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SYSTEMATIC REVIEW AND META-ANALYSIS

Predictors of Permanent Pacemaker Implantation in Patients Undergoing Transcatheter Aortic Valve Replacement - A Systematic Review and Meta-Analysis

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BACKGROUND: As transcatheter aortic valve replacement (TAVR) technology expands to healthy and lower-risk populations, the burden and predictors of procedure-related complications including the need for permanent pacemaker (PPM) implantation needs to be identified.

METHODS AND RESULTS: Digital databases were systematically searched to identify studies reporting the incidence of PPM implantation after TAVR. A random- and fixed-effects model was used to calculate unadjusted odds ratios (OR) for all predictors. A total of 78 studies, recruiting 31,261 patients were included in the final analysis. Overall, 6212 patients required a PPM, with a mean of 18.9% PPM per study and net rate ranging from 0.16% to 51%. The pooled estimates on a random-effects model indicated significantly higher odds of post-TAVR PPM implantation for men (OR, 1.16; 95% CI, 1.04–1.28); for patients with baseline mobitz type-1 second-degree atrioventricular block (OR, 3.13; 95% CI, 1.64–5.93), left anterior hemiblock (OR, 1.43; 95% CI, 1.09–1.86), bifascicular block (OR, 2.59; 95% CI, 1.52–4.42), right bundle-branch block (OR, 2.48; 95% CI, 2.17–2.83), and for periprocedural atrioventricular block (OR, 4.17; 95% CI, 2.69–6.46). The mechanically expandable valves had 1.44 (95% CI, 1.18–1.76), while self-expandable valves had 1.93 (95% CI, 1.42–2.63) fold higher odds of PPM requirement compared with self-expandable and balloon-expandable valves, respectively.

CONCLUSIONS: Male sex, baseline atrioventricular conduction delays, intraprocedural atrioventricular block, and use of mechanically expandable and self-expanding prosthesis served as positive predictors of PPM implantation in patients undergoing TAVR.

Key Words: aortic disease ■ aortic valve ■ aortic valve implantation ■ aortic valve stenosis ■ atrioventricular block ■ pacemaker ■ transcathether aortic valve replacement

As the rheumatic etiology of aortic stenosis (AS) has significantly waned over time, age-related AS remains the most common valvular disease in the developed world.1 Valve replacement is the only definitive and effective treatment to improve survival in these patients, however, a multitude of coexisting comorbidities, including but not limited to chronic cardiac or pulmonary diseases, operative risks, extremes of age and poor physical health serve as barriers to surgical aortic valve replacement (SAVR). Transcatheter aortic valve replacement (TAVR) has recently emerged as a reasonable alternative to rescue these high-risk patients.2 The first TAVR was performed in 2002, in France, on a 57-year-old man in whom SAVR was...

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CONTRARY to medical therapy in patients with severe AS, but is also no-inferior to SAVR, even in low-risk patients.4–6

However, like any other therapeutic intervention, the advent of TAVR has presented its own set of challenges urging the need for a favorable risk-benefit estimation. With the widespread availability and expanded indication of TAVR to a lower-risk healthy population, there are concerns about the rising trend of procedural complications associated with TAVR. A frequent issue encountered with this procedure is conduction defects requiring permanent pacemaker (PPM) implantation.7,8 The bundle of His and the bundle branches run in the vicinity of where the prosthesis is being placed. These conduction abnormalities arise primarily due to the proximity of the aortic annulus to the atrioventricular conduction system that gets manipulated during the procedure.7 Data suggests that the prevalence of conduction defects post-procedure also depends upon the type of valve implanted during the TAVR procedure.8 The 2 most common prostheses used are balloon-expandable Edwards Sapien Valve (ESV) and self-expanding Medtronic Corevalve Revealing System (MCRS) with a 5%-12% incidence of PPM implantation post-procedure in the former and 24%-33% in the latter.9 Due to the manipulation of the old valve, aortic annulus dilatation and subsequent implantation of a prosthetic valve, conduction defects are common. In our study, we intend to identify various cardiac and non-cardiac predictors that lead to PPM implantation following TAVR. We also aim to gauge the risk of conduction abnormalities based on the type of prosthesis and access site used in TAVR.

METHODS

Data was obtained from published articles on the topic. All data can be obtained from the references mentioned in the supplementary file. The consolidated extracted data is available on demand.

Search Strategy

PubMed, Embase, Ovid, and Cochrane databases were queried with various combinations of keywords and medical subject headings (MeSH) to identify studies of interest. There were no time filters or language restrictions placed. Backward snowballing by screening the references of relevant articles were also performed to retrieve unidentified articles that were missed on the primary search. The MeSH used included 2 subsets: one for TAVR using the keywords “percutaneous prosthetic valve,” “transcatheter aortic valve replacement,” “TAVR,” “transcatheter aortic valve implantation,” “TAVI,” “percutaneous approach,” “minimal invasive aortic valve replacement,” “transapical aortic valve replacement,” and the other for PPM and heart block including “LAFB,” “LPFB,” “LBBB,” “pacemaker implantation,” “heart block,” “conduction abnormalities,” and “conduction delays.” The 2 subsets of MeSH were systematically combined using Boolean operators. The final results from all possible combinations were downloaded into an EndNote library. All randomized control trials (RCT) and
observational cohort studies (OCS) until April 2021, were screened for relevance. Any OCS or RCT that assessed the post-TAVR rate of atrioventricular conduction or cardiac rhythm abnormalities and subsequent PPM implantation during the same hospitalization or within 30-days of TAVR procedure were included. To avoid the inclusion of duplicate data, we only selected the most contemporary data when overlapping study populations (according to the period of recruitment and participating institutions) were reported; however, we cautiously included all patients reporting different predictors from studies of overlapping populations. To measure the impact of the procedure on PPM implantation, all patients with prophylactic implantation of PPM before the TAVR procedure were excluded from the analysis.

**Data Extraction**

Raw data about the events of PPM implantation in different predictor comparison groups were extracted for analysis by the first 9 authors independently. Detailed study- and patient-level baseline characteristics including the type of study design; recruitment period, region, and follow-up duration; sample size, number of post-TAVR PPM implantations, sex, age, procedural risk assessment (by logistic EuroSCORE [European System for Cardiac Operative Risk Evaluation] or STS-PROM [Society of Thoracic Surgeons Predicted Risk of Mortality] score), and baseline comorbidities were abstracted. Additionally, data related to the access site (transfemoral versus trans subclavian, transapical versus transvascular), type of prosthesis (MCRS versus ESV versus LOTUS), inclusion criteria, and definition of outcomes were obtained from individual studies (Table S1). Finally, the post-TAVR indications for PPM implantation in each article were also extracted. Based on previous reviews, the following proposed potential predictors were selected: age, sex, baseline conduction abnormalities, anatomical features, access route, and valve types. Case reports, review articles, conference papers, and articles with insufficient data or no control arms were excluded. Patients with prior PPM implantation unrelated to TAVR were also excluded from our analysis. All data was validated by the corresponding author; in case of missing data authors of the original article were contacted. The detailed search map is given in Data S1.

**Statistical Analysis**

The statistical analysis was performed using the DerSimonian and Laird (DL) and Mantel Haenszel (MH) methods on random- and fixed-effects models, respectively. The unadjusted odds ratio (OR) for dichotomous outcomes of RCTs and OCS were calculated. The “test for overall effect” was reported as a z value corroborating the inference from the 95% confidence interval. To avoid the influence of study design on pooled estimates, a stratified analysis based on the type of study (OCS versus RCT) was performed. A subgroup analysis based on the type of implanted valve (mechanically expandable versus self-expanding versus balloon-expansible), access route (transfemoral versus trans subclavian), and procedure type (transapical versus transvascular) was also performed. Sensitivity analysis after exclusion of small studies with fewer than 200 patients was done to determine the impact of sample size on pooled estimates. Descriptive characteristics for continuous data were reported as mean and SD, whereas categorical variables were presented as frequencies and percentages. Higgins I-squared (I²) statistical model was used to determine heterogeneity in outcomes of the included studies. The observed heterogeneity was regarded statistically significant if the I² statistics P value was <0.05. Publication bias was illustrated graphically using a funnel plot. The methodological quality assessment of the included RCTs was performed using the risk of bias-2 (RoB-2) tool and the Oxford quality scoring system (Jadad score). The Newcastle-Ottawa Scale was used for assessing non-randomized studies. The probability value of two-sided P<0.05 was considered statistically significant. All statistical analysis was performed using the Cochrane Review Manager (RevMan) version 5.3 and STATA software (version 16.0, STATA Corp., College Station, Texas).

**Quality of the Included Studies**

The overall quality of the included studies was high. The risk of bias-2 (RoB-2) tool used 5 different bias assessments: selection, detection, performance, attrition, and reporting. All 3 of the included RCTs in our meta-analysis were open-label, posing some theoretical risk to “allocation concealment;” however, the overall risk of selection bias was reduced due to adequate randomization. Because most RCTs used an “intention to treat model” or had a lower loss at follow-up, the risk of attrition bias was minimal. Similarly, the risk of reporting, detection and performance bias was lower due to appropriate reporting and adequate blinding of outcome assessors, respectively. The RoB-2 plots are given in Figure 1. 10–12 The methodological quality of included RCTs was also high on the Jadad scale with a score >3 (Table S2). Observational studies were mostly matched in terms of clinical profile and demographics to curtail selection bias. The Newcastle-Ottawa Scale for assessing nonrandomized studies indicated the inclusion of high-quality observational studies (score >7) (Table S3).
RESULTS

Search Results

The initial search revealed 4118 articles. After the removal of irrelevant (1561) and duplicate (2109) items, 448 studies were selected for full-text review. Of these, 370 articles were excluded based on different reasons including: review articles (35), meta-analyses (41), insufficient data for analysis (162), duplicate population studies (47), no risk factors data (80), and other reasons (5). A total of 78 articles (3 RCTs, 75 observational studies) qualified for quantitative analysis. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram is shown in Figure 2 and the PRISMA checklist is given in Data S2.

Study Characteristics

A total of 31,261 patients undergoing TAVR from 78 studies were included, of these 6212 (19.8%) received PPM, while 25,049 (80.2%) did not require a PPM.79–85 Most of the studies were from the United States and

![Figure 1. Overall (A) and study-level (B) methodological bias assessment of the included randomized clinical trials with the Cochrane risk of bias tool-2.](image-url)
Europe. Two of the RCTs were multi-continental, recruiting patients from the US, Australia, Germany, and Brazil. All included studies were published between 2009 and 2020 with an average recruitment period of approximately 4 years. The mean age of the included population was 81±8 years, comprising on average 46% male patients. The proportion of PPM implantation across different baseline comorbidities was comparable between the 2 groups. The detailed baseline characteristics are given in Tables S4 and S5, while the procedure characteristics of TAVR are given in Table S6. The summary is illustrated in Figure 1. The overall study-level rate of post-TAVR PPM ranged from 0.16% to 51.1%. The need for PPM implantation across different baseline comorbidities was variable as shown in Table S7 and Figure 3. The etiology for PPM implantation was only mentioned in 19.9% of patients (n=1238/6212). Post-TAVR complete atrioventricular block was the most commonly observed indication for PPM implantation; other causes included bradycardia,

Figure 2. PRISMA flow diagram showing the included studies.
new-onset left bundle-branch block (LBBB), and trifascicular block (Table). Patients with a prior history of PPM before the index TAVR procedure were mostly excluded from the analysis of their respective study. Two studies (De-Carlo and Hamandi et al) had prophylactic PPM implantation before the TAVR procedure in 158 patients; these patients were excluded from the analysis. Most PPM implantations were performed during the same hospitalization or within 30-days of the TAVR procedure. Most studies employed a transfemoral approach for TAVR, while 31 studies used transapical access in about 32% of its population. Mechanical (LOTUS) self-expanding (MCRS and Evolut R) and balloon-expandable (ESV) aortic prosthesis were the major valves used in the included studies. MCRS was used in 55, while ESV and Lotus were used in 46 and 12 studies, respectively. The mean log EuroSCORE for patients among the included studies was around 18.9±10 and the mean Society of Thoracic Surgeons score was found to be 5.85. The overall follow-up duration ranged from 2 to 36 months, with a mean follow-up of 8.02 months (Tables S4 through S6).

Pooled Analysis of Overall Studies

Twenty-nine different potential predictors for the PPM implantation were evaluated. The number of patients having post-TAVR PPM implantation (n=6212) from all studies contributed to the pooled OR calculation for each predictor. On a random effects model of binary data, the aggregate odds for post-TAVR PPM implantation irrespective of the type of valve was higher in the male population compared with the female patients (OR, 1.16; 95% CI, 1.04–1.28). The baseline electrocardiographic conduction abnormalities, mobitz type-1 second-degree heart block (OR, 3.13; 95% CI, 1.64–5.93), mobitz type-2 second-degree heart block (OR, 3.89; 95% CI, 2.54–5.95), left anterior fascicular hemiblock (LAFB; OR, 1.43; 95% CI, 1.09–1.86), bifascicular block (OR, 2.59; 95% CI, 1.52–4.42), right bundle-branch block (RBBB; OR, 2.48; 95% CI, 2.17–2.83), and intraprocedural atroventricular block (OR, 4.17; 95% CI, 2.69–6.46) were associated with significantly higher odds of PPM implantation. The baseline predictor variables that were not statistically significantly associated with PPM implantation were age (OR, 1.19; 95% CI, 0.95–1.49), first-degree heart block (OR, 1.09; 95% CI, 0.85–2.37), atrial fibrillation (AF; OR, 1.05; 95% CI, 0.93–1.20), left posterior fascicular hemiblock (LPFB; OR, 3.34; 95% CI, 1.1–11.13), left bundle branch block (LBBB; OR, 1.06; 95% CI, 0.87–1.29), severe pulmonary hypertension (OR, 1.78; 95% CI, 0.82–3.89), moderate/severe mitral regurgitation (MR; OR, 3.3; 95% CI, 0.59–18.32), unspecified heart failure; OR, 1.06; 95% CI, 0.72–1.55), and heart failure with preserved ejection fraction (OR, 1.01; 95% CI, 0.51–2.01). Of note, patients receiving 29 mm of prosthesis had significantly higher odds of PPM implantation compared with 23 mm prosthesis (OR, 1.49; 95% CI, 1.06–2.08). However, there appeared to be a statistically nonsignificant difference in the odds of PPM implantation between 23 mm versus 26 mm prosthesis (OR, 1.12; 95% CI, 0.62–2.03) and for patients with intraventricular septum size >11 mm (OR, 1.71; 95% CI, 0.17–17.41) and >22 mm (OR, 1.65; 95% CI, 0.55–4.93). The detailed valvular and anatomical variant estimates for PPM need are given Table S8.

Analysis of all predictors on a fixed-effects model mirrored the findings of the random-effects model with 2 exceptions; first-degree heart block (OR, 0.35; 95% CI, 0.30–0.40) was found to be associated with a significantly lower risk, while LBBB (OR, 1.29; 95% CI, 1.14–1.46) had significantly higher odds of need for PPM. The detailed forest plots for both random and fixed effects are given in Figures S1 through S16. The heterogeneity in the outcomes of these studies was P<0.05, except for the studies comparing the RBBB and male populations, which showed significant heterogeneity (I²=52% and I²=74%, both P<0.05), respectively (Figure 4). There was no significant difference in the odds of mortality in patients receiving PPM compared with those who did not receive PPM at 30 days and 1 year in 12 studies that included survival data (Figure 5).

On pooled analysis of continuous data, membranous septal length (MSL) was inversely, while the depth of prosthesis was directly, associated with the risk of PPM implantation. The mean MSL was 5.6 mm for patients requiring PPM implantation compared with 6.8 mm for those who did not require PPM, while the mean depth for prosthesis implantation for the former group was 6.86 mm compared with 5.34 mm in patients who did not require PPM (Figures S17 and S18).

Subgroup and Sensitivity Analyses

Overall, a head-to-head comparison based on the type of prosthesis favored the balloon-expandable valves irrespective of the prevalence of different predictors. On a random-effects model, the mechanically expandable valve (OR, 1.44; 95% CI, 1.18–1.76) and self-expanding valves (OR, 1.93; 95% CI, 1.42–2.63) had higher PPM requirements compared with the self-expanding and balloon-expandable valves, respectively. Based on a breakdown data of 16 studies, MCRS implantation was associated with significantly higher odds of PPM implantation compared with ESV (OR, 2.48; 95% CI, 1.91–3.22). By contrast, the LOTUS valve implantation was associated with higher odds (OR, 1.61; 95% CI, 1.23–2.1) of PPM implantation compared with MCRS. Compared with EVOLUT-R, the risk of PPM implantation was not significantly different in LOTUS and ESV (Table S9). There was no significant difference in the odds of PPM implantation
in patients undergoing a transarterial versus transapical approach (OR 1.02; 95% CI, 0.1–10.1), transfemoral versus subclavian approach (OR 1.13; 95% CI, 0.6–2.1). These findings remained invariant on a fixed-effects model. The heterogeneity among these studies ranged from $I^2=0\%$ to $I^2=54\%$ (Figure 6, Figures S14 through S16).

