

## **Thirty-day readmissions in surgical and transcatheter aortic valve replacement: a systematic review and meta-analysis**

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## Abstract

### Background

The 30-day all-cause readmission rate after surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR) vary substantially. We conducted a systematic review and meta-analysis to examine the overall incidence, causes, and risk factors of 30-day all-cause readmission rate after SAVR and TAVR.

### Methods

Eight medical research databases were searched; Cochrane, Medline, Embase, UpToDate, PROSPERO, National Guideline Clearinghouse, SweMed and Oria. We followed The Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) for this study.

### Results

Thirty-three articles were included in the systematic review, 32 of which were appropriate for the meta-analysis. Overall, 17% (95% CI: 16-18%) of patients in the SAVR group, and 16% (95% CI: 15-18%) in the TAVR groups were readmitted within 30 days. Heart failure, arrhythmia, infection, and respiratory problems were the most frequent causes of all-cause readmission after SAVR and TAVR. Most frequent reported prior risk factors for all-cause readmission following TAVR were diabetes, chronic lung disease/chronic obstructive pulmonary disease, atrial fibrillation, kidney problems, and transapical approach/nonfemoral access. For SAVR, no risk factors for 30-day all-cause readmission were reported in the literature to date.

### Conclusion

In conclusion, the overall proportion of 30-day all-cause readmission after SAVR and TAVR are high. Interventions to prevent avoidable readmissions ought to be developed and implemented.

## **Introduction**

Today, surgical aortic valve replacement (SAVR) is the standard treatment for patients with operable severe aortic stenosis (AS) (1, 2). Surgical treatment for AS improves survival and enhances patients' quality of life (3-5). In older patients (>75 years) with symptomatic severe AS and who are at high surgical risk, transcatheter aortic valve replacement (TAVR) is the established alternative to SAVR (1, 6, 7). TAVR yields favorable outcomes compared to medical treatment (8).

Arrhythmias, infections, or other complications after SAVR and TAVR are relatively frequent (9) and often require readmission to the hospital. Unplanned readmissions are costly for individuals and the public and negatively affect patients' quality of life and rehabilitation (10). Furthermore, it increases the risk for hospital-acquired complications (10). In the literature, it is reported that the incidence of 30-day all-cause readmissions after SAVR and TAVR is about one out of every four discharges results in a readmission (9, 11, 12). However, reported readmission rates vary substantially. Hence, the precise estimation of the magnitude of the problem remains unaddressed. Moreover, risk factors for and causes of readmissions following SAVR and TAVR have not yet been systematically scrutinized. This information is important, because it can guide clinicians, hospital administrators, and policy-makers in developing and implementing programs to improve the quality of care for SAVR and TAVR patients following hospital discharge. This will be even more important in the coming years, as the increasing trend in life expectancy translates to more SAVR and TAVR procedures (5, 13-15). An accurate estimation of readmission rates and risk factors leading up to them is also relevant for researchers in the area of valve replacement, because resulting data could be used for benchmarking and would enable researchers to calculate the sample sizes needed for future trials that assess interventions to reduce readmissions.

These issues prompted us to conduct a systematic literature review and meta-analysis. Our aims were (i) to estimate the overall 30-day all-cause readmission rate in patients following SAVR and TAVR, and (ii) to identify risk factors for and causes of 30-day all-cause readmissions after discharge of these patients.

## **Methods**

The protocol for this systematic literature review and meta-analysis was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; no. 42016032670). The Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) guidelines were used. (16).

### *Literature search*

The first author (SOD) developed the search strategy in collaboration with an experienced research librarian. The following databases were consulted: Cochrane (Cochrane database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register, NHS Economic Evaluation Database, Health Technology Assessment Database and Other Reviews); Medline (accessed through PubMed; <http://www.ncbi.nlm.nih.gov/pubmed>); Embase; UpToDate; PROSPERO; National Guideline Clearinghouse; SveMed; and Oria.no. In addition, reference lists of candidate articles were screened to find additional references missed by our search strings (i.e., snowball method). Details on the search terms and the search strings can be found in online Table 2. Publication date limits were set from database inception to October 8, 2017. Language search was limited to English, and the Scandinavian languages. If necessary information was missing, we emailed the authors to obtain additional information.

Articles were eligible for inclusion if they reported study results on 30-day all-cause readmission following SAVR and TAVR procedures. For the present review, we defined 30-day all-cause readmission as an unplanned readmission for any reason within 30 days after discharge (17). We excluded articles that reported results from studies dealing with multiple valves or specific diseases/conditions related to the SAVR and TAVR treatment. We also excluded articles that reported results from studies dealing with procedural or cardiac-related causes or other specific causes for readmissions, because they did not address all-cause readmissions. One researcher (SOD) screened all the records identified by title, and two researchers (SOD/IL) assessed the full-text candidate articles of the first screening using the inclusion criteria listed above. Before our review was completed, we consulted the databases several more times to check whether we had missed any eligible articles (Online Table 2).

#### *Data abstraction*

Data from included articles were extracted onto a standard form according to an *a priori* protocol. Extracted data included information on study-related characteristics, patient-related characteristics, and main findings. The study-related variables included the article's year of publication; country where the study took place; representativeness of the cohort (single-center, multicenter, or nationwide data); whether the cohort was prospectively or retrospectively studied; and whether 30-day all-cause readmission was reported as a primary or secondary endpoint. Patient-related variables included mean age and proportion of the study population that were males. The results we were interested in, and what we extracted, pertained to the total sample size reported in the article and the number of events (30-day all-cause readmission).

### *Quality of the studies*

Two researchers independently assessed the quality of the studies (SOD/IL) using the Newcastle-Ottawa Scale (NOS). NOS is an established scale for assessment of cohort studies (18). For studies with no relevant data accordingly to NOS items for appraisal, we noted them as “not relevant” (NR). Consensus by discourse resolved disagreements.

