,<br>Evolut R | * | | | | | |
| **171.** | Tébar Márquez (Catheter Cardiovasc Interv, 2022; 1286-1290) | Observational single arm (n=8) | Spain | Allegra | * | | | | | |
| **172.** | Testa (Cardiovasc Revasc Med, 2023; 22-27) | Observational registry (n=100) | Italy | Myval | * | | | | | |
| **173.** | Thiele (Eur Heart J 2020a; 41:1890–1899) | RCT [SOLVE-TAVI] (n=438) | Germany | Sapien 3,<br>Evolut R | | ✓ | | ✓ | ✓ | ✓ |
| **174.** | Thyregod (Eur Heart J, 2024; 1116-1124) | RCT (TAVI, SAVR, n=145) | Denmark, Sweden | CoreValve | * | | | | | |
| **175.** | Tichelbäcker (PLoS One 2018; 13:e0204503) | Observational (n=181) | NR | Portico,<br>DFM,<br>Sapien 3 | | | | | ✓ | |
| **176.** | Toggweiler (Cardiovasc Revasc Med, 2022; 37-43) | Non-randomised (n=60) | Switzerland | ACURATE neo2,<br>ACURATE neo | * | | | | | |
| **177.** | Toggweiler (2018) | Case report (n=1) | Switzerland | Allegra | * | | | | | |
| **178.** | Trebacz (Kardiol Pol, 2023: 515-516) | Case report (n=1) | Poland | ACURATE neo2 | * | | | | | |
| **179.** | Treede (EuroIntervention, 2012; Q88-93) | Observational, single arm (n=73) | Germany | JenaValve | * | | | | | |
| **180.** | Van Belle (Circulation 2020; 141:243–59) | Observational with PSM (n=7,820) | NR | CoreValve,<br>Sapien 3/Sapien XT | | | | | | ✓ |
| **181.** | van Gils 2017 (J Am Heart Assoc 2017;6:e005028) | Observational (n=52) | NR | Lotus,<br>Sapien 3 | | | | | ✓ | |
| **182.** | van Nieuwkerk (J Clin Med. 2021; 10(17):4005) | Observational with PSM [CENTER] (n=1,405) | NR | Evolut R,<br>Sapien 3 | | | | ✓ | | |
| **183.** | Vera Vera (Rev Esp Cardiol (Engl Ed) 2021; 74:1032–41) | Observational with PSM, registry (n=514) | Spain | Evolut R/Pro,<br>ACURATE neo,<br>Portico,<br>Allegra | * | | | | ✓ [comparison of Evolut R/Pro, AUCRATE neo, Portico only] | |
| **184.** | Veulemans (Int J Cardiol 2019; 278:40–5) | Observational (n=204) | Germany | Sapien 3,<br>†Evolut R | | ✓ | | | ✓ | |
| **185.** | Vlastra (Eur Heart J 2019; 40:456–65) | Observational, registries with PSM [CENTER] (†n=8,192) | International | †Sapien/SapienXT/Sapien 3, CoreValve/Evolut | | ✓ | | ✓ | ✓ | ✓ |

| # | Study | Study design (n, patients) | Country | Valves included | EAG report (2024); *non-key study | Lerman (IJC, 2023; 100-108) | Siddiqui (J Soc Cardiovasc Angiogr Interv, 2024; 102146) | Wang (BMC Cardiovasc Disord, 2023; 382 | Yang (Int J Surg, 2023; 2414-2426 | Zhang (J Cardiol, 2022; 204-210) |
|---|---|---|---|---|---|---|---|---|---|---|
| **186.** | Voigtländer (Clin Res Cardiol 2021; 110:1957–66) | Observational (n=1,069) | NR | Evolut/Evolut R/Pro, ACURATE neo, Portico, Lotus, Sapien 3 | ✓ | | | | ✓ | |
| **187.** | Vondran (Thorac Cardiovasc Surg Rep, 2021; e1-e5) | Case report (n=1) | Germany | Allegra | * | | | | | |
| **188.** | Wenaweser (EuroIntervention, 2016; 71-7) | Observational, prospective, single arm (n=21) | Switzerland, Germany | Allegra | * | | | | | |
| **189.** | Wijeysundera (Am J Cardiol 2017; 119:1094–9) | Observational with PSM (n=714) | NR | CoreValve, Sapien/Sapien XT | | | | | | ✓ |
| **190.** | Wöhrle (Int J Cardiol 2015; 195:171–5) | Observational (n=78) | NR | Lotus, Sapien 3 | | | | | ✓ | |
| **191.** | Wolfrum (J Invasive Cardiol, 2023) | Observational registry (n=103) | Switzerland | Allegra | ✓ | | | | | |
| **192.** | Wolfrum (Catheter Cardiovasc Interv, 2021; 1204-1209) | Observational, registry single arm (n=255) | Switzerland, Finland, Spain, the Netherlands | Allegra | * | | | | | |
| **193.** | Wyler von Ballmoos (Cardiovasc Revasc Med, 2021; 12-16) | Observational, retrospective single cohort (n=60) | US | Evolut Pro | ✓ | | | | | |
| **194.** | Yashige (Catheter Cardiovasc Interv, 2022; 1331-1335) | Case report (n=1) | Japan | Evolut Pro+ | * | | | | | |
| **195.** | Zaid (JACC Cardiovasc Interv, 2023b; 1626-35) | Non-randomised, registry (n=604) | US | Evolut FX, Evolut Pro+ | ✓ | | | | | |
| **196.** | Zhang (Catheter Cardiovasc Interv 2015; 85: 1217–25) | Observational with PSM (n=80) | NR | CoreValve, Sapien XT | | | | | | ✓ |
| **TOTAL** | **196** | **-** | **-** | **-** | **98** | **19** | **16** | **18** | **79** | **15** |