Overall, a subgroup analysis based on the type of valve used, study design and access site mirrored the
The present meta-analysis represents the most contemporary and largest evidence on the predictors of PPM implantation in patients with severe AS undergoing TAVR. Our findings revealed that male sex, pre-TAVR baseline atrioventricular conduction abnormalities (including Mobitz type-1 second-degree heart block, LAFB, RBBB), and intraprocedural atrioventricular block were associated with higher odds of PPM implantation, irrespective of the type of prosthesis or choice of the access site. A stratified analysis based on the prosthesis design showed a 2.4-fold increased risk of PPM implantation with MCRS (self-expanding) compared with ESV (balloon-expandable), and 1.61 times higher odds of PPM-need in LOTUS (mechanically expandable) compared with MCRS. The overall odds of PPM implantation remained identical in patients aged >80 years versus the younger population and those having first-degree heart block, AF, prolonged PR-interval, LPFB, and LBBB, when compared with their corresponding control groups who had an absence of these rhythm abnormalities. The type of approach (transapical versus transvascular) or choice of access site (transfemoral versus trans-subclavian) also had no impact on the risk of PPM implantation. Among the anatomical and valvar variants, the membranous septal length (MSL) was inversely, while the depth of prosthesis implantation was directly associated with the risk of PPM implantation. Larger devices (29 mm) had a higher risk of PPM implantation, while there was no impact of interventricular septum thickness, mitral regurgitation, or pulmonary hypertension on the need for PPM implantation.
for PPM during TAVR. On subgroup analysis, only the MCRS data followed the results of the pooled analysis, indicating that the overall findings were mostly driven by the data obtained from patients receiving self-expanding valves. The major post-procedural etiology for PPM implantation was a periprocedural occurrence of high-degree heart block, new-onset LBBB, or persistent bradycardia.

It is imperative to identify patients at an increased risk of PPM implantation before a TAVR procedure, as timely detection of high-risk patients can potentially prevent the occurrence of atrioventricular block and its associated complications (including syncope and sudden cardiac death). Also, patients with post-TAVR atrioventricular nodal abnormalities are prone to prolonged hospitalization, putting a high financial burden on the healthcare budget. PPM predictors in this context can help in the effective allocation of limited resources. With all its benefits, PPM placement comes at the cost of loss of atrioventricular synchrony, lack of physiological heart rate control, and increased risk of bleeding and pocket infection. Early detection of patients at high risk of PPM implantation and identification of pre-specified predictors, therefore provides an opportunity to mitigate these risks and to favorably lower the harm-benefit ratio.

Among the measured predictors for PPM implantation, the demographic risk factors including age and sex are of paramount importance. Current evidence on sex-related differences in post-TAVR complications and the need for PPM is conflicting in recently published studies. Our large-scale analysis shows a
16% higher rate of PPM implantation in men. This can partly be explained by the relatively larger-sized bioprosthesis (>25 mm) they receive, but mostly because of the higher prevalence of baseline comorbidities, putting men at a greater risk of procedural complications.\(^{63,90}\) Additionally, our results also revealed a numerically higher rate of PPM use (by 19%) in a population age >80 years, however, the difference did not reach statistical significance. These findings contrast the results of Ramkumar et al. and Ledwoch et al. studies, which denoted a significantly higher risk of post-TAVR PPM placement in octogenarians by 30% and 35%, respectively.\(^{37,44}\) Amongst the cardiac predictors, the presence of a LAFB, bifascicular block and second degree atrioventricular block are known to be associated with higher chances of receiving a PPM after TAVR.\(^{7–9}\) Our study echoes the same trend and expands these findings by demonstrating a 1.3-, 2.1-, and 3.1-fold increase in the odds of the need for PPM implantation in LAFB, bifascicular block and second degree atrioventricular block, respectively.\(^{9}\) Regarding the baseline first-degree atrioventricular block, Dolci et al and Naveh et al showed an increased incidence of PPM placement at 1 year of TAVR.\(^{46,91}\) By contrast, we believe that a first-degree atrioventricular block is a mere delay of atrioventricular conduction rather than a true block and that is why our study demonstrated no impact of first-degree heart block on the need for PPM implantation.

Studies have shown a higher incidence of post-TAVR atrioventricular blocks in patients with baseline conduction blocks, due to the manipulation of an already diseased conduction system.\(^{37,44,46,61,73,92,93}\) Pre-procedure LBBB and RBBB resulted in up to 1.5 times greater risk of PPM implantation after TAVR.\(^{92,93}\) In our study, RBBB conferred a 2.48 times greater risk of PPM implantation, much higher than the expected rise seen in previous studies. Intriguingly, baseline LBBB on our analysis did not increase the peri-procedural odds of atrioventricular block or the need for PPM implantation on a random-effects model. These effects were consistent across the different types of prosthesis and
Figure 6. Forest plot showing the pooled estimate comparison of (A) self expanding vs balloon expandable and (B) mechanically expandable vs self-expanding.

DL indicates DerSimonian and Laird; MH, Mantel-Haenszel; PPM, permanent pacemaker.
access sites used for the TAVR procedure. When comparing the risk of atrial arrhythmias induced conduction abnormalities, we found that AF had no impact on the need for PPM implantation after TAVR. These findings were in line with the previous literature that also demonstrated an identical rate of need for PPM. While a subset of the PARTNER registry showed that patients with sinus rhythm before TAVR and AF at discharge were twice more likely to get a PPM, patients with chronic AF had <6% risk of PPM, not significantly different from patients having no-AF at baseline.

On review, we found 40 previous meta-analyses discussing the risk factors of PPM implantation, however in light of the current evidence the applicability of those studies is limited. Most of these meta-analyses included a smaller number of previously published studies ranging from 4 to 41 articles, missing a large amount of contemporary data. The selection criteria and measured predictors were limited with respect to conduction abnormalities evaluated, indications for TAVR, and in some incidences inclusive of SAVR patients. More importantly, these studies had conflicting results. By contrast, our meta-analysis is the largest study (78 studies), including all patients who underwent TAVR for symptomatic AS (irrespective of the etiology), a wider range of demographics predictors, conduction abnormalities and procedural characteristics (29 predictors). Our study also provides a subgroup analysis on the type of valve and sensitivity analysis based on the sample size and study design. The detailed study-level characteristics and differences of our study from previous meta-analyses are given in Table S12.

Previous small-scale studies have also shown that atrioventricular conduction disturbances and a subsequent requirement for PPM were more common after the implantation of non-balloon expandable valves. Our results validated these findings by demonstrating a 1.93 and 2.8 times higher rate of PPM implantation in the self-expanding and mechanically expandable prosthesis compared with the balloon-expandable valves. MCRS and LOTUS, being a self-expanding and mechanically expandable valve increases the risk of complete heart block due to deeper implantation into the aortic annulus, tissue edema, and sustained pressure on the conduction pathway (atrioventricular

Figure 7. Factors increasing the risk of PPM implantation post-TAVR (red text indicates a higher risk).
node and left bundle branches). These effects might be delayed in the balloon-expandable valves (ESV) due to the intermittent nature of expansion and lower risk of tissue impingement. Although relatively lower, the newer generation balloon-expandable prosthesis is not devoid of the risk of PPM implantation. A study by Bisson and colleagues noted that in an effort to decrease a paravalvular leak, the newer ESV comes with an outer skirt, increasing the odds of PPM implantation. In contrast to the studies by Puls et al and Rouge et al that showed a higher prevalence of PPM implantation in transfemoral approach compared with trans subclavian access, we found no impact of the choice of the TAVR access site (transapical versus transvascular) and (transfemoral versus trans subclavian) on the need for PPM implantation. To summarize, men, patients with baseline conduction abnormalities and those receiving the self-expanding or mechanically expandable prostheses are at higher risk of PPM implantation after TAVR.

Limitations
Our study is constrained by the limitations of the included studies. A multivariate logistic regression model is required to control for potential confounders and to obtain an independent impact of the predictor. Patient-level data were missing to determine the adjusted odds of PPM predictors. For the same reason, we could not assess the impact of the procedure technique and could not account for the differential use of medications or other causes of atrioventricular conduction abnormalities. The impact of unmeasured confounding factors and operators’ skills could not be measured. Although we selected a wide range of potential, previously proven predictors, the available data for some comparisons were sparse. Due to the lack of extended follow-up data the long-term effectiveness of PPM could not be evaluated. It is also important to note that the reasons for PPM implantation were variable in included studies, hence PPM implantation in our analysis should not be interpreted as a surrogate marker of atrioventricular conduction disturbances. The need for PPM in post-TAVR patients can be influenced by several economic and logistic factors out of the scope of the current study.

CONCLUSIONS
Patients with baseline conduction abnormalities, men, and those receiving mechanical- or self-expanding larger-sized prostheses for transcatheter aortic valve replacement are at an increased risk of pacemaker implantation. Given the clinical and economic impact of TAVR, interventionists should cautiously risk-stratify and identify patients at a high risk of the need for PPM.

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Ullah et al. PPM in TAVR

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Supplemental Material
Data S1.

A. SEARCH STRATEGY and MAP:

((((((((((per-cutaneous aortic valve implantation AND cardiac pacemaker)) OR (per-cutaneous aortic valve implantation AND artificial pacemaker)) OR (per-cutaneous aortic valve implantation AND pacer)) OR (per-cutaneous aortic valve implantation AND cardiac pacemaker)) OR (g transcatheter aortic valve implantation AND artificial pacemaker)) OR ((transcatheter aortic valve implantation AND cardiac pacemaker)) OR (transcatheter aortic valve implantation AND artificial pacemaker)) OR (transcatheter aortic valve implantation AND pacer)) OR (transcatheter aortic valve implantation AND pacemaker))) OR (((tavr AND cardiac pacemaker)) OR (tavr AND artificial pacemaker)) OR (tavr AND pacer)) OR (tavr AND pacemaker)))) OR (((((((per-cutaneous aortic valve replacement AND cardiac pacemaker)) OR (per-cutaneous aortic valve replacement AND artificial pacemaker)) OR (per-cutaneous aortic valve replacement AND pacemaker)) OR (transcatheter aortic valve replacement AND artificial pacemaker)) OR (transcatheter aortic valve replacement AND pacer)) OR (transcatheter aortic valve replacement AND pacemaker))) OR (((tavr AND cardiac pacemaker)) OR (tavr AND artificial pacemaker)) OR (tavr AND pacer)) OR (tavr AND pacemaker)))))
# PRISMA 2020 Checklist

**Data S2.**

| Section and Topic | Item # | Checklist item                                                                 | Location where item is reported |
|-------------------|--------|-------------------------------------------------------------------------------|--------------------------------|
| **TITLE**         | 1      | Identify the report as a systematic review.                                  | Page 1                          |
| **ABSTRACT**      | 2      | See the PRISMA 2020 for Abstracts checklist.                                | Page 2                          |
| **INTRODUCTION**  | 3      | Describe the rationale for the review in the context of existing knowledge. | Page 3                          |
|                   | 4      | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Page 3                          |
| **METHODS**       | 5      | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Page 4                          |
|                   | 6      | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 3                          |
|                   | 7      | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Page 3, Supplementary page 3    |
|                   | 8      | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Page 4                          |
|                   | 9      | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 4                          |
|                   | 10a    | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Page 4                          |
|                   | 10b    | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Page 4                          |
|                   | 11     | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Page 5,7                        |
|                   | 12     | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 4                          |
| **Synthesis methods** | 13a   | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Page 5                          |
|                   | 13b    | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Page 4-5                        |
|                   | 13c    | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Page 4-5                        |
|                   | 13d    | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Page 4-5                        |
|                   | 13e    | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Page 4,6,7                      |
### PRISMA 2020 Checklist

| 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Page 7 |
| --- | --- | --- |
| 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Page 7 |
| 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Page 7 |

### RESULTS

| 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page 5 |
| 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Page 5 |
| 17 | Cite each included study and present its characteristics. | Page 5 |
| 18 | Present assessments of risk of bias for each included study. | Page 5, Figure 1 |
| 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | S.Figure 1-21 |
| 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | S.Table 4 |
| 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Page 6-7 |
| 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Page 6-7 |
| 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | S.Table 11 |
| 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | S.Figure 25 |
| 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Page 6-7 |

### DISCUSSION

| 23a | Provide a general interpretation of the results in the context of other evidence. | Page 7,8,9 |
| 23b | Discuss any limitations of the evidence included in the review. | Page 9 |
| 23c | Discuss any limitations of the review processes used. | Page 10 |
| 23d | Discuss implications of the results for practice, policy, and future research. | Page 9 |

### OTHER INFORMATION

| 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | NA |
| 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | NA |
| 24c | Describe and explain any amendments to information provided at registration or in the protocol. | NA |
| 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Page 1 |
| 26 | Declare any competing interests of review authors. | Page 1 |
| 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Page 1 |
### Table S1: Inclusion criteria of the included RCTs

| Author/Study/Year/Ref | Inclusion Criteria | MACCE Components |
|-----------------------|--------------------|------------------|
| **Meduri (REPRISE III)** 2019 | Symptomatic Aortic Stenosis and STS predicted risk of Mortality >8%. | Cardiovascular Mortality, MI, Stroke, Conduction abnormality requiring new-pacemaker placement, Paravalvular leakage. |
| **Thiele (SOLVE-TAVI)** 2020 | Symptomatic Aortic Stenosis, Age >75 years and high predicted surgical risk of Mortality defined as Logistic Euroscore >20% or STS score >10%. | Cardiovascular Mortality, MI, Stroke, Conduction abnormality requiring new-pacemaker placement, Paravalvular leakage. |
| **Reardon (REPRISE III)** 2019 | Severe Native Aortic stenosis, and STS predicted risk of Mortality >8% | Cardiovascular Mortality, MI, Stroke, Conduction abnormality requiring new-pacemaker placement, Paravalvular leakage. |
Table S2: Randomized studies quality assessment using the Oxford Quality Scoring System. (Jadad score ≥ 3 considered high quality)

| Author/Study/Year/Ref | Rating Scale List | Jadad Score |
|-----------------------|-------------------|-------------|
| Meduri (REPRISE III) 2019 | Was the study described as random | Yes | 3 |
|                       | Was the randomization described and appropriate | Yes | |
|                       | Was the study described as double-blind | No | |
|                       | Was the method of double-blinding appropriate | No | |
|                       | Was there a description of dropouts and withdrawals | Yes | |
| Thiele (SOLVE-TAVI) 2020 | Was the study described as random | Yes | 3 |
|                       | Was the randomization described and appropriate | Yes | |
|                       | Was the study described as double-blind | No | |
|                       | Was the method of double-blinding appropriate | No | |
|                       | Was there a description of dropouts and withdrawals | Yes | |
| Reardon (REPRISE III) 2019 | Was the study described as random | Yes | 3 |
|                       | Was the randomization described and appropriate | Yes | |
|                       | Was the study described as double-blind | No | |
|                       | Was the method of double-blinding appropriate | No | |
|                       | Was there a description of dropouts and withdrawals | Yes | |
### Table S3: Quality Assessment of the included observational studies

| Author/Study          | Year | Representativeness of the exposed | Selection of the non-exposed cohort | Ascertainment of exposure | Outcome not present at baseline | Comparability of the cohort | Assessment of outcome | Enough follow-up duration | Adequate follow-up | Total score |
|----------------------|------|-----------------------------------|-------------------------------------|---------------------------|---------------------------------|-----------------------------|----------------------|------------------------|-------------------|-------------|
| Hamandi              | 2020 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Kochman              | 2020 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Sharma               | 2020 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Ay                   | 2019 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Giordano             | 2019 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Kaneo                | 2019 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Karacop              | 2019 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Ball                 | 2018 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Bhargava             | 2018 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Doshi                | 2018 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Eitan                | 2018 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Finkelstein          | 2018 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Gonska               | 2018 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Yousef               | 2018 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Enriquez-Rodriguez   | 2017 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Monteiro             | 2017 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Rogers               | 2017 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Soliman              | 2017 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Van Mourik           | 2017 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Ben-Shoshan          | 2016 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Kahraman             | 2016 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Kley                 | 2016 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Ramkumar             | 2016 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Sawaya               | 2016 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Zaman                | 2016 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Gauthier             | 2015 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Rouge                | 2015 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Boerlage-Van Dijk    | 2014 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Simms                | 2013 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Akin                 | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Bagur                | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| De Carlo             | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Gilard               | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Ledwoch              | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Mouillet             | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Muniz-Garcia         | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Nuis                 | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Pulse                | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Saia                 | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Salinas              | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Schroeter            | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Van der Boon         | 2012 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Bosmans              | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 7           |
| Calvi                | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Chorianopoulos      | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| D’Ancona             | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Ewe                  | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Fraccaro             | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 8           |
| Guetta               | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Khawaja              | 2011 | *                                 | *                                   | *                         | *                               | *                           | *                    | *                      | *                 | 9           |
| Author          | Year | Quality Score |
|-----------------|------|---------------|
| Pilgrim         | 2011 | * * * * * * * | 8   |
| Baan            | 2010 | * * * *       | 9   |
| Bleiziffer      | 2010 | * * * *       | 8   |
| Elchnameff      | 2010 | * * * *       | 9   |
| Erkpic          | 2010 | * * * *       | 9   |
| Ewe             | 2010 | * * * *       | 9   |
| Ferriera        | 2010 | * * * *       | 9   |
| Godino          | 2010 | * * * *       | 8   |
| Haworth         | 2010 | * * * *       | 9   |
| Lefevre         | 2010 | * * * *       | 8   |
| Piazza          | 2010 | * * * *       | 8   |
| Rodes-Cabau     | 2010 | * * * *       | 9   |
| Roten           | 2010 | * * * *       | 9   |
| Thielmann       | 2009 | * * * *       | 9   |
| Aslan           | 2020 | * * * *       | 9   |
| Hamdan          | 2015 | * * * *       | 9   |
| Jilaihawi       | 2019 | * * * *       | 9   |
| Matsushita      | 2020 | * * * *       | 7   |
| Tretter         | 2019 | * * * *       | 9   |
| Zaid            | 2020 | * * * *       | 9   |
| Ahmad           | 2019 | * * * *       | 7   |