### *Statistical analysis*

To calculate an overall incidence of 30-day all-cause readmission, we used a random effects meta-analysis of single proportions according to the DerSimonian-Laird method (19). We used the Freeman-Turkey double arcsine transformation to stabilize the variance (20). Heterogeneity between studies was assessed with the Cochran’s Q test, and its magnitude was evaluated by the  $I^2$  statistic. This describes the proportion of total variation due to heterogeneity rather than chance (21). To investigate possible sources of heterogeneity, we performed analyses stratified by the study characteristic, prospective versus retrospective timing of the study, representativeness of the cohort (single- versus multi-center), country where the study took place (USA versus others), and whether or not 30-day all-cause readmission was reported as the primary endpoint. Further univariable random effects meta-regression analyses were used to examine whether estimates were affected by the study-level covariates. Source of heterogeneity was considered to be important if the covariate decreased between-study variance. The estimate of  $\tau^2$  in the presence of a covariate versus its omission allows the proportion of the heterogeneity variance explained by the covariate to be calculated. For power consideration, we determined that a minimum of 10 studies per covariate was required in a single model of meta-regression (22). An additional sensitivity analysis was conducted by iteratively omitting one study at a time from the meta-analysis and assessing its influence on the overall results (23). Publication bias was evaluated visually by

funnel plots and further assessed using a test of asymmetry (Egger's test of the intercept) applied to funnel plots (24).

All statistical analyses were performed with STATA 14.0 (STATA Data Analysis and Statistical Software; StataCorp LP, College Station, TX, USA.)

## **Results**

### *Included articles*

One article was excluded because it reported results from another article we had already included. Another article was excluded because the mean age of participants in the study was >80 years. We identified a total of 6867 candidate articles (Fig.1). After duplicates were removed, we reviewed the title and abstract of 6848 articles, 6588 of which were not relevant for our purposes. The remaining 260 articles were assessed for eligibility based on full-text review; 227 were deemed ineligible. We included 33 articles in the systematic review and 32 in the meta-analysis, 12 on the SAVR population and 20 on the TAVR population.

### *Study characteristics in included articles*

The characteristics of the studies included are presented in Online Table 1. We identified 12 cohort studies (14, 25-35) on SAVR, all of which were published from 2008 to 2017. Ten studies used a retrospective design, 8 studies were conducted in the USA, and 7 designated 30-day all-cause readmission as the primary endpoint. Overall, 558,396 patients were included in our review of SAVR studies, yielding 111,909 readmissions. Mean age of the included patients ranged from 61 to 81 years; the proportion of males ranged from 48% to 71%.



For articles reporting TAVR results, we identified 20 cohort studies (6, 7, 11-13, 28, 34-47), which were published from 2015 to 2017. Sixteen studies employed a retrospective design; 11 studies were performed in the USA; and 11 studies had 30-day all-cause readmission as a primary endpoint. In these 20 studies, 109,730 patients were included, yielding 21,192 readmissions. Mean age ranged from 80.7 to 84.3 years; the proportion of males ranged from 34% to 57%.

#### *Quality assessment and publication bias*

The overall quality of studies in the included articles was moderate on the NOS. Many of these retrospective studies failed to provide descriptions of how the outcome was derived and how it was validated. Thus, this produced an overall assessment of moderate quality (online Table 3). We found no publication bias, neither in SAVR studies (Egger test,  $p=0.255$ ) nor in TAVR studies (Egger test,  $p=0.140$ ). Funnel plots are presented in online material (Online Fig. 1).

#### *Incidence of 30-day all-cause readmission rate following SAVR or TAVR*

The incidence of 30-day all-cause readmission rate for SAVR ranged from 7-23%, and for TAVR, from 5-27%. The pooled estimated proportion of the 30-day all-cause readmission after SAVR was 17% (95% CI: 16-18), with substantial heterogeneity ( $I^2=98.44\%$ ) (Fig. 2). Subgroup analysis of heterogeneity in the SAVR population revealed a significantly higher readmission rate in multicenter studies (20%) compared to single-center studies (12%) (Table 1). Regional differences were also observed, with higher readmission rates in the USA (18%) compared to other countries (14%). A lower incidence of readmissions was found in prospective (14%) compared to retrospective (17%) studies. We also found a difference in

studies reporting on readmission as a primary (17%) versus secondary (15%) endpoint (Table 1).

The pooled estimated proportion of the 30-day all-cause readmission after TAVR was 16% (95% CI: 15-18), also with substantial heterogeneity ( $I^2=97.06\%$ ) (Fig. 2). Subgroup analysis revealed more readmissions in multicenter studies (18%) compared to single-center studies (12%) (Table 1). Regional differences were observed, with a higher incidence in the USA (18%) compared to other countries (14%). A lower incidence was found in prospective (11%) studies compared to retrospective (17%) studies.

We also extended the analyses by using a random effect meta-regression model in the univariable mode. With this approach, we found that the only study-level variable significantly associated with readmission rate was single-center studies versus multicenter studies (Table 2). Sixty-nine percent of between-study heterogeneity was accounted for by this study-level variable in the SAVR population ( $p=0.013$ ), and 24% in the TAVR population ( $p=0.038$ ). Furthermore, USA versus other countries was marginally associated with readmission in the TAVR population ( $p=0.091$ ).

In the meta-analysis, the results from the sensitivity analyses appeared to be robust against the influence of individual studies.

#### *Cause of 30-day all-cause readmissions after SAVR and TAVR*

We found three articles reporting on causes of 30-day all-cause readmissions for SAVR patients (28, 31, 34). Heart failure (15-19%) and cardiac rhythm disorder (10-14%) were the most frequently reported causes of 30-day all-cause readmission after SAVR. Infections, lung complications/respiratory problems, and bleedings ranged from 3-14%, as causes of readmissions after SAVR (Online Table 4).

We found nine articles reporting on causes of 30-day all-cause readmissions after TAVR. Heart failure (up to 30%), respiratory problems (up to 14%), infections (up to 13%), and arrhythmia (up to 10%) were the most frequently reported causes of 30-day all-cause readmission after TAVR (Online Table 5).

