SUPPLEMENTAL MATERIAL
Data S1.

SUPPLEMENTAL METHODS

**Baseline Doppler echocardiography at rest and under dobutamine stress**

Resting Doppler echocardiograms and under dobutamine stress were performed using commercially available ultrasound systems. Echo analyses were performed in the Echo CoreLab of Quebec Heart and Lung Institute using the Tomtec Arena software (Tomtec Corporation USA, Chicago, IL, USA). LV dimensions were measured at rest according to American Society of Echocardiography/European Association of Cardiovascular Imaging recommendations\(^ {14,35} \). AVA was calculated by the continuity equation; MG was obtained by the Bernoulli formula; LVEF was measured using the biplane Simpson method\(^ {36} \). Projected aortic valve area (AVA\(_{\text{Proj}}\)) at a normal transvalvular flow rate (250ml/min) was calculated using the formula\(^ {18,11} \):

\[
AVA_{\text{Proj}} = AVA_{\text{Rest}} + \frac{AVA_{\text{Peak}} - AVA_{\text{Rest}}}{Q_{\text{Peak}} - Q_{\text{Rest}}} \times (250 - Q_{\text{Rest}})
\]

Where AVA\(_{\text{Rest}}\) and AVA\(_{\text{Peak}}\) are the AVA at rest and at peak stress, and Q\(_{\text{Rest}}\) and Q\(_{\text{Peak}}\) were mean transvalvular flows at rest and at peak stress. This method reduces the flow dependence of AVA under dobutamine stress by standardizing AVA to a fixed normal flow rate of 250 ml/s. AVA\(_{\text{Proj}}\) was previously demonstrated to be superior to AVA\(_{\text{Peak}}\) and MG at peak stress to distinguish true from pseudo-severe AS and to predict death under conservative management\(^ {6} \).

**Statistical analysis**

- **Inverse probability-of-treatment-weighting to limit confusion**

Inverse probability-of-treatment-weighting allows improving baseline imbalances between treatment groups by giving a higher or lower weight to underrepresented and overrepresented
observations, respectively. A propensity score was built using multiple logistic regression taking early AVR vs. ConsRx as a binary endpoint (Table S1). We chose the variables with significantly different distributions between treatment arms in addition to those associated with all-cause mortality in multivariate analysis (see below). The C-index of the propensity score to predict early AVR vs. conservative management was 0.85 ([0.82-0.88], p<0.001). To compare the different types of AVR, the propensity score using the same regression model was recalculated for each of the following pairs of treatments: TAVR vs ConsRx (C-index=0.92 [0.89-0.95], p<0.001), SAVR vs ConsRx (C-index=0.88 [0.85-0.92], p<0.001), TAVR vs SAVR (C-index=0.96 [0.94-0.98], p<0.001). Each patient was weighted by the inverse probability of treatment (e.g. 1/propensity score for AVR patients and 1/(1-propensity score) for ConsRx patients). Trimming of the 99th percentile outliers of the resulting weights (25.1 [n=4], 18.1 [n=2], 19.0 [n=2] and 16.8 [n=6] respectively in the AVR vs. ConsRx, SAVR vs. ConsRx, TAVR vs. ConsRx, and TAVR vs. SAVR pars of treatment) allowed preventing excessive weighting. The resulting weights’ distributions stratified by the treatment arm are illustrated in Figure S1. Then, baseline characteristics were compared between treatment groups in the resulting pseudo-population using weighted standardized mean difference (SMD i.e. percentage of the pooled standard deviation). SMD values were considered acceptable when ≤20%. In case of significant residual differences (SMD>20%), Cox multivariate regression adjustment was done by forcing the variables that remained unbalanced in the unadjusted IPTW model.

- Outcome analyses in the non-weighted population

A Cox proportional hazards regression model was built to predict all-cause mortality comprising clinically relevant variables in addition to variables with a p value <0.1 in univariate analysis. The resulting model comprised age, sex, true severe AS, previous coronary artery bypass grafting, chronic obstructive pulmonary disease, diabetes, chronic kidney disease
(eGFR<60 ml/min/1.73m²), New York Heart Association functional class III-IV, classical/paradoxical low-flow, beta-blockers, and the need for diuretics. The different treatment types were forced into this model to calculate adjusted hazard ratios of all cause mortality. In all multivariate analyses, the number of events per independent variable was maintained ≥10.\textsuperscript{37} To assess clustering effect, we used multilevel mixed effect survival models. In this method, the conventional univariable and multivariable models were enhanced by a random effect term i.e. representing the participating centers. We used the \textit{mestreg} command of Stata software. When the enhancement was significant (likelihood ratio test p<0.05) the results of the mixed effect survival model was reported. Otherwise, we reported the results of the conventional analysis.

