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Permanent pacemaker implantation after On-X surgical aortic valve replacement: SWEDEHEART observational study

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ABSTRACT

Objective Bioprosthetic aortic valves with an extended subannular component, such as transcatheter valves, exert increased compression on the cardiac conduction system and increase the risk for permanent pacemaker implantation. It is unknown if the On-X mechanical prosthetic valve, which has an elongated subannular valve housing, increases the risk of permanent pacemaker implantation following aortic valve replacement.

Design Observational nationwide cohort study.

Setting Swedish population-based study.

Participants All patients aged 18–65 years who underwent primary mechanical aortic valve replacement in Sweden between 2005 and 2018. We used the Swedish Web system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies register and other Swedish national health-data registers.

Exposure Patients implanted with an On-X valve versus patients implanted with other bileaflet mechanical valves.

Primary and secondary outcome measures Primary outcome measure was permanent pacemaker implantation within 30 days of surgery.

Results A total of 2602 patients were included, and 581 patients received an On-X valve and 2021 patients received a St Jude Masters/Regent (n=945) or Carbomedics Reduced valve (n=1076). In the total study population, 115 (4.4%) permanent pacemaker implantations were performed within 30 days after aortic valve replacement. In the propensity score matched population, there was no significant difference in the rate of permanent pacemaker implantation in the On-X group compared with the control group: 3.6% (95% CI: 2.4% to 5.5%) vs 4.0% (95% CI: 2.7% to 5.9%), p=0.877.

Conclusions The On-X prosthetic heart valve was associated with a similarly low risk for permanent pacemaker implantation after aortic valve replacement compared with other conventional bileaflet mechanical valves. The On-X elongated subannular valve housing does not interfere with the cardiac conduction system.

Strengths and limitations of this study

- ► Data were obtained from high-quality national Swedish health data registers.
- ► Long and complete follow-up in a nationwide cohort.
- ► One limitation of the study was that data did not include preoperative conduction disorders known to increase the risk for postoperative pacemaker requirement, such as bundle branch block.
- ► Another limitation was that we had no information about specific indications of postoperative pacemaker implantation.

INTRODUCTION

Surgical aortic valve replacement can induce cardiac conduction disorders that require permanent pacemaker implantation in 2%–6% of the patients.[1–4] The close proximity of the atrioventricular node and the bundle of His to the aortic valve annulus and the left ventricular outflow tract makes the cardiac conduction system prone to injury during implantation of an aortic valve prosthesis.[3] Compared with conventional intra-/supraannulary prosthetic valves, bioprosthetic valves with an extended subannular component, such as transcatheter and rapid deployment valves, exerts increased compression on the conduction system.[5 6] These prosthetic valves, as well as the subannular implantation depth, are associated with markedly increased risks for permanent pacemaker implantation.[5–8] The current standard for mechanical aortic valves used in contemporary clinical practice are bileaflet valves implanted intra- or supraannulary. The On-X prosthetic valve (On-X Life Technologies, Austin, Texas) is one of the most commonly used bileaflet mechanical valves today. Its' design differs from other contemporary mechanical valves,[9] and it is the only mechanical heart valve approved for reduced international normalised ratio target range.[10 11] In order to reduce turbulence and enhance blood flow over the prosthetic valve, the On-X consists of an elongated valve housing with a flared inlet that protrudes subannulary into the left ventricular outflow tract.[9] It is unknown

whether this design increases the risk for conduction disorders requiring permanent pacemaker implantation.

We performed a nationwide population-based cohort study to analyse whether aortic valve replacement with implantation of the On-X prosthetic heart valve, compared with other conventional bileaflet mechanical valves, was associated with an increased risk for permanent pacemaker implantation.

METHODS

This nationwide population-based observational cohort study followed the Strengthening the Reporting of Observational Studies in Epidemiology and the REporting of studies Conducted using Observational Routinely collected health Data guidelines for observational studies using routinely collected data.[12 13] The study was approved by the Swedish Ethical Review Authority and the need for informed consent was waived (Registration number: 2019–04131).

Study population

The Swedish Web system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies register[14 15] was used to identify all adult patients aged 18–65 who underwent primary mechanical aortic valve replacement between 2005 and 2018. Patients who had a permanent pacemaker or implantable cardioverter-defibrillator prior to surgery or who underwent valve replacement because of infective endocarditis, or who had concomitant mitral valve surgery were excluded. Implantation of the On-X prosthetic valve was the exposure and the two most common valve types (Carbomedics Reduced (LivaNova, London, United Kingdom) and St Jude Masters/Regent (St Jude Medical, St Paul, Minnesota, USA)) served as the control group. Thus, patients who received other valve models were excluded.

As previously described, individual-level data linking to other nationwide healthcare registries was performed using the unique personal identity numbers assigned to all Swedish residents.[16 17] The National Patient Register[18] was used to acquire information regarding relevant prior medical history, and the LISA (Longitudinal integration database for health insurance and labour market studies) database, managed by Statistics Sweden, was used to obtain information regarding socioeconomic variabels.[19]

Outcomes

The primary outcome measure was the implantation of a permanent pacemaker or implantable cardioverter-defibrillator within 30 days following aortic valve replacement as identified by the International Classification of Diseases-codes (FPE00, FPE10, FPE20, FPE26, FPF00, FPF10, FPF20, FPG10, FPG20, FPG30 and FPG33) from the Swedish National Patient Register.[18] We included implantable cardioverter defibrillator in the primary outcome measure in order to capture patients who had dual indications for both pacing and defibrillation.

Statistical methods

Baseline characteristics were described with frequencies and percentages for categorical variables and means and SD for continuous variables. To minimise confounding due to measured baseline covariates, we estimated propensity scores (the probability of receiving an On-X valve based on the observed data) using a logistic regression model that included all variables reported in table 1. A propensity score matched cohort was created by 1:1 nearest neighbour matching on the logit of the propensity score without replacement and a calliper width of 0.2 times the SD of the logit of the propensity score.[20] In a separate analysis, we also estimated propensity scores using generalised boosted regression modeling[21 22] and used the scores for inverse probability of treatment weighting. Finally, we applied the propensity scores from a logistic regression model to construct overlap weights, a weighting method that yields exact covariate balance between the exposed and reference groups by construction.[23] Balance between the groups was assessed by standardised mean differences. An absolute standardised difference ≤0.1 was considered an ideal balance.[24] In the matched and weighed populations, respectively, the percentage of pacemaker implants and 95% CI were compared between the groups using McNemar's and χ^2 tests, respectively. To illustrate the pacemaker implantation rate the first 90 days postoperatively, we constructed Kaplan-Meier curves. Although death could be considered a competing event, it occurred rarely during the first 90 days of follow-up and was therefore not accounted for. The statistical analyses were performed with R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) and the Matching[25] and twang[22] packages.

Missing data

Although data were complete for most variables, including exposure and outcome, there were some missing data. The variables with missing data were body mass index, estimated glomerular filtration rate, valve size and educational level with 6.9%, 1.5%, 0.7% and 0.6% missing data, respectively. For these variables, missing data was imputed with the most common category. Missing data was handled differently in the inverse probability of treatment weighted analysis because the weights were constructed to also balance rates of missingness in both groups.[21 22]

Patient and public involvement

There was no patient or public involvement in the design or conduct of this study.

RESULTS

A total of 2602 patients were included in the study, and 581 patients received an On-X valve and 2021 patients

Table 1 Baseline characteristics in patients who underwent aortic valve replacement in Sweden with an On-X valve or other mechanical valves before and after propensity score matching

