Supplemental Material

Table S1. Definition of each outcome.

Author	Year	Major bleeding	Stroke	Reintervention
Doss	2005	Bleeding requiring hospitalization	Stroke	Any operation involving the aortic and/or pulmonary valves
El-Hamamsy	2010	N/A	Stroke	Any operation involving the aortic and/or pulmonary valves
Mokhles	2011	Bleeding requiring transfusion, surgical or endoscopic intervention, or inpatient care or causing long-term impairment	N/A	N/A
Mazine	2016	Bleeding leading to death or stroke or requiring hospitalization and/or transfusion	Stroke and transient ischemic attack	Any surgical or percutaneous reintervention on any operated valve
Sharabiani	2016	N/A	N/A	N/A
Bouhout	2017	N/A	N/A	N/A
Buratto	2018	N/A	N/A	N/A
Gofus	2022	N/A	N/A	Any operation involving the aortic and/or pulmonary valves
El-Hamamsy	2022	Bleeding which required inpatient	Hemorrhagic or ischemic stroke.	Any operation involving the aortic and/or pulmonary valves
Mazine	2022	N/A	Stroke, transient ischemic attack, and noncerebral systemic embolism	Any surgical or percutaneous reintervention on any operated valve

N/A=not applicable.

Table S2. Inclusion age criteria and exclusion criteria.

Author	Year	Age (yrs)	Exclusion criteria
Doss	2005	18-55	Patients with isolated or predominant aortic regurgitation, previous valve surgeries, concomitant valve procedures, active endocarditis, emergency procedures, and a history of myocardial infarction, and severe calcification of the aortic root.
El-Hamamsy	2010	18-69	Patients with Marfan’s syndrome, rheumatoid arthritis, Reiter’s syndrome.

Mokhles	2011	18-60	Patients with an urgent operation, aortic dissection or aortic aneurysm, concomitant mitral valve replacement.
Mazine	2016	16-63	Patients with acute aortic dissection, active endocarditis, or requiring emergency surgery
Sharabiani	2016	16-40	Patients with complex heart abnormalities, rheumatic fever, unclassified aortic valve procedures.
Bouhout	2017	18-65	Patients with concomitant procedures other than ascending aortic replacement, redo operations, or urgent surgery
Buratto	2018	18-65	Patients with urgent surgery, concomitant cardiovascular procedures, aortic dissection, or endocarditis.
Gofus	2022	18-60	Patients with concomitant procedure, acute aortic syndrome and in a critical preoperative state (those in need of artificial ventilation, catecholamines, cardiopulmonary resuscitation or in cardiogenic shock).
El-Hamamsy	2022	18-50	Patients with concomitant valve surgery or coronary artery bypass grafting, end-stage renal disease, intravenous drug use, acute aortic dissection, infective endocarditis, history of carcinoid disease or Marfan syndrome.
Mazine	2022	16-60	Patients with active endocarditis, acute aortic dissection, end-stage renal disease, or emergency surgery.

Table S3. Variables used in propensity-score matching studies.

Author	Year	Variables
Mokhles	2011	Age, sex, pathology, endocarditis, hemodynamic manifestation, preoperative NYHA grade, creatinine, preoperative rhythm, diabetes, hypertension, lung disease, LVEF, LVEDO, LVESD, previous cardiac operation, concomitant surgery.
Mazine	2016	Age, sex, residential location, year of surgery, body weight and body surface area, preoperative creatinine level, diabetes control (if applicable), history of cardiac intervention (i.e. previous aortic/mitral valve surgery, any other cardiac surgery, non-surgical intervention), clinical presentation (i.e. congestive heart failure, severe angina pectoris, left ventricular ejection fraction, results of stress testing and NYHA functional classification) 10. presence of cardiovascular risk factors (i.e. diabetes mellitus, hypertension, hyperlipidemia and smoking history) 11. presence of other associated diseases (i.e. chronic obstructive pulmonary disease, previous stroke or transient ischemic attack, peripheral vascular disease, atrial