**SUPPLEMENTAL RESULTS**

\textit{Comparison of baseline characteristics between TSAS and PSAS patients:}

Baseline characteristics according to the actual AS severity (i.e TSAS or PSAS) are summarized in Table S2. PSAS patients had a higher prevalence of chronic kidney disease (35\% vs 24\%, p=0.02) and previous myocardial infarction (49\% vs 33\%, p=0.002), but less atrial fibrillation (9\% vs 21\%, p=0.004). The mean age and the median EuroSCORE were similar between treatment groups (p>0.05). Symptoms were more severe in the TSAS group as reflected by a higher prevalence of NYHA functional class III-IV (47\% versus 58\%, p=0.02), although the median Duke activity status index was comparable between groups. The indexed LV diastolic diameter was 1 mm/m² larger in the PSAS group, while median NT-proBNP was comparable. Baseline AVA was smaller and MG and peak jet velocity were higher in the TSAS group (Table S2). The results of the different flow-independent AS grading schemes (also detailed in Table S2) are illustrated in Figure S3.
Baseline characteristic before and after inverse-probability-of-treatment weighting:

Fifty seven percent of the patients had early AVR (n=274) and 43% had ConsRx (n=207). Baseline characteristics before and after IPTW are summarized in Table S3. The most important differences between Early AVR and ConsRx group were in the year of inclusion (SMD=32%), previous myocardial infarction (SMD=29%), chronic obstructive pulmonary disease (SMD=25%), coronary artery disease (SMD=30%), NYHA functional class III-IV (SMD=41%), Duke Activity Status Index (SMD=64%), AVA (SMD=30%), MG (SMD=35%), and TSAS (SMD=74%). After IPTW, all differences were well balanced (SMD≤20%). However slight differences emerged in LVEF (SMD=24%) and peripheral artery disease (SMD=25%).

Baseline characteristics according to the type of AVR i.e. SAVR (n=176) and TAVR (n=96) are reported and briefly described in the main manuscript. Pairwise comparisons of baseline characteristics before and after IPTW are reported in tables S4, S5 and S6. Briefly:

- Between ConsRx vs. SAVR: before weighting, there were important differences regarding age (SMD=40%), chronic obstructive pulmonary disease (SMD=25%), previous coronary artery bypass grafting (SMD=25%), myocardial infarction (SMD=38%), peripheral artery disease (SMD=28%), New York Heart Association functional class (SMD=34%), Duke Activity Status Index (SMD=28%), AVA (SMD=41%), MG (SMD=69%), TSAS (SMD=91%), LVEF (SMD=29%), and the EuroSCORE II (SMD=29%). After IPTW, all these imbalances were corrected except peripheral artery disease (weighted SMD=26%) and a slight difference in sex category emerged (weighted SMD=21).

- Between TAVR and ConsRx groups there were differences in age (SMD=59%), hypertension (SMD=45%), chronic kidney disease (SMD=51%), chronic obstructive pulmonary disease (SMD=39%), coronary artery disease (SMD=48%), peripheral
artery disease (SMD=29%), atrial fibrillation/flutter (SMD=33%), diastolic blood pressure (SMD=26%), New York Heart Association functional class III-IV (SMD=56%), Duke Activity Status Index (SMD=117%), mean gradient (SMD=47%), TSAS (SMD=47%), NT-proBNP (SMD=40%), and the EuroSCORE II (SMD=90%). These major differences were partially balanced after IPTW. DASI was refractory to IPTW (weighted SMD=121%), while the differences in age (weighted SMD=33%), hypertension (weighted SMD=25%), chronic kidney disease (weighted SMD=23%), mean gradient (weighted SMD=27%), and the euroSCORE II (weighted SMD=33%) were attenuated but not balanced. These differences were only equilibrated with unacceptably high weights. A difference in pulmonary hypertension not present before emerged after IPTW (weighted SMD=23%). Of note, except for pulmonary hypertension, all the residual balances favored a healthier conservative treatment group.

- Between TAVR vs. SAVR, there were also major baseline differences in age (SMD=104%), body mass index (SMD=34%), hypertension (SMD=59%), chronic kidney disease (SMD=56%), chronic obstructive pulmonary disease (SMD=22%), previous coronary artery bypass grafting (SMD=70%), previous myocardial infarction (SMD=25%), coronary artery disease (SMD=28%), peripheral artery disease (SMD=58%), atrial fibrillation/flutter (SMD=25%), diastolic blood pressure (SMD=39%), congestive heart failure (SMD=21%), New York Heart Association function class II-IV (SMD=22%), Duke activity status index (SMD=90%), mean gradient (SMD=21%), TSAS (SMD=40%), LVEF (SMD=40%), NTproBNP (SMD=31%) and the euroSCORE II (SMD=116%). Duke activity status index was refractory to IPTW (weighted SMD=90%). The remaining differences were corrected (weighted SMD≤20%), except for age (weighted SMD=36%), peripheral artery
disease (weighted SMD=29%), TSAS (weighted SMD=21%) and the euroSCORE II (weighted SMD=50%) which were only attenuated. Again, these differences would have required unacceptably high weights to be addressed.
Table S1. Multiple Logistic Regression to Predict Aortic Valve Replacement. This Model Allowed Generating the Propensity Score Used For Inverse Probability-Of-Treatment Weighting.