#### *Risk factors for 30-day all-cause readmissions after SAVR and TAVR*

We identified six articles reporting data on risk factors for 30-day all-cause readmission after TAVR (7, 11, 37, 39, 40, 48). Independent risk factors of diabetes (OR: 1.13-1.18); chronic lung disease/chronic obstructive pulmonary disease (COPD) (OR: 1.18-1.32, HR: 1.16); atrial fibrillation (OR: 1.26-1.70); kidney-related access (OR: 1.33-1.62, HR: 1.20-1.23); and transapical approach/nonfemoral access (OR: 1.21-1.43) were among the most frequently reported risk factors. Risk factors with an OR value of  $>2.0$  were major/life threatening bleeding (2.41), length of stay of 7-10 days during primary admission (2.32), length of stay of  $>10$  days during primary admission (3.06), and second prior admission in the year before TAVR (2.33). Details are included in online Table 6.

We found no articles that comprehensively reported on risk factors for 30-day all-cause readmission after SAVR.

## **Discussion**

Reported hospital readmission rates vary substantially following SAVR and TAVR, obscuring rational guidance for clinicians, hospital administrators, and policy-makers. An accurate estimation of readmission rates and risk factors is also relevant for researchers, because reliable estimates are needed for benchmarking new valve replacement prototypes and to calculate study population sample sizes.

The meta-analysis we report here estimated a pooled 30-day all-cause readmission rate of 17% for SAVR and 16% for TAVR. The readmission rates are high, which we know are an additional burden for patients and caregivers, costly for society, and increase the risk of hospital-acquired infections and other errors (10). Poor quality of care and transitional care contributes to high numbers of readmissions, but some readmissions are not necessarily attributable to the quality of care (49). Some are unavoidable and occur due to expected complications after the treatments (49). We don't know the proportion of avoidable readmissions after SAVR and TAVR, and this makes the interpretation of readmissions as a quality indicator difficult. Greater age and higher comorbidity, and major surgery, suggest a need to examine the proportions of avoidable and unavoidable readmissions after SAVR and TAVR. Having firm data on avoidable and unavoidable readmissions would help healthcare professionals to tailor new interventions to prevent readmissions, especially avoidable ones, and to improve transitional care in order to reduce burdens associated with readmissions.

Studies on 30-day all-cause readmission rates in SAVR and TAVR populations, support the notion that the proportion of readmissions in these two groups of patients are not significantly different (28, 34), and are approximately similar to the estimates of the meta-analysis. However, because the populations differ (e.g., in age and comorbidity), one cannot obtain generalizable data by directly comparing the 30-day all-cause readmission rates between SAVR and TAVR patients (28). When the two groups of patients were matched, though, the 30-day all-cause readmission rates seem to be similar (28). Interestingly, studies have shown that TAVR done with a transapical approach (TAVR-TA) seems to produce a higher proportion of readmissions than TAVR done with a transfemoral approach (TAVR-TF) and SAVR (43), possibly due to a higher risk profile (34).

In the SAVR and TAVR studies we analyzed, we found a significant increase in the proportion of 30-day all-cause readmissions in multicenter studies compared to single-center

studies. Cohort studies with 30-day all-cause readmission numbers retrieved from large administrative databases might capture more readmissions than single-center studies. Single-center studies might not capture all readmissions if patients are admitted to other hospitals outside their area (33). Moreover, registry data can also be biased/corrupt (50). Indeed, studies depending on administrative data from a registry rarely contain detailed descriptions of how the data were validated (50). When evaluating the methodological quality of the included studies, we found that none of them provided a detailed transparent statement on the validity of the 30-day all-cause readmission numbers.

We observed regional differences among studies in the meta-analysis, with more 30-day all-cause readmissions in the USA versus other countries. In October 2012, the USA began to penalize hospitals (Medicare) as part of the Hospital Readmission Reduction Program (HRRP) under the Patient Protection and Affordable Care Act. HRRP has led to increased interest and research into the field of readmissions in the USA, and this might explain a difference between the USA and other countries. Even though readmissions have declined since 2012 for certain diagnoses for Medicare fee-for-service patients (51), more readmissions after 30 days and 1 year are reported for the USA compared to other countries in, for example, the TAVR population (52).

Causes of 30-day all-cause readmissions after SAVR are poorly described. In this systematic review, we found that heart failure and heart rhythm disturbances are prominent causes. This is similar to the reported causes for readmissions after cardiac surgery, in general, in addition to infections and bleeding (53). In the TAVR population, heart failure is the most frequently reported cause of 30-day all-cause readmission. However, heart blocks are also common (35), requiring postoperative implantations of permanent pacemakers in 10-30% of the patients (54, 55).

Examining the risk factors for 30-day all-cause readmission after TAVR showed that these patients harbor high comorbidity and an underlying frailty (11, 34). COPD, diabetes, heart failure, greater age, and being female have been reported to be predictors for 30-day all-cause readmission after cardiac surgery (9, 33, 53, 56-59). Many of these predictors for readmissions are also described in the general cardiac surgery population. Risk factors for 30-day all-cause readmission after SAVR are not comprehensively described, at least for articles included in our exhaustive search.

### *Clinical implications*

Recent evidence suggests a slight increase in mortality among heart-failure patients, simultaneously with the reduction of readmissions due to the implementation of HRRP in the USA (60). Knowing that heart failure is a prominent cause and risk factor of readmissions after invasive cardiac procedures, such as SAVR and TAVR, this gives rise to concern for the care of these populations in the discharge and early rehabilitation phase.

Given that the population of older ones continues to increase, we expect that SAVR and TAVRs procedures also will increase in the coming years. If most readmissions after SAVR and TAVR are unavoidable, then we should tolerate a higher number of readmissions to avoid unintended consequences of focusing exclusively on avoiding readmissions. One meta-analysis showed that 27% of readmissions are considered to have been avoidable (61). Increasing the quality of symptom monitoring in the early phase after discharge might prevent avoidable readmissions and maintain patient safety for those who must be readmitted (62).

### *Research implications*

The overall numbers of 30-day all-cause readmissions after SAVR and TAVR can be used to achieve more robustly powered studies. Indeed, the present meta-analysis provides reliable figures for calculating sample sizes for future intervention studies (e.g., aiming to reduce readmissions) (63) or for improving the transition of care. Furthermore, the high number of readmissions underscores a greater need for research aimed at determining the proportion of avoidable readmissions, because that type of readmission is auspicious for quality-enhancing interventions. Completing more prospective studies will ensure higher data quality and detailed follow-up. Finally, to understand and to be able to appraise the readmission statistics, transparency on how the readmission numbers are validated in research should be comprehensively reported in the publications.