The methodological quality of retrospective or prospective observational studies was done using Newcastle–Ottawa scale (NOS) quality scale. Each asterisk/star in the Newcastle-Ottawa Scaling System (NOS) represents responses of the biases questionnaire. Each bias assessment part gets one star except comparability that gets a maximum of 2 stars. Each star counts towards the total score. Score <5 represents poor quality, 5-6 represents moderate quality and 7 to 9 are considered as high quality. Total of 30 studies had a NOS score >7 representing a high quality. Rest of the studies had moderate to poor quality owing to the ascertainment bias, comparability, and follow up limitations.
## Table S4: The demographics of the population in all the included studies

| Author         | Year | Study  | Country                        | Period     | F  | U | Size | PPM | PPM % | Mean age | Male | EuroSCORE | STS | Valve type                |
|----------------|------|--------|--------------------------------|------------|----|---|------|-----|-------|----------|------|------------|----|---------------------------|
| Hamandi        | 2020 | OCS    | US                             | 2012-2016  | 12 | 424| 110  | 25.9| 82    | 52.9     | Sapien, CoreValve, Evolut |
| Sharma         | 2020 | OCS    | US                             | 2012-2016  | 1  | 226| 25   | 11.1| 81±7  | 50.4     | Edwards Sapien            |
| Thiele         | 2020 | OCS    | Germany                        | 2016-2018  | 438| 90 | 20.6 | 81.7±5| 48.9  | 4.10     | Evolut R vs Sapien 3      |
| Kochman        | 2020 | OCS    | Poland                         | 2015-2016  | 24 | 24 | 6    | 75.3±7| 50.0  | lotus     | CoreValve                 |
| Meduri         | 2019 | RCT    | US, Brazil, Australia          | 2014-2015  | 12 | 704| 245  | 26.9| 82±8  | 49.0     | LOTUS and CoreValve       |
| Karacop        | 2019 | OCS    | Turkey                         | 2013-2018  | 3  | 150| 49   | 32.7| 81±8  | 72.7     | CoreValve                 |
| Ay             | 2019 | OCS    | Turkey                         | 2012-2017  | 27 | 274| 25   | 9.1 | 78    | 37.2     | ESV XR, Corevalve, Lotus  |
| Kaneko         | 2019 | OCS    | Germany                        | 2015-2017  | 92 | 17 | 18.5 | 82±7 | 32.6  | 17±13    | Evolut R                 |
| Reardon        | 2019 | RCT    | US, Europe, Australia          | 2014-2018  | 2  | 912| 263  | 28.8| 82±8  | 49.0     | Corevalve vs Lotus        |
| Giordanj       | 2019 | OCS    | Italy                          | 2012-2018  | 1  | 197| 284  | 14.4| 83.5  | 42.3     | ESV, portico, evol, evol  |
| Doshi          | 2018 | OCS    | US                             | 2012-2014  | 12 | 821| 194  | 9   | 23    | 81±8     | Not mentioned            |
| Bhawardwaj     | 2018 | OCS    | US                             | 2012-2016  | 12 | 383| 44   | 11.5| 83±8  | 50.9     | Edward Sapien and CoreValve |
| Gonska         | 2018 | OCS    | Germany                        | 2014-2016  | 12 | 612| 168  | 27.5| 80±6  | 47.1     | Corevalve, ESV and Lotus Edge |
| Yousif         | 2018 | OCS    | Switzerland                    | 2008-2014  | 12 | 546| 103  | 18.9| 81.35 | 48.5     | Corevalve, ESV, Symetis, Ventor |
| Ball           | 2018 | OCS    | US                             | 2012-2016  | 209| 44 | 21.1 |     |      | 56.5     | CoreValve, ESV, Lotus, CoreValve |
| Eitau          | 2018 | OCS    | Germany                        | 2014-2017  | 92 | 18 | 23   | 82.4 | 93.5  | 21.04    | ESV & core valve         |
| Finkelstei     | 2018 | OCS    | Israel                         | 2012-2016  | 735| 122| 16.6 | 81   | 44.6  | 3.40     | ESV core valve            |
| Monteiro       | 2017 | OCS    | Brazil                         | 2008-2015  | 1  | 670| 135  | 20.2| 82±7  | 47.9     | CoreValve and Sapien XT   |
| Enríquez-R     | 2017 | OCS    | Spain                          | 2013-2016  | 1  | 144| 18   | 12.5| 83±6  | 47.9     | CoreValve and Sapien XT   |
| Rogers         | 2017 | OCS    | US                             | 2013-2016  | 257| 17 | 6.6  | 82±8 | 49.4  | 6.96     | sapien corevalve          |
| Soliman        | 2017 | OCS    | Egypt                          | 2013-2016  | 6  | 40 | 5    | 12.5| 73.9±8.4 | 52.5     | medtronic                 |
| vanMourik      | 2017 | OCS    | Netherlands                    | 2010-2013  | 36 | 114| 5    | 4.4 | 79±8.7 | 32.5     | sapien                   |
| Kley           | 2016 | OCS    | Netherlands                    | 2007-2013  | 12 | 240| 25   | 10.4| 81    | 0.0      | Edward Sapien XT, Corevalve |
| Zaman          | 2016 | OCS    | Australia                      | 2012-2015  | 95 | 27 | 27.4 | 83±6 | 44.5  | 7.3±8    | Lotus                   |
| Kahraman       | 2016 | OCS    | Turkey                         | 2012-2014  | 6  | 136| 6    | 4.4 | 79.4  | 38.2     | NA                      |
| Sawaya         | 2016 | OCS    | France                         | 2010-2015  | 12 | 790| 87   | 11  | 82±8  | 47.9     | sapien                   |
| Ben-Shoshan    | 2016 | OCS    | Israel                         | 2014-2016  | 1  | 232| 48   | 24.5| 82.3±6.1| 46.1     | ESV, Medtronic            |
| Ramkumar       | 2016 | OCS    | Australia                      | 2012-2015  | 1  | 104| 25   | 24   | 46.2  | lotus     | CoreValve                |
| Rouge          | 2015 | OCS    | France                         | 2009-2015  | 6  | 150| 18   | 12  | 82.6  | 45.3     | ESV and Medtronic         |
| Gauthier       | 2015 | OCS    | France                         | 2009-2013  | 176| 13 | 7.4  | 85   | 51.7  | 25.28    | ESV, Evolut and portico  |
| Boerlage       | 2014 | OCS    | Netherlands                    | 2007-2011  | 12 | 121| 23   | 19  | 80.5±7 | 38.1     | 19.2±12    | Corevalve |
| Simms          | 2013 | OCS    | UK                             | 2008-2010  | 12 | 100| 17   | 17  | 81±6  | 48.0     | Medtronic CoreValve       |
| Nuis           | 2012 | OCS    | Columbia, Nether              | 2005-2011  | 1  | 235| 48   | 20.4| 80±7  | 48.9     | medtronic                |
| Pulse          | 2012 | OCS    | Germany                        | 2008-2010  | 12 | 180| 9    | 5   | 82.1±5.4| 30.0     | medtronic and sapien     |
| Ledwoch        | 2012 | OCS    | Germany                        | 2009-2010  | 1  | 114| 7    | 386  | 33.7  | 82±6     | Medtronic and sapien     |
| Akin           | 2012 | OCS    | Germany                        | 2007-2008  | 0  | 2   | 45   | 23   | 51.1  | 81±6     | Medtronic CoreValve       |
| Bagur          | 2012 | OCS    | Canada                         | 2005-2010  | 1  | 411| 30   | 7.3  | 81±11 | 42.8     | Medtronic CoreValve       |
| De Carlo       | 2012 | OCS    | Italy                          | 2007-2010  | 12 | 275| 66   | 24   | 82±6  | 46.6     | Medtronic CoreValve       |
| Name          | Year | Country | Year Range | Values | Comment                  |
|---------------|------|---------|------------|--------|--------------------------|
| Gilard        | 2012 | France  | 2010-2011  | 3.8    | 319 497 15.6 83±7 51.0 22±14 14±2 | CoreValve and ESV |
| Muniz-Garcia  | 2012 | Spain   | 2008-2011  | 1.8    | 174 48 27.6 79±7 37.4 19±6 7.5 | Medtronic CoreValve |
| Saia          | 2012 | Italy   | 2008-2010  | 20.8   | 12 60 17 82±6 43.3 23±8 9±7 | Medtronic CoreValve |
| Salinas       | 2012 | Spain   | 2008-2010  | 20.8   | 12 34 3 8.8 84 38.2 23.0 | Edward SAPIEN |
| Schroeter     | 2012 | Germany | 2008-2009  | 20.8   | 88 32 36.4 80±6 23±12 | Medtronic CoreValve |
| van der Boon  | 2012 | Netherlands | 2005-2011  | 20.8   | 12 167 36 21.6 81±7 46.0 13.0 | Medtronic CoreValve |
| Mouillet      | 2012 | France  | 2007-2011  | 20.8   | 10 79 21 26.6 82±17 31.0 23±10 | Medtronic CoreValve |
| Liang         | 2012 | New Zealand | 2008-2011  | 20.8   | 21 53 5 9.4 80±7 56.6 26±16 6±1 | CoreValve and ESV |
| Pilgrim       | 2011 | Switzerland | 2007-2010  | 20.8   | 12 256 60 23.4 82±6 56.3 40±15 | Medtronic and ESV |
| Bosmans       | 2011 | Belgium | 2010      | 20.8   | 12 328 40 12.2 83±6 46.0 28±16 | CoreValve and ESV |
| D’Ancona      | 2011 | Germany | 2008-2011  | 20.8   | 12 322 20 6.2 82±6 33.2 39±12 10±1 | Edward SAPIEN |
| Ewe           | 2011 | Netherlands | 2009-2011  | 20.8   | 29 104 4 3.8 80.6±7.9 50.0 21±12 8.7±3.6 | Edward SAPIEN |
| Fracaro       | 2011 | Italy   | 2007-2009  | 20.8   | 6 64 25 39.1 81±7 45.0 24±15 | Medtronic CoreValve |
| Guetta        | 2011 | Israel  | 2008-2010  | 20.8   | 3 70 28 40 83±5 37.0 | Medtronic CoreValve |
| Khawaja       | 2011 | UK      | 2007-2009  | 20.8   | 243 81 33.3 81±7 50.6 | Medtronic CoreValve |
| Calvi         | 2011 | Italy   | 2007-2011  | 20.8   | 12 162 52 32.1 81±5 39.5 28±15 | Medtronic CoreValve |
| Chorianopoulos| 2011 | Germany | 2009-2011  | 20.8   | 1 130 46 35.4 81±6 41.5 24±13 | Medtronic CoreValve |
| Hayashida     | 2011 | France  | 2006-2010  | 20.8   | 7 260 17 6.5 83±6.3 49.6 24±11.3 | CoreValve and ESV |
| Bleiziffer    | 2010 | Germany | 2007-2009  | 20.8   | 0.5 159 35 22 80.8±6.2 43.0 21±13 | CoreValve and ESV |
| Elliottnoff   | 2010 | France  | 2009-2009  | 20.8   | 1 244 29 11.9 82±7.3 56.6 25±11.1 18.9±12.8 | CoreValve and ESV |
| Baan          | 2010 | Netherlands | 2009-2011  | 20.8   | 1 34 7 0.2 80±8 53.0 5±13 | Medtronic CoreValve |
| Ewe           | 2010 | Netherlands | 2007-2010  | 20.8   | 12 147 7 4.8 80±7 42.9 21.8±11 | Edward SAPIEN |
| Ferreira      | 2010 | Portugal | 2007-2009  | 20.8   | 32 8 25 81 34.0 23±9 14.9 | Medtronic CoreValve |
| Godino        | 2010 | Italy   | 2007-2010  | 20.8   | 6 137 23 0.16 | 53.3 | CoreValve and ESV |
| Erkapic       | 2010 | Germany | 2008-2009  | 20.8   | 0.4 50 17 34 80±6 46.0 20±15 | CoreValve and ESV |
| Hawthorn      | 2010 | UK      | 2007-2008  | 20.8   | 5 33 8 24 81.5±6.7 57.0 24±15 | Medtronic CoreValve |
| Piazza        | 2010 | Netherlands | 2005-2009  | 20.8   | 6 91 17 18.7 81±7 42.9 16±9 | Medtronic CoreValve |
| Rodes-Cabau   | 2010 | Canada  | 2005-2009  | 20.8   | 8 339 17 5 81±8 44.8 9±8 6.4 | Edward SAPIEN |
| Roten         | 2010 | Switzerland | 2007-2009  | 20.8   | 2.6 67 23 34.3 83 46.0 23.0 | CoreValve and ESV |
| Lefevre       | 2010 | Europe  | 2007-2008  | 20.8   | 12 130 3 2.3 82±6.5 44.6 30±13.7 11.6±8.5 | Edward SAPIEN |
| Attias        | 2010 | France  | 2006-2009  | 20.8   | 1 83 7 8.4 81±9 53.0 26±14 15±13 | CoreValve and ESV |
| Petronio      | 2010 | Italy   | 2007-2009  | 20.8   | 6 514 84 16.3 83 44.0 20.1 | Medtronic CoreValve |
| Thielmann     | 2009 | Germany | 2005-2008  | 20.8   | 12 39 4 10.3 81±5 38.0 44.2±12.6 17.9±16 | Edward SAPIEN |
| Aslan         | 2020 | Turkey  | 2017-2020  | 20.8   | 140 24 17 78±8 36.4 | Edward SAPIEN XT, Medtronic CoreValve evolut |
| Hamdan        | 2015 | Israel  | 2015      | 20.8   | 73 21 29 79±6 45.0 | CoreValve, Engager |
| Jilaihawi     | 2019 | US      | 2016-2018  | 20.8   | 1 248 24 9.6 83±7 57.3 6±0.2 9 Evolut R, Evolut Pro, XL |
| Matsushita    | 2020 | France  | 2014-2018  | 20.8   | 3 242 114 47 38.4 | Sapiens 3, Evolut R |
| Trettter      | 2019 | US      | 2013-2017  | 20.8   | 6 200 41 20.5 81±7.7 49.0 4.7±2.8 | Sapiens XT, Sapiens 3, LOTUS, CoreValve, Evolut R, Evolut |
| Zaid          | 2020 | US      | 2015-2019  | 20.8   | 1 532 57 10.7 80.7±8 57.9 5.5 | Sapiens 3 |
Excluded patients with prophylactic PPM: Hamandi (126), De Carlo (32); Excluded patients with prior PPM: Kochman (4), Elan (14), Ben-Shoshan 36, Meduri (160), Sharma (36), Doshi (62), D'Ancona (36), Chorianopoulos (32); OCS: Observational Cohort Study, RCT: Randomized Controlled Trial, FU: Follow up in years, STS: Society of Thoracic Surgeons Score
Table S5: The baseline comorbidities of the population in all the included studies (all numbers indicate percentages).