Key: †value edited by EAG on review of primary evidence source (conflicting information between systematic reviews)

## Appendix G – Critical appraisal

### RCTs

#### Feistritzer (JACC, 2025)

Reviewer 1: KB, Reviewer 2: KK

| Bias domain | Source of bias | Support for Judgement | Review authors' judgement (assess as low, unclear, or high risk of bias |
|---|---|---|---|
| Selection bias | Random sequence generation | Permuted blocks, stratified by centre. Characteristics appear well-balanced between arms (by TAVI device, described by Thiele et al. 2020a) | Low |
| | Allocation concealment | Opaque sealed envelopes | Low |
| Performance bias | Blinding of participants and personnel | Open-label (participants and clinical staff not blinded) | High |
| Detection bias | Blinding of outcome assessment | "*In all but 5 patients, prosthetic valve regurgitation was also analyzed by an independent core laboratory (blinded to treatment allocation).*" Unclear on other outcomes | Unclear |
| Attrition bias | Incomplete outcome data | Echocardiographic data at 5 years were available in only a small proportion of patients (n=37) limiting the analysis of structural valve deterioration. | High |
| Reporting bias | Selective reporting | All primary and secondary outcomes listed in trial registration were reported NCT02737150. Additional detail provided in Supplementary Material. Power calculation reported in Thiele et al. 2020a. | Low |
| Other bias | Anything else, ideally pre-specified. | Trial was a priori powered for equivalence of the primary combined endpoint at 30 days. Funded by the German Heart Research Foundation and Leipzig Hear Institute Germany. | Low |

## Nuche (JACC Cardiovasc Interv, 2023)

Reviewer 1: KB, Reviewer 2: KK

| Bias domain | Source of bias | Support for Judgement | Review authors' judgement (assess as low, unclear, or high risk of bias |
|---|---|---|---|
| Selection bias | Random sequence generation | *"Each local heart team evaluated the suitability of the patient to receive any of the transcatheter valves studied in the trial. Only patients who were candidates to receive any of the 2 valve types were finally randomized. […].* Randomisation was centralized and considered the mechanism of surgical bioprosthesis failure (predominant stenosis or regurgitation)" Method unreported. | Unclear |
| | Allocation concealment | Not reported | Unclear |
| Performance bias | Blinding of participants and personnel | Open-label | High |
| Detection bias | Blinding of outcome assessment | NR | Unclear |
| Attrition bias | Incomplete outcome data | For the primary outcomes reasons for attrition reported by Rodes-Cabau (JACC, 2022, 681-693). Authors acknowledge that "missing echocardiography data at 1-year follow up accounted for 22% of patients at risk". | High |
| Reporting bias | Selective reporting | Trial registration: NCT03520101; study design reported in Rodes-Cabau et al. 2022 (no power calculation reported). Primary outcomes of hemodynamic performance at 30 days. Cannot find mention of 6-min walk test or hypertrophy secondary outcomes in Nuche (including suppl mat) or Rodes-Cabau paper. | High |
| Other bias | Anything else, ideally pre-specified. | Multiple authors have received research grants, consultant fees, or advisory board members for TAVI valve manufacturer(s) including: Edwards, Medtronic, Abbot, JenaValve. | Unclear |