### *Methodological considerations*

The present systematic review and meta-analysis has methodological strengths. In both the SAVR and TAVR groups, there were more than 10 appropriate articles evaluated, which enabled us to perform a random effects meta-regression on study-level variables.

Furthermore, none of the included articles reported on studies that were of poor quality. The extensive search we conducted implies that we likely missed few or no relevant studies. In addition, we found no publication bias, and the sensitivity analysis shows that the results are robust and strengthens validity of the results from the meta-analysis.

However, there were also some methodological limitations of our review and analysis that warrant discussion. First, there was great heterogeneity between the studies reported on which could be caused by differences in competence among surgeons, cardiologists, intervention radiologists, etc. There were also differences in patient volumes among the hospitals, device usage, and follow-up strategies after discharge. This heterogeneity limits to

some degree what can be interpreted from the results. Second, the reporting of clinical data was inconsistent. This inconsistency prevented us from doing a random meta-regression analysis on patient-level variables. Third, none of the included articles provided a detailed, transparent validation of the readmission data presented in the articles. In large retrospective trials, administrative databases are often used to obtain the readmissions figures. It is well known that, with these databases, there are errors in coding practice and methodological problems regarding extraction of exact, relevant data (50, 64). Fourth, English-language bias can have been introduced due to our language limitations, but likely with less effect (65). Fifth, the proportions of avoidable and unavoidable readmissions are not described, making it difficult to evaluate to what degree the readmissions after SAVR and TAVR are a matter of quality of care or an anticipated clinical outcome due to the natural course of the condition after treatment. Because of this issue, some believe that readmission is not a reliable quality measurement of hospital care for cardiac surgery patients (66).

## **Conclusions**

Our findings demonstrate a high proportion of 30-day all-cause readmissions after SAVR (17%) and TAVR (16%). In the SAVR group, higher readmission rates were reported in multicenter studies, the USA, retrospective studies, and studies with readmission as the primary outcome. In the TAVR group, higher readmission rates were reported in multicenter studies, the USA, and in retrospective studies. Heart failure and heart rhythm disturbances are common causes of readmission in patients with heart valve problems. The results of the present systematic review and meta-analysis provide new impetus for conducting quality-enhancing projects and provide the necessary data for accurately calculating sample sizes for future trials.



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Figure 1, heading: Figure 1. PRISMA flowchart describing literature search and article selection.

Figure 2, heading: Figure 2. Forest plots summarizing the proportions of 30-day all-cause readmission after surgical and transcatheter aortic valve replacement (SAVR and TAVR).



**Table 1** Pooled estimate of total incidence of readmission with stratification on study-level characteristics using the random effect model.

Subdivision	SAVR*			TAVR†		
	N	Incidence (95% CI)	I <sup>2</sup> (%)	N	Incidence (95%CI)	I <sup>2</sup> (%)
All studies	12	0.17 (0.16-0.18)	98.44	20	0.16 (0.15-0.18)	97.06
Single center	6	0.12 (0.08-0.17)	93.31	6	0.12 (0.08-0.13)	80.00
Multi center	6	0.20 (0.18-0.21)	98.95	14	0.18 (0.16-0.19)	97.64
Country						
USA	8	0.18 (0.17-0.19)	98.75	11	0.18 (0.16-0.20)	98.21
Other	4	0.14 (0.09-0.20)	94.53	9	0.14 (0.11-0.17)	79.80
Primary endpoint						
Yes	7	0.17 (0.16-0.19)	98.43	11	0.17 (0.16-0.19)	96.82
No	5	0.15 (0.10-0.20)	97.14	9	0.15 (0.12-0.18)	97.11
Timing of study						
Prospective	2	0.14 (0.12-0.17)	99.80	4	0.11 (0.06-0.18)	97.53
Retrospective	10	0.17 (0.16-0.18)	98.59	16	0.17 (0.16-0.19)	79.69

\*SAVR= surgical aortic valve replacement, †TAVR= transcatheter aortic valve replacement





**Table 2** Estimate of the random effect meta-regression model between incidence of readmission and the study-level variables.

Covariates	N	Level	$\beta$ -coefficient	Std. Error ( $\beta$ )	t	p-value	$\tau^2$	*Adj R <sup>2</sup> (%)
<b>SAVR<sup>†</sup></b>								
None	12	-	0.1723	0.0149	11.54	<0.001	0.00157	-
Single center	12	Yes/no	-0.0698	0.0231	-3.01	0.013	0.0004	69.20
Prospective	12	Yes/no	-0.0129	0.0523	-0.25	0.810	0.0016	-8.48
Primary endpoint	12	Yes/no	0.0270	0.0311	0.87	0.406	0.0014	1.16
USA	12	Yes/no	0.0488	0.0321	4.82	0.160	0.0008	46.48
<b>TAVR<sup>‡</sup></b>								
None	20	-	0.1793	0.0093	19.18	<0.001	0.0008	-
Single center	20	Yes/no	-0.0529	0.0315	-2.24	0.038	0.0006	23.78
Prospective	20	Yes/no	0.0209	0.0393	-1.35	0.195	0.0008	5.53
Primary endpoint	20	Yes/no	-0.0014	0.0209	-0.07	0.946	0.0009	-10.71
USA	20	Yes/no	0.0420	0.0235	1.79	0.091	0.0009	14.87

\*Heterogeneity accounted by the covariate, <sup>†</sup>SAVR=surgical aortic valve replacement, <sup>‡</sup>TAVR=transcatheter aortic

valve replacement



Figure 1. PRISMA flowchart describing literature search and article selection.