	Before matching				After propensity score matching			
	Overall	Control	On-X	SMD	Overall	Control	On-X	SMD
Number of patients	2602	2021	581		1160	580	580	
Age (years), mean (SD)	53.4 (9.5)	54.1 (9.0)	51.0 (10.7)	0.322	51.4 (10.6)	51.9 (10.6)	51.0 (10.6)	0.079
Female sex	631 (24.3)	525 (26.0)	106 (18.2)	0.187	207 (17.8)	101 (17.4)	106 (18.3)	0.023
Non-Nordic birth region	239 (9.2)	207 (10.2)	32 (5.5)	0.176	52 (4.5)	20 (3.4)	32 (5.5)	0.100
Educational level				0.147				0.017
<10 years	720 (27.7)	588 (29.1)	132 (22.7)		266 (22.9)	135 (23.3)	131 (22.6)	
10–12 years	1263 (48.5)	959 (47.5)	304 (52.3)		604 (52.1)	300 (51.7)	304 (52.4)	
>12 years	619 (23.8)	474 (23.5)	145 (25.0)		290 (25.0)	145 (25.0)	145 (25.0)	
Disposable household income (quartiles)				0.119				0.074
Q1 (low)	651 (25.0)	520 (25.7)	131 (22.5)		260 (22.4)	129 (22.2)	131 (22.6)	
Q2	651 (25.0)	506 (25.0)	145 (25.0)		289 (24.9)	144 (24.8)	145 (25.0)	
Q3	650 (25.0)	512 (25.3)	138 (23.8)		262 (22.6)	124 (21.4)	138 (23.8)	
Q4 (high)	650 (25.0)	483 (23.9)	167 (28.7)		349 (30.1)	183 (31.6)	166 (28.6)	
Married	1326 (51.0)	1065 (52.7)	261 (44.9)	0.156	531 (45.8)	270 (46.6)	261 (45.0)	0.031
Body mass index (tertiles)				0.053				0.082
T1 (low)	808 (31.1)	623 (30.8)	185 (31.8)		387 (33.4)	203 (35.0)	184 (31.7)	
T2	987 (37.9)	778 (38.5)	209 (36.0)		418 (36.0)	209 (36.0)	209 (36.0)	
T3 (high)	807 (31.0)	620 (30.7)	187 (32.2)		355 (30.6)	168 (29.0)	187 (32.2)	
Atrial fibrillation	233 (9.0)	183 (9.1)	50 (8.6)	0.016	99 (8.5)	49 (8.4)	50 (8.6)	0.006
Heart failure	382 (14.7)	310 (15.3)	72 (12.4)	0.085	134 (11.6)	62 (10.7)	72 (12.4)	0.054
Left ventricular ejection fraction (%)				0.079				0.015
>50	1953 (75.1)	1518 (75.1)	435 (74.9)		872 (75.2)	437 (75.3)	435 (75.0)	
30–50	511 (19.6)	389 (19.2)	122 (21.0)		239 (20.6)	118 (20.3)	121 (20.9)	
<30	138 (5.3)	114 (5.6)	24 (4.1)		49 (4.2)	25 (4.3)	24 (4.1)	
Chronic obstructive pulmonary disease	155 (6.0)	136 (6.7)	19 (3.3)	0.159	33 (2.8)	14 (2.4)	19 (3.3)	0.052
Diabetes	361 (13.9)	301 (14.9)	60 (10.3)	0.138	114 (9.8)	54 (9.3)	60 (10.3)	0.035
eGFR (ml/min/1,73 m2)				0.153				0.068
>60	2457 (94.4)	1894 (93.7)	563 (96.9)		1124 (96.9)	562 (96.9)	562 (96.9)	
45–59	97 (3.7)	85 (4.2)	12 (2.1)		22 (1.9)	10 (1.7)	12 (2.1)	
30–44	28 (1.1)	24 (1.2)	4 (0.7)		11 (0.9)	7 (1.2)	4 (0.7)	
<30	20 (0.8)	18 (0.9)	2 (0.3)		3 (0.3)	1 (0.2)	2 (0.3)	
Preoperative dialysis	21 (0.8)	19 (0.9)	2 (0.3)	0.075	2 (0.2)	0 (0.0)	2 (0.3)	0.083
Prior myocardial infarction	235 (9.0)	193 (9.5)	42 (7.2)	0.084	91 (7.8)	49 (8.4)	42 (7.2)	0.045
Prior percutaneous coronary intervention	127 (4.9)	102 (5.0)	25 (4.3)	0.035	55 (4.7)	30 (5.2)	25 (4.3)	0.041
Peripheral vascular disease	305 (11.7)	208 (10.3)	97 (16.7)	0.188	184 (15.9)	87 (15.0)	97 (16.7)	0.047
Hypertension	920 (35.4)	703 (34.8)	217 (37.3)	0.053	431 (37.2)	215 (37.1)	216 (37.2)	0.004
Hyperlipidemia	433 (16.6)	344 (17.0)	89 (15.3)	0.046	187 (16.1)	98 (16.9)	89 (15.3)	0.042
Prior stroke	136 (5.2)	105 (5.2)	31 (5.3)	0.006	63 (5.4)	32 (5.5)	31 (5.3)	0.008
History of cancer	128 (4.9)	98 (4.8)	30 (5.2)	0.014	69 (5.9)	39 (6.7)	30 (5.2)	0.066

Continued

Table 1 Continued

	Before matching				After propensity score matching			
	Overall	Control	On-X	SMD	Overall	Control	On-X	SMD
Alcohol dependence	84 (3.2)	69 (3.4)	15 (2.6)	0.049	28 (2.4)	13 (2.2)	15 (2.6)	0.022
Liver disease	21 (0.8)	18 (0.9)	3 (0.5)	0.045	7 (0.6)	4 (0.7)	3 (0.5)	0.022
Prior bleeding event	82 (3.2)	67 (3.3)	15 (2.6)	0.043	27 (2.3)	12 (2.1)	15 (2.6)	0.034
Prior endocarditis	118 (4.5)	92 (4.6)	26 (4.5)	0.004	49 (4.2)	23 (4.0)	26 (4.5)	0.026
Emergent operation	43 (1.7)	32 (1.6)	11 (1.9)	0.024	20 (1.7)	9 (1.6)	11 (1.9)	0.026
Coronary artery bypass grafting	442 (17.0)	363 (18.0)	79 (13.6)	0.120	164 (14.1)	85 (14.7)	79 (13.6)	0.030
Valve size (mm)				0.390				0.030
19	106 (4.1)	74 (3.7)	32 (5.5)		63 (5.4)	31 (5.3)	32 (5.5)	
21	493 (18.9)	376 (18.6)	117 (20.1)		238 (20.5)	121 (20.9)	117 (20.2)	
23	998 (38.4)	739 (36.6)	259 (44.6)		520 (44.8)	262 (45.2)	258 (44.5)	
25	741 (28.5)	584 (28.9)	157 (27.0)		308 (26.6)	151 (26.0)	157 (27.1)	
27	264 (10.1)	248 (12.3)	16 (2.8)		31 (2.7)	15 (2.6)	16 (2.8)	

Numbers are n (%) unless otherwise specified.
eGFR, estimated glomerular filtration rate; SMD, standardized mean difference.

received a St Jude Masters/Regent (n=945) or Carbomedics Reduced valve (n=1076) at the eight hospitals performing cardiac surgery in Sweden during the study period. The proportion of On-X valve implantations increased during the study period but varied markedly by hospital as shown in online supplemental figures 1 and 2 and online supplemental tables 1 and 2. The mean age in the total study population was 53.4 years, and 24% were women. Before propensity score matching, there were differences in baseline characteristics between the groups as shown in table 1. There were more women and the mean age was higher in the control group. Peripheral vascular disease was more common in the On-X valve group, whereas pulmonary disease, diabetes and concomitant coronary artery bypass grafting were more common in the control group. The 30-day all-cause mortality was 0.69% in the On-X valve group vs 0.64% in the control group (p=0.905). After propensity score matching, the two groups were well balanced across all baseline characteristics and no standardised mean differences were greater than 10% (table 1 and online supplemental figures 3 and 4).

Permanent pacemaker implantation following mechanical aortic valve replacement

In the total study population, 115 (4.4%) permanent pacemaker implantations were performed within 30 days after aortic valve replacement. In the On-X group, the number of pacemakers implanted was 21 (3.6%) vs 94 (4.6%) in the control group (p=0.284). Implantable cardioverter-defibrillators accounted for 5% of the implantations in both groups. The pacemaker implantation rate increased slightly during the study period but was fairly similar between hospitals (online supplemental figures 5 and 6 and online supplemental tables 3 and 4).

The Kaplan-Meier estimated rate of permanent pacemaker implantation in the propensity score matched population is shown in figure 1. There was no significant difference in the rate of permanent pacemaker implantation within 30 days after aortic valve replacement with the On-X valve compared with the control group: 3.6% (95% CI: 2.4% to 5.5%) vs 4.0% (95% CI: 2.7% to 5.9%), p=0.877. The OR (95% CI) for a permanent pacemaker implantation within 30 days after On-X aortic valve replacement was 0.91 (0.49–1.67). The majority of

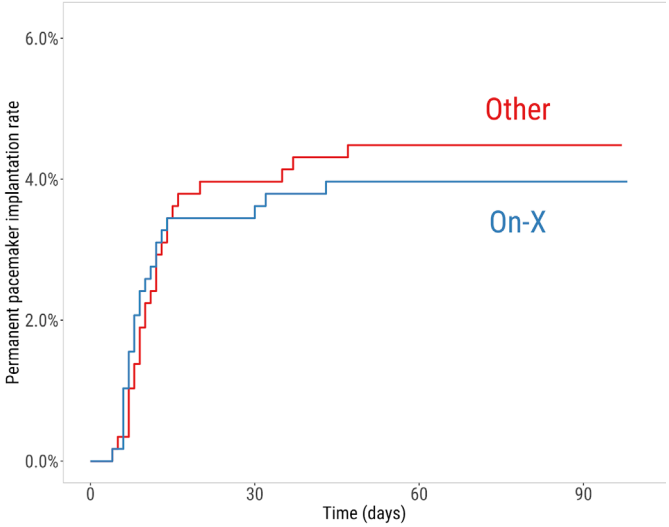

Figure 1 The graph shows the Kaplan-Meier estimated permanent pacemaker implantation rate in propensity score matched patients who received an On-X valve compared with other valves. There was no significant difference in the pacemaker implant rate between the groups. The majority of permanent pacemaker implantations occurred during the first 30 days. No pacemakers were implanted from day 60 to day 120.

permanent pacemaker implantations occurred during the first 30 days. No pacemakers were implanted from postoperative day 60 to postoperative day 120.