| Author     | AF  | LBBB | RBBB | EF  | Sm | DM | HTN | HLD | CKD | CVA | Ob | LC  | PAD | MI | PCI | CABG | CAD | COPD |
|------------|-----|------|------|-----|----|----|-----|-----|-----|-----|----|-----|-----|----|-----|------|-----|------|
| Sharma     | 10  | 12   |      |     |    |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Thiele     | 45  |      |      | 38  | 91 | 41 | 82  | 12  |     |     |    |     |     |    |     |      |     |      |
| Kochman    | 25  |      |      | 21  | 67 |    | 13  |     |     |     |    |     |     |    |     |      |     |      |
| Meduri     | 29  | 8    | 12   | 31  | 92 |    | 13  | 1   | 28  | 17  | 31 | 24  | 21  |    |     |      |     |      |
| Karacop    |      | 52   | 34   | 35  | 79 | 16 | 62  |     |     |     |    |     |     |    |     |      |     |      |
| Ay         | 32  |      |      | 50  |    | 29 | 62  | 17  |     |     |    |     |     |    |     |      |     |      |
| Kaneko     | 34  | 8    | 10   | 67  | 77 | 32 | 49  |     |     |     |    |     |     |    |     |      |     |      |
| Reardon    | 34  |      |      | 56  |    |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Giordano   |     |      |      |     |    |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Doshi      | 44  | 9    | 3    | 28  | 79 | 37 | 14  | 2   |     |     |    |     |     |    |     |      |     |      |
| Bhardwaj   | 43  | 10   | 13   | 3   | 36 | 94 |     |     |     |     |    |     |     |    |     |      |     |      |
| Gonska     | 36  | 20   | 30   | 30  |    | 10 | 10  |     |     |     |    |     |     |    |     |      |     |      |
| Yousif     |     |      |      |     |    |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Ball       | 32  | 10   | 11   | 39  | 91 |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Eitan      | 47  | 14   | 28   | 87  | 65 | 11 |     |     |     |     |    |     |     |    |     |      |     |      |
| Finkeleitei| 29  |      |      | 6   | 4  | 85 | 71  | 64  | 17  | 66  |     | 10  |     |    |     |      |     |      |
| Monteiro   | 14  | 14   | 11   | 32  | 75 | 49 | 76  | 7   |     |     |    |     |     |    |     |      |     |      |
| Enriquez-R | 34  |      |      | 37  | 80 | 46 | 19  |     |     |     |    |     |     |    |     |      |     |      |
| Rogers     | 38  |      |      |     |    |    |     |     | 33  | 6   |    | 1   | 14  | 13 | 25  | 10   |    |      |
| Soliman    | 35  | 53   | 65   |     |    |    |     |     |     |     |    |     |     |    |     |      |     |      |
| vanMourik  | 25  |      |      | 26  | 65 | 36 | 33  |     |     |     |    | 1   |     |    |     |      |     |      |
| Kley       | 18  |      |      | 52  | 29 | 75 | 22  |     |     |     |    |     |     |    |     |      |     |      |
| Zaman      | 28  | 8   | 7    |      | 23 | 75 | 14  |     |     |     |    |     |     |    |     |      |     |      |
| Kahraman   | 21  |      |      | 30  | 70 | 15 |     |     |     |     |    |     |     |    |     |      |     |      |
| Sawaya     | 27  | 2    | 4    | 54  | 3  | 25 | 64  | 46  | 2   | 8   |     | 25  | 10  |    |     |      |     |      |
| Ben-Shoshan| 32  |      |      | 56  | 23 | 40 | 88  | 76  |     |     |    |     |     |    |     |      |     |      |
| Ram Kumar   | 32  |      |      | 23  | 76 |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Rouge      | 31  | 28   | 59   |     |    |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Gautier    | 20  |      |      |     |    |    |     |     |     |     |    |     |     |    |     |      |     |      |
| Boerlage   | 31  | 12   | 12   | 28  | 50 | 12 |     |     |     |     |    |     |     |    |     |      |     |      |
| Simms      | 29  |      |      | 28  | 23 | 19 |     |     |     |     |    |     |     |    |     |      |     |      |
| Nuis       | 21  |      |      | 24  | 56 | 5  |     |     |     |     |    |     |     |    |     |      |     |      |
| Pulse      | 7   |      |      | 36  |    | 61 | 12  |     |     |     |    |     |     |    |     |      |     |      |
| Ledwoch    | 24  |      |      | 34  | 65 | 6  | 8   |     |     |     |    |     |     |    |     |      |     |      |
| Akin       | 16  | 2    | 4    | 27  | 38 | 91 |     |     |     |     |    |     |     |    |     |      |     |      |
| Bagur      | 23  | 8   | 5    | 54  | 29 | 79 | 60  | 24  |     |     |    |     |     |    |     |      |     |      |
| Name           | 14 | 12 | 52 | 53 | 10 | 21 | 16 | 18 | 48 | 25 |
|----------------|----|----|----|----|----|----|----|----|----|----|
| De Carlo       |    |    |    |    |    |    |    |    |    |    |
| Gilard         | 26 |    |    |    |    |    |    |    |    |    |
| Muniz-Garcia   | 32 | 17 | 17 | 37 | 76 | 52 | 17 | 16 |    |    |
| Saia           | 15 | 18 | 59 | 15 |    | 5  |    | 23 | 2  | 12 |
| Salinas        | 50 |    |    | 56 | 41 | 68 | 9  | 14 | 15 |    |
| Schroeter      | 32 | 8  | 7  |    |    |    |    |    |    | 56 |
| van der Boon   | 25 | 8  | 10 | 51 | 22 | 55 | 5  | 21 | 10 | 24 |
| Mouillet       | 25 | 20 | 9  | 49 | 18 | 68 | 25 |    | 24 |    |
| Liang          | 32 | 15 | 9  |    |    |    |    |    | 26 | 57 |
| Pilgrim        | 26 | 56 | 16 | 24 | 78 | 60 | 9  |    | 25 | 18 |
| Bosmans        |    |    |    |    |    |    |    |    |    | 9  |
| D'Ancona       | 29 |    |    |    |    |    |    |    | 29 | 24 |
| Ewe            | 21 | 37 | 60 | 12 | 43 | 23 | 40 |    |    |    |
| Fracca         | 16 | 14 | 13 | 52 |    |    |    |    | 55 | 11 |
| Guetta         | 27 | 24 | 16 | 16 | 83 |    |    |    | 23 | 54 |
| Khawaja        | 19 | 13 | 10 |    |    |    |    |    |    |    |
| Calvi          | 17 | 3  | 50 | 30 | 31 | 85 | 58 | 16 |    |    |
| Chorianopoulos| 22 | 7  | 14 |    |    |    |    |    |    | 32 |
| Hayashida      | 50 | 7  | 71 | 49 | 13 |    |    | 34 | 15 | 30 |
| Bleiziffer     | 26 | 17 | 4  |    |    |    |    |    |    |    |
| Elchnainoff    |    | 51 | 27 | 69 | 10 |    |    | 73 | 23 | 25 |
| Baan           | 42 | 6  | 9  | 32 | 53 | 21 |    |    | 27 | 12 |
| Ewe            | 20 |    |    | 35 | 25 | 77 | 46 |    | 35 | 18 |
| Ferriera       | 28 |    |    |    |    |    |    | 50 | 97 |    |
| Godino         |    | 29 | 26 | 37 | 23 |    |    |    | 35 | 29 |
| Erkapic        | 34 | 1  | 14 | 51 | 30 | 82 |    |    |    |    |
| Haworth        | 18 | 9  | 21 | 9  |    | 17 |    | 21 | 23 | 23 |
| Piazza         | 28 | 15 | 6  |    |    |    |    |    |    |    |
| Rodes-Cabau    | 34 | 55 | 6  | 23 | 74 | 71 | 23 |    | 35 | 51 |
| Roten          | 12 | 16 | 19 | 51 | 22 | 72 |    |    |    |    |
| Lefevre        | 25 |    |    | 53 | 32 | 74 | 42 |    | 34 | 21 |
| Attias         |    |    |    |    | 52 |    |    |    | 28 | 13 |
| Petronio       | 12 | 8  | 5  | 27 | 75 | 8  |    | 19 | 22 | 16 |
| Thielmann      | 51 | 28 | 92 | 54 | 18 |    |    | 62 | 53 | 36 |
| Aslan          | 21 | 38 |    |    |    | 61 | 28 |    |    |    |
| Hamdan         | 14 | 1  | 10 | 38 | 84 | 70 |    |    | 14 | 22 |
| Jilaihawi      | 17 | 6  | 15 | 65 | 31 | 24 | 2  |    |    |    |
| Matsushita     | 31 | 15 | 57 | 30 | 85 | 56 | 42 | 13 |    |    |
| Tretter        | 31 | 7  | 17 | 31 | 90 | 29 | 9  |    | 19 |    |
| Zaid       | 37 | 5   | 45  | 91 | 21 | 32 |
|------------|----|-----|-----|----|----|----|
| Ahmad      |    |     |     |    |    |    |
Table S6: Procedural characteristics and type of valves used across the included studies (all numbers indicate percentages).

| Author          | Apical access | Femoral access | MR-Pro ADM >/= 1.3 nmol/l | TAVR using ACURATE TA device | Medtronic Corevalve | Edward Sapien | Lotus Transarterial vs transapical comparison (y or n) | Trans Subclavien vs Transfemoral (y or n) |
|-----------------|---------------|----------------|---------------------------|-----------------------------|--------------------|---------------|---------------------------------------------------|------------------------------------------|
| Hamandi         | 12.7          | 84.5           |                           | 9.8                        | 86.9               | y             | n                                                 |                                          |
| Sharma          | 17.6          | 77.8           |                           | 100                        | y                  | n             |                                                   |                                          |
| Thiele          | 100           | 50             |                           | 100                        | 50                 | n             | n                                                 |                                          |
| Kochman         | 100           | 100            |                           | 33.8                       | 66.1               | n             | n                                                 |                                          |
| Meduri          | 36.6(100%)    | 36.6           |                           | 36.6                       | 50                 | 2.9           | n                                                 |                                          |
| Karazop         | 100           | 100            |                           | 79.6                       | 18                 | 82            |                                                   |                                          |
| Ay              | 100           | 100            |                           | 100                        | 100                | n             | n                                                 |                                          |
| Kaneko          | 100           | 100            |                           | 100                        | 100                | y             | n                                                 |                                          |
| Reardon         | 90.2          | 11.8           |                           | 35.6                       | 27.3               | 7.6           | n                                                 | 66.5                                     |
| Giordano        | 79.6          | 100            |                           | 79.6                       | 100                | n             | n                                                 |                                          |
| Hamandi         | 12.7          | 84.5           |                           | 9.8                        | 86.9               | y             | n                                                 |                                          |
| Sharma          | 17.6          | 77.8           |                           | 100                        | y                  | n             |                                                   |                                          |
| Thiele          | 100           | 50             |                           | 100                        | 50                 | n             | n                                                 |                                          |
| Kochman         | 100           | 100            |                           | 33.8                       | 66.1               | n             | n                                                 |                                          |
| Meduri          | 36.6(100%)    | 36.6           |                           | 36.6                       | 50                 | 2.9           | n                                                 |                                          |
| Karazop         | 100           | 100            |                           | 79.6                       | 18                 | 82            |                                                   |                                          |
| Ay              | 100           | 100            |                           | 100                        | 100                | y             | n                                                 |                                          |
| Kaneko          | 100           | 100            |                           | 100                        | 100                | n             | n                                                 |                                          |
| Reardon         | 90.2          | 11.8           |                           | 35.6                       | 27.3               | 7.6           | n                                                 | 66.5                                     |
| Giordano        | 79.6          | 100            |                           | 79.6                       | 100                | n             | n                                                 |                                          |
| Hamandi         | 12.7          | 84.5           |                           | 9.8                        | 86.9               | y             | n                                                 |                                          |
| Sharma          | 17.6          | 77.8           |                           | 100                        | y                  | n             |                                                   |                                          |
| Thiele          | 100           | 50             |                           | 100                        | 50                 | n             | n                                                 |                                          |
| Kochman         | 100           | 100            |                           | 33.8                       | 66.1               | n             | n                                                 |                                          |
| Meduri          | 36.6(100%)    | 36.6           |                           | 36.6                       | 50                 | 2.9           | n                                                 |                                          |
| Karazop         | 100           | 100            |                           | 79.6                       | 18                 | 82            |                                                   |                                          |
| Ay              | 100           | 100            |                           | 100                        | 100                | n             | n                                                 |                                          |
| Kaneko          | 100           | 100            |                           | 100                        | 100                | y             | n                                                 |                                          |
| Reardon         | 90.2          | 11.8           |                           | 35.6                       | 27.3               | 7.6           | n                                                 | 66.5                                     |
| Giordano        | 79.6          | 100            |                           | 79.6                       | 100                | n             | n                                                 |                                          |
| Hamandi         | 12.7          | 84.5           |                           | 9.8                        | 86.9               | y             | n                                                 |                                          |
| Sharma          | 17.6          | 77.8           |                           | 100                        | y                  | n             |                                                   |                                          |
| Thiele          | 100           | 50             |                           | 100                        | 50                 | n             | n                                                 |                                          |
| Kochman         | 100           | 100            |                           | 33.8                       | 66.1               | n             | n                                                 |                                          |
| Meduri          | 36.6(100%)    | 36.6           |                           | 36.6                       | 50                 | 2.9           | n                                                 |                                          |
| Karazop         | 100           | 100            |                           | 79.6                       | 18                 | 82            |                                                   |                                          |
| Ay              | 100           | 100            |                           | 100                        | 100                | y             | n                                                 |                                          |
| Kaneko          | 100           | 100            |                           | 100                        | 100                | n             | n                                                 |                                          |
| Reardon         | 90.2          | 11.8           |                           | 35.6                       | 27.3               | 7.6           | n                                                 | 66.5                                     |
| Giordano        | 79.6          | 100            |                           | 79.6                       | 100                | n             | n                                                 |                                          |
| Name   | 25 | 75 | 61.2 | 38.8 | y  | n |
|--------|----|----|------|------|----|---|
| Roten  | 47 | 53 | 100  | 13.3 | 100| 100| 100 |
| Lefevre| 100| 100| 86.7 | 89.5 | 100| 100| 100 |
| Attias | 100| 100| 100  | 100  | 100| 100| 100 |
| Petronio| 61.5| 38.5| 52.9 | 47.1 | 100| 100| 100 |
| Thielmann| 100| 100| 86.7 | 89.5 | 100| 100| 100 |
| Aslan | 8.2 | 80.8| 91.7 | 99.6 | 74.4| 74.4| 74.4 |
| Hamdan | 100| 100| 100  | 100  | 100| 100| 100 |
| Jilaihawi | 100| 100| 100  | 100  | 100| 100| 100 |
| Matsushita | 100| 100| 100  | 100  | 100| 100| 100 |
| Tretter | 100| 100| 100  | 100  | 100| 100| 100 |
| Zaid | 100| 100| 100  | 100  | 100| 100| 100 |
| Ahmad | 100| 100| 100  | 100  | 100| 100| 100 |

*n=no, y=yes
Table S7: Proportion of PPM implantation across different baseline comorbidities in the included studies

| Variable        | Total | PPM  | PPM (%) | No PPM | No PPM (%) |
|-----------------|-------|------|---------|--------|------------|
| Diabetes Mellitus| 5904  | 1034 | 17.51   | 4870   | 82.49      |
| Hypertension    | 14879 | 3401 | 22.86   | 11478  | 77.14      |
| Hyperlipidemia  | 2634  | 104  | 3.95    | 2530   | 96.05      |
| COPD            | 3034  | 314  | 10.35   | 2720   | 89.65      |
| Prior CVA       | 1747  | 135  | 7.73    | 1612   | 92.27      |
| CKD             | 5839  | 1168 | 20.00   | 4671   | 80.00      |
| Liver Cirrhosis | 215   | 50   | 23.26   | 165    | 76.74      |
| PAD             | 2928  | 292  | 9.97    | 2636   | 90.03      |
| Smokers         | 425   | 38   | 8.94    | 387    | 91.06      |
| Prior MI        | 2776  | 233  | 8.39    | 2543   | 91.61      |
| Prior PCI       | 2581  | 353  | 13.68   | 2228   | 86.32      |
| Prior CABG      | 2453  | 234  | 9.54    | 2219   | 90.46      |

COPD- Chronic Obstructive Pulmonary Disease, CVA- Cerebrovascular Accident, CKD- Chronic Kidney Disease, PAD- Peripheral arterial disease, MI- Myocardial Infarction, PCI- Percutaneous coronary intervention, CABG- Coronary Artery Bypass graft
Table S8: Pooled estimates of anatomical and valvular predictors for PPM implantation in TAVR

| Anatomical Variants          | Valvular Variants                  |                   |
|------------------------------|-----------------------------------|-------------------|
| 23mm vs. 26mm prosthesis (2) | LOTUS vs. EvolutR                 | 1.12 (0.62-2.03)  |
| 29mm vs. 23mm (7)            | LOTUS vs. ESV                     | 1.49 (1.06-2.08)  |
| IV septum >22mm vs. <22mm (1)| LOTUS vs. MCRS                    | 1.65 (0.55-4.93)  |
| IV septum>11mm vs. <11mm (1) | P-HTN (>60mmHg) vs. No P-HTN (3)  | 1.71 (0.17-17.41) |
| LVOT>22mm vs. <22mm (1)      | Severe MR vs. No MR (3)           | 1.65 (0.55-4.93)  |
|                             |                                   | 1.78 (0.82-3.89)  |
|                             |                                   | 3.30 (0.59-18.32) |

Abbreviations: mm: millimeter, PPM- Permanent pacemaker, TAVR- Transaortic valve replacement, IV septum- interventricular septum, LVOT- Left ventricular outflow tract, P-HTN: Pulmonary hypertension, MCRS - Medtronic CoreValve Revalving System, ESV: Edwards SAPIEN valve,
Table S9: Predictors of PPM Implantation across different valve types

| Variables          | Medtronic CoreValve | Edward SAPIENS Valve | LOTUS | EVOLUT R   |
|--------------------|---------------------|----------------------|-------|------------|
|                    | OR (95%CI)          | OR (95%CI)           | OR (95%CI) | OR (95%CI) |
| Male vs. Female (MCV) | 1.33 (1.02-1.73)    | 1.25 (0.70-2.24)     | -     | 2.14 (0.73-6.27)* |
| 1st HB vs. No 1st HB | 1.95 (1.18-3.24)    | 1.56 (0.20-11.8)     | 0.19 (0.04-0.89)* | 1.47 (0.41-5.23)* |
| LBBB vs. No LBBB   | 0.99 (0.66-1.48)    | 0.28 (0.03-2.39)     | 0.34 (0.04-2.86)* | 0.29 (0.02-2.28)* |
| LAHB vs. No LAHB   | 1.94 (1.11-3.38)    | 1.95 (0.32-12.01)    | -     | -          |
| LPHB vs. No LPHB   | 1.19 (0.05-29.88)   | 2.29 (0.12-41.9)     | -     | -          |
| RBBB vs. No RBBB   | 4.03 (2.47-6.56)    | 14 (0.51-387)*       | 1.01 (0.18-5.54)* | 4.31 (1.02-18.22)* |
| Bifascicular Block | -                   | 3.84 (0.67-21.9)     | -     | -          |
| IPB vs. No IPB     | 8.04 (3.53-18.2)    | 12.83 (1.26-130)*    | -     | -          |
| AF vs. No AF       | 1.39 (0.86-2.26)    | 0.70 (0.34-1.43)     | 0.12 (0.01-0.92)* | 0.55 (0.16-1.85)* |
| Transfemoral vs. Subclavian | 0.35 (0.09-1.31) | -                     | -     | -          |
| Transapical        | -                   | 1.11 (0.46-2.72)     | -     | -          |