|                          | β coefficient ± | Wald    | p value  |
|--------------------------|-----------------|---------|----------|
| **Year of inclusion**    | 0.16±0.04       | 17.694  | <0.001   |
| **Age**                  | -0.03±0.01      | 5.332   | 0.021    |
| **Female**               | -0.1±0.28       | 0.138   | 0.710    |
| **True severe AS**       | 1.54±0.28       | 29.732  | 0.000    |
| **Previous coronary artery bypass grafting** | 0.36±0.33   | 1.190   | 0.275    |
| **Peripheral artery disease** | -1.08±0.46 | 5.532   | 0.019    |
| **Diabetes**             | 0.08±0.26       | 0.106   | 0.745    |
| **Chronic kidney disease** | -0.53±0.3     | 3.192   | 0.074    |
| **Hypertension**         | 0.04±0.3        | 0.016   | 0.900    |
| **Previous stroke**      | 0.18±0.34       | 0.268   | 0.605    |
| **Hyperlipidemia**       | -0.32±0.28      | 1.308   | 0.253    |
| **Chronic obstructive pulmonary disease** | -0.82±0.28 | 8.365   | 0.004    |
| **Previous myocardial infarction** | 0.93±0.28 | 10.786  | 0.001    |
| **Any coronary artery disease** | -1.01±0.48 | 4.494   | 0.034    |
| **Multivessel coronary artery disease** | 0.08±0.19 | 0.197   | 0.657    |
| **Congestive heart failure** | 0.23±0.29    | 0.607   | 0.436    |
| **History of pulmonary oedema** | -1.1±0.38  | 8.513   | 0.004    |
| **Body mass index**      | 0±0.02         | 0.005   | 0.945    |
| **Systolic blood pressure** | -0.01±0.01    | 1.668   | 0.197    |
| **Diastolic blood pressure** | 0.01±0.01   | 0.755   | 0.385    |
| **Heart rate**           | -0.01±0.01      | 0.906   | 0.341    |
| **Paced rhythm**         | -0.21±0.26      | 0.606   | 0.436    |
| **Atrial fibrillation**  | 0.3±0.33        | 0.816   | 0.366    |
| **EuroSCORE II**         | 0.03±0.03       | 1.524   | 0.217    |
| **Betablockers**         | 0.16±0.25       | 0.437   | 0.509    |
| **Diuretics**            | 0.31±0.27       | 1.281   | 0.258    |
| **New York Heart Association functional class III-IV** | 0.83±0.25   | 10.914  | 0.001    |
| **Mean gradient**        | 0.01±0.04       | 0.149   | 0.700    |
| **Aortic valve area**    | -0.43±0.63      | 0.464   | 0.496    |
| **Left ventricular ejection fraction** | 0.02±0.02 | 1.906   | 0.167    |
| **Paradoxical vs. Classical LFLG-AS** | -0.39±0.51 | 0.586   | 0.444    |
| **Duke Activity Status Index** | -0.03±0.01 | 3.090   | 0.079    |
| **Intercept**            | -315.35±75.11   | 17.628  | 0.001    |

Results are β coefficients ± standard errors
Table S2. Baseline Characteristics in Patients with True Severe Aortic Stenosis (TSAS) Compared to Patients with Pseudo-Severe Aortic Stenosis (PSAS).