Alternative approaches for confounding adjustment

Two alternative approaches for confounding adjustment using propensity scores for construction of weights were conducted: inverse probability of treatment weighting and overlap weighting. Both approaches resulted in excellent balance in baseline characteristics between the groups (online supplemental tables 5 and 6 and online supplemental figures 7 and 8). The results were very similar to the results obtained in the propensity score matched analysis, and we found no significant difference in the rate of permanent pacemaker implantation within 30 days after aortic valve replacement with an On-X valve compared with the control group.

In the inverse probability of treatment weighted population, the rate of permanent pacemaker implantation within 30 days after aortic valve replacement was 3.8% (95% CI: 2.0% to 5.6%) with an On-X valve vs 4.7% (95% CI: 3.7% to 5.6%) in the control group, p=0.428. The odds ratio (95% CI) for a permanent pacemaker implantation within 30 days after On-X aortic valve replacement was 0.81 (0.48–1.37).

In the population where overlap weights were used, the rate of permanent pacemaker implantation within 30 days after aortic valve replacement was 3.7% (95% CI: 2.1% to 5.3%) with an On-X valve vs 4.7% (95% CI: 3.6% to 5.8%) in the control group, p=0.357. The odds ratio (95% CI) for a permanent pacemaker implantation within 30 days after On-X aortic valve replacement was 0.79 (0.47–1.31).

The Kaplan-Meier estimated rates of permanent pacemaker implantation in the inverse probability of treatment weighted population, and the population where overlap weights were used, respectively, are shown in online supplemental figures 9 and 10.

The results from all approaches are summarised in online supplemental figure 11. As height and weight were not included in the propensity score model, these data are presented in online supplemental table 7.

DISCUSSION

The On-X prosthetic heart valve has an elongated subannular valve housing with a flared inlet that protrudes subannulary into the left ventricular outflow tract. This design distinguishes the On-X prosthetic valve from other contemporary bileaflet mechanical aortic valves that are implanted intra-/supraannulary and that do not extend subannulary (figure 2). In this nationwide cohort study, aortic valve replacement with implantation of the On-X prosthetic heart valve was not associated with an increased risk for permanent pacemaker implantation compared with other intra-/supraannulary bileaflet mechanical valves.

Cardiac conduction abnormalities requiring permanent pacemaker implantation is a well-known complication of aortic valve replacement.[1] The widespread use of transcatheter and rapid deployment prosthetic valves, which are associated with a significant risk of injury to the conduction system, has generated an increased interest in research concerning permanent pacemaker implantation after aortic valve replacement.[5–7] Although the use of mechanical prosthetic valves has decreased during later years, these valves are still the primary choice for younger patients, for whom mechanical valves have been shown to be superior to biological valves, in terms of mortality and reoperation rates.[17 26] Permanent pacemaker requirement has in some studies been associated with adverse events and impaired long-term survival.[2]

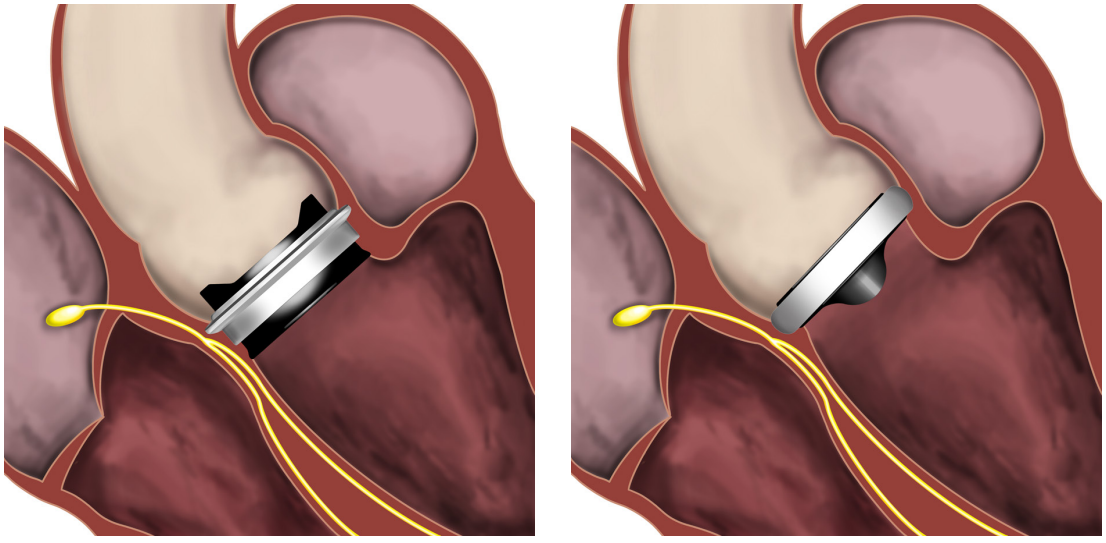

Figure 2 The On-X prosthetic heart valve (On-X Life Technologies, Austin, Texas, USA; left panel) has an elongated subannular valve housing with a flared inlet that protrudes subannulary into the left ventricular outflow tract, in close proximity to the cardiac conduction system. This design distinguishes the On-X prosthetic valve from other contemporary bileaflet mechanical aortic valves, such as the St Jude Regent (St Jude Medical, St Paul, Minnesota, USA; right panel), that are implanted intra-/supraannulary and do not extend subannulary. Illustration: Magnus Dalén.

The potential risks associated with permanent pacemaker requirement are particularly relevant for younger patients since they have a longer life expectancy.[27]

The incidence of permanent pacemaker implantation in the current study (4.4%) is in line with previous studies of mechanical aortic valve replacement in younger adults, reporting rates of 2.5%–5%.[28 29] Few head-to-head comparisons of mechanical bileaflet prosthetic valves have been reported[30] and none of these have analysed permanent pacemaker implantation rates between different valves. Generally, there are very few reports regarding rates of permanent pacemaker implantation after mechanical aortic valve replacement and most prior studies concerning mechanical prosthetic valves are completely lacking information on permanent pacemaker rates.

Compression on the subannunlar tissue, and thereby subsequent possible compression of the cardiac conduction system can induce conduction disturbances necessitating permanent pacemaker implantation. Because bioprosthetic valves with an extended subannular component, such as transcatheter and rapid deployment prosthetic valves, have been associated with a markedly increased risk for permanent pacemaker implantation,[5–7] we aimed to analyse whether this would also be true for the On-X prosthetic valve. Despite its' elongated subannular valve housing, our results demonstrated that the On-X prosthetic heart valve did not confer a higher risk of permanent pacemaker implantation compared with other conventional intra-/supraannulary bileaflet mechanical valves. This might be explained by the differences in design and annular fixation between the On-X prosthetic valve and transcatheter/rapid deployment prosthetic valves. These valves, unlike the On-X, are balloon- or self-expandable bioprosthetic valves that rely on radial forces for deployment of a subannular frame for stabilisation in the aortic annulus and left ventricular outflow tract. These valves are therefore oversized in relation to the aortic annulus. This is in contrast with the On-X valve, which is sutured to the aortic annulus with no expansion of the subannular valve component. Correct implantation requires that the On-X subannular valve housing fit into the left ventricular outflow tract and oversizing is thereby not possible.

Limitations

This analysis has limitations. First, the data did not include preoperative conduction disorders known to increase the risk for postoperative pacemaker requirement, such as bundle branch block, as well as other risk factors for postoperative pacemaker requirement such as mitral annular calcification, left ventricular outflow tract calcification and surgical suture technique that was used for valve implantation. We were therefore not able to adjust for such risk factors. We were unable to account for possible centre effects, owing to a low number of events (pacemaker implantations) in the On-X group. Second, we did not have information about specific indications of postoperative pacemaker implantation. Third, we included implantable cardiac defibrillators in the primary outcome measure, in order to capture patients who had dual indications for both pacing and defibrillation. It is possible that some of these patients only had indication for defibrillation.

CONCLUSIONS

The On-X prosthetic heart valve was associated with a similarly low risk for permanent pacemaker implantation after aortic valve replacement compared with other conventional bileaflet mechanical valves. This indicates that the On-X elongated subannular valve housing does not seem to inflict on the cardiac conduction system.

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Contributors All authors (MD, MP, NG, US) have made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and drafting the work and revising it critically for important intellectual content; and made final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. MD is the guarantor.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the Swedish Ethical Review Authority and the need for informed consent was waived (Registration number: 2019-04131).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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SUPPLEMENTAL MATERIAL

Permanent pacemaker implantation after On-X aortic valve replacement:

SWEDEHEART observational cohort study

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Contents

Supplemental Table 1. Number of patients by year of surgery.

Year of surgery	Total study population *n = 2602*	On-X valve	
		No *n = 2021*	Yes *n = 581*
2005	251 (100%)	244 (97%)	7 (2.8%)
2006	237 (100%)	230 (97%)	7 (3.0%)
2007	215 (100%)	187 (87%)	28 (13%)
2008	214 (100%)	176 (82%)	38 (18%)
2009	152 (100%)	110 (72%)	42 (28%)
2010	166 (100%)	120 (72%)	46 (28%)
2011	133 (100%)	100 (75%)	33 (25%)
2012	145 (100%)	110 (76%)	35 (24%)
2013	157 (100%)	120 (76%)	37 (24%)
2014	158 (100%)	112 (71%)	46 (29%)
2015	141 (100%)	100 (71%)	41 (29%)
2016	221 (100%)	148 (67%)	73 (33%)
2017	193 (100%)	121 (63%)	72 (37%)
2018	219 (100%)	143 (65%)	76 (35%)

Numbers are n (%).