*Less than 3 studies with small sample size were used to calculate these values

Abbreviations: PPM- Permanent pacemaker, MCV- medtronic corevalve, HB- Heart block, LBBB- left bundle branch block, LAHB- Left anterior hemiblock, LPHB- Left posterior hemiblock, RBBB- Right bundle branch block, IPB- intraprocedural block, AF- atrial fibrillation
### Table S10: Sensitivity and subgroup analysis based on sample size and study design

| Variable                                      | Sensitivity analysis based on sample size (<200 removed) | Sensitivity analysis based on study design (RCT removed) |
|-----------------------------------------------|--------------------------------------------------------|---------------------------------------------------------|
| Age                                           | 1.25 (0.98-1.60)                                        | -                                                       |
| Male sex                                      | 1.47 (1.12-1.91)                                        | -                                                       |
| First degree heart block                      | 0.68 (0.14-3.30)                                        | 0.86 (0.27-2.80)                                        |
| Mobitz type 1 2nd Degree Heart Block          | 6.77 (2.82-16.22)                                       | -                                                       |
| Mobitz type 2 2nd Degree Heart Block          | 3.89 (2.54-5.95)                                        | -                                                       |
| Atrial Fibrillation                           | 1.08 (0.89-1.32)                                        | -                                                       |
| Left Anterior Hemiblock                       | 1.60 (1.17-2.18)                                        | 1.87 (1.19-2.93)                                        |
| Left Posterior Hemiblock                      | 1.23 (0.05-30.77)                                       | -                                                       |
| Intraprocedural AV Block                      | 8.04 (3.53-18.29)                                       | -                                                       |
| Left bundle branch block                      | 1.14 (0.84-1.55)                                        | 1.01 (0.76-1.35)                                        |
| Right bundle branch block                     | 4.12 (2.83-6)                                           | 4.21 (3.13-5.66)                                        |
| Bifascicular Block                            | 2.38 (1.94-6.01)                                        | -                                                       |
| Heart Failure with Preserved Ejection Fraction | 1.60 (0.88-2.91)                                        | -                                                       |
| Transarterial Approach with Transapical Approach (Edward Sapien) | 1.44 (0.34-6.04)                                        | -                                                       |
| Transfemoral approach with Subclavian Approach (MCV) | 0.84 (0.41-1.75)                                        | -                                                       |
| Medtronic CoreValve with Edward SAPIEN        | 2.87 (1.96-4.21)                                        | 3.03 (2.57-3.56)                                        |
| LOTUS valve with Medtronic CoreValve           | 1.76 (1.38-2.25)                                        | 1.75 (1.38-2.22)                                        |
| Edward SAPIEN valve with Medtronic EvolutR valve | 0.81 (0.58-1.14)                                        | -                                                       |
Table S11: Number of studies and patients with PPM and total patients across different predictors.

| Variable                     | PPM/Predictor present | PPM/Predictor absent |
|------------------------------|------------------------|----------------------|
| **Age >80 (n=5)**            |                        |                      |
| Ledwoch                      | 278/788                | 108/359              |
| Kley                         | 14/135                 | 11/105               |
| Ay                           | 14/132                 | 11/142               |
| Kahraman                     | 4/69                   | 2/67                 |
| Ramkumar                     | 7/23                   | 18/81                |
| **Sex (male) (n=31)**        |                        |                      |
| Monteiro                     | 80/321                 | 55/349               |
| Meduri                       | 122/345                | 123/359              |
| Bharadwaj                    | 20/195                 | 24/188               |
| Gonska                       | 88/288                 | 80/324               |
| Karacop                      | 35/109                 | 14/41                |
| Yousif                       | 59/270                 | 44/276               |
| Kaneko                       | 8/30                   | 9/62                 |
| Boerlage-Van Dijk            | 6/40                   | 17/65                |
| Ball                         | 25/118                 | 19/91                |
| Tretter                      | 21/93                  | 20/107               |
| Ledwoch                      | 174/468                | 212/679              |
| Bleiziffer                    | 13/68                  | 22/91                |
| Baan                         | 2/14                   | 5/13                 |
| Roten                        | 13/31                  | 10/36                |
| D’Ancona                     | 8/107                  | 12/215               |
| Fraccaro                     | 15/29                  | 10/35                |
| Akın                         | 10/18                  | 13/27                |
| Calvi                        | 22/64                  | 30/98                |
| Bagur                        | 14/176                 | 16/235               |
| De Carlo                     | 37/128                 | 29/147               |
| Munoz-Garcia                 | 21/65                  | 27/109               |
| Saia                         | 8/24                   | 9/36                 |
| Simms                        | 10/48                  | 7/52                 |
| van der Boon                 | 19/77                  | 17/90                |
| Mouillet                      | 7/25                   | 14/54                |
| Ahmad                        | 11/136                 | 6/133                |
| Matsushita                   | 45/94                  | 69/148               |
| Hamdan                       | 7/33                   | 14/40                |
| Aslan                        | 9/51                   | 15/89                |
| Zaid                         | 31/308                 | 26/224               |
| Jilawahi                     | 10/142                 | 14/106               |
| Hayashida                    | 10/129                 | 7/131                |
| **Atrial fibrillation (n=31)**|                        |                      |
| Monteiro                     | 19/91                  | 116/579              |
| Doshi                        | 925/3653               | 1086/4557            |
| Meduri                       | 78/202                 | 167/502              |
| Bharadwaj                    | 11/163                 | 33/220               |
| Gonska                       | 66/220                 | 102/392              |
| Kaneko                       | 4/31                   | 13/61                |
| Zaman                        | 3/19                   | 23/76                |
| Name                     | Count 1 | Count 2 |
|--------------------------|---------|---------|
| Boerlage-Van Dijk        | 7/30    | 98/75   |
| Ball                     | 18/67   | 26/142  |
| Matsushita               | 40/76   | 74/166  |
| Hamadan                  | 4/10    | 17/63   |
| Ledwoch                  | 103/277 | 283/870 |
| Bleiziffer               | 9/41    | 26/118  |
| Baan                     | 4/10    | 3/17    |
| Erkapic                  | 5/17    | 12/33   |
| Roten                    | 4/8     | 19/59   |
| D’Ancona                 | 5/93    | 15/229  |
| Calvi                    | 11/27   | 41/135  |
| Bagur                    | 4/96    | 26/315  |
| Chorianopoulos           | 6/29    | 40/101  |
| Munoz-Garcia             | 14/56   | 34/118  |
| Salinas                  | 2/17    | 1/17    |
| Schroeter                | 16/28   | 16/60   |
| Simms                    | 7/29    | 10/71   |
| Aslan                    | 6/29    | 18/111  |
| Van der Boon             | 12/41   | 24/126  |
| Roten                    | 4/8     | 19/59   |
| Mouillet                 | 6/21    | 15/58   |
| Tretter                  | 13/61   | 28/139  |
| Ahmad                    | 8/99    | 9/170   |
| Jilawahi                 | 4/43    | 20/205  |

**1st degree AV block (n=16)**

| Name                     | Count 1 | Count 2 |
|--------------------------|---------|---------|
| Monteiro                 | 29/104  | 106/566 |
| Doshi                    | 127/2857| 1822/5353|
| Meduri                   | 25/56   | 220/648 |
| Sharma                   | 5/47    | 20/179  |
| Kaneko                   | 4/17    | 13/75   |
| Zaman                    | 8/23    | 18/192  |
| Boerlage-Van Dijk        | 5/19    | 18/86   |
| Hamadan                  | 3/13    | 18/60   |
| Baan                     | 2/5     | 5/22    |
| Tretter                  | 2/22    | 27/187  |
| Bleiziffer               | 7/22    | 28/137  |
| Erkapic                  | 4/10    | 13/40   |
| Bagur                    | 1/38    | 29/373  |
| Jilawahi                 | 4/29    | 20/219  |
| Chorianopoulos           | 9/15    | 37/115  |
| De Carlo                 | 17/50   | 49/225  |

**2nd degree Mobitz I AV block (n=3)**

| Name                     | Count 1 | Count 2 |
|--------------------------|---------|---------|
| Monteiro                 | 1/1     | 134/669 |
| Doshi                    | 14/21   | 1935/8189|
| Liang                    | 1/1     | 4/52    |

**2nd degree Mobitz II AV block (n=2)**

| Name                     | Count 1 | Count 2 |
|--------------------------|---------|---------|
| Monteiro                 | 0/1     | 135/669 |
| Doshi                    | 48/86   | 1963/8124|

**3rd degree AV block (n=4)**

| Name                     | Count 1 | Count 2 |
|--------------------------|---------|---------|
| Doshi                    | 622/777 | 1351/7457|
| Karacop                  | 49/49   | 0/101   |
| First Name     | Last Name     | Number of Patients |
|----------------|---------------|--------------------|
| Sharma         | Liang         | 3/3                |

**Left anterior hemiblock (n=9)**

| First Name     | Last Name     | Number of Patients |
|----------------|---------------|--------------------|
| Meduri         | 51/121        | 194/583            |
| Sharma         | 7/34          | 18/192             |
| Ball           | 2/7           | 42/202             |
| Erkapic        | 4/8           | 13/42              |
| Calvi          | 1/4           | 51/158             |
| Bagur          | 3/29          | 27/382             |
| De Carlo       | 18/46         | 48/229             |
| Jilawahi       | 1/12          | 23/236             |
| Van der Boon   | 5/19          | 31/148             |

**Left posterior hemiblock (n=4)**

| First Name     | Last Name     | Number of Patients |
|----------------|---------------|--------------------|
| Sharma         | 2/3           | 23/223             |
| Ball           | 0/1           | 44/208             |
| Jilawahi       | 1/4           | 23/244             |
| Van der Boon   | 0/1           | 36/166             |

**Intraprocedural AV block (n=3)**

| First Name     | Last Name     | Number of Patients |
|----------------|---------------|--------------------|
| Sharma         | 13/30         | 12/196             |
| Bleiziffer     | 18/37         | 17/122             |
| Munoz-Garcia   | 22/34         | 26/140             |

**Left bundle branch block (n=29)**

| First Name     | Last Name     | Number of Patients |
|----------------|---------------|--------------------|
| Monteiro       | 15/93         | 120/577            |
| Doshi          | 260/731       | 1751/7479          |
| Meduri         | 20/56         | 225/648            |
| Bharadwaj      | 3/39          | 41/344             |
| Hamandi        | 13/52         | 97/372             |
| Sharma         | 1/23          | 24/203             |
| Kaneko         | 0/7           | 17/92              |
| Zaman          | 1/8           | 26/87              |
| Boerlage-Van Dijk | 1/14    | 22/91              |
| Ball           | 28/100        | 16/109             |
| Sawaya         | 0/14          | 43/230             |
| Hamadan        | 1/9           | 12/72              |
| Roten          | 1/11          | 22/56              |
| Bleiziffer     | 7/27          | 28/132             |
| Eltchnainoff   | 4/27          | 25/182             |
| Baan           | 0/2           | 7/25               |
| Erkapic        | 0/5           | 17/45              |
| Haworth        | 1/3           | 7/27               |
| Roten          | 1/11          | 22/56              |
| Khawaja        | 14/32         | 67/211             |
| Calvi          | 2/5           | 50/157             |
| Bagur          | 1/33          | 29/378             |
| Chorianopoulos | 3/9           | 43/121             |
| De Carlo       | 9/37          | 57/238             |
| Saia           | 1/9           | 16/51              |
| Schroeter      | 2/7           | 30/81              |
| Jilawahi       | 0/14          | 24/234             |
| Tretter        | 1/14          | 40/186             |
| Van der Boon   | 3/14          | 33/153             |
| Right bundle branch block (n=29) |
|--------------------------------|
| Monteiro                      | 36/71 | 99/599 |
| Doshi                         | 96/220| 1791/7990 |
| Meduri                        | 68/85 | 177/619 |
| Bharadwaj                     | 11/50 | 33/333 |
| Sharma                        | 10/28 | 15/198 |
| Kaneko                        | 4/9   | 13/83  |
| Zaman                         | 6/7   | 21/88  |
| Boerlage-Van Dijk             | 5/11  | 18/94  |
| Ball                          | 11/23 | 33/186 |
| Sawaya                        | 12/29 | 31/215 |
| Hamadan                       | 4/7   | 17/66  |
| Matsushita                    | 19/35 | 95/207 |
| Bleiziffer                     | 3/6   | 32/153 |
| Baan                          | 0/2   | 7/25   |
| Ferreira                      | 4/7   | 4/20   |
| Erkapic                       | 6/7   | 11/43  |
| Haworth                       | 6/7   | 2/23   |
| Piazza                        | 5/5   | 12/75  |
| Roten                         | 10/13 | 13/54  |
| Guetta                        | 10/11 | 18/59  |
| Khawaja                       | 15/23 | 66/220 |
| Bagur                         | 7/20  | 23/391 |
| Chorianopoulos                | 12/18 | 34/112 |
| De Carlo                      | 15/32 | 51/243 |
| Saia                          | 4/11  | 13/49  |
| Van der Boon                  | 11/17 | 25/150 |
| Jilawahi                      | 8/37  | 16/211 |
| Tretter                       | 18/34 | 23/166 |
| Mouillet                      | 3/7   | 18/72  |

| Bifascicular block (n=4) |
|--------------------------|
| Sharma                   | 7/16 | 18/210 |
| Ball                     | 2/3  | 42/206 |
| Jilawahi                 | 2/8  | 22/240 |
| Sawaya                   | 12/45| 31/199 |

| 23mm vs 26mm prosthesis (n=2) |
|-----------------------------|
| D’Ancona                    | 6/115| 14/207 |
| Bagur                       | 16/187| 14/223 |

| 23mm vs 29mm prosthesis (n=7) |
|------------------------------|
| Akin                         | 10/22| 13/23 |
| Saia                         | 10/35| 7/28 |
| Fraccaro                     | 12/36| 13/28 |
| Guetta                       | 10/33| 15/37 |
| Boon                         | 10/56| 26/109 |
| Chorianopoulos               | 12/46| 34/84 |
| Garcia                       | 24/97| 24/77 |

| Severe Pulmonary Hypertension (n=3) |
|-------------------------------------|
| Guetta                              | 9/15 | 16/55 |
| Munoz-Garcia                        | 16/39| 32/135 |
| Calvi                               | 26/83| 26/79 |