|                                | True-severe AS (n=293) | Pseudo-severe AS (n=133) | P value |
|--------------------------------|-------------------------|---------------------------|---------|
| **Clinical data**              |                         |                           |         |
| Age, y                         | 74±11                   | 74±9                      | 0.61    |
| Male sex, n(%)                 | 203(69)                 | 102(77)                   | 0.09    |
| Diabetes, n(%)                 | 101(35)                 | 44(33)                    | 0.82    |
| Chronic kidney disease i.e. eGFR≤60ml/min, n(%) | 71(24)                 | 46(35)                    | 0.02    |
| Chronic obstructive pulmonary disease, n(%) | 69(24)                 | 40(30)                    | 0.14    |
| Previous CAGB                  | 76(26)                  | 38(29)                    | 0.54    |
| Previous myocardial infarction, n(%) | 97(33)                 | 64(49)                    | 0.002   |
| Coronary artery disease        | 184(63)                 | 84(64)                    | 0.87    |
| Peripheral artery disease, n(%) | 26(9)                  | 7(5)                      | 0.20    |
| Previous stroke/transient ischemic attack | 40(14)                 | 21(16)                    | 0.56    |
| Atrial fibrillation/flutter, n(%) | 60(21)                 | 12(9)                     | 0.004   |
| Heart rate, bpm                | 72±14                   | 69±13                     | 0.06    |
| **Symptoms and functional status** |                       |                           |         |
| History of CHF, n(%)           | 147(50)                 | 77(58)                    | 0.12    |
| NYHA Functional class, n(%)    |                         |                           | 0.03    |
| I-II                           | 123(42)                 | 70(53)                    |         |
| III-IV                         | 170(58)                 | 61(47)                    |         |
| Duke activity status index     | 19[18-31]               | 19[12-36]                 | 0.24    |
| **The Aortic valve hemodynamics** |                       |                           |         |
| Aortic valve area, cm²         | 0.76±0.18               | 0.92±0.25                 | <0.001  |
| Mean gradient, mmHg            | 29±8                    | 20±7                      | <0.001  |
| Peak aortic jet velocity, m/s  | 3.5±1.8                 | 3.0±1.8                   | <0.001  |
| **True AS severity**           |                         |                           |         |
| Confirmed true severe AS, n(%) | 281(100)               | 0(0)                      |         |
| AVAProj cm²                    | 0.89±0.16               | 1.19±0.13                 |         |
| AVAProj ≤1.0 cm², n/available (%) | 121/140(86)          | 0/66(0)                   |         |
| Aortic valve calcification ratio* | 1.51±0.62              | 0.59±0.25                 | <0.001  |
| Aortic valve calcification ratio ≥1.0, n/available (%) | 88/100(88)             | 0/54(0)                   |         |
| Aortic valve weight ratio*     | 1.34±0.42               | 0.81±0.11                 |         |
| Aortic valve weight ratio ≥1.0, n/available (%) | 72/93(77)             | 0/13(0)                   |         |
| Macroscopic assessment of surgically explanted valve, n/available (%) | 91/117(78)             | 0/14(0)                   |         |
| **Left ventricular function**  |                         |                           |         |
| Stroke volume index, ml/beat/m² | 31[25-36]             | 32[26-36]                 | 0.80    |
| LVEF, %                        | 32[25-49]               | 33[25-50]                 | 0.99    |
| Indexed LVEDD, mm²             | 29±5                    | 30±6                      | 0.02    |
| Classical/Paradoxical LFLG     | 204(70)                 | 98(74)                    | 0.33    |
| n(%)                           |                         |                           |         |
| NT-proBNP, pg/ml               | 2216                    | 1478                      | 0.13    |
| Systolic pulmonary artery pressure | 44±13                 | 40±13                     | 0.02    |
| **Operative risk**             |                         |                           |         |
| EuroSCORE, %                   | 6.6±5.7                 | 6.8±6.0                   | 0.77    |
Values are mean ±SD, median [IQR], and n (%)

*Aortic valve calcification ratio was calculated by dividing the actual aortic valve calcium score by the sex-specific threshold that defines severe AS i.e. 1200 and 2000 arbitrary units respectively for women and men. Similarly, aortic valve weight ratio is the actual valve weight divided by the sex-specific valve weight that defines true severe AS i.e. 1.2 g and 2.0 g respectively for women and men (13)*

eGFR: estimated filtration rate; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; DASI: Duke activity status index; AVA: aortic valve area; AVAProj projected AVA at normal flow i.e. mean systolic flow 250 ml/s; AS: aortic stenosis ; LVEF: left ventricular ejection fraction ; LVEDD: left ventricular end diastolic volume ; NT-proBNP: aminoterminal proB-type natriuretic peptide.
Table S3. Baseline Characteristics in Patients Undergoing Early Aortic Valve Replacement (AVR) Compared to Patients Conservatively Managed (ConsRx) Before and After Inverse Probability-of-Treatment Weighting.