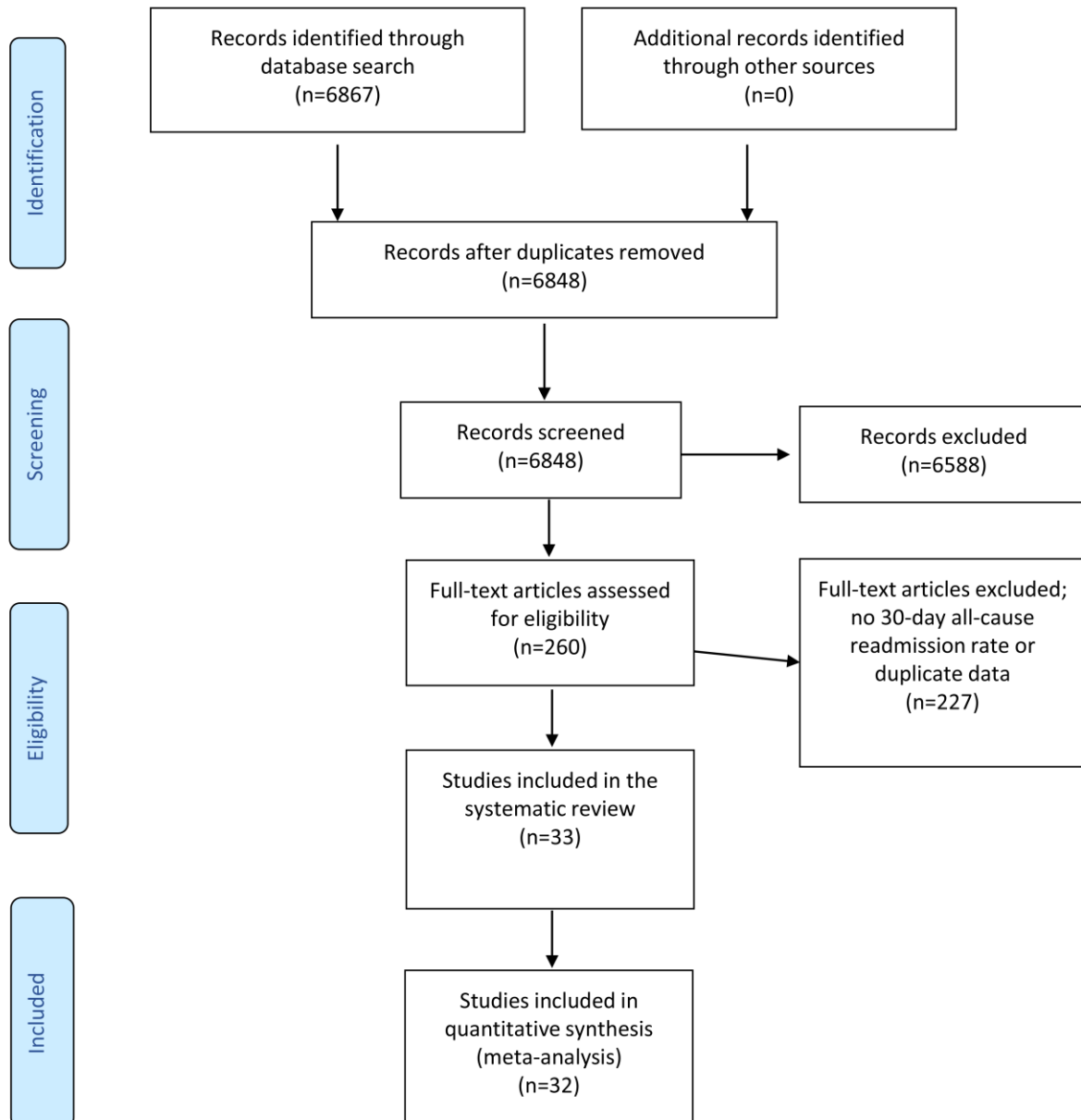
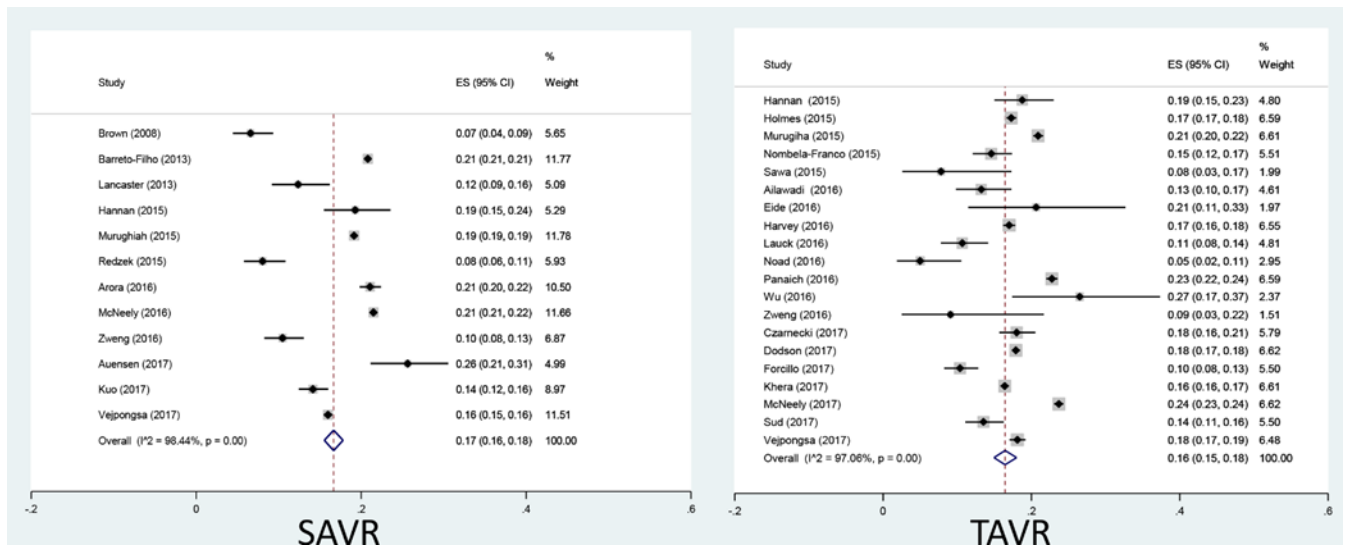


Figure 2. Forest plots summarizing the proportions of 30-day all-cause readmission after surgical and transcatheter aortic valve replacement (SAVR and TAVR).



Online Table 1. Study- and patient-level characteristics of 32 articles included in the meta-analysis stratified by surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR).