| Interventricular septum greater than 11mm (1) |
| Metric                                      | Value     |
|---------------------------------------------|-----------|
| Interventricular septum greater than 22mm   | 1/4       |
| Moderate/Severe MR                         |           |
| Akim                                        | 1/45      |
| Boon                                        | 30/143    |
| Bagur                                       | 21/307    |
| MCRS vs. Edwards SAPIEN(n=16)              |           |
| Monteiro                                    | 16/172    |
| Thiele                                      | 41/214    |
| Ball                                        | 1/24      |
| Soliman                                     | 1/17      |
| Ledwoch                                     | 34/235    |
| Bleiziffer                                   | 2/35      |
| Godino                                      | 7/61      |
| Erkapic                                     | 1/14      |
| Roten                                       | 3/26      |
| Bosmans                                     | 9/163     |
| Gilard                                      | 243/1793  |
| Liang                                       | 0/15      |
| Attitias                                    | 5/72      |
| Ben-Shoshan                                  | 26/108    |
| Eltchnainoff                                | 9/166     |
| Rogue                                       | 12/135    |
| LOTUS vs. MCV (n=4)                         |           |
| Ball                                        | 36/148    |
| Meduri                                      | 16/53     |
| Gonska                                      | 49/150    |
| Reardon                                     | 61/305    |
| LOTUS vs. Evolut R (n=1)                    |           |
| Giordana                                    | 122/703   |
| LOTUS vs. Edwards SAPIEN (n=2)              |           |
| Ball                                        | 1/24      |
| Giordana                                    | 72/541    |
| Edwards SAPIEN vs. EVOLUT R (n=5)           |           |
| Eitan                                       | 8/28      |
| Rodriguez                                   | 6/80      |
| Rogers                                      | 9/74      |
| Ben-Shoshan                                 | 22/88     |
| Finklestein                                 | 90/512    |
| Preserved LVEF (n=5)                        |           |
| Simms                                       | 17/90     |
| Fraccaro                                    | 53/313    |
| Ewe                                         | 6/94      |
| Munoz-Garcia                                | 40/151    |
| Access route (transfemoral vs. transapical (n=12) |   |
| Eltchnainoff                                | 4/71      |
| Sharma                                      | 4/40      |
| Rodes-Cabau                                 | 11/177    |
| Roten                                       | 3/17      |
|                |        |        |
|----------------|--------|--------|
| Bosmans        | 35/232 | 5/88   |
| Ewe            | 2/45   | 2/59   |
| Lefevre        | 1/61   | 3/69   |
| Bagur          | 15/223 | 15/188 |
| Gauthier       | 10/66  | 3/59   |
| Thielmann      | 4/14   | 0/20   |
| Godino         | 17/107 | 3/15   |
| Erkapic        | 16/36  | 1/14   |
| **Access route (transfemoral vs. subclavian) - MCRS (n=4)** |        |        |
| Petronio       | 74/460 | 10/54  |
| Saia           | 10/49  | 7/11   |
| Fraccaro       | 22/60  | 3/4    |
| Etchnainoff    | 22/161 | 3/12   |
| **Self-Expanding vs. Balloon-Expanding valves (n=18)** |        |        |
| Liang          | 5/38   | 0/15   |
| Soliman        | 4/23   | 1/17   |
| Erkapic        | 16/36  | 1/14   |
| Ball           | 36/148 | 1/24   |
| Attitias       | 2/11   | 5/72   |
| Bleiziffer     | 33/124 | 2/35   |
| Roten          | 20/41  | 3/26   |
| Eitan          | 9/37   | 5/55   |
| Rodriguez      | 6/80   | 12/64  |
| Giordana       | 12/46  | 7/61   |
| Rogers         | 9/74   | 9/108  |
| Bosman         | 31/121 | 9/163  |
| Ben-Shoshan    | 22/88  | 26/108 |
| Montiero       | 119/498| 16/172 |
| Thiel          | 49/213 | 41/214 |
| Finkelstein    | 90/512 | 32/223 |
| Ledowoch       | 352/912| 34/235 |
| Aslan          | 15/74  | 9/66   |
| Gilard         | 252/874| 243/1793|
| **Mechanically-Expandable vs. Self-Expanding Valves (n=5)** |        |        |
| Ball           | 3/10   | 36/148 |
| Meduri         | 71/192 | 16/53  |
| Gonska         | 98/225 | 49/150 |
| Giordana       | 35/151 | 122/703|
| Reardon        | 202/607| 61/305 |
| **Heart Failure (Unspecified) (n=4)** |        |        |
| Meduri         | 182/531| 63/173 |
| Bharadwaj      | 8/105  | 36/278 |
| Ahmad          | 3/39   | 14/230 |
| Kaneko         | 4/9    | 13/83  |
| Pilgrim        | 12/37  | 48/219 |
| Author         | Year | S  | PPM risk factors                              | Comparison arms                        | Model      | Results                                                                 |
|----------------|------|----|-----------------------------------------------|---------------------------------------|------------|-------------------------------------------------------------------------|
| Erkapic        | 2011 | 32 | Bradycardia, bifascicular block, RBBB         | CVP VS ESP                            | Random and Fixed | Higher risk of PPM in CVP, with prior RBBB                             |
| Gozdek         | 2020 | 11 | Lotus valve                                   | Lotus Vs Sapiens 3                    | Random     | Higher risk of PPM with Lotus                                           |
| Zhan           | 2019 | 5  | Access (transfemoral vs transaxial)           | Transfemoral vs Transaxial            | Random     | No difference in PPM implantation with different access                |
| Zafar          | 2020 | 4  | Chest radiation in patients with thoracic malignancy | Hx of chest radiation vs no chest radiation | Random     | No difference in PPM implantation in patients who received chest radiation |
| Xi             | 2019 | 20 | Long term outcomes of TAVR and Self expandable prosthesis | Self expandable vs balloon expandable prosthesis | Random and Fixed | Self expandable prosthesis had 2.5 fold increased risk of PPM implantation compared to balloon expandable prosthesis |
| Siontis        | 2014 | 41 | Age, sex, Afib, LBBB, RBBB, preserved EF, access route, first degree AV block, left anterior and posterior hemiblock, intraprocedural AV Block, medtronic vs Edwards valve, PR >200 | Predictors of pacemaker | Random     | Male sex, intraprocedural AV block, baseline conduction abnormalities predicted PPM implantation |
| Shoar          | 2020 | 3  | Preexisting LBBB                             | TAVR in patients with LBBB vs no LBBB | Random     | LBBB has an increased risk of PPM after TAVR                           |
| Biondi         | 2014 | 4  | Valve type (TAVR vs. SAVR risk factors)       | CoreValve vs Sapien                   | Fixed      | Higher PPM risk in CoreValve                                           |
| Alperi         | 2020 | 35 | Implantation depth, different types of valves and pre TAVR balloon aortic valvuloplasty | sapien3 vs EvoluR vs acurate neo vs portico | -          | Pre-TAVR BAV has no impact. Sapien 3 and Acurate Neo valves had lowest risk for PPM. Deeper valve implantation and a shorter MS length has high risk |
| An lee         | 2020 | 27 | SEV, BEV                                     | SEV vs BEV in post TAVR               | Random     | Transcatheter aortic IV, SEV was associated with larger postprocedural effective orifice area but higher rates of PPM. |
| Ando           | 2016 | 7  | RBBB, self-expandable prosthesis valve, and depth of implantation | NO-LBBB vs Non NO LBBB (NO=New onset) | Random     | LBBB after TAVI was associated with an increased rate of PPM          |
| Faroux         | 2020 | 30 | New onset persistent (NOP)-LBBB               | NOP-LBBB                              | Random and Fixed | NOP-LBBB had increased risk of all-cause death and PPM at 1-year follow-up. |
| Fu             | 2019 | 15 | PPM in TAVR                                  | PPM in SAVR                           | Random     | PPM implantation rate for TAVR is higher than SAVR at 1-year           |
| Gozdek (duplicate, same as 3) | 2020 | 11 | Lotus valve                                   | Sapien 3                              | Random     | Lotus was associated with higher rate of PPM implantation              |
| Haddad         | 2019 | 12 | Core Valve                                   | Jena Valve                            | Random     | Early gen. Valve associated with increased PPM compared to new gen valves for TAVI in AR |
| Kanjanahattakij | 2018 | 9  | Bicuspid aortic valve (BAV) TAVR             | Tricuspid valve TAVR                  | Random     | No difference in pacemaker implantation, major bleeding, and major vascular complication |
| Khan           | 2017 | 12 | TAVR                                         | SAVR                                  | Random     | High PPM and paravalvular leaks in TAVR.                               |
| Khan          | 2020  | 7     | TAVR | SAVR | Random | High risk of PPM in TAVR |
|--------------|-------|-------|------|------|--------|--------------------------|
| Khatri       | 2021  | 49    | CoreValve, Transarterial route | CoreValve vs Edwards Sapien valve | Random | PPI was 5 times more common with the CoreValve than the Sapien valve |
| Lee          | 2020  | 31    | Transaxillary route | Transaxillary vs direct aortic approach | Random | Direct aortic TAVR was associated with lower risks of permanent pacemaker implantation and valve malposition than transaxillary TAVR |
| Li           | 2020  | 13    | TAVR | SAVR | Random | No difference in PPM between TAVR and SAVR |
| Lou          | 2020  | 21    | TAVR | TAVR vs SAVR | Random | TAVR had high complication, paravalvular leak, and PPM |
| Krasopolous  | 2016  | 8     | CoreValve | Transfemoral Edwards Sapiens vs Transapical Edwards Sapiens vs CoreValve | Random | CoreValve implantation was associated with an increased risk of PPM |
| Liu          | 2018  | 3     | TAVR | SAVR and Medical therapy | Fixed | No differences in the risk of PPM, myocardial infarction, acute kidney injury or endocarditis |
| Liu          | 2020  | 5     | Nonagenarians | Younger patients | Random and Fixed | Nonagenarians had higher complications but no difference in PPM risk |
| Wagner       | 2019  | 19    | TAVR | TAVR vs SAVR, BAV, and medical therapy | Random and Fixed | TAVR had lower risk of PPM compared to SAVR |
| Wang         | 2020  | 6     | TAVR | SUAVR (sutureless aortic valve replacement) | Random and Fixed | No significant difference in need for PPM |
| Williams     | 2020  | 4     | Sutureless and rapid-deployment aortic valve replacement (SURD-AVR) | Edwards Lifeciences (Edwards Lifesciences, California) valves | Random | PPM insertion rate was 8.2% |
| Xie          | 2016  | 17    | BAV pts with TAVR | non-BAV | Random and Fixed | No difference in the risk of PPM |
| Seimens      | 2016  | 4     | Trans-arterial vs surgical approach | TAVR vs SAVR | Randomized | TAVI had lower risk of PPM |
| Rosendael    | 2018  | 40    | Pre-procedural conduction abnormalities including RBBB, prolonged PR interval, Atrial fibrillation and first degree AV block; LVOT calcification amount; Implantation depth. | Preprocedural anatomical and conduction abnormalities, present vs not present. | Random and Fixed | Electrical factor, calcification of the left ventricular outflow tract, balloon valvuloplasty and depth of implantation had increased risk of PPI. |
| Regueiro     | 2016  | 17    | Pre-procedural conduction abnormalities. New onset LBBB post-TAVR | Edward SApiens vs Medtronic valve. | Fixed | New-onset LBBB had higher PPM risk |
| R Khan       | 2020  | 7     | Undergoing TAVR. Moderate vs low surgical risk | TAVR vs SAVR. | Randomized | High PPM in TAVR |
| Quintana     | 2019  | 5     | BAV | TAV | Fixed | No difference of PPM in BAV and TAV |
| Panchal      | 2015  | 27    | Valve type used for TAVR | Edwards vs Medronic Corevalve | Random and Fixed | PPM higher in Corevalve compared to EV |
| Author         | Year | Case Number | Intervention | Comparator | Study Type | Conclusion |
|---------------|------|-------------|--------------|------------|------------|------------|
| Nagaraja      | 2014 | 39          | TAVR         | TAVR vs SAVR | Random and Fixed | No difference in risk of PPM in TAVR and SAVR |
| Malik         | 2020 | 4           | TAVR         | TAVR vs SAVR | Random           | High risk of PPM in TAVR |
| Ma            | 2020 | 7           | Chronic liver disease (CLD) | No CLD | Fixed | CLD has lower PPM risk |
| M Gozdek      | 2020 | 6           | Valve type used for TAVR | Self expandable valve vs Balloon-expandable Valve | Random and Fixed | Lower risk of PPM in Accurate neo self expandable valve |
| Arora         | 2016 | 29          | TAVR         | SAVR       | Random       | Increase risk of PPM in TAVR. |
| Croix         | 2020 | 11          | RBBB         | TAVR in No RBBB | Fixed | RBBB had higher incidence of PPM & mortality at 30 days |
SUPPLEMENTAL FOREST PLOTS FOR ALL STUDIES:

**Figure S1: Forest Plot showing an individual and pooled OR of PPM Implantation in patients age>80**

| Study          | Age<80 | Age≥80 | Odds Ratio with 95% CI | Weight (%) |
|----------------|--------|--------|------------------------|------------|
|                | Events | Total  | Events | Total |                   |            |
| Kley 2016 2016 | 14     | 135    | 11     | 105   | 0.99 [0.43, 2.27] | 7.38       |
| Ay 2019        | 14     | 132    | 11     | 142   | 1.37 [0.60, 3.12] | 7.48       |
| Kahraman 2016  | 4      | 69     | 2      | 67    | 1.94 [0.34, 10.96]| 1.70       |
| Ramkumar 2016  | 7      | 23     | 18     | 81    | 1.37 [0.51, 3.68] | 5.20       |
| Ledwoch 2012   | 278    | 788    | 108    | 359   | 1.17 [0.91, 1.51] | 78.24      |
| **Overall**    |        |        |        |       | 1.19 [0.95, 1.49] |            |
| **Random-DL model** |    |        |        |       | 1.19 [0.95, 1.49] |            |
| **Fixed-MH model** |    |        |        |       | 1.19 [0.95, 1.49] |            |

Heterogeneity: τ² = 0.00, I² = 0.00%, H² = 1.00

Test of θ = θ₀: Q(4) = 0.70, p = 0.95

Test of θ = 0: z = 1.52, p = 0.13

Decreases PPM Implantation

Increases PPM Implantation
Figure S2: Forest Plot showing an individual and pooled OR of PPM Implantation in Male Patients
| Study           | Male Events | Male Total | Female Events | Female Total | Odds Ratio with 95% CI | Weight (%) |
|-----------------|-------------|------------|---------------|--------------|------------------------|------------|
| Monteiro        | 80          | 321        | 55            | 349          | 1.58 [ 1.09, 2.30]     | 7.30       |
| Meduri          | 122         | 345        | 123           | 359          | 1.03 [ 0.77, 1.38]     | 12.15      |
| Bharadwaj       | 20          | 195        | 24            | 188          | 0.80 [ 0.43, 1.50]     | 2.82       |
| Gonska          | 88          | 288        | 80            | 324          | 1.24 [ 0.88, 1.74]     | 8.79       |
| Karacop         | 35          | 109        | 14            | 41           | 0.94 [ 0.46, 1.92]     | 2.00       |
| Yousef          | 59          | 270        | 44            | 276          | 1.37 [ 0.90, 2.10]     | 5.69       |
| Kaneko          | 8           | 30         | 9             | 62           | 1.84 [ 0.64, 5.24]     | 0.94       |
| Boonlage-Van Dijk | 4           | 40         | 17            | 65           | 0.57 [ 0.21, 1.58]     | 1.01       |
| Ball            | 25          | 118        | 19            | 91           | 1.01 [ 0.53, 1.96]     | 2.39       |
| Trettter        | 21          | 93         | 20            | 107          | 1.21 [ 0.62, 2.37]     | 2.27       |
| Ledwoch         | 174         | 468        | 212           | 679          | 1.19 [ 0.94, 1.50]     | 19.01      |
| Bleijffer       | 13          | 68         | 22            | 91           | 0.79 [ 0.37, 1.66]     | 1.81       |
| Bean            | 2           | 14         | 5             | 13           | 0.37 [ 0.06, 2.26]     | 0.32       |
| Roten           | 13          | 31         | 10            | 36           | 1.51 [ 0.58, 3.92]     | 1.13       |
| D’Ancona        | 8           | 107        | 12            | 215          | 1.34 [ 0.63, 3.38]     | 1.20       |
| Fraccaro        | 15          | 29         | 10            | 35           | 1.81 [ 0.71, 4.63]     | 1.16       |
| Akin            | 10          | 18         | 13            | 27           | 1.15 [ 0.42, 3.18]     | 0.99       |
| Calvi           | 22          | 64         | 30            | 98           | 1.12 [ 0.60, 2.12]     | 2.56       |
| Bagur           | 14          | 176        | 16            | 235          | 1.17 [ 0.56, 2.46]     | 1.86       |
| De Carlo        | 37          | 128        | 29            | 147          | 1.47 [ 0.85, 2.52]     | 3.51       |
| Munoz-Garcia    | 21          | 65         | 27            | 109          | 1.30 [ 0.68, 2.49]     | 2.45       |
| Saia            | 8           | 24         | 9             | 36           | 1.33 [ 0.45, 3.94]     | 0.88       |
| Simms           | 10          | 48         | 7             | 52           | 1.55 [ 0.55, 4.39]     | 0.95       |
| van der Boon    | 19          | 77         | 17            | 90           | 1.31 [ 0.63, 2.69]     | 1.97       |
| Mouillet        | 7           | 25         | 14            | 54           | 1.08 [ 0.39, 3.01]     | 0.98       |
| Ahmad           | 11          | 136        | 6             | 133          | 1.79 [ 0.64, 4.99]     | 0.98       |
| Matsushita      | 45          | 94         | 69            | 148          | 1.03 [ 0.65, 1.62]     | 4.94       |
| Hamdan          | 7           | 33         | 14            | 40           | 0.61 [ 0.22, 1.68]     | 0.99       |
| Astaran         | 9           | 51         | 15            | 89           | 1.05 [ 0.43, 2.56]     | 1.28       |
| Zaid            | 31          | 308        | 26            | 224          | 0.87 [ 0.50, 1.50]     | 3.41       |
| Jillawali       | 10          | 142        | 14            | 106          | 0.53 [ 0.23, 1.25]     | 1.42       |
| Hayashida       | 10          | 129        | 7             | 131          | 1.45 [ 0.54, 3.93]     | 1.04       |

**Random-DL model**

**Fixed-MH model**

Heterogeneity: $I^2 = 0.00$, $F^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta = 0$: $Q(31) = 20.62$, $p = 0.92$

Test of $\theta = 0$: $z = 2.81$, $p = 0.00$
Figure S3: Forest Plot showing an individual and pooled OR of PPM Implantation with First Degree Heart Block

| Study          | 1st HB Events | Total | No 1st HB Events | Total | Odds Ratio with 95% CI | Weight (%) |
|---------------|--------------|-------|------------------|-------|------------------------|------------|
| Monteiro      | 29           | 104   | 106              | 566   | 1.49 [0.94, 2.36]      | 8.50       |
| Doshi         | 127          | 2,857 | 1,822            | 5,353 | 0.13 [0.11, 0.16]      | 9.15       |
| Meduri        | 25           | 56    | 220              | 648   | 1.31 [0.80, 2.16]      | 8.38       |
| Sharma        | 5            | 47    | 20               | 179   | 0.95 [0.34, 2.67]      | 6.34       |
| Kaneko        | 4            | 17    | 13               | 75    | 1.36 [0.39, 4.68]      | 5.56       |
| Zaman         | 8            | 23    | 18               | 192   | 3.71 [1.45, 9.48]      | 6.70       |
| Boerlage-Van Dijk | 5          | 19    | 18               | 86    | 1.26 [0.42, 3.81]      | 6.04       |
| Hamadan       | 3            | 13    | 18               | 60    | 0.77 [0.20, 3.00]      | 5.13       |
| Baan          | 2            | 5     | 5                | 22    | 1.76 [0.26, 11.84]     | 3.59       |
| Trotter       | 2            | 22    | 27               | 187   | 0.63 [0.14, 2.83]      | 4.67       |
| Bleiziffer    | 7            | 22    | 28               | 137   | 1.56 [0.61, 4.00]      | 6.69       |
| Erkapic       | 4            | 10    | 13               | 40    | 1.23 [0.33, 4.60]      | 5.28       |
| Bagur         | 1            | 38    | 29               | 373   | 0.34 [0.04, 2.55]      | 3.33       |
| Jilawahi      | 4            | 29    | 20               | 219   | 1.51 [0.48, 4.73]      | 5.91       |
| Chorianopoulos | 9           | 15    | 37               | 115   | 1.86 [0.75, 4.61]      | 6.83       |
| De Carlo      | 17           | 50    | 49               | 225   | 1.56 [0.83, 2.93]      | 7.91       |