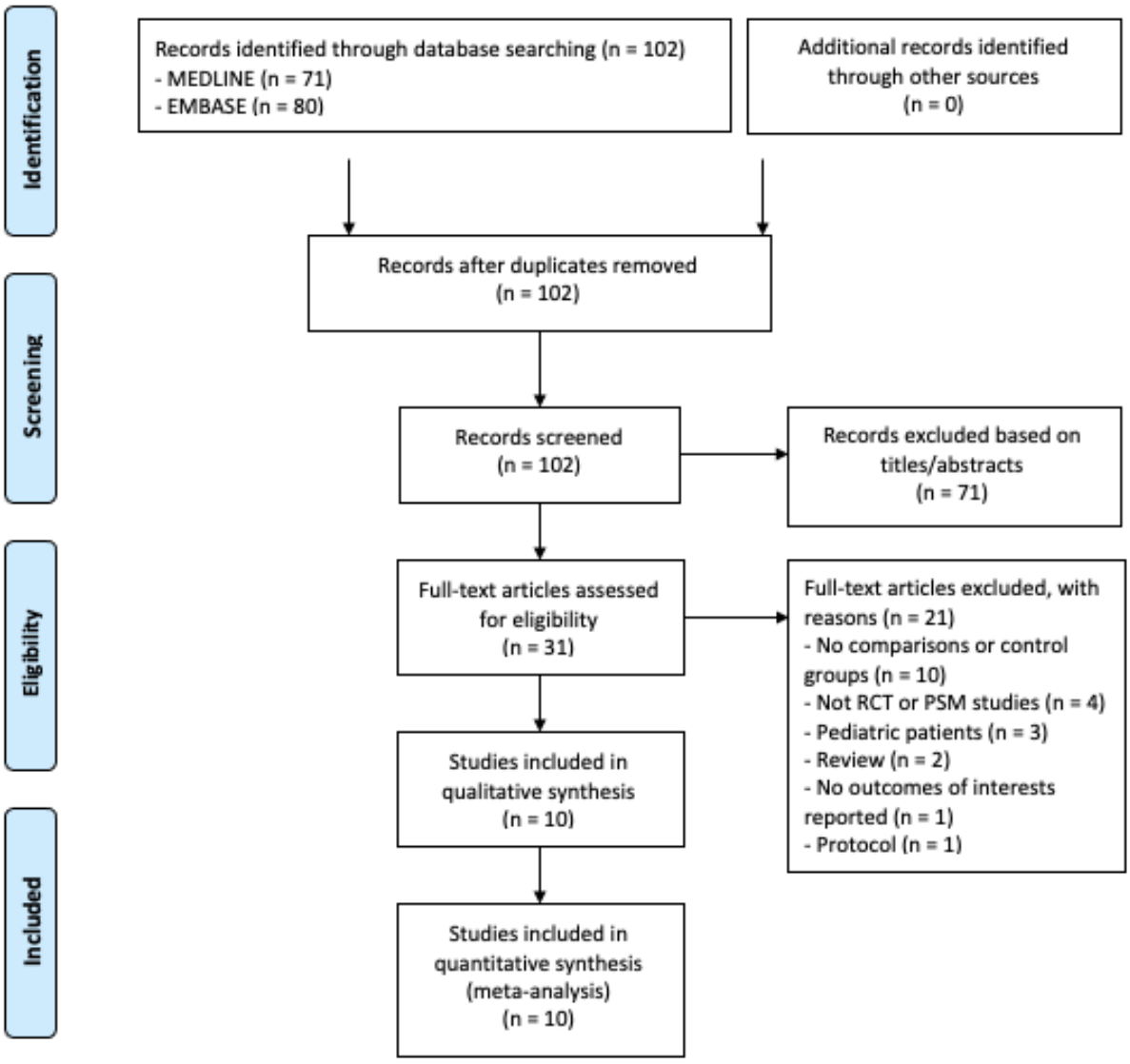
		fibrillation, complete heart block) 12. pre-operative use of medications (i.e. statin or aspirin within 7 days before the surgery) 13. disease characteristics (i.e. aortic valve pathology, presence of ascending aortic disease, mitral valve disease and coronary artery disease 14. concomitant procedures
Sharabiani	2016	Age, sex, aortic disease type, mitral disease, coarctation, subaortic stenosis, genetic syndrome, mitral valve procedure, coarctation repair, and subaortic stenosis repair at index
Bouhout	2017	Age, ascending aorta aneurysm, aortic root aneurysm, NYHA functional class, hypertension, pulmonary hypertension, surgical indication for AVR, left ventricle ejection fraction <50% and dyslipidemia.
Buratto	2018	Age, sex, era of surgery, hypertension, diabetes mellitus, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, myocardial infarction, dialysis, New York Heart Association functional class, ejection fraction <45%, aortic stenosis, aortic regurgitation, mixed aortic valve disease, reoperation, congestive heart failure.
Gofus	2022	Age, sex, body mass index, creatinine, LVEF, angina pectoris, NYHA class, heart failure, previous heart surgery, smoking status, diabetes, hypertension, dyslipidemia, chronic pulmonary disease, rhythm, cerebral vascular disease, coronary artery disease, endocarditis, urgent surgery, valve pathology, concomitant procedures
El-Hamamsy	2022	Age, sex, race, history of hypertension, diabetes, congestive heart failure, chronic kidney disease, coronary artery disease, atrial fibrillation, peripheral vascular disease, chronic obstructive pulmonary disease, liver disease, cancer, cerebrovascular disease, coagulation disorders, previous endocarditis), and admission year.
Mazine	2022	Age, sex, year of surgery, weight, body surface area, preoperative diabetes, congestive heart failure, angina, severe chronic obstructive pulmonary disease, hypertension, medically treated hyperlipidemia, previous stroke or transient ischemic attack, atrial fibrillation or complete heart block preoperatively, ascending aortic disease, use of aspirin or statins within 7 days before surgery, concurrent coronary artery bypass grafting, concurrent mitral and/or tricuspid valve procedure, and history of cardiac intervention (ie, previous aortic or mitral valve surgery, any other cardiac surgery, or nonsurgical cardiac intervention).

Table S4. Quality assessment based on NOS (range, 1-9). NOS score≥8 is low risk, 6-7 is moderate risk and ≤5 is high risk.

Studies	Representativeness of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Absence of outcome at start of study	Comparability of cohorts	Outcome assessment	Length of follow-up	Adequacy of follow-up	NOS score
Mokhles	1	0	1	1	2	1	1	1	8
Mazine	1	1	1	1	2	1	1	1	9
Sharabiani	1	1	1	1	2	1	1	1	9
Bouhout	1	1	1	1	2	1	0	1	8
Buratto	1	0	1	1	2	1	1	1	8
Gofus	1	1	1	1	2	1	1	1	9
El-Hamamsy	1	1	1	1	2	1	1	1	9
Mazine	1	1	1	1	2	1	1	1	9

NOS=Newcastle-Ottawa Scale

Figure S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.



RCT, randomized controlled trial; PSM, propensity-score-matched

Figure S2. Risk of bias summary according to the Cochrane Collaboration Manual.

Yellow: unclear risk; Green: low risk, Red: high risk.

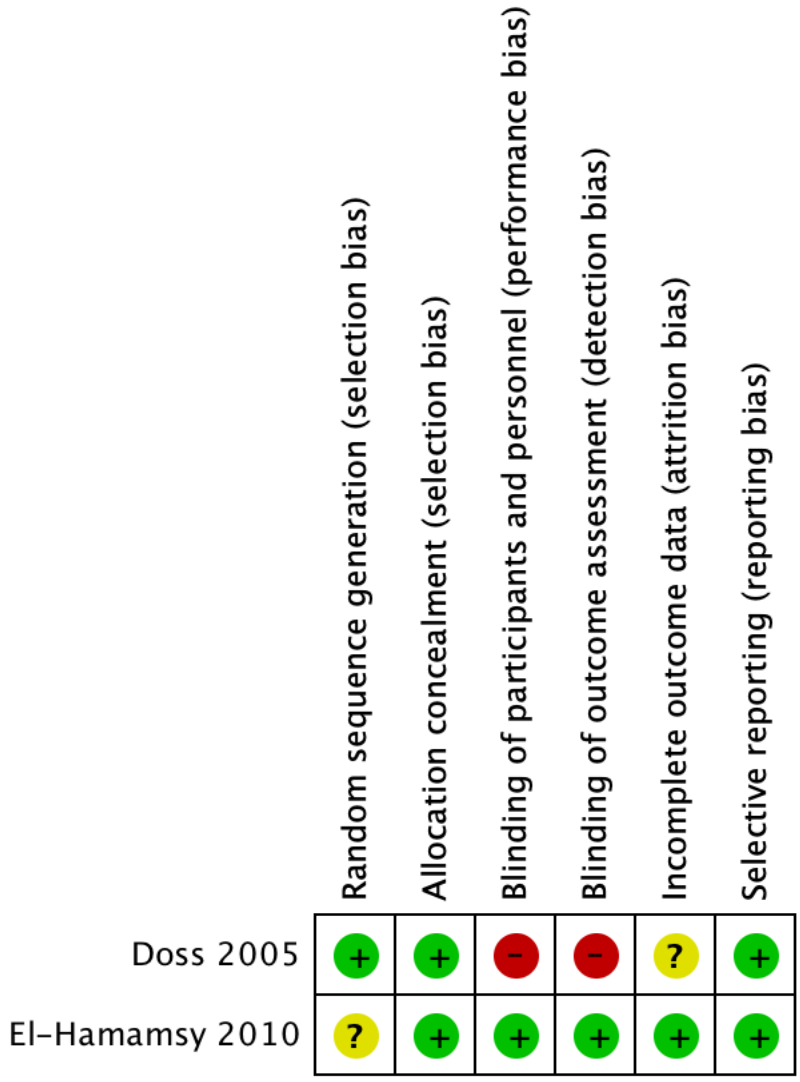
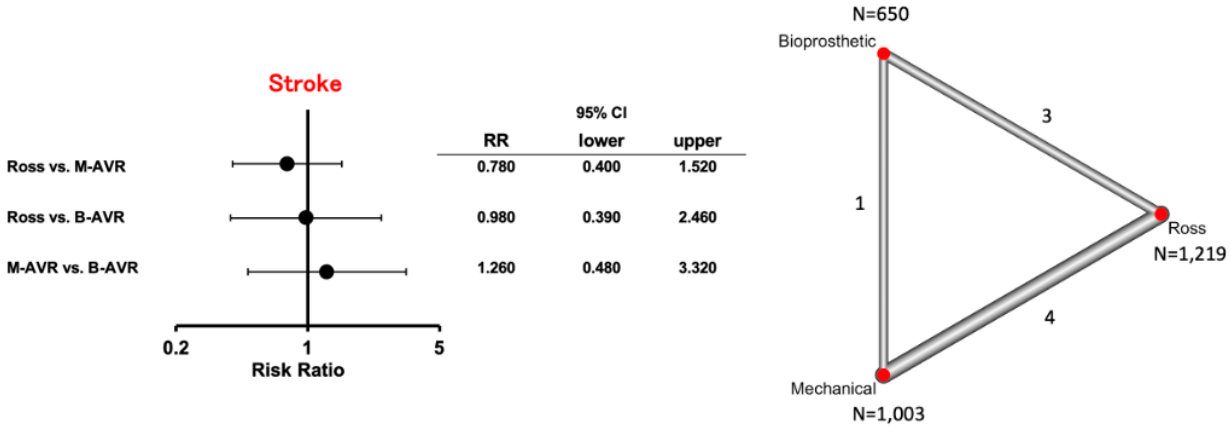