Supplemental Table 2. Number of patients according to hospital.

Hospital	Total study population *n = 2602*	On-X valve	
		No *n = 2021*	Yes *n = 581*
1	467 (100%)	413 (88%)	54 (12%)
2	340 (100%)	227 (67%)	113 (33%)
3	329 (100%)	304 (92%)	25 (7.6%)
4	120 (100%)	120 (100%)	0 (0%)
5	398 (100%)	398 (100%)	0 (0%)
6	331 (100%)	243 (73%)	88 (27%)
7	221 (100%)	215 (97%)	6 (2.7%)
8	396 (100%)	101 (26%)	295 (74%)

Numbers are n (%).

Supplemental Table 3. Number of pacemaker implants by year of surgery.

Year of surgery	Total study population *n = 2602*	Pacemaker within 30 days	
		No *n = 2487*	Yes *n = 115*
2005	251 (100%)	243 (97%)	8 (3.2%)
2006	237 (100%)	226 (95%)	11 (4.6%)
2007	215 (100%)	209 (97%)	6 (2.8%)
2008	214 (100%)	207 (97%)	7 (3.3%)
2009	152 (100%)	144 (95%)	8 (5.3%)
2010	166 (100%)	157 (95%)	9 (5.4%)
2011	133 (100%)	130 (98%)	3 (2.3%)
2012	145 (100%)	139 (96%)	6 (4.1%)
2013	157 (100%)	151 (96%)	6 (3.8%)
2014	158 (100%)	153 (97%)	5 (3.2%)
2015	141 (100%)	135 (96%)	6 (4.3%)
2016	221 (100%)	207 (94%)	14 (6.3%)
2017	193 (100%)	182 (94%)	11 (5.7%)
2018	219 (100%)	204 (93%)	15 (6.8%)

Numbers are n (%).

Supplemental Table 4. Number of pacemaker implants according to hospital.

Hospital	Total study population *n = 2602*	Pacemaker within 30 days	
		No *n = 2487*	Yes *n = 115*
1	467 (100%)	442 (95%)	25 (5.4%)
2	340 (100%)	316 (93%)	24 (7.1%)
3	329 (100%)	311 (95%)	18 (5.5%)
4	120 (100%)	115 (96%)	5 (4.2%)
5	398 (100%)	389 (98%)	9 (2.3%)
6	331 (100%)	319 (96%)	12 (3.6%)
7	221 (100%)	213 (96%)	8 (3.6%)
8	396 (100%)	382 (96%)	14 (3.5%)

Numbers are n (%).

Supplemental Table 5. Baseline characteristics after IPTW.
Baseline characteristics in patients who underwent mechanical aortic valve replacement with an On-X valve or other mechanical valves in Sweden from 2005 to 2018 before and after inverse probability of treatment weighting.

	Unweighted			**IPTW***		
	Control	On-X	SMD	Control	On-X	SMD
Number of patients	2021	581		2573.7	2204.4	
Age (years), mean (SD)	54.1 (9.0)	51.0 (10.7)	0.322	53.5 (9.4)	52.8 (9.6)	0.067
Female sex	525 (26.0)	106 (18.2)	0.187	631.4 (24.5)	517.8 (23.5)	0.024
Non-Nordic birth region	207 (10.2)	32 (5.5)	0.176	238.7 (9.3)	148.1 (6.7)	0.094
Educational level			0.151			0.039
<10 years	588 (29.3)	132 (22.8)		716.6 (28.0)	579.0 (26.4)	
10-12 years	945 (47.1)	303 (52.2)		1230.2 (48.1)	1091.8 (49.8)	
>12 years	474 (23.6)	145 (25.0)		611.6 (23.9)	520.9 (23.8)	
Disposable household income (quartiles)			0.119			0.024
Q1 (low)	520 (25.7)	131 (22.5)		642.7 (25.0)	557.5 (25.3)	
Q2	506 (25.0)	145 (25.0)		648.0 (25.2)	547.9 (24.9)	
Q3	512 (25.3)	138 (23.8)		645.7 (25.1)	535.6 (24.3)	
Q4 (high)	483 (23.9)	167 (28.7)		637.3 (24.8)	563.5 (25.6)	
Married	1065 (52.7)	261 (44.9)	0.156	1318.3 (51.2)	1058.1 (48.0)	0.065
Body mass index (tertiles)			0.012			0.042
T1 (low)	623 (33.5)	185 (33.0)		804.0 (33.6)	743.2 (35.5)	

T2	618 (33.2)	189 (33.7)		798.0 (33.3)	685.6 (32.8)	
T3 (high)	620 (33.3)	187 (33.3)		791.3 (33.1)	663.3 (31.7)	
Atrial fibrillation	183 (9.1)	50 (8.6)	0.016	227.8 (8.9)	210.8 (9.6)	0.025
Heart failure	310 (15.3)	72 (12.4)	0.085	379.4 (14.7)	309.3 (14.0)	0.020
Left ventricular ejection fraction (%)			0.079			0.035
>50	1518 (75.1)	435 (74.9)		1935.0 (75.2)	1679.7 (76.2)	
30-50	389 (19.2)	122 (21.0)		499.8 (19.4)	422.0 (19.1)	
<30	114 (5.6)	24 (4.1)		138.8 (5.4)	102.7 (4.7)	
Chronic obstructive pulmonary disease	136 (6.7)	19 (3.3)	0.159	155.5 (6.0)	96.5 (4.4)	0.075
Diabetes	301 (14.9)	60 (10.3)	0.138	360.6 (14.0)	254.6 (11.5)	0.074
eGFR (ml/min/1,73 m^2)			0.154			0.050
>60	1865 (93.6)	554 (96.9)		2392.7 (94.3)	2066.5 (95.0)	
45-59	85 (4.3)	12 (2.1)		97.5 (3.8)	78.0 (3.6)	
30-44	24 (1.2)	4 (0.7)		27.1 (1.1)	22.7 (1.0)	
<30	18 (0.9)	2 (0.3)		20.3 (0.8)	9.2 (0.4)	
Preoperative dialysis	19 (1.0)	2 (0.4)	0.077	21.5 (0.9)	9.5 (0.5)	0.052
Prior myocardial infarction	193 (9.5)	42 (7.2)	0.084	235.7 (9.2)	173.2 (7.9)	0.047
Prior percutaneous coronary intervention	102 (5.0)	25 (4.3)	0.035	123.8 (4.8)	116.7 (5.3)	0.022
Peripheral vascular disease	208 (10.3)	97 (16.7)	0.188	297.4 (11.6)	294.6 (13.4)	0.055
Hypertension	703 (34.8)	217 (37.3)	0.053	905.7 (35.2)	789.8 (35.8)	0.013
Hyperlipidemia	344 (17.0)	89 (15.3)	0.046	431.7 (16.8)	317.2 (14.4)	0.066
Prior stroke	105 (5.2)	31 (5.3)	0.006	139.3 (5.4)	119.6 (5.4)	0.001

History of cancer	98 (4.8)	30 (5.2)	0.014	126.0 (4.9)	116.2 (5.3)	0.017
Alcohol dependence	69 (3.4)	15 (2.6)	0.049	84.6 (3.3)	50.8 (2.3)	0.059
Liver disease	18 (0.9)	3 (0.5)	0.045	20.9 (0.8)	9.5 (0.4)	0.049
Prior bleeding event	67 (3.3)	15 (2.6)	0.043	81.4 (3.2)	72.6 (3.3)	0.008
Prior endocarditis	92 (4.6)	26 (4.5)	0.004	118.3 (4.6)	116.2 (5.3)	0.031
Emergent operation	32 (1.6)	11 (1.9)	0.024	41.5 (1.6)	36.9 (1.7)	0.005
Coronary artery bypass grafting	363 (18.0)	79 (13.6)	0.120	438.9 (17.1)	296.2 (13.4)	0.101
Valve size (mm)			0.254			0.075
19-21	450 (22.7)	149 (25.8)		589.5 (23.2)	548.5 (25.3)	
23	704 (35.4)	256 (44.3)		944.9 (37.3)	841.0 (38.8)	
25-27	832 (41.9)	173 (29.9)		1001.4 (39.5)	780.5 (36.0)	

Numbers are n (%) unless otherwise specified.
eGFR = estimated glomerular filtration rate, SD = standard deviation, SMD = standardized mean difference
* The overall numbers of patients in each group are not necessarily integers owing to inverse probability of treatment weighting.

Supplemental Table 6. Baseline characteristics after overlap weighting.
Baseline characteristics in patients who underwent mechanical aortic valve replacement with an On-X valve or other mechanical valves in Sweden from 2005 to 2018 before and after overlap weighting.