**Random-DL model**

**Fixed-MH model**

Heterogeneity: $\tau^2 = 0.59$, $I^2 = 82.43\%$, $H^2 = 5.69$

Test of $\theta = \theta_0$: $Q(15) = 270.14$, $p = 0.00$

Test of $\theta = 0$: $z = 0.33$, $p = 0.74$

Decreases PPM Implantation

Increases PPM Implantation
Figure S4: Forest Plot showing an individual and pooled OR of PPM Implantation with Mobitz type 1 2nd Degree Heart Block

| Study      | Mobitz-1 | No Mobitz-1 | Odds Ratio with 95% CI | Weight (%) |
|------------|----------|-------------|------------------------|------------|
| Monteiro 2017 | 1 1 | 134 669 | 4.99 [0.31, 80.31] | 5.36 |
| Doshi 2018    | 14 21 | 1,935 8,189 | 2.82 [1.43, 5.56] | 89.90 |
| Liang 2012    | 1 1 | 4 52 | 13.00 [0.68, 248.99] | 4.74 |

**Overall**

**Random-DL model**

**Fixed-MH model**

Heterogeneity: $I^2 = 0.00\%$, $H^2 = 1.00$  
Test of $θ_i = θ_r$: $Q(2) = 1.09$, $p = 0.58$  
Test of $θ = 0$: $z = 3.48$, $p = 0.00$
Figure S5: Forest Plot showing an individual and pooled OR of PPM Implantation with Atrial Fibrillation
| Study                | AF Events | AF Total | No AF Events | No AF Total | Odds Ratio with 95% CI | Weight (%) |
|---------------------|-----------|----------|--------------|-------------|------------------------|------------|
| Monteiro            | 19        | 91       | 116          | 579         | 1.04 [0.61, 1.76]      | 2.04       |
| Doshi               | 925       | 3,653    | 1,068        | 4,557       | 1.06 [0.96, 1.17]      | 60.50      |
| Meduri              | 78        | 202      | 167          | 502         | 1.16 [0.85, 1.59]      | 5.86       |
| Bharadwaj           | 11        | 163      | 33           | 220         | 0.45 [0.22, 0.92]      | 1.14       |
| Gonska              | 66        | 220      | 102          | 392         | 1.15 [0.81, 1.64]      | 4.71       |
| Kaneko              | 4         | 31       | 13           | 61          | 0.61 [0.18, 2.01]      | 0.40       |
| Zaman               | 3         | 19       | 23           | 76          | 0.52 [0.14, 1.92]      | 0.34       |
| Boerlage-Van Dijk   | 7         | 30       | 98           | 75          | 0.18 [0.07, 0.43]      | 0.76       |
| Ball                | 18        | 67       | 26           | 142         | 1.47 [0.75, 2.88]      | 1.30       |
| Matsushita          | 40        | 76       | 74           | 166         | 1.18 [0.74, 1.89]      | 2.62       |
| Hamadan             | 4         | 10       | 17           | 63          | 1.46 [0.41, 5.32]      | 0.36       |
| Ledwoch             | 103       | 277      | 283          | 870         | 1.14 [0.88, 1.49]      | 8.39       |
| Bleiziffer           | 9         | 41       | 26           | 118         | 1.00 [0.43, 2.30]      | 0.83       |
| Baan                | 4         | 10       | 3            | 17          | 2.27 [0.42, 12.27]     | 0.20       |
| Erkapic             | 5         | 17       | 12           | 33          | 0.81 [0.24, 2.68]      | 0.41       |
| Roten               | 4         | 8        | 19           | 59          | 1.55 [0.42, 5.74]      | 0.34       |
| D'Ancona            | 5         | 93       | 15           | 229         | 0.82 [0.29, 2.52]      | 0.54       |
| Calvi               | 11        | 27       | 41           | 135         | 1.34 [0.61, 2.94]      | 0.95       |
| Bagur               | 4         | 96       | 26           | 315         | 0.50 [0.17, 1.48]      | 0.50       |
| Chorianopoulos      | 6         | 29       | 40           | 101         | 0.52 [0.20, 1.35]      | 0.64       |
| Munoz-Garcia        | 14        | 56       | 34           | 118         | 0.87 [0.43, 1.75]      | 1.19       |
| Salinas             | 2         | 17       | 1            | 17          | 2.00 [0.17, 24.19]     | 0.09       |
| Schroeter           | 16        | 28       | 16           | 60          | 2.14 [0.94, 4.89]      | 0.85       |
| Simms               | 7         | 29       | 10           | 71          | 1.71 [0.59, 4.94]      | 0.52       |
| Asian               | 6         | 29       | 18           | 111         | 1.28 [0.46, 3.50]      | 0.57       |
| Van der Boon        | 12        | 41       | 24           | 126         | 1.54 [0.71, 3.34]      | 0.96       |
| Roten               | 4         | 8        | 19           | 59          | 1.55 [0.42, 5.74]      | 0.34       |
| Mouillet            | 6         | 21       | 15           | 58          | 1.10 [0.38, 3.22]      | 0.51       |
| Tretter             | 13        | 61       | 28           | 139         | 1.06 [0.51, 2.18]      | 1.11       |
| Ahmad               | 8         | 99       | 9            | 170         | 1.53 [0.57, 4.08]      | 0.80       |
| Jillawi             | 4         | 43       | 20           | 205         | 0.95 [0.31, 2.93]      | 0.46       |

**Random-DL model**

**Fixed-MH model**

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\beta_j = 0$: $Q(50) = 37.54$, $p = 0.16$

Test of $\beta = 0$: $z = 1.64$, $p = 0.10$

Decreases PPM Implantation

Increases PPM Implantation

1/32 1/4 2 16
Figure S6: Forest Plot showing an individual and pooled OR of PPM Implantation with Left Anterior Fascicular Block (LAFB)

| Study         | LAFB Events | LAFB Total | No LAFB Events | No LAFB Total | OR with 95% CI | Weight (%) |
|---------------|-------------|------------|----------------|---------------|----------------|------------|
| Meduri        | 51          | 121        | 194            | 583           | 1.27 [0.88, 1.83] | 53.33      |
| Sharma        | 7           | 34         | 18             | 192           | 2.20 [0.85, 5.66] | 7.95       |
| Ball          | 2           | 7          | 42             | 202           | 1.37 [0.28, 6.85] | 2.76       |
| Erkapic       | 4           | 8          | 13             | 42            | 1.62 [0.42, 6.24] | 3.89       |
| Calvi         | 1           | 4          | 51             | 158           | 0.77 [0.08, 7.09] | 1.45       |
| Bagur         | 3           | 29         | 27             | 382           | 1.46 [0.42, 5.11] | 4.55       |
| De Carlo      | 18          | 46         | 48             | 229           | 1.87 [1.00, 3.50] | 18.08      |
| Jilawahi      | 1           | 12         | 23             | 236           | 0.86 [0.11, 6.87] | 1.64       |
| Van der Boon  | 5           | 19         | 31             | 148           | 1.26 [0.44, 3.62] | 6.35       |

Random-DL model
1.43 [1.09, 1.86]

Fixed-MH model
1.43 [1.09, 1.86]

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta_1 = \theta_2$: $Q(8) = 2.53$, $p = 0.96$

Decreases PPM Implantation

Increases PPM Implantation

Test of $\theta = 0$: $z = 2.60$, $p = 0.01$

Figure S7: Forest Plot showing an individual and pooled OR of PPM Implantation with Left Posterior Fascicular Block (LPFB)

| Study        | LPFB Events | LPFB Total | No LPFB Events | No LPFB Total | OR with 95% CI | Weight (%) |
|--------------|-------------|------------|----------------|---------------|----------------|------------|
| Sharma       | 2           | 3          | 23             | 223           | 6.46 [1.03, 40.70] | 42.87      |
| Ball         | 0           | 1          | 44             | 208           | 1.56 [0.06, 38.97] | 14.02      |
| Jilawahi     | 1           | 4          | 23             | 244           | 2.65 [0.28, 24.73] | 29.12      |
| Van der Boon | 0           | 1          | 36             | 166           | 1.52 [0.06, 38.08] | 13.99      |

Random-DL model
3.34 [1.00, 11.13]

Fixed-MH model
3.34 [1.00, 11.13]

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta_1 = \theta_2$: $Q(3) = 0.98$, $p = 0.81$

Decreases PPM Implantation

Increases PPM Implantation

Test of $\theta = 0$: $z = 1.96$, $p = 0.05$
Figure S8: Forest Plot showing an individual and pooled OR of PPM Implantation with Intraprocedural AV Block

| Study           | Periprocedural Block | Odds Ratio with 95% CI | Weight (%) |
|-----------------|----------------------|------------------------|------------|
|                 | Events   | Total | Events | Total |                   |            |
| Sharma          | 13       | 30    | 12     | 196   | 7.08 [ 2.95, 16.96] | 25.14      |
| Bleiziffer       | 18       | 37    | 17     | 122   | 3.49 [ 1.64, 7.45]  | 33.39      |
| Munoz-Garcia    | 22       | 34    | 26     | 140   | 3.48 [ 1.76, 6.88]  | 41.47      |

Random-DL model
Fixed-MH model
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta = 0$: $Q(2) = 1.89$, $p = 0.39$
Test of $\theta = 0$: $z = 6.39$, $p = 0.00$

Figure S9: Forest Plot showing an individual and pooled OR of PPM Implantation with Left Bundle Branch block.
| Study               | LBBB Events | LBBB Total | No LBBB Events | No LBBB Total | Odds Ratio with 95% CI | Weight (%) |
|---------------------|-------------|------------|----------------|---------------|------------------------|------------|
| Monteiro            | 15          | 93         | 120            | 577           | 0.78 [0.43, 1.36]     | 8.90       |
| Doshi               | 260         | 731        | 1,751          | 7,479         | 1.52 [1.31, 1.77]     | 19.40      |
| Meduri              | 20          | 56         | 225            | 648           | 1.03 [0.60, 1.75]     | 9.78       |
| Bharadwaj           | 3           | 39         | 41             | 344           | 0.65 [0.19, 2.18]     | 2.98       |
| Hamandi             | 13          | 52         | 97             | 372           | 0.96 [0.50, 1.83]     | 7.78       |
| Sharma              | 1           | 23         | 24             | 203           | 0.37 [0.05, 2.85]     | 1.16       |
| Kaneko              | 0           | 7          | 17             | 92            | 0.35 [0.02, 6.46]     | 0.59       |
| Zaman               | 1           | 8          | 26             | 87            | 0.42 [0.05, 3.50]     | 1.08       |
| Boerlage-Van Dijk   | 1           | 14         | 22             | 91            | 0.30 [0.04, 2.37]     | 1.13       |
| Ball                | 28          | 100        | 16             | 109           | 1.91 [0.97, 3.73]     | 7.42       |
| Sawaya              | 0           | 14         | 43             | 230           | 0.18 [0.01, 3.12]     | 0.62       |
| Hamadan             | 1           | 9          | 12             | 72            | 0.67 [0.08, 5.75]     | 1.05       |
| Roten               | 1           | 11         | 22             | 56            | 0.23 [0.03, 1.90]     | 1.10       |
| Bleiziffer          | 7           | 27         | 28             | 132           | 1.22 [0.48, 3.09]     | 4.68       |
| Ettchmaïnoff        | 4           | 27         | 25             | 182           | 1.08 [0.35, 3.34]     | 3.39       |
| Baan                | 0           | 2          | 7              | 25            | 0.68 [0.03, 15.77]    | 0.51       |
| Erkagic             | 0           | 5          | 17             | 45            | 0.24 [0.01, 4.50]     | 0.58       |
| Haworth             | 1           | 3          | 7              | 27            | 1.29 [0.12, 14.33]    | 0.85       |
| Roten               | 1           | 11         | 22             | 56            | 0.23 [0.03, 1.90]     | 1.10       |
| Khawaja             | 14          | 32         | 87             | 211           | 1.38 [0.24, 6.67]     | 7.23       |
| Calvi               | 2           | 5          | 50             | 157           | 1.26 [0.24, 2.73]     | 1.70       |
| Bagur               | 1           | 33         | 29             | 378           | 0.39 [0.05, 2.99]     | 1.19       |
| Chorianopoulos      | 3           | 9          | 43             | 121           | 0.94 [0.24, 3.63]     | 2.49       |
| De Carlo            | 9           | 37         | 57             | 238           | 1.02 [0.46, 2.22]     | 6.01       |
| Saia                | 1           | 9          | 16             | 51            | 0.35 [0.04, 3.01]     | 1.07       |
| Schreeter           | 2           | 7          | 30             | 81            | 0.77 [0.15, 3.92]     | 1.78       |
| Jilawahi            | 0           | 14         | 24             | 234           | 0.33 [0.02, 5.70]     | 0.62       |
| Trotter             | 1           | 14         | 40             | 186           | 0.33 [0.04, 2.60]     | 1.15       |
| Van der Boon        | 3           | 14         | 33             | 153           | 0.99 [0.27, 3.85]     | 2.66       |

**Random-DL model**

**Fixed-MH model**

Heterogeneity: $I^2 = 0.06$, $I^2 = 23.92\%$, $H^2 = 1.31$

Test of $\theta = \theta$: $Q(28) = 31.99$, $p = 0.27$ (Decreases PPM Implantation)

Test of $\theta = 0$: $z = -0.10$, $p = 0.92$ (Increases PPM Implantation)
Figure S10: Forest Plot showing an individual and pooled OR of PPM Implantation with RBBB

| Study          | RBBB Events | RBBB Total | No RBBB Events | No RBBB Total | Odds Ratio with 95% CI | Weight (%) |
|----------------|-------------|------------|----------------|---------------|------------------------|------------|
| Monteiro       | 36          | 71         | 99             | 599           | 3.07 [1.95, 4.83]      | 8.54       |
| Doshi          | 96          | 220        | 1,791          | 7,990         | 1.95 [1.52, 2.49]      | 16.67      |
| Meduri         | 68          | 85         | 177            | 619           | 2.80 [1.95, 4.01]      | 11.47      |
| Bharadwaj      | 11          | 50         | 33             | 333           | 2.22 [1.05, 4.67]      | 3.95       |
| Sharma         | 10          | 28         | 15             | 198           | 4.71 [1.93, 11.51]     | 2.87       |
| Kaneko         | 4           | 9          | 13             | 83            | 2.84 [0.76, 10.57]     | 1.40       |
| Zaman          | 6           | 7          | 21             | 88            | 3.59 [1.09, 11.80]     | 1.69       |
| Boerlage-Van Dijk | 5       | 11         | 18             | 94            | 2.37 [0.74, 7.66]      | 1.74       |
| Ball           | 11          | 23         | 33             | 186           | 2.70 [1.20, 6.05]      | 3.42       |
| Sawaya         | 12          | 29         | 31             | 215           | 2.87 [1.33, 6.20]      | 3.72       |
| Hamadan        | 4           | 7          | 17             | 66            | 2.22 [0.58, 8.47]      | 1.35       |
| Matsushita     | 19          | 35         | 95             | 207           | 1.18 [0.64, 2.17]      | 5.50       |
| Bleiziffer      | 3           | 6          | 32             | 153           | 2.39 [0.57, 10.06]     | 1.18       |
| Baan           | 0           | 2          | 7              | 25            | 0.68 [0.03, 15.77]     | 0.26       |
| Ferreira       | 4           | 7          | 4              | 20            | 2.86 [0.56, 14.60]     | 0.93       |
| Erkapic        | 6           | 7          | 11             | 43            | 3.35 [0.94, 12.00]     | 1.48       |
| Haworth        | 6           | 7          | 2              | 23            | 9.88 [1.61, 60.24]     | 0.76       |
| Piazza         | 5           | 5          | 12             | 75            | 6.25 [1.57, 24.87]     | 1.28       |
| Roten          | 10          | 13         | 13             | 54            | 3.20 [1.15, 8.89]      | 2.24       |
| Guetta         | 10          | 11         | 18             | 59            | 2.98 [1.09, 8.15]      | 2.31       |
| Khawaja        | 15          | 23         | 86             | 220           | 2.17 [1.07, 4.41]      | 4.32       |
| Bagur          | 7           | 20         | 23             | 391           | 5.95 [2.28, 15.51]     | 2.53       |
| Chorianopoulos | 12         | 18         | 34             | 112           | 2.20 [0.96, 5.01]      | 3.30       |
| De Carlo       | 15          | 32         | 51             | 243           | 2.23 [1.13, 4.42]      | 4.56       |
| Saia           | 4           | 11         | 13             | 49            | 1.37 [0.37, 5.02]      | 1.44       |
| Van der Boon   | 11          | 17         | 25             | 150           | 3.88 [1.63, 9.25]      | 3.01       |
| Jilawahi       | 8           | 37         | 16             | 211           | 2.85 [1.14, 7.14]      | 2.73       |
| Tretter        | 18          | 34         | 23             | 166           | 3.82 [1.86, 7.84]      | 4.19       |
| Mouillet       | 3           | 7          | 18             | 72            | 1.71 [0.40, 7.29]      | 1.17       |

**Random-DL model**

**Fixed-MH model**

Heterogeneity: $\tau^2 = 0.02$, $I^2 = 14.34\%$, $H^2 = 1.17$

Test of $\theta = 0$: $Q(28) = 25.67$, $p = 0.59$  **Decreases PPM Implantation**