## Terkelsen (Lancet, 2025)

Reviewer 1: KB, Reviewer 2: KK

| Bias domain | Source of bias | Support for Judgement | Review authors' judgement (assess as low, unclear, or high risk of bias |
|---|---|---|---|
| Selection bias | Random sequence generation | Randomisation by treating physicians using a web-based system (corolog.net) with block permutation (block sizes 2–6), stratified by centre and sex. | Low |
| | Allocation concealment | Electronic randomisation form (Trial Partner). | Unclear |
| Performance bias | Blinding of participants and personnel | Operators and patients were not masked to randomisation ('not possible'). Statistical difference in pre-dilatation between arms (21% Sapien 3, 45% Myval; p<0.0001) | High |
| Detection bias | Blinding of outcome assessment | *"An independent data and safety monitoring board, comprising two cardiologists, an epidemiologist, and a statistician, reported no safety issues and recommended that trial inclusion continued on Aug 23, 2023, when 575 patients had reached 1-year follow-up."* | Unclear |
| Attrition bias | Incomplete outcome data | Composite endpoint was performed according to the intention-to-treat principle, but per-protocol analyses were also conducted if crossover occurred (7 cross-overs from Myval to Sapien arm). Echocardiograms available at 1-year for 957/1020 (95%), 1 month for 5% and post-procedure in 1% | Low |
| Reporting bias | Selective reporting | Trial registration (NCT04443023). Power calculation reported. Additional detail provided in Supplementary Material. *"Endpoints related to the multislice CT and cardiac MRI substudies, valve thrombosis, and degree of aortic regurgitation and gradients according to annular calcium on multislice CT, and 3-year, 5-year, and 10-year findings are planned to be published separately (appendix p 5)."*<br>Authors noted the margin was altered due to higher than expected *blinded* event rate. | Low |
| Other bias | Anything else, ideally pre-specified. | Funded by Meril Life Sciences (manufacturer of Myval), however papers explicitly stated that the funder had no role in the study design, data collection, data analysis, data interpretation or writing of the report. Secondary outcomes considered by authors to be exploratory (hypothesis generating). Limited Bonferonni-corrected secondary endpoints reported in Table 3. | Low |

## Observational studies (with propensity score matching)

Kim (JACC, 2025)

Reviewer 1: PL, Reviewer 2: KB

| # | Question | Yes | No | Unclear | N/A |
|---|---|---|---|---|---|
| 1 | Were the two groups similar and recruited from the same population? | - | ✓ | - | - |
| 2 | Were the exposures measured similarly to assign people to both exposed and unexposed groups? | ✓ | - | - | - |
| 3 | Was the exposure measured in a valid and reliable way? | ✓ | - | - | - |
| 4 | Were confounding factors identified? | ✓ | - | - | - |
| 5 | Were strategies to deal with confounding factors stated? | ✓ | - | - | - |
| 6 | Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? | ✓ | - | - | - |
| 7 | Were the outcomes measured in a valid and reliable way? | ✓ | - | - | - |
| 8 | Was the follow up time reported and sufficient to be long enough for outcomes to occur? | ✓ | - | - | - |
| 9 | Was follow up complete, and if not, were the reasons to loss to follow up described and explored? | ✓ | - | - | - |
| 10 | Were strategies to address incomplete follow up utilized? | ✓ | - | - | - |
| 11 | Was appropriate statistical analysis used? | ✓ | - | - | - |

Comments: Propensity score matched (1:1; based on 11 variables); baseline characteristics appear balanced. Differences in valve size, pre-dilation, volume of contrast agent between arms which may influence findings. No correction for multiple hypothesis testing; however multivariable analysis reported in Supplementary Material.

## Loewenstein (Cardiovas Revascul Med, 2024)

Reviewer 1: PL, Reviewer 2: KB

| # | Question | Yes | No | Unclear | N/A |
|---|---|---|---|---|---|
| **1** | Were the two groups similar and recruited from the same population? | - | ✓ | - | - |
| **2** | Were the exposures measured similarly to assign people to both exposed and unexposed groups? | ✓ | - | - | - |
| **3** | Was the exposure measured in a valid and reliable way? | ✓ | - | - | - |
| **4** | Were confounding factors identified? | ✓ | - | - | - |
| **5** | Were strategies to deal with confounding factors stated? | ✓ | - | - | - |
| **6** | Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? | - | - | ✓ | - |
| **7** | Were the outcomes measured in a valid and reliable way? | ✓ | - | - | - |
| **8** | Was the follow up time reported and sufficient to be long enough for outcomes to occur? | - | ✓ | - | - |
| **9** | Was follow up complete, and if not, were the reasons to loss to follow up described and explored? | - | - | ✓ | - |
| **10** | Were strategies to address incomplete follow up utilized? | - | - | ✓ | - |
| **11** | Was appropriate statistical analysis | - | ✓ | - | - |

Comments: Old and new generation captured during recruitment period. Statistical differences in baseline characteristics (for example: STS, coronary artery calcium, CT aortic valve area, small valve size, medium valve size, pre-dilatation size) noted despite propensity score matching. No correction for multiple univariate tests applied. Only mortality reported at 30 days; remaining in-hospital outcomes.