	Unweighted			Overlap weighting		
	Control	On-X	SMD	Control	On-X	SMD
Number of patients	2021	581		407	407	
Age (years), mean (SD)	54.15 (9.01)	50.97 (10.70)	0.322	51.8 (10.3)	51.8 (10.2)	<0.001
Female sex	525 (26.0)	106 (18.2)	0.187	83 (20.4)	83 (20.4)	<0.001
Non-Nordic birth region	207 (10.2)	32 (5.5)	0.176	25 (6.2)	25 (6.2)	<0.001
Educational level			0.147			<0.001
<10 years	588 (29.1)	132 (22.7)		97 (23.8)	97 (23.8)	
10-12 years	959 (47.5)	304 (52.3)		210 (51.6)	210 (51.6)	
>12 years	474 (23.5)	145 (25.0)		100 (24.6)	100 (24.6)	
Disposable household income (quartiles)			0.119			<0.001
Q1 (low)	520 (25.7)	131 (22.5)		95 (23.4)	95 (23.4)	
Q2	506 (25.0)	145 (25.0)		102 (25.1)	102 (25.1)	
Q3	512 (25.3)	138 (23.8)		98 (24.0)	98 (24.0)	
Q4 (high)	483 (23.9)	167 (28.7)		112 (27.5)	112 (27.5)	
Married	1065 (52.7)	261 (44.9)	0.156	190 (46.7)	190 (46.7)	<0.001
Body mass index (tertiles)			0.053			<0.001
T1 (low)	623 (30.8)	185 (31.8)		131 (32.1)	131 (32.1)	

T2	778 (38.5)	209 (36.0)		149 (36.7)	149 (36.7)	
T3 (high)	620 (30.7)	187 (32.2)		127 (31.2)	127 (31.2)	
Atrial fibrillation	183 (9.1)	50 (8.6)	0.016	35 (8.5)	35 (8.5)	<0.001
Heart failure	310 (15.3)	72 (12.4)	0.085	52 (12.9)	52.4 (12.9)	<0.001
Left ventricular ejection fraction (%)			0.079			<0.001
>50	1518 (75.1)	435 (74.9)		307 (75.4)	307 (75.4)	
30-50	389 (19.2)	122 (21.0)		83 (20.3)	83 (20.3)	
<30	114 (5.6)	24 (4.1)		17 (4.3)	17 (4.3)	
Chronic obstructive pulmonary disease	136 (6.7)	19 (3.3)	0.159	16 (3.8)	16 (3.8)	<0.001
Diabetes	301 (14.9)	60 (10.3)	0.138	45 (11.0)	45 (11.0)	<0.001
eGFR (ml/min/1,73 m^2)			0.153			<0.001
>60	1894 (93.7)	563 (96.9)		392 (96.4)	392 (96.4)	
45-59	85 (4.2)	12 (2.1)		10 (2.4)	10 (2.4)	
30-44	24 (1.2)	4 (0.7)		3 (0.8)	3 (0.8)	
<30	18 (0.9)	2 (0.3)		2 (0.4)	2 (0.4)	
Preoperative dialysis	19 (0.9)	2 (0.3)	0.075	2 (0.4)	2 (0.4)	<0.001
Prior myocardial infarction	193 (9.5)	42 (7.2)	0.084	32 (7.9)	32 (7.9)	<0.001
Prior percutaneous coronary intervention	102 (5.0)	25 (4.3)	0.035	19 (4.6)	19 (4.6)	<0.001
Peripheral vascular disease	208 (10.3)	97 (16.7)	0.188	60 (14.7)	60 (14.7)	<0.001
Hypertension	703 (34.8)	217 (37.3)	0.053	149 (36.6)	149 (36.6)	<0.001
Hyperlipidemia	344 (17.0)	89 (15.3)	0.046	63 (15.6)	63 (15.6)	<0.001
Prior stroke	105 (5.2)	31 (5.3)	0.006	22 (5.4)	22 (5.4)	<0.001

History of cancer	98 (4.8)	30 (5.2)	0.014	22 (5.3)	22 (5.3)	<0.001
Alcohol dependence	69 (3.4)	15 (2.6)	0.049	11 (2.7)	11 (2.7)	<0.001
Liver disease	18 (0.9)	3 (0.5)	0.045	2 (0.6)	2 (0.6)	<0.001
Prior bleeding event	67 (3.3)	15 (2.6)	0.043	11 (2.7)	11 (2.7)	<0.001
Prior endocarditis	92 (4.6)	26 (4.5)	0.004	18 (4.4)	18 (4.4)	<0.001
Emergent operation	32 (1.6)	11 (1.9)	0.024	7 (1.7)	7 (1.7)	<0.001
Coronary artery bypass grafting	363 (18.0)	79 (13.6)	0.120	59 (14.5)	59 (14.5)	<0.001
Valve size (mm)			0.390			<0.001
19	74 (3.7)	32 (5.5)		21 (5.2)	21 (5.2)	
21	376 (18.6)	117 (20.1)		83 (20.4)	83 (20.4)	
23	739 (36.6)	259 (44.6)		176 (43.2)	176 (43.2)	
25	584 (28.9)	157 (27.0)		113 (27.7)	113 (27.7)	
27	248 (12.3)	16 (2.8)		14 (3.5)	14 (3.5)	

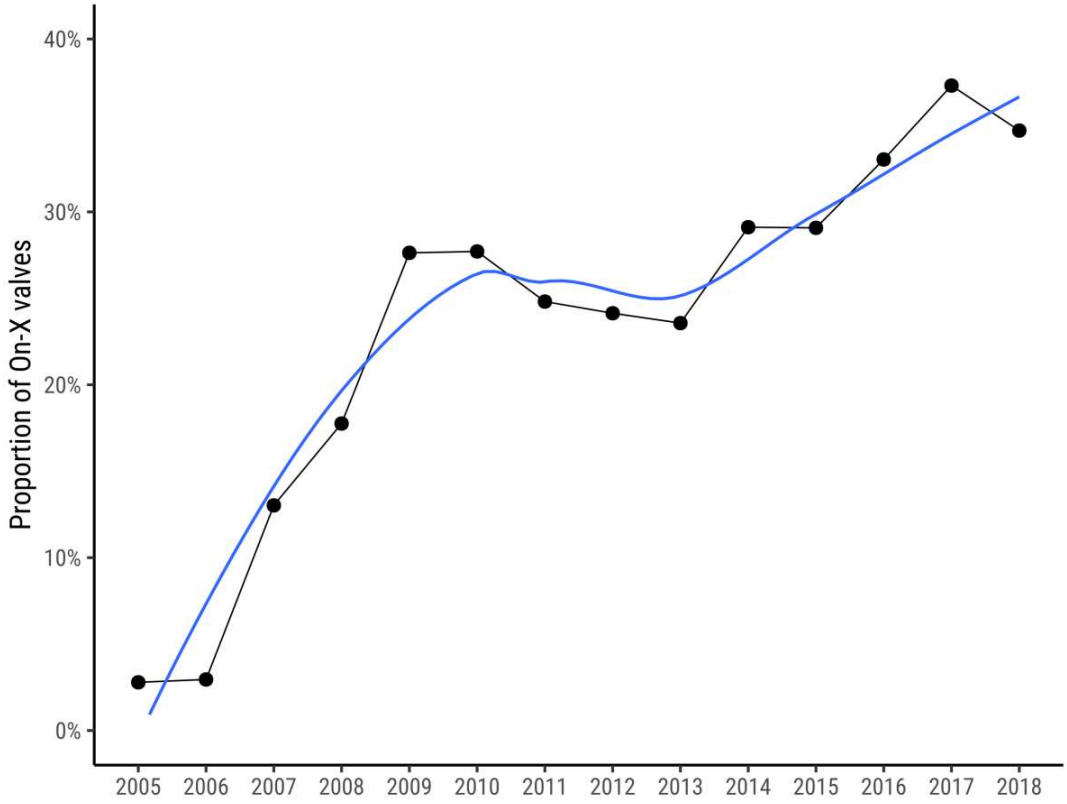
Numbers are n (%) unless otherwise specified.
eGFR = estimated glomerular filtration rate, SD = standard deviation, SMD = standardized mean difference

Supplemental Table 7. Height, weight and body surface area.

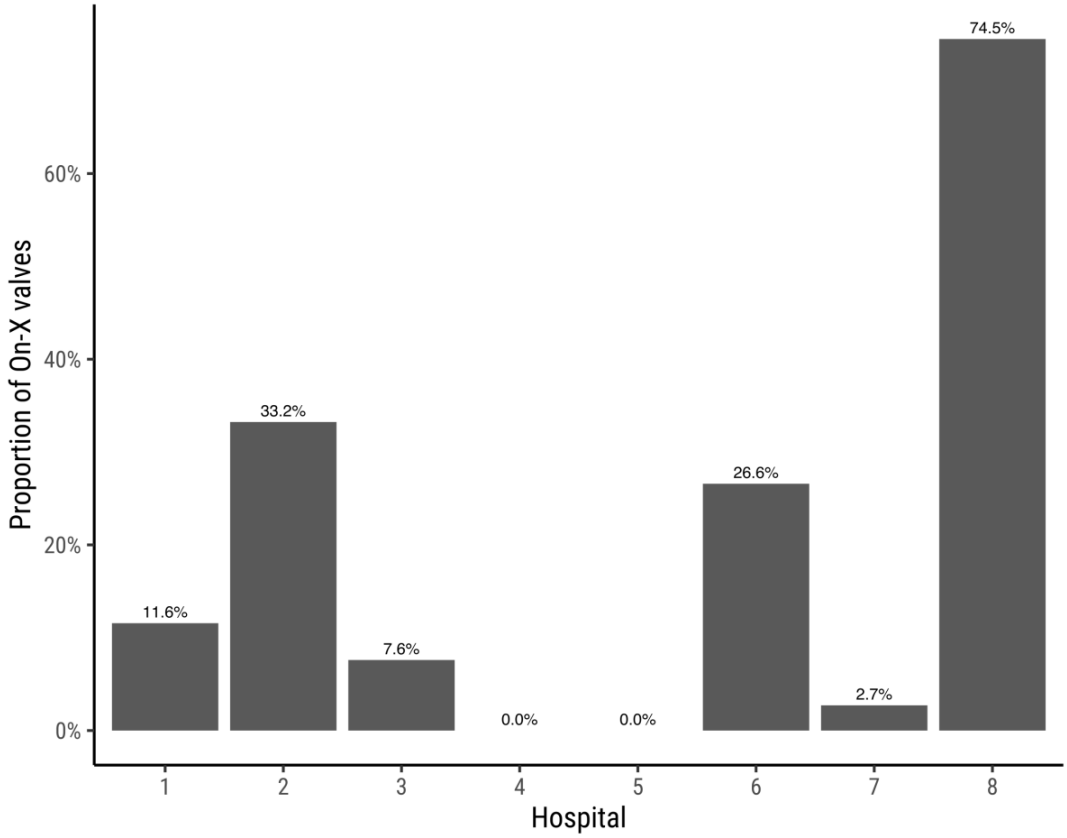
	Before matching			
	Overall	Control	On-X	SMD
Number of patients	2602	2021	581	
Height, cm	175 (9.4)	175 (9.5)	177 (8.8)	0.216
Weight, kg	86.0 (17.3)	85.5 (17.1)	87.5 (17.8)	0.116
BSA, m^2	2.04 (0.23)	2.03 (0.23)	2.07 (0.23)	0.154

Numbers are mean and standard deviation.
BSA = body surface area, SMD = standardized mean difference

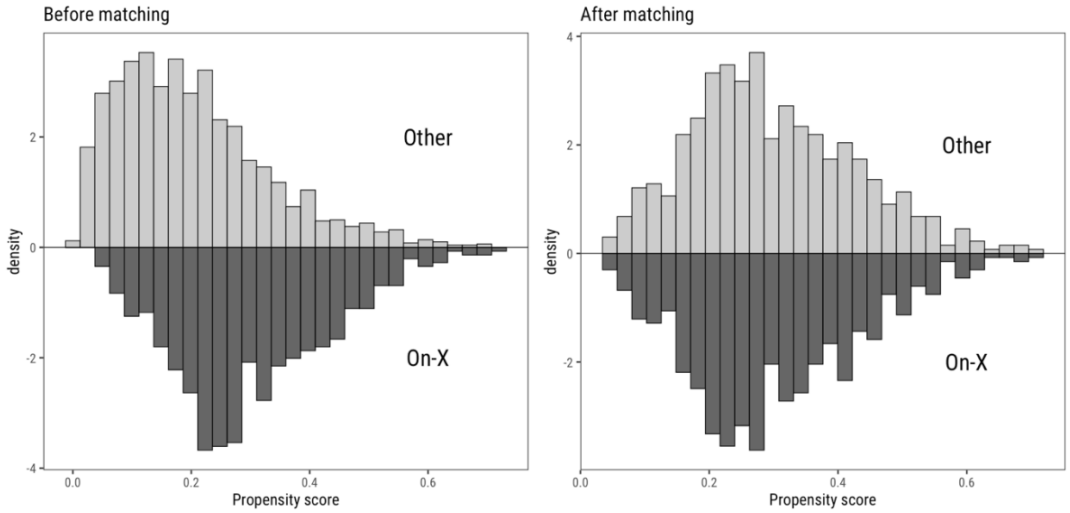
Supplemental Figure 1. Proportion of On-X valves by year of surgery.



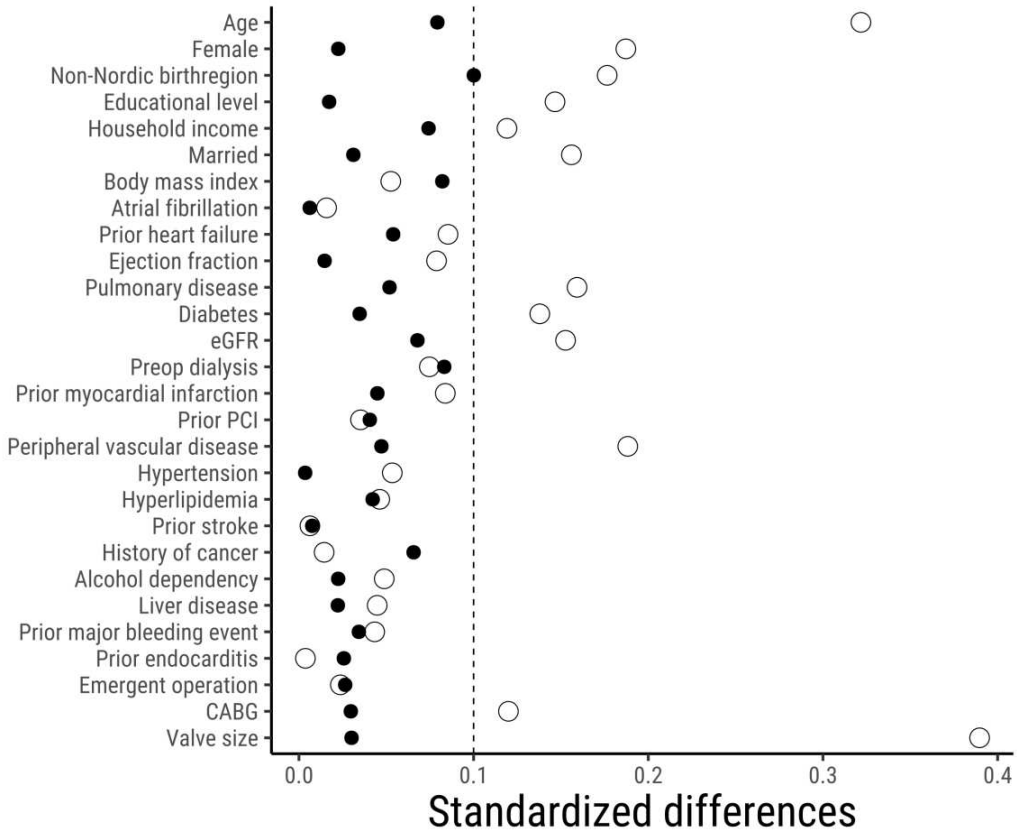
Supplemental Figure 2. Proportion of On-X valves according to hospital.



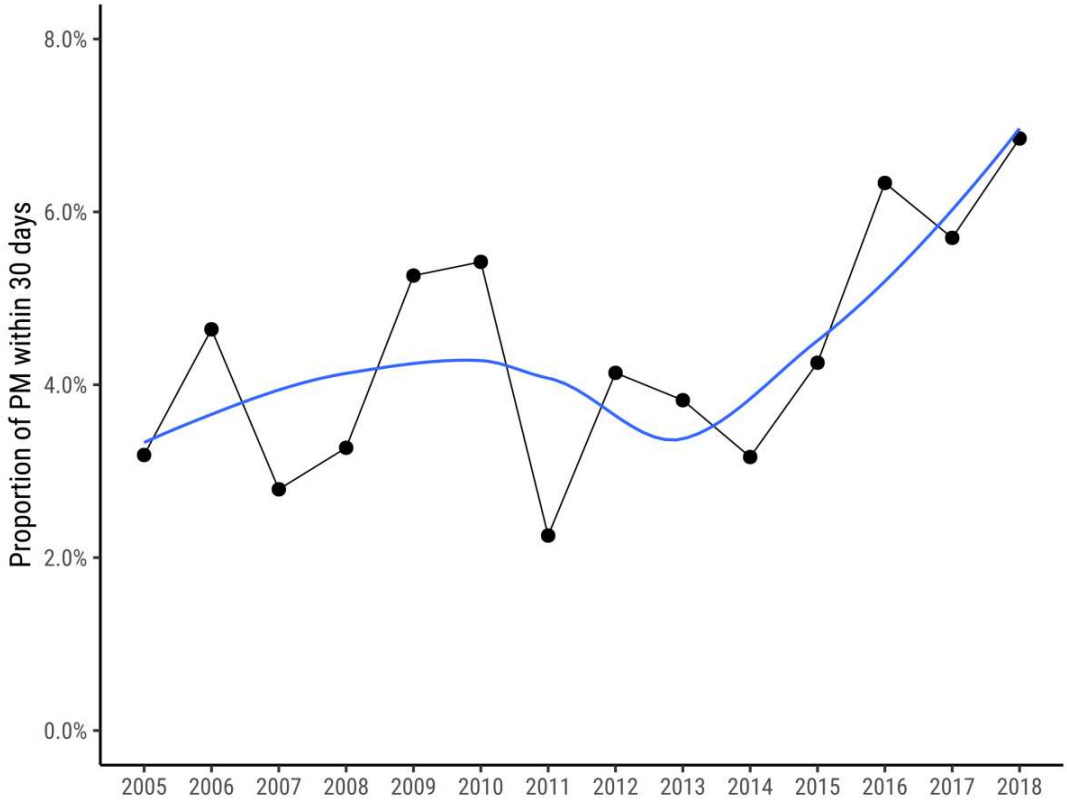
Supplemental Figure 3. Histogram of propensity scores before and after matching.



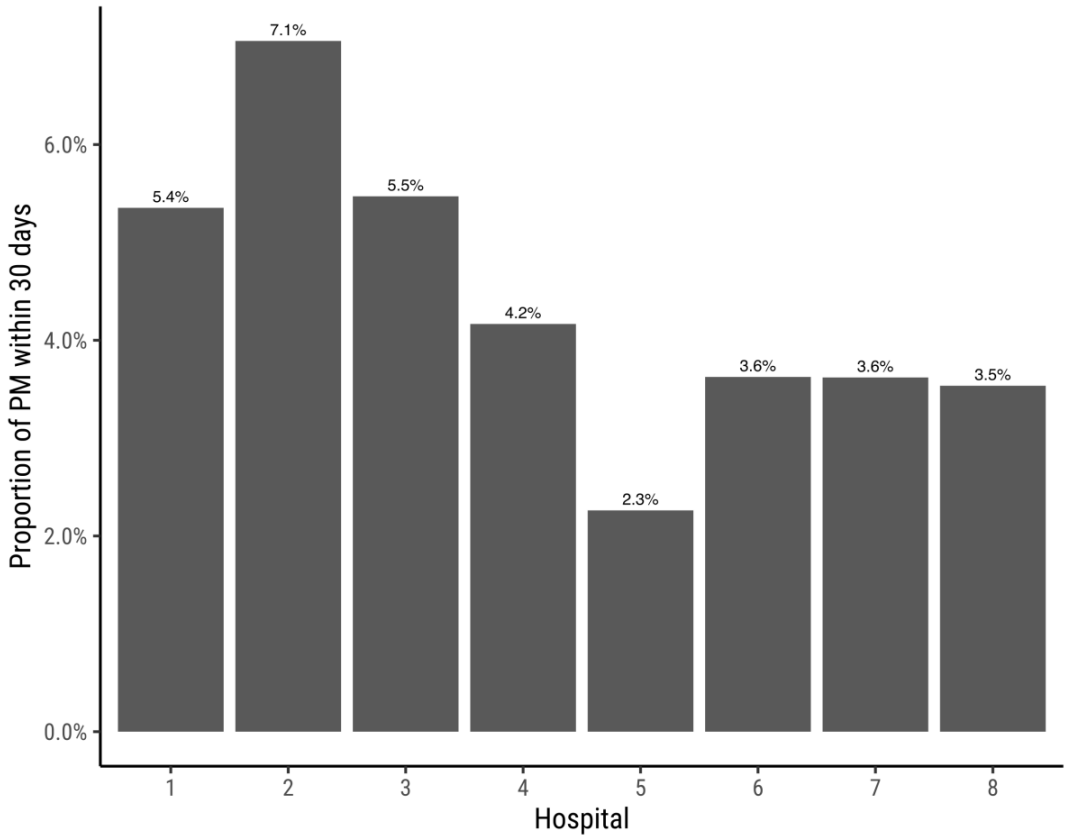
Supplemental Figure 4. Absolute standardized differences before (hollow circles) and after (filled circles) propensity score matching.



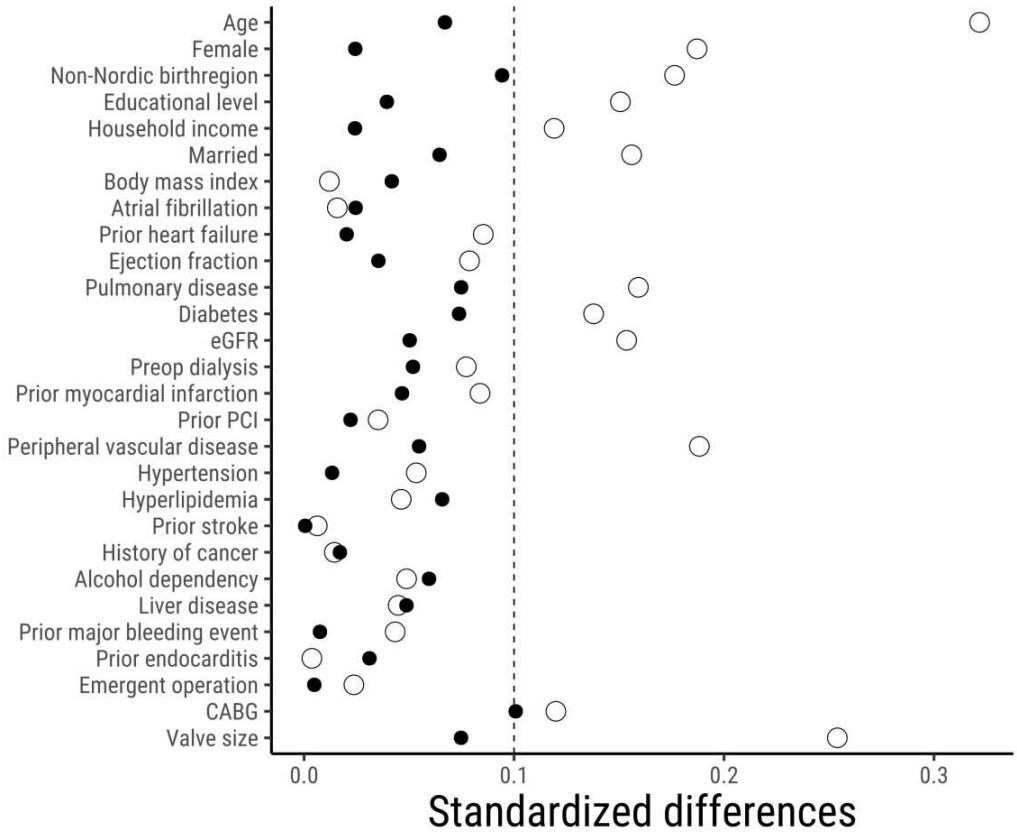
Supplemental Figure 5. Proportion of permanent pacemaker implants by year of surgery.



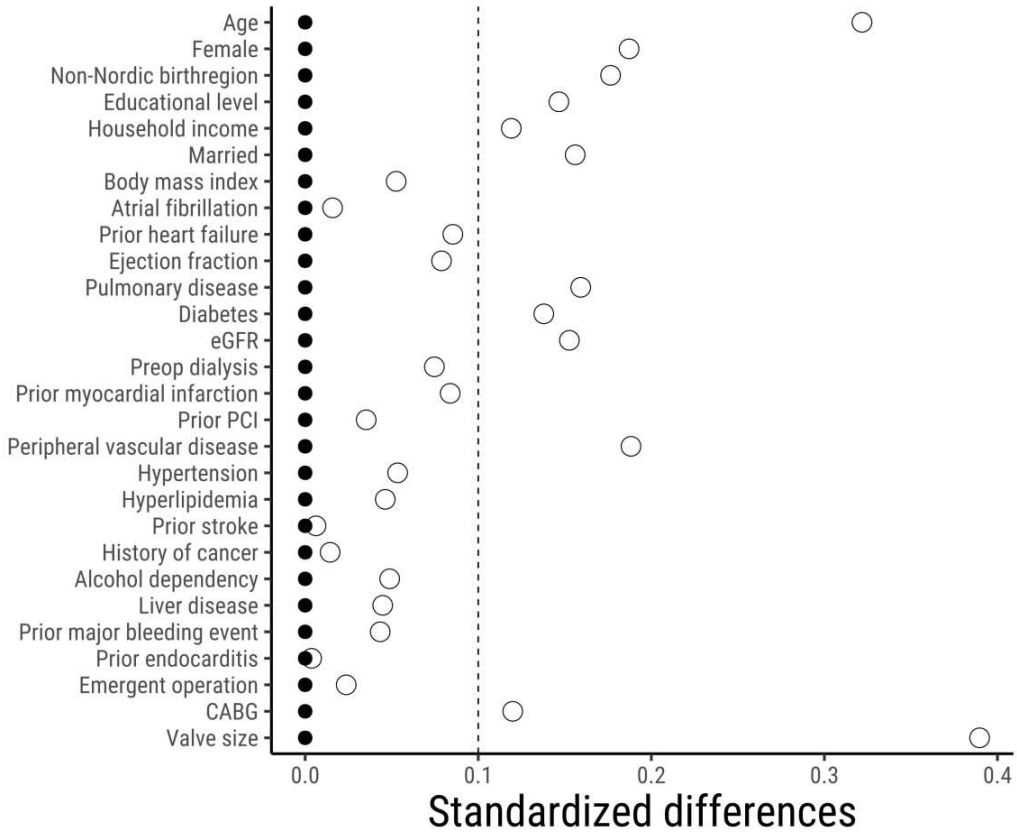
Supplemental Figure 6. Proportion of permanent pacemaker implants according to hospital.



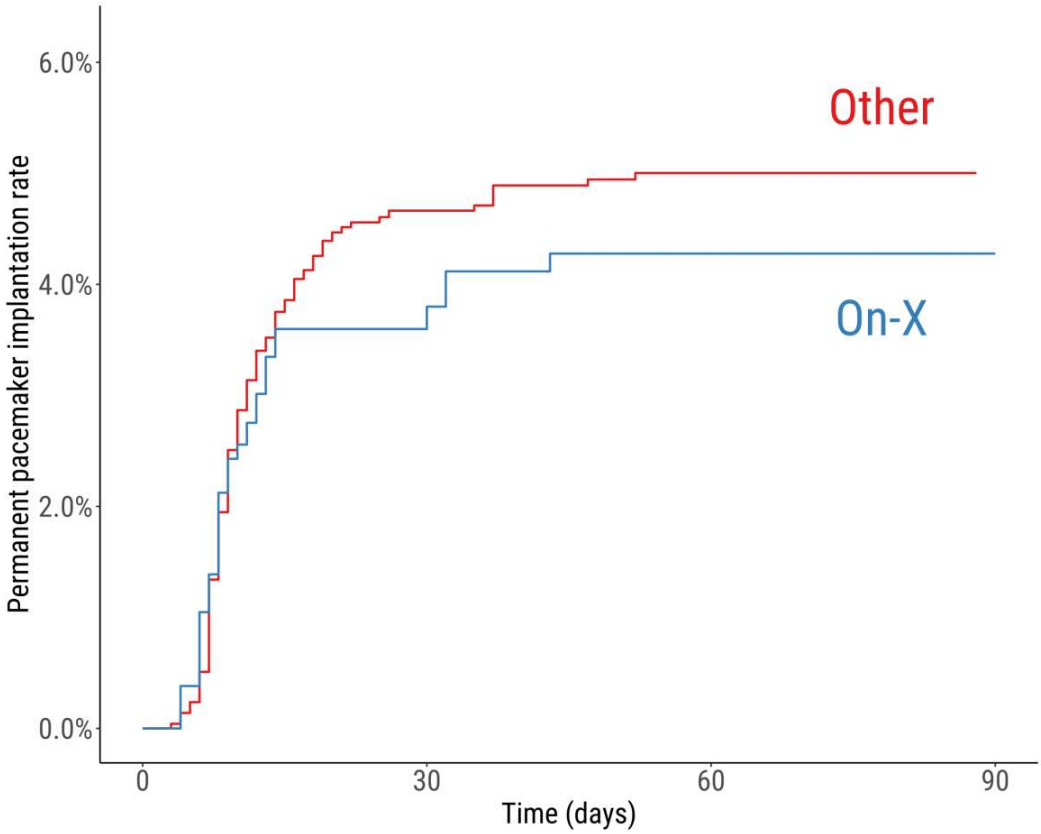
Supplemental Figure 7. Absolute standardized differences before (hollow circles) and after (filled circles) inverse probability of treatment weighting.



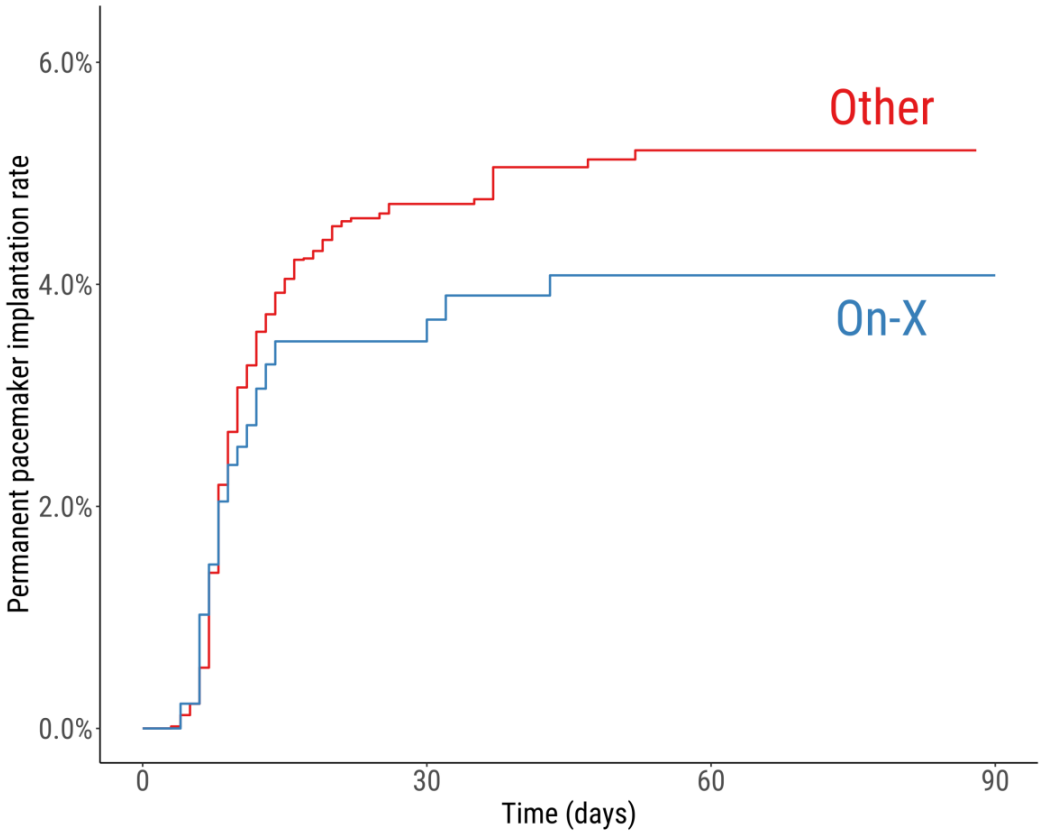
Supplemental Figure 8. Absolute standardized differences before (hollow circles) and after (filled circles) overlap weighting.
Note: This method yields exact covariate balance between treated and reference groups by construction.



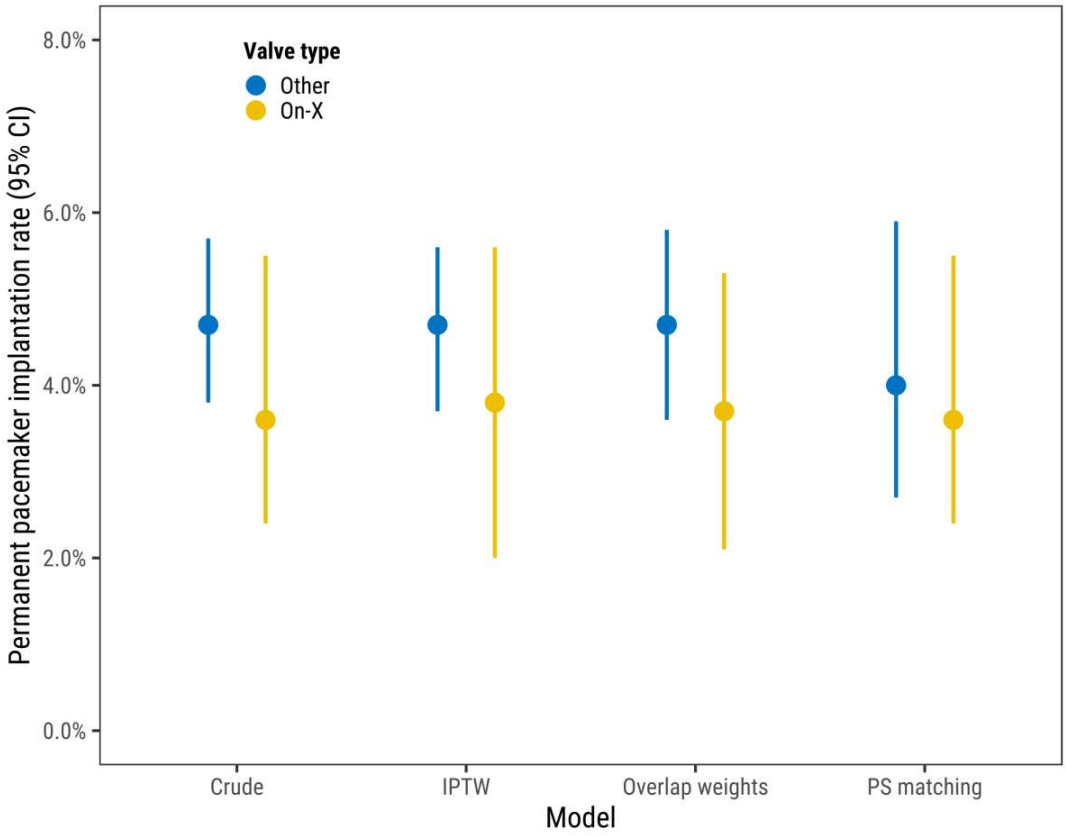
Supplemental Figure 9. Kaplan-Meier estimated pacemaker implantation rate in the inverse probability of treatment weighted population.



Supplemental Figure 10. Kaplan-Meier estimated pacemaker implantation rate in the overlap weighted population.



Supplemental Figure 11. Crude and adjusted pacemaker implantation rate after On-X valve aortic valve replacement according to alternative approaches for confounding adjustment.



Note: IPTW = inverse probability of treatment weighting, PS = propensity score