First author of article	Publication year	Country	Data source	Year of study	Primary endpoint*	Prospective cohort study	Mean age	Male (%)	Sample size	Readmission s n (%)
<b>SAVR</b>										
Brown	2008	USA	Single center	1991-2000	No	No	66.2	70.5	440	29 (7)
Lancaster	2013	USA	Single center	2008-2011	Yes	No	60.5	64.5	364	45 (12)
Barreto-Filho	2013	USA	Multicenter	1999-2011	Yes	No	76.6	58.4	197,876	41,179 (21)
Hannan	2015	USA	Multicenter	2011-2012	Yes	No	81.2	48.0	389	75 (19)
Murughiah	2015	USA	Multicenter	1999-2010	No	No	76.4	59.0	293,853	56,229 (19)
Redzek	2015	Serbia	Single center	2012	Yes	Yes	65.3	68.0	484	39 (8)
Arora <sup>‡</sup>	2016	USA	Multicenter	2013	Yes	No	79.5	54.0	3,886	819 (21)
Zweng	2016	Australia	Single center	2008-2015	No	No	71.0	68.0	669	70 (10)
McNeely	2016	USA	Multicenter	2011-2013	Yes	No	76 <sup>†</sup>	NR	40,751	8,761 (21)
Vejpongsa	2017	USA	Multicenter	2013	Yes	No	75.5	62.1	19,118	3,053 (16)
Kuo	2017	Canada	Single center	1995-2014	No	No	72 <sup>†</sup>	63.9	215	1,520 (14)
Auensen	2017	Norway	Single center	2010-2013	No	Yes	73.0	58.0	351	90 (26)
<b>Total</b>		-	-		-				<b>55,8396</b>	<b>111,909</b>
<b>TAVR</b>										
Hannan	2015	USA	Single center	2011-2012	Yes	No	81.7	46	389	79 (19)
Murughiah <sup>§</sup>	2015	USA	Multicenter	2011-2013	Yes	No	NR	NR	14,722	3,077 (21)
Sawa	2015	Japan	Multicenter	2010-2011	No	Yes	84.3	34.4	64	5 (8)

Holmes	2015	USA	Multicenter	2011-2013	No	No	84.0	48.1	12,182	2,106 (17)
Nombela-Franco	2015	Spain	Multicenter	NR	Yes	Yes	82.0	41.8	720	105 (15)
Ailawadi	2016	USA	Multicenter	2011-2013	No	No	81.0	48.0	340	45 (13)
Panaich	2016	USA	Multicenter	2013	Yes	No	83.8	50.4	12,110	2,757 (23)
Noad	2016	N. Ireland	Single center	2013-2014	No	Yes	82.9	41.9	120	6 (5)
Zweng	2016	Australia	Single center	2009-2015	No	No	82.3	41.0	44	4 (9)
Wu	2016	New Zealand	Single center	2011-2015	No	No	80.7	57	83	22 (27)
Harvey <sup>‡</sup>	2016	USA	Multicenter	2014	Yes	No	NR	NR	8,073	1,372 (17)
Eide	2016	Norway	Single center	2011-2013	Yes	Yes	NR	NR	63	13 (21)
Lauck	2016	Canada	Single center	2012-2014	No	No	81.5	60.6	393	42 (11)
Veijpongsa	2017	USA	Multicenter	2013	Yes	No	82.3	49.7	4,902	888 (18)
Sud	2017	Canada	Multicenter	2007-2014	Yes	No	84	58	709	96 (14)
Czarnecki	2017	Canada	Multicenter	2007-2013	No	No	84 <sup>†</sup>	54.6	999	180 (18)
Dodson	2017	USA	Multicenter	2011-2015	Yes	No	84 <sup>†</sup>	51.4	18,568	3,324 (18)
Forcillo	2017	USA	Single center	2007-2015	Yes	No	NR	53.5	714	74 (10)
Khera	2017	USA	Multicenter	2016	Yes	No	81.2	53.8	16,252	2,665 (16)
McNeely	2017	USA	Multicenter	2011-2013	No	No	84 <sup>†</sup>	50.9	18,283	4,333 (24)
<b>Total</b>		-	-		-				<b>109,730</b>	<b>21,193</b>

\* Primary endpoint is 30-day all-cause readmission rate after surgical or transcatheter aortic valve replacement (SAVR or TAVR), <sup>†</sup>Median age, <sup>‡</sup>Abstract,

<sup>§</sup>Letter

Online Table 2. Search strings used for database searches.

Database	String
Cochrane Library (Cochrane Reviews, Other Reviews, Technology Assessment, Economic Evaluations)	<p data-bbox="562 344 1736 560"><u>Search</u>  (readmi* or re-admi* or rehosp* or re-hosp* or (admi* and (repeat* or subseq*))) and (aort* or avr or tavr or pavr or savr or tavi): in Title, Abstract, Keyword</p> <p data-bbox="562 647 1736 887"><u>Search</u>  (readmi* or re-admi* or rehosp* or re-hosp* or (admi* and (repeat* or subseq*))) and (card* or heart* or coronar*): in Title, Abstract, Keyword</p>
Medline	<p data-bbox="562 903 1736 1377"><u>Search</u>  ("Heart Valve Prosthesis Implantation"[Mesh] OR "Transcatheter Aortic Valve Replacement"[Mesh] OR "Heart Valve Prosthesis/surgery"[Mesh] OR "Heart Valve Diseases/surgery"[ Mesh:NoExp] OR "Aortic Valve Insufficiency/surgery"[Mesh] OR "Aortic Valve Stenosis/surgery"[Mesh] OR "Heart Valves/surgery"[Mesh:NoExp] OR "Aortic Valve/surgery"[Mesh] OR avr OR tavr OR pavr OR savr OR tavi OR ((aorta OR aortic) AND valve AND (replacement[ti] OR surgery[ti] OR implant*[ti]))) AND ("Patient Readmission"[Mesh] OR readmi* OR re-admi* OR rehospital* OR re-hospital* OR "subsequent admission"</p>



OR "subsequent admissions" OR "repeated admission" OR "repeated admissions" OR "subsequent hospitalization" OR "subsequent hospitalizations" OR "repeated hospitalization" OR "repeated hospitalizations") AND (Danish[lang] OR English[lang] OR Norwegian[lang] OR Swedish[lang])

Search

("Heart Valve Prosthesis Implantation"[Majr] OR "Transcatheter Aortic Valve Replacement"[Majr] OR "Heart Valve Prosthesis/surgery"[Majr] OR "Heart Valve Diseases/surgery"[Majr:NoExp] OR "Aortic Valve Insufficiency/surgery"[Majr] OR "Aortic Valve Stenosis/surgery"[Majr] OR "Heart Valves/surgery"[Majr:NoExp] OR "Aortic Valve/surgery"[Majr]) AND ("Disease-Free Survival"[Mesh] OR ("Postoperative Complications"[Majr:NoExp] AND Time Factors[mesh]) OR "Recurrence"[Mesh] OR Treatment Outcome[Majr]) AND (Danish[lang] OR English[lang] OR Norwegian[lang] OR Swedish[lang]) AND (aortic[ti] AND valve[ti])

Search

("Cardiovascular Diseases/surgery"[Majr:NoExp] OR "Heart Diseases/surgery"[Majr:NoExp] OR "Cardiovascular Surgical Procedures"[Majr:NoExp] OR "Cardiac Surgical Procedures"[Majr:NoExp] OR "Thoracic Surgical Procedures"[Majr:NoExp] OR "Thoracic Surgery"[Majr] OR "Aortic

	<p>Diseases/surgery"[Majr:NoExp] OR "Aorta/surgery"[Majr:NoExp] OR Vascular Stiffness[Majr]) AND "Patient Readmission"[Majr] AND (Danish[lang] OR English[lang] OR Norwegian[lang] OR Swedish[lang])</p> <p><u>Additional search</u></p> <p>(Savr[ti] OR avr[ti] OR (aortic[ti] AND valve[ti] AND replacement[ti])) AND (pavr[ti] OR tavi[ti] OR tavr[ti] OR percutaneous[ti] OR transcatheter[ti] OR implantation[ti]) AND (Danish[lang] OR English[lang] OR Norwegian[lang] OR Swedish[lang])</p> <p>((aortic[ti] AND valve[ti] AND (replacement[ti] OR implantation[ti])) OR avr[ti] OR savr[ti] OR tavi[ti] OR pavr[ti] OR tavr[ti]) AND Treatment Outcome[MeSH] AND systematic[sb] AND (Danish[lang] OR English[lang] OR Norwegian[lang] OR Swedish[lang])</p>
Embase	<ol style="list-style-type: none"> <li>1 *aorta valve replacement/</li> <li>2 *transcatheter aortic valve implantation/</li> <li>3 Transcatheter Aortic Valve implantation.ti.</li> <li>4 Aortic Valve Replacement.ti.</li> <li>5 (avr or savr or tavi or tavr or pavr).ti.</li> <li>6 1 or 2 or 3 or 4 or 5</li> </ol>

	<p>7 *hospital readmission/  8 (readmi* or re-admi* or rehospital* or re-hospital*).ti.  9 7 or 8  10 6 and 9</p>
SweMed	<p>1 exp:"Heart Valve Prosthesis Implantation"  2 Transcatheter Aortic Valve Replacement  3 Transcatheter Aortic Valve implantation  4 exp:"Heart Valve Diseases/surgery"  5 exp:"Aortic Valve Insufficiency/surgery"  6 exp:"Aortic Valve Stenosis/surgery"  7 exp:"Heart Valves/surgery"  8 exp:"Aortic Valve/surgery"  9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8  10 exp:"Patient Readmission"  11 Readmission*  12 rehospital*  13 reinnlegg*  14 #10 OR #11 OR #12 OR #13  15 #9 AND #14</p>

	16	exp:"Treatment Outcome"
	17	#9 AND #16
National Guideline Clearinghouse, Clinical Trials.gov, ORIA.no (University of Oslo), Google Scholar, Google.com (grey literature), and search for unpublished literature.	1	*aorta valve replacement/
	2	*transcatheter aortic valve implantation/
	3	Transcatheter Aortic Valve implantation.ti.
	4	Aortic Valve Replacement.ti.
	5	(avr or savr or tavi or tavr or pavr).ti.
	6	1 or 2 or 3 or 4 or 5
	7	*hospital readmission/
	8	(readmi* or re-admi* or rehospital* or re-hospital*).ti.
	9	7 or 8
	10	6 and 9



Sawa	2015	*	NR	*	*	NR	NR	*	*	-	5/6
Holmes	2015	*	NR	*	-	NR	NR	*	*	-	4/6
Nombela-Franco	2015	*	NR	*	*	NR	NR	*	*	*	6/6
Ailawadi	2016	*	NR	*	-	NR	NR	*	*	-	4/6
Panaich	2016	*	NR	*	-	NR	NR	*	*	-	4/6
Noad	2016	*	NR	*	*	NR	NR	*	*	*	6/6
Zweng	2016	*	NR	*	-	NR	NR	*	*	-	4/6
Wu	2016	*	NR	*	-	NR	NR	*	*	-	4/6
Harvey	2016	-	-	-	-	-	-	-	-	-	-
Eide	2016	*	NR	*	*	NR	NR	*	*	*	6/6
Lauck	2016	*	NR	*	-	NR	NR	*	*	*	5/6
Vejpongsa	2017	*	NR	*	-	NR	NR	*	*	-	4/6
Sud	2017	*	NR	*	-	NR	NR	*	*	-	4/6
Czarnecki	2017	*	NR	*	-	NR	NR	*	*	-	4/6
Dodson	2017	*	NR	*	-	NR	NR	*	*	-	4/6
Forcillo	2017	*	NR	*	-	NR	NR	*	*	*	5/6
Khera	2017	*	NR	*	-	NR	NR	*	*	-	4/6
McNeely	2017	*	NR	*	-	NR	NR	*	*	-	4/6

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\*No. of stars given= relevant score possibility; S1, How representative is the exposed cohort?; S2, Selection of the non-exposed cohort?; S3, Ascertainment of exposure?; S4, Outcome not present at start of study?; C1, Comparability of readmission outcome?; C2, Comparability of the design?; E1, Assessment of outcome?; E2, Sufficiently long follow-up for outcome to occur?; E3, Adequacy of follow-up?; NR=Not relevant

Online Table 4. Cause for 30-day all-cause readmission after surgical aortic valve replacement (SAVR).

<b>Causes for readmission</b>	<b>Hannan 2015 (%)</b>	<b>McNeely 2016 (%)</b>	<b>Vejpongsa 2017 (%)</b>
Heart failure (HF)	19.2	18.2	15.3
Cardiac rhythm disorder	9.6		13.7
Stroke or TIA	5.5		
Pneumonia	5.5		
Pneumothorax, pleural effusion	5.5		
GI Bleeding	5.5		3.1
GI Problems			6.9
Respiratory failure	4.1		
Respiratory			13.6
Sepsis	2.7		
Postoperative infection	2.7		7.3
AMI	1.4		
Hemorrhage or hematoma	0		
Noninflammatory complication of cardiac device or implant	0		
Surgical complication			14.7



Online Table 5. Causes for all-cause 30-day readmission after TAVR.

Causes	Nombela- Franco 2015	Hannan 2015	Murugiha 2015	Panaich 2016	Kolte 2016	Vejpongsa 2017	Khera 2017	Forcillo 2017	McNeely 2017
HF	30.4%	21,9%	4.8%	22.38%	22.5%	20.7%	1. cardiac cause	25.7%	25.7%
Arrhythmia	9.6%	2,7%	1.1%	5.52%	6.6%	7.1%	2. cardiac cause	6.8%	
Conduction disorders							4. cardiac cause		
Acute coronary syndrome	1,7%	0							
Prosthesis related	0.9%								
Respiratory	9.6%					14.3%	2.non-cardiac cause	9.5%	
Respiratory incl. Pneumonia					14.6%				
Infection	10.4%	11%		12.78%	12.9%	7.3%	3.non-cardiac cause		
Bleeding	8.7%			15.84%			4.non-cardiac cause		

Peripheral vascular event	6.1%			
Cerebrovascular event	7.8%			
Traumatology	5.2%			
Strok or TIA	4.1%			3.3%
Pneumonia	2.7%	0.8%	5.08%	
Pneumothorax, pleural effusion	1.4%			
GI Bleeding	1.4%	0.6%		4.3%
Respiratory failure	4.1%			
Sepsis	1.4%	0.9%		
Hemorrhage or hematoma	5.5%			
Noninflammatory complication of cardiac device or implant	2			
Postoperative complications (shock, hematoma, wound dehiscence and infection)		1.4%		
Mechanical device complication		0.5%		
Kidney/Urinary complication			6.78%	
Surgical complication				9.7%

Gastrointestinal problems	8.8%	5. non-cardiac cause
Valve disorders	2.1%	3. cardiac cause
Vascular complications		6.8%

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Online Table 6. Risk factors of 30-day all-cause readmission rate after transcatheter aortic valve replacement (TAVR).

	<b>Nombela-Franco 2015</b>	<b>Panaich 2016</b>	<b>Harvey 2016</b>	<b>Kolte 2017</b>	<b>Dodson 2017</b>	<b>Forcillo 2017</b>
<b>Risk factor</b>	OR	OR	OR	HR	OR	HR
Major/life threatening bleeding	2.41 (1.57-3.70)					
LVEF at hospital discharge	1.08 (1.00-1.17)					
Hb at hospital discharge	1.19 (1.03-1.39)					
Single or dual antiplatelet therapy	1.62 (1.10-2.39)					
Trans apical		1.23 (1.10-1.38)		1.21 (1.05-1.39)	1.43 (1.31-1.57)	
Diabetes		1.18 (1.06-1.32)			1.13 (1.04-1.23)	
Chronic lung disease		1.32 (1.18-1.47)	1.18 (1.03-1.34)	1.16 (1.01-1.34)	1.22 (1.21-1.33)	
Renal failure		1.43 (1.24-1.65)				
Facility/others		1.28 (1.14-1.42)	1.30 (1.10-1.53)	1.16 (1.01-1.34)		

Length of stay, primary admission:			
3 to 6 days	1.76 (1.31-2.76)		
7 to 10 days	2.32 (1.70-3.17)		
>10 days	3.06 (2.22-4.22)		
2 prior admissions in year before TAVI		2.33 (2.02-2.70)	
History of dialysis		1.78 (1.26-2.51)	
Stroke		1.76 (1.24-2.49)	1.47 (1.13-1.89)
Blood loss		1.73 (1.14-2.61)	
Anemia			0.78 (0.62-0.99)
New onset atrial fibrillation		1.70 (1.24-2.49)	
Baseline atrial fibrillation		1.46 (1.29-1.66)	
Atrial fibrillation/Flutter			1.26 (1.17-1.36)
1 prior admission in year before TAVI		1.65 (1.41-1.92)	

Acute kidney injury	1.62 (1.36-1.94)	1.23 (1.05-1.44)	
Chronic kidney disease		1.20 (1.04-1.39)	
Baseline atrial fibrillation	1.46 (1.29-1.66)		
Paroxysmal tachycardia	1.38 (1.07-1.77)		
Respiratory failure	1.25 (1.01-1.55)		
Length of stay >5 days		1.47 (1.24-1.73)	
>4 Elixhauser comorbidities		1.22 (1.03-1.46)	
In-hospital vascular complication			1.34 (1.18-1.53)
Transfusion			1.30 (1.19-1.42)
Glomerular filtration rate (<30 vs ≥30)			1.33 (1.14-1.56)

Glomerular filtration rate (On dialysis vs $\geq 30$ )	1.61 (1.34-1.93)
Hours in Intensive Care Unit	1.00 (1.00-1.00)
Prior cardiac surgery (1 vs 0)	0.85 (0.77-0.94)
Female	0.91 (0.84-0.99)
NYHA (moderate/severe)	1.12 (1.00-1.25)
Age	1.00 (1.00-1.01)
Mitral insufficiency (moderate/severe)	1.08 (1.00-1.18)

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Online Figure 1. Analysis of publication bias by Funnel plots of studies of included articles for surgical and transcatheter aortic valve replacement (SAVR and TAVR).