|                                | Before IPTW |                          | After IPTW |                          |                          |                          |
|--------------------------------|-------------|--------------------------|------------|--------------------------|--------------------------|--------------------------|
|                                | Early AVR (n=274) | Conservative (n=207) | SMD (%)    | Early AVR (n=476) | Conservative (n=446) | SMD (%)    |
| Year of surgery                | 2009.6±3.4  | 2008.4±4.1              | 32         | 2009.0±3.7  | 2009.3±4.1              | 08          |
| Age, y                         | 74.0±10.0   | 75.0±10.0               | 10         | 73.8±10.4   | 75.7±9.8               | 19          |
| Male sex, %                    | 70.1        | 72.5                    | 5          | 66.2        | 73.1                    | 15          |
| Body mass index, kg/m²         | 27.7±5.5    | 27.5±5.7                | 4          | 27.3±5.3    | 27.2±5.3                | 2           |
| Diabetes, %                    | 35.4        | 32.9                    | 5          | 32.4        | 36.8                    | 9           |
| Hypertension, %                | 25.2        | 27.5                    | 5          | 70.3        | 70.0                    | 1           |
| Hyperlipidemia, %              | 71.9        | 64.7                    | 16         | 66.9        | 72.2                    | 12          |
| Chronic kidney disease i.e. eGFR≤60ml/min, % | 31.4 | 24.2 | 16 | 25.5 | 29.8 | 10 |
| Chronic obstructive pulmonary disease, % | 29.6 | 18.8 | 25 | 22.9 | 23.3 | 1 |
| Previous CABG, %               | 26.3        | 25.1                    | 3          | 23.4        | 29.1                    | 13          |
| Previous myocardial infarction, % | 30.7 | 44.4 | 29 | 32.0 | 39.0 | 15 |
| Coronary artery disease, %     | 67.5        | 53.1                    | 30         | 57.8        | 64.6                    | 14          |
| Previous stroke or transient ischemic attack, % | 14.2 | 14.5 | 1 | 14.1 | 13.5 | 2 |
| History of peripheral artery disease, % | 8.0 | 8.7 | 3 | 5.7 | 12.8 | 25 |
| Atrial fibrillation/flutter, % | 19.0        | 13.0                    | 16         | 15.3        | 19.3                    | 11          |
| Heart rate, bpm                | 71±12       | 71±13                   | 0          | 71±12       | 72±14                   | 8           |
| Systolic blood pressure, mmHg  | 122±20      | 124±19                  | 10         | 123±18      | 121±19                  | 11          |
| Diastolic blood pressure, mmHg | 71±11       | 71±10                   | 0          | 72±12       | 71±11                   | 9           |
| Variable                                      | Value 1 | Value 2 | Value 3 | Value 4 | Value 5 | Value 6 |
|----------------------------------------------|---------|---------|---------|---------|---------|---------|
| History of CHF, %                            | 51      | 54      | 6       | 51      | 59      | 18      |
| Previous acute pulmonary oedema, %           | 19.7    | 14.5    | 14      | 17.5    | 11.9    | 16      |
| NYHA III-IV, %                               | 64      | 44      | 41      | 57.6    | 56.7    | 02      |
| Duke activity status index                   | 18±13   | 27±15   | 64      | 23.4±16.6| 23.4±15.6| 00      |
| Aortic valve area, cm²                        | 0.78±0.19| 0.85±0.21| 35     | 0.80±0.19| 0.82±0.2| 10      |
| Mean gradient, mmHg                          | 27±8    | 22±8    | 63      | 25.5±7.8| 24.6±8.2| 11      |
| Confirmed true severe AS, %                  | 75.5    | 41.5    | 74      | 65.9    | 60.1    | 12      |
| LVEF, %                                      | 39±17   | 36±15   | 19      | 38±18   | 34±14   | 24      |
| Classical LFLG, %                            | 75      | 69      | 13      | 69.7    | 81.8    | 29      |
| Moderate mitrale regurgitation, %            | 12      | 12      | 0       | 10.7    | 12.2    | 05      |
| SPAP >35 mmHg, %                             | 50      | 45      | 10      | 45.1    | 50.1    | 10      |
| Ln NT-proBNP                                 | 7.8±1.4| 7.1±6.3| 15      | 7.7±1.3| 7.9±1.7| 13      |
| EuroSCORE II, %                              | 7.1±6.3| 6±4.9   | 19      | 6.4±6.1| 6.6±4.9| 04      |

Values are mean ±SD and %

In bold: variables with SMD >20 i.e. insufficiently balanced

eGFR: estimated filtration rate; IPTW: inverse probability-of-treatment weighting; LFLG: low-flow, low-gradient; LVEF: left ventricular ejection fraction ; NYHA: New York Heart Association; SMD: standardized mean difference; SPAP: systolic pulmonary artery pressure
Table S4. Baseline Characteristics in Patients Undergoing Early Surgical Aortic Valve Replacement (SAVR) Compared to Patients Conservatively Managed (ConsRx) Before and After Inverse Probability-of-Treatment Weighting.

|                        | Before IPTW              | After IPTW              |
|------------------------|--------------------------|-------------------------|
|                        | SAVR (n=177)             | Conservative (n=207)    | SMD (%)     | SAVR (n=397) | Conservative (n=316) | SMD (%)     |
| year of inclusion      | 2008.0±3.3               | 2008.0±4.1              | 2           | 2008.0±3.4   | 2008.0±4              | 3           |
| Age, y                 | 70.8±10.3                | 75.0±10.0               | 41          | 72.5±10.1    | 74.1±10.3             | -15         |
| Male sex, %            | 72.2                     | 72.5                    | 1           | 67.0         | 76.0                   | 21          |
| Body mass index, kg/m² | 28.3±5.7                 | 27.5±5.7                | 14          | 27±5.5       | 27.5±5.4              | 8           |
| Diabetes, %            | 34.1                     | 32.9                    | 3           | 28.0         | 33.2                   | 11          |
| Hypertension, %        | 50.6                     | 44.9                    | 11          | 43.5         | 46                      | 6           |
| Hyperlipidemia, %      | 70.5                     | 64.7                    | 12          | 67.2         | 68.6                    | 2           |
| Chronic kidney disease i.e. eGFR≤60ml/min, % | 22.2       | 24.2                   | 5           | 21.3         | 22.3                   | 3           |
| Chronic obstructive pulmonary disease, % | 15.3             | 25.1                   | 25          | 23.2         | 23.9                   | 0           |
| Previous CABG, %       | 15.3                     | 25.1                    | 25          | 23.0         | 23.6                   | 0           |
| Previous myocardial infarction, % | 26.7             | 44.4                   | 38          | 32.1         | 39.1                   | 15          |
| Coronary artery disease, % | 63.1         | 53.1                   | 20          | 54.0         | 57.0                   | 5           |
| Previous stroke or transient ischemic attack, % | 11.9       | 14.5                   | 8           | 12.4         | 13.4                   | 4           |
| History of peripheral artery disease, % | 2.3              | 8.7                    | 28          | 2.2          | 7.1                    | 26          |
| Atrial fibrillation/flutter, % | 15.3         | 12.6                   | 8           | 11.1         | 15.2                   | 13          |
| Heart rate, bpm         | 72.0±13.2                | 71.0±13.3               | 7           | 71.7±12.2    | 71.4±13                | 2           |
| Systolic blood pressure, mmHg | 121.6±19.1       | 123.8±19.4              | 12          | 123.4±18.2   | 123.1±18.9             | 2           |
| Diastolic blood pressure, mmHg | 72.7±11.2 | 71.1±10.3               | 15          | 73.1±11.2    | 72.2±10.8              | 8           |
| History of CHF, %      | 47.2                     | 53.6                    | 13          | 53.4         | 55.0                   | 5           |
| Previous acute pulmonary oedema, % | 18.8          | 14.5                   | 12          | 17.1         | 14.2                   | 8           |
|                          |        |        |        |        |        |        |
|--------------------------|--------|--------|--------|--------|--------|--------|
| **NYHA III-IV, %**       | 60.2   | 43.5   | 34     | 58     | 49     | 18     |
| Duke activity status index | 22.7±14.1 | 26.7±15.3 | 28   | 26±15.5 | 26.5±15.7 | 3     |
| Aortic valve area, cm²   | 0.7±0.1 | 0.8±0.2 | 41   | 0.8±0.1 | 0.8±0.2 | 17    |
| Mean gradient, mmHg      | 27.7±7.5 | 22.2±8.2 | 69   | 25.2±7.2 | 23.7±8.3 | 19    |
| Confirmed True Severe AS, % | 81.8   | 41.5   | 91   | 58     | 54     | 9     |
| **LVEF, %**              | 41.4±18.7 | 36.3±16   | 29   | 37.9±18.4 | 34.9±15.4 | 18    |
| Classical LFLG, %        | 65.3   | 74.9   | 21   | 72     | 77     | 10    |
| Moderate mitrale regurgitation, % | 10.0   | 12.0   | 6    | 9      | 9      | 0     |
| SPAP >35 mmHg, %         | 50.6   | 44.9   | 11   | 43     | 46     | 6     |
| Ln NT-proBNP             | 7.5±1.5 | 7.4±1.5 | 9    | 7.6±1.4 | 7.4±1.5 | 11    |
| EuroSCORE II, %          | 4.6±4.4 | 6±4.8  | 29   | 5.3±4.4 | 5.9±4.6 | 15    |

Values are mean ±SD and %

In bold: variables with SMD >20 i.e. insufficiently balanced

eGFR: estimated filtration rate; IPTW: inverse probability-of-treatment weighting; LFLG: low-flow, low-gradient; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; SMD: standardized mean difference; SPAP: systolic pulmonary artery pressure
Table S5. Baseline Characteristics in Patients Undergoing Early Transcatheter Aortic Valve Replacement (TAVR) Compared to Patients Conservatively Managed (ConsRx) Before and After Inverse Probability-of-Treatment Weighting.

|                                | Before weighting |                              | After weighting |                              |
|--------------------------------|------------------|------------------------------|----------------|------------------------------|
|                                | TAVR (n=98)      | Conservative (n=207) SMD (%) | TAVR (n=202)   | Conservative (n=320) SMD (%) |
| year of inclusion              | 2011.7±2.3       | 2008.4±4.1                  | 97             | 2011.2±2.5                  | 2009.7±4.1               | 45             |
| Age, y                         | 80.2±7.4         | 75.0±10.0                   | 59             | 79.8±8.1                    | 76.9±9.2                 | 33             |
| Male sex, %                    | 66.3             | 72.5                        | 13             | 70.9                        | 75.9                     | 11             |
| Body mass index, kg/m²         | 26.5±4.6         | 27.5±5.7                    | 19             | 27±4.8                      | 27.7±5.3                 | 14             |
| Diabetes, %                    | 37.8             | 32.9                        | 10             | 34.2                        | 35.3                     | 2              |
| Hypertension, %                | 89.8             | 72.8                        | 45             | 89.2                        | 80.3                     | 25             |
| Hyperlipidemia, %              | 74.5             | 64.7                        | 21             | 73.9                        | 71.8                     | 5              |
| Chronic kidney disease i.e. eGFR≤60ml/min, % | 48.0             | 24.2                        | 51             | 38.6                        | 27.9                     | 23             |
| Chronic obstructive pulmonary disease, % | 35.7             | 18.8                        | 39             | 29.2                        | 31.9                     | 6              |
| Previous CABG, %               | 45.9             | 25.1                        | 45             | 38.6                        | 38.2                     | 1              |
| Previous myocardial infarction, % | 37.8             | 44.4                        | 13             | 44.3                        | 38.9                     | 11             |
| Coronary artery disease, %     | 75.5             | 53.1                        | 48             | 73.9                        | 64.7                     | 20             |
| Previous stroke or transient ischemic attack, % | 18.4             | 14.5                        | 11             | 19.2                        | 19.4                     | 1              |
| History of peripheral artery disease, % | 18.4             | 8.7                         | 29             | 13.9                        | 11.9                     | 6              |
| Atrial fibrillation/flutter, % | 25.5             | 12.6                        | 33             | 22.2                        | 15.9                     | 16             |
| Heart rate, bpm                | 69.6±10.7        | 71±13.3                     | 12             | 69.8±10.5                   | 68.9±14.3                | 7              |
| Systolic blood pressure, mmHg  | 122.2±18.7       | 123.8±19.4                  | 9              | 126.3±18.6                  | 126.0±19.0               | 2              |
| Variable                                      | Group 1        | Group 2        | Group 3        | Group 4        | Group 5        | SMD |
|-----------------------------------------------|----------------|----------------|----------------|----------------|----------------|-----|
| Diastolic blood pressure, mmHg                | 68.3±11.4      | 71.1±10.3      | 69.5±10.6      | 70.0±10.5      | 5              |     |
| History of CHF, %                             | 57.1           | 53.6           | 53.5           | 59.4           | 12             |     |
| Previous acute pulmonary oedema, %            | 21.4           | 14.5           | 12.8           | 10.9           | 6              |     |
| NYHA III-IV, %                                | 70.4           | 43.5           | 56             | 69.5           | 56.7           | 27  |
| Duke activity status index                    | 12.3±8.2       | 26.7±15.3      | 117            | 11.2±7.6       | 25.9±15.4      | 121 |
| Aortic valve area, cm²                         | 0.8±0.2        | 0.8±0.2        | 20             | 0.8±0.2        | 0.8±0.2        | 11  |
| Mean gradient, mmHg                           | 26.1±7.9       | 22.2±8.2       | 47             | 25.1±7.6       | 23.1±7.4       | 27  |
| Confirmed True Severe AS, %                   | 64.3           | 41.5           | 47             | 50.0           | 48.3           | 3   |
| LVEF, %                                       | 34.8±12.5      | 35.7±15.4      | 6              | 34.9±11.9      | 33.9±15.2      | 8   |
| Classical LFLG, %                             | 75.5           | 74.9           | 1              | 74.9           | 76.9           | 5   |
| Moderate mitral regurgitation                 | 15.4           | 12             | 10             | 13.7           | 21.8           | 21  |
| SPAP >35 mmHg, %                              | 49.0           | 44.9           | 8              | 40.1           | 51.6           | 23  |
| Ln NT-proBNP                                  | 7.9±1.1        | 7.4±1.5        | 40             | 7.9±1          | 7.9±1.6        | 2   |
| EuroSCORE II, %                               | 11.3±6.8       | 6±4.8          | 90             | 9.3±6.1        | 7.4±5.2        | 33  |

Values are mean ±SD and %

In bold: variables with SMD >20 i.e. insufficiently balanced

eGFR: estimated filtration rate; IPTW: inverse probability-of-treatment weighting; LFLG: low-flow, low-gradient; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; SMD: standardized mean difference; SPAP: systolic pulmonary artery pressure
Table S6. Baseline Characteristics in Patients Undergoing Transcatheter Aortic Valve Replacement (TAVR) Compared to Patients Undergoing Surgical Aortic Valve Replacement (SAVR) Before and After Inverse Probability-of-Treatment Weighting.

| Feature                                         | Before IPTW | After IPTW |
|-------------------------------------------------|-------------|------------|
|                                                 | TAVR        | SAVR       | SMD   | TAVR       | SAVR       | SMD   |
|                                                 | (n=98)      | (n=177)    |       | (n=174)    | (n=267)    |       |
| Year of inclusion                               | 2011.7±2.4  | 2008.4±3.3 | 116   | 2011.3±2.4 | 2009.2±3.4 | 74    |
| Age, y                                          | 80.3±7.5    | 70.9±10.4  | 104   | 77.8±9.1   | 74.2±10.8  | 36    |
| Male sex, %                                     | 66.3        | 72.6       | 14    | 71.3       | 72.4       | 2     |
| Body mass index, kg/m²                          | 26.5±4.7    | 28.3±5.8   | 34    | 27.2±5.1   | 27.7±5.2   | 10    |
| Diabetes, %                                     | 37.8        | 34.3       | 7     | 36.8       | 30.1       | 14    |
| Hypertension, %                                 | 89.8        | 66.3       | 59    | 82.3       | 75         | 18    |
| Hyperlipidemia, %                               | 74.5        | 70.9       | 8     | 72.4       | 71.3       | 2     |
| Chronic kidney disease i.e. eGFR≤60ml/min, %    | 48.0        | 22.3       | 56    | 35.6       | 32.0       | 8     |
| Chronic obstructive pulmonary disease, %        | 35.7        | 25.7       | 22    | 28.7       | 23.8       | 11    |
| Previous CABG, %                                | 45.9        | 15.4       | 70    | 34.5       | 25.8       | 19    |
| Previous myocardial infarction, %               | 37.8        | 26.3       | 25    | 33.3       | 31.9       | 3     |
| Coronary artery disease, %                      | 75.5        | 62.9       | 28    | 70.7       | 65.6       | 11    |
| Previous stroke or transient ischemic attack, % | 18.4        | 12         | 18    | 19.0       | 16.3       | 7     |
| History of peripheral artery disease, %         | 18.4        | 1.7        | 58    | 10.9       | 3.5        | 29    |
| Atrial fibrillation/flutter, %                  | 25.5        | 15.4       | 25    | 19.0       | 15.6       | 9     |
| Heart rate, bpm                                 | 69.6±10.7   | 72±13.2    | 20    | 69.4±10.2  | 71.4±12.7  | 18    |
| Systolic blood pressure, mmHg                   | 122.3±18.8  | 121.6±19.1 | 3     | 126.7±18.7 | 125.3±18.8 | 7     |
| Diastolic blood pressure, mmHg                  | 68.3±11.4   | 72.8±11.3  | 39    | 70.4±10.1  | 72.5±10.7  | 21    |
| History of CHF, %                               | 57.1        | 46.9       | 21    | 44.3       | 52.5       | 16    |
| Previous acute pulmonary oedema, %              | 21.4        | 18.9       | 6     | 19.5       | 23.0       | 9     |
| NYHA III-IV, %                                  | 70.4        | 60.0       | 22    | 66.9       | 61.1       | 12    |
| Duke activity status index                      | 12.3±8.3    | 22.7±14.1  | 90    | 10.7±7.7   | 20.9±14.1  | 90    |
| Variable                                      | Mean ± SD | Median ± IQR | Max | Min | Max ± SD | Median ± IQR | Min ± SD |
|-----------------------------------------------|-----------|--------------|-----|-----|----------|--------------|----------|
| Aortic valve area, cm²                         | 0.8±0.2   | 0.8±0.2      | 20  | 0.8±0.2 | 0.8±0.2   |              |          |
| Mean gradient, mmHg                           | 26.1±8    | 27.8±7.6     | 21  | 26.5±8.7 | 27.6±7.3 |              |          |
| Confirmed True Severe AS, %                   | 64.3      | 81.7         | 40  | 64.9 | 74.7     |              |          |
| LVEF, %                                       | 34.9±12.6 | 41.3±18.7    | 40  | 57.3±15.1 | 56.7±10.6 |              |          |
| Classical LFLG, %                             | 75.5      | 65.3         | 22  | 65.5 | 61.7     |              |          |
| Moderate mitral regurgitation, %              | 15.4      | 10.0         | 16  | 11.2 | 11.2     |              |          |
| SPAP >35 mmHg, %                              | 49.0      | 50.6         | 3   | 46.0 | 52.1     |              |          |
| Ln NT-proBNP                                  | 8±1.1     | 7.6±1.6      | 31  | 7.9±1.1 | 7.8±1.5 |              |          |
| EuroSCORE II, %                               | 11.4±6.8  | 4.7±4.5      | 116 | 9.1±6.6 | 6.2±5   |              |          |

Values are mean ± SD and %

In bold: variables with SMD >20 i.e. insufficiently balanced

eGFR: estimated filtration rate; IPTW: inverse probability-of-treatment weighting; LFLG: low-flow, low-gradient; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; SMD: standardized mean difference; SPAP: systolic pulmonary artery pressure
Figure S1. Distribution of inverse probability-of-treatment weights stratified by the different pairs of treatment arm.

In Panel A, conservative strategy (median weight [1\textsuperscript{st}-3\textsuperscript{rd} quartile] 1.41 [1.16-2.19]) vs. early AVR (1.30 [1.12-1.70]);

In Panel B, conservative (1.16 [1.06-1.68]) vs. early SAVR (1.46 [1.13-2.12]);

In Panel C, conservative (1.05 [1.01-1.21]) vs. TAVR (1.30 [1.09-1.92]);

In Panel D, SAVR (1.02 [1.00-1.17]) vs. TAVR (1.10 [1.02-1.59]).
Figure S2. Survival benefit associated with aortic valve replacement (non-weighted population).

The benefit of aortic valve replacement was studied in the original population to corroborate the findings with inverse probability of treatment weighting. A multilevel, mixed effect survival model was used to account for potential clustering effect of the participating centers.

Adjusted hazard ratio (HR): see supplemental methods for details regarding multivariate analysis. AVR: aortic valve replacement.
Figure S3. Survival Benefit Associated With Aortic Valve Replacement After Stratification According to the Presence of True or Pseudo-Severe AS (Non-Weighted Population).

The benefit of aortic valve replacement was studied in the original population to corroborate the findings with inverse probability of treatment weighting.

Adjusted hazard ratio (HR): see supplemental methods for details regarding multivariate analysis

TSAS/PSAS: true/pseudo-severe aortic stenosis; AVR: aortic valve replacement; ConsRx: conservative management.

*Patients with indeterminate AS severity (n=56) were excluded and 3 of 425 remaining patients were lost to follow up
Figure S4. Survival Benefit Associated With Aortic Valve Replacement in Classical (Left Panel) and Paradoxical LFLG-AS (Right Panel) Using Inverse Probability-of-Treatment Weighting.

The adjusted weighted hazard ratios are adjusted for peripheral artery disease which remained significant despite IPTW (see Table S3).

AVR: aortic valve replacement.