Test of $\theta = 0$: $z = 11.67$, $p = 0.00$  **Increases PPM Implantation**

Odds Ratio with 95% CI: $2.48 [2.17, 2.83]$
Figure S11: Forest Plot showing an individual and pooled OR of PPM Implantation with Bifascicular Block

| Study  | Bifascicular Block | No Bifascicular Block | Odds Ratio with 95% CI | Weight (%) |
|--------|-------------------|-----------------------|------------------------|------------|
|        | Events | Total    | Events | Total    |                      |            |
| Sharma | 7  | 16       | 18     | 210      | 5.10 [1.86, 14.02]   | 29.87      |
| Ball   | 2  | 3        | 42     | 206      | 3.27 [0.53, 20.18]   | 11.66      |
| Jilawahi | 2  | 8        | 22     | 240      | 2.73 [0.55, 13.64]   | 14.42      |
| Sawaya | 12 | 45       | 31     | 199      | 1.71 [0.82, 3.59]    | 44.05      |

Random-DL model

Fixed-MH model

Heterogeneity: $I^2 = 0.12$, $P = 24.58\%$, $H^2 = 1.33$

Test of $\theta = \theta^*$; $Q(3) = 3.00$, $p = 0.39$

Test of $\theta = 0$: $z = 2.98$, $p = 0.00$

Figure S12: Forest Plot showing an individual and pooled OR of PPM Implantation in Heart Failure

| Study   | HF | Total | No HF | Total | Odds Ratio with 95% CI | Weight (%) |
|---------|----|-------|-------|-------|------------------------|------------|
|         | Events | Total    | Events | Total    |                      |            |
| Meduri  | 182 | 531    | 63    | 173    | 0.94 [0.67, 1.31]     | 56.29      |
| Bharadwaj | 8  | 105    | 36    | 278    | 0.59 [0.26, 1.31]     | 14.59      |
| Ahmad   | 3  | 39     | 14    | 230    | 1.26 [0.35, 4.60]     | 5.94       |
| Kaneko  | 4  | 9      | 13    | 83     | 2.84 [0.76, 10.57]    | 5.75       |
| Pilgrim | 12 | 37     | 48    | 219    | 1.48 [0.72, 3.05]     | 17.43      |

Random-DL model

Fixed-MH model

Heterogeneity: $I^2 = 0.02$, $P = 11.57\%$, $H^2 = 1.13$

Test of $\theta = \theta^*$; $Q(4) = 5.49$, $p = 0.24$

Test of $\theta = 0$: $z = 0.19$, $p = 0.85$

Figure S13: Forest Plot showing an individual and pooled OR of PPM Implantation in Heart Failure with Preserved Ejection Fraction.
| Study         | HFpEF Events | HFpEF Total | No HFpEF Events | No HFpEF Total | Odds Ratio with 95% CI | Weight (%) |
|--------------|--------------|-------------|-----------------|----------------|------------------------|------------|
| Simms        | 0            | 10          | 17              | 90             | 0.25 [0.01, 4.40]     | 3.43       |
| Fraccaro     | 10           | 39          | 53              | 313            | 1.51 [0.71, 3.22]     | 50.25      |
| Ewe          | 1            | 41          | 6               | 94             | 0.38 [0.04, 3.28]     | 6.18       |
| Ewe          | 0            | 97          | 2               | 50             | 0.10 [0.00, 2.20]     | 3.05       |
| Munoz-Garcia | 8            | 23          | 40              | 151            | 1.31 [0.55, 3.16]     | 37.09      |

**Random-DL model**

**Fixed-MH model**

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta = 0$: $Q(4) = 5.09$, $p = 0.28$

Test of $\theta = 0$: $z = 0.49$, $p = 0.63$

Decreases PPM Implantation Increases PPM Implantation
Figure S14: Forest Plot showing an individual and pooled OR of PPM Implantation comparing Transfemoral approach with Transapical Approach

| Study       | Transfemoral | Transapical | Odds Ratio with 95% CI | Weight (%) |
|-------------|--------------|-------------|------------------------|------------|
|             | Events       | Total       | Events                 | Total      |            |
| Eltchnainoff| 22           | 161         | 4                      | 71         | 2.43 [ 0.81, 7.30] | 10.68      |
| Sharma      | 21           | 176         | 4                      | 40         | 1.19 [ 0.39, 3.67] | 10.39      |
| Rodes-Cabau | 6            | 168         | 11                     | 177        | 0.57 [ 0.21, 1.59] | 11.88      |
| Roten       | 20           | 50          | 3                      | 17         | 2.27 [ 0.60, 8.59] | 8.10       |
| Bosmans     | 35           | 232         | 5                      | 88         | 2.66 [ 1.01, 6.99] | 12.65      |
| Ewe         | 2            | 45          | 2                      | 59         | 1.31 [ 0.18, 9.67] | 4.14       |
| Lefevre     | 1            | 61          | 3                      | 69         | 0.38 [ 0.04, 3.72] | 3.25       |
| Bagur       | 15           | 223         | 15                     | 188        | 0.84 [ 0.40, 1.77] | 17.11      |
| Gauthier    | 10           | 66          | 3                      | 59         | 2.98 [ 0.78, 11.35] | 8.05       |
| Thielmann   | 4            | 14          | 0                      | 20         | 12.72 [ 0.63, 255.10] | 1.97    |
| Godino      | 17           | 107         | 3                      | 15         | 0.79 [ 0.21, 3.04] | 8.02       |
| Erkapic     | 16           | 36          | 1                      | 14         | 6.22 [ 0.75, 51.45] | 3.76       |

Random-DL model

Fixed-MH model

Heterogeneity: $\tau^2 = 0.14, I^2 = 25.78\%$, $H^2 = 1.35$

Test of $\theta = \theta_0$; $Q(11) = 15.13, p = 0.18$ Decreases PPM Implantation

Test of $\theta = 0$: $z = 1.70, p = 0.09$ Increases PPM Implantation
Figure S16: Forest Plot showing an individual and pooled OR of PPM Implantation comparing Transfemoral approach with subclavian approach

| Study     | Transfemoral Events | Total | Subclavian Events | Total | Odds Ratio with 95% CI | Weight (%) |
|-----------|---------------------|-------|-------------------|-------|------------------------|------------|
| Petronio  | 74                  | 460   | 10                | 54    | 0.87 [0.42, 1.78]      | 50.99      |
| Saia      | 10                  | 49    | 7                 | 11    | 0.32 [0.10, 1.03]      | 21.04      |
| Fraccaro  | 22                  | 60    | 3                 | 4     | 0.49 [0.10, 2.36]      | 11.84      |
| Eltchnainoff | 22             | 161   | 3                 | 12    | 0.55 [0.14, 2.09]      | 16.13      |

Random-DL model
Fixed-MH model
Heterogeneity: $\tau^2 = 0.02, I^2 = 5.71\%, H^2 = 1.06$
Test of $\theta = 0; Q(3) = 2.20, p = 0.53$
Test of $\theta = 0; z = -1.76, p = 0.08$

Decreases PPM Implantation
Increases PPM Implantation

Figure S17: Forest plot showing the mean difference of implantation depth for patients with and without PPM

| Study or Subgroup | PPM Mean ± SD | Total Mean ± SD | Weight | Mean Difference IV, Random, 95% CI | Mean Difference IV, Random, 95% CI |
|-------------------|---------------|-----------------|--------|-----------------------------------|-----------------------------------|
| Hamadian 2016     | 8.5 ± 4.7     | 21              | 5.6 ± 2.8 | 52 | 6.09 [0.88, 6.11] | 3.60 [0.52, 3.87] |
| Treble 2019       | 6.4 ± 2.9     | 41              | 5.5 ± 2.6 | 169 | 1.81 [0.97, 1.95] | 1.09 [0.57, 1.50] |
| Jilliham 2019     | 4.5 ± 1.9     | 24              | 3.2 ± 1.0 | 224 | 2.50 [0.81, 3.20] | 1.30 [0.50, 2.10] |
| Asian 2020        | 9.2 ± 1.7     | 24              | 7.4 ± 2.1 | 118 | 2.03 [0.80, 3.26] | 1.80 [0.72, 2.88] |
| Enoshiba 2020     | 5.7 ± 2.3     | 114             | 5.1 ± 1.9 | 129 | 2.64 [0.88, 3.40] | 0.65 [0.38, 1.14] |
| Total (95% CI)    | 224           | 679             | 100.0%  | 1.25 [0.64, 1.87] | 0.65 [0.38, 1.14] |

Heterogeneity: Tau² = 0.27, Chi² = 9.58, df = 4 (P = 0.04), I² = 59%
Test for overall effect Z = 3.98 (P < 0.0001)

Figure S18: Forest plot showing the pooled mean membranous septal length for patients with and without PPM
Figure S19: Forest Plot showing an individual and pooled OR of PPM Implantation comparing Medtronic CoreValve with Edwards SAPIEN valve

| Study       | Events | Total | Events | Total | MCV Odds Ratio with 95% CI | ESV Weight (%) |
|-------------|--------|-------|--------|-------|---------------------------|----------------|
| Monteiro    | 119    | 498   | 16     | 172   | 2.57 [1.48, 4.45]         | 10.27          |
| Thiele      | 49     | 213   | 41     | 214   | 1.20 [0.76, 1.89]         | 11.43          |
| Ball        | 36     | 148   | 1      | 24    | 5.84 [0.76, 44.60]        | 2.00           |
| Soliman     | 4      | 23    | 1      | 17    | 2.96 [0.30, 28.88]        | 1.64           |
| Ledwoch     | 325    | 912   | 34     | 235   | 2.67 [1.82, 3.90]         | 12.38          |
| Bleiziffer  | 33     | 124   | 2      | 35    | 4.66 [1.06, 20.37]        | 3.40           |
| Godino      | 12     | 46    | 7      | 61    | 2.27 [0.83, 6.23]         | 5.81           |
| Erkapic     | 16     | 36    | 1      | 14    | 6.22 [0.75, 51.45]        | 1.87           |
| Roten       | 20     | 41    | 3      | 26    | 4.23 [1.14, 15.66]        | 4.07           |
| Bosmans     | 31     | 121   | 9      | 163   | 4.64 [2.13, 10.11]        | 7.74           |
| Gilard      | 252    | 874   | 243    | 1,793 | 2.13 [1.75, 2.58]         | 14.37          |
| Liang       | 5      | 38    | 0      | 15    | 4.43 [0.23, 84.99]        | 1.02           |
| Attalas     | 2      | 11    | 5      | 72    | 2.62 [0.45, 15.19]        | 2.56           |
| Ben-Shoshan | 22     | 88    | 26     | 108   | 1.04 [0.55, 1.96]         | 9.28           |
| Eltchmanoff | 20     | 78    | 9      | 166   | 4.73 [2.06, 10.86]        | 7.24           |
| Rogue       | 6      | 12    | 12     | 135   | 5.62 [1.79, 17.66]        | 4.93           |

Random-DL model

Fixed-MH model

Heterogeneity: T² = 0.16, I² = 59.62%, H² = 2.48

Test of θ = θ: Q(15) = 26.99, p = 0.03 (Decreases PPM Implantation)

Test of θ = 0: z = 6.05, p = 0.00 (Increases PPM Implantation)
**Figure S20:** Forest Plot showing an individual and pooled OR of PPM Implantation comparing LOTUS valve with Medtronic CoreValve

| Study     | Lotus Events | Total | Corevalve Events | Total | Odds Ratio with 95% CI | Weight (%) |
|-----------|--------------|-------|------------------|-------|------------------------|------------|
| Meduri 2019 | 71           | 192   | 16               | 53    | 1.22 [ 0.66, 2.28]     | 18.59      |
| Gonska 2018 | 98           | 225   | 4                | 27    | 2.94 [ 1.00, 8.63]     | 6.20       |
| Reardon 2019 | 202          | 607   | 61               | 305   | 1.66 [ 1.21, 2.29]     | 71.21      |
| Ball 2018  | 3            | 10    | 36               | 148   | 1.23 [ 0.32, 4.71]     | 4.00       |
| **Overall** |              |       |                  |       | 1.61 [ 1.23, 2.10]     |            |
| **Random-DL model** |         |       |                  |       | 1.61 [ 1.23, 2.10]     |            |
| **Fixed-MH model** |          |       |                  |       | 1.61 [ 1.23, 2.10]     |            |

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta = \theta_0$: $Q(3) = 2.14$, $p = 0.54$  
\textbf{Decreases PPM Implantation}

Test of $\theta = 0$: $z = 3.48$, $p = 0.00$  

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**Figure S21:** Forest Plot showing an individual and pooled OR of PPM Implantation comparing Edwards SAPIEN valve with Medtronic EvolutR valve

| Study     | ESV Events | Total | EVOLUT-R Events | Total | Odds Ratio with 95% CI | Weight (%) |
|-----------|------------|-------|------------------|-------|------------------------|------------|
| Eitan     | 10         | 50    | 8                | 28    | 0.70 [ 0.25, 1.98]     | 8.63       |
| Rodriguez | 12         | 64    | 6                | 80    | 2.50 [ 0.89, 7.03]     | 8.71       |
| Rogers    | 9          | 108   | 9                | 74    | 0.69 [ 0.26, 1.81]     | 9.88       |
| Ben-Shoshan | 26         | 108   | 22               | 88    | 0.96 [ 0.51, 1.81]     | 23.16      |
| Finklestein | 32         | 223   | 90               | 512   | 0.82 [ 0.53, 1.26]     | 49.62      |
| **Random-DL model** |         |       |                  |       | 0.92 [ 0.65, 1.29]     |            |
| **Fixed-MH model** |          |       |                  |       | 0.91 [ 0.67, 1.23]     |            |

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta = \theta_0$: $Q(4) = 4.52$, $p = 0.34$  
\textbf{Decreases PPM Implantation}

Test of $\theta = 0$: $z = -0.63$, $p = 0.53$  

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Figure S22: Sensitivity Analysis on the pooled estimate of PPM implantation in patients with First Degree HB.
Figure S23: Sensitivity Analysis on the pooled estimate of PPM implantation in patients with RBBB.
Figure S24: Sensitivity Analysis on the pooled estimate of PPM implantation in patients with LBBB.

Sorted by $I^2$

- Omitting Doshi
- Omitting Monteiro
- Omitting Roten.1
- Omitting Roten
- Omitting Boereange-Van Dijk
- Omitting Tretter
- Omitting Salo
- Omitting Sharma
- Omitting Bharadwaj
- Omitting Zaman
- Omitting Sawaya
- Omitting Bagur
- Omitting Erkacpic
- Omitting Ball
- Omitting Hamandi
- Omitting Meduri
- Omitting Jilawahi
- Omitting Kaneko
- Omitting Schroeter
- Omitting De Carlo
- Omitting Baan
- Omitting Hamadan
- Omitting Chrorianopoulos
- Omitting Van der Boon
- Omitting Elshnainoff
- Omitting Khawaja
- Omitting Beiziffer
- Omitting Haworth
- Omitting Calvi

$I^2$ values:
- $I^2 = 6\%$, $\hat{\sigma} = 0.93$ [0.73-1.18]
- $I^2 = 40\%$, $\hat{\sigma} = 0.95$ [0.71-1.27]
- $I^2 = 41\%$, $\hat{\sigma} = 0.97$ [0.74-1.25]
- $I^2 = 41\%$, $\hat{\sigma} = 0.97$ [0.74-1.25]
- $I^2 = 43\%$, $\hat{\sigma} = 0.95$ [0.73-1.25]
- $I^2 = 44\%$, $\hat{\sigma} = 0.95$ [0.72-1.24]
- $I^2 = 44\%$, $\hat{\sigma} = 0.95$ [0.72-1.24]
- $I^2 = 44\%$, $\hat{\sigma} = 0.94$ [0.72-1.24]
- $I^2 = 44\%$, $\hat{\sigma} = 0.94$ [0.71-1.24]
- $I^2 = 44\%$, $\hat{\sigma} = 0.94$ [0.71-1.24]
- $I^2 = 45\%$, $\hat{\sigma} = 0.93$ [0.71-1.22]
- $I^2 = 45\%$, $\hat{\sigma} = 0.94$ [0.71-1.24]
- $I^2 = 45\%$, $\hat{\sigma} = 0.93$ [0.71-1.22]
- $I^2 = 45\%$, $\hat{\sigma} = 0.85$ [0.65-1.11]
- $I^2 = 45\%$, $\hat{\sigma} = 0.91$ [0.68-1.22]
- $I^2 = 45\%$, $\hat{\sigma} = 0.89$ [0.67-1.20]
- $I^2 = 45\%$, $\hat{\sigma} = 0.93$ [0.70-1.22]
- $I^2 = 45\%$, $\hat{\sigma} = 0.93$ [0.70-1.22]
- $I^2 = 46\%$, $\hat{\sigma} = 0.92$ [0.70-1.23]
- $I^2 = 46\%$, $\hat{\sigma} = 0.90$ [0.68-1.21]
- $I^2 = 46\%$, $\hat{\sigma} = 0.92$ [0.70-1.22]
- $I^2 = 46\%$, $\hat{\sigma} = 0.92$ [0.69-1.22]
- $I^2 = 46\%$, $\hat{\sigma} = 0.91$ [0.69-1.21]
- $I^2 = 46\%$, $\hat{\sigma} = 0.91$ [0.68-1.20]
- $I^2 = 46\%$, $\hat{\sigma} = 0.87$ [0.65-1.15]
- $I^2 = 47\%$, $\hat{\sigma} = 0.89$ [0.87-1.19]
- $I^2 = 47\%$, $\hat{\sigma} = 0.94$ [0.69-1.20]
- $I^2 = 47\%$, $\hat{\sigma} = 0.91$ [0.68-1.20]
Figure S25: Funnel plot showing minimal publication bias comparing the pooled estimate of PPM predictor across studies for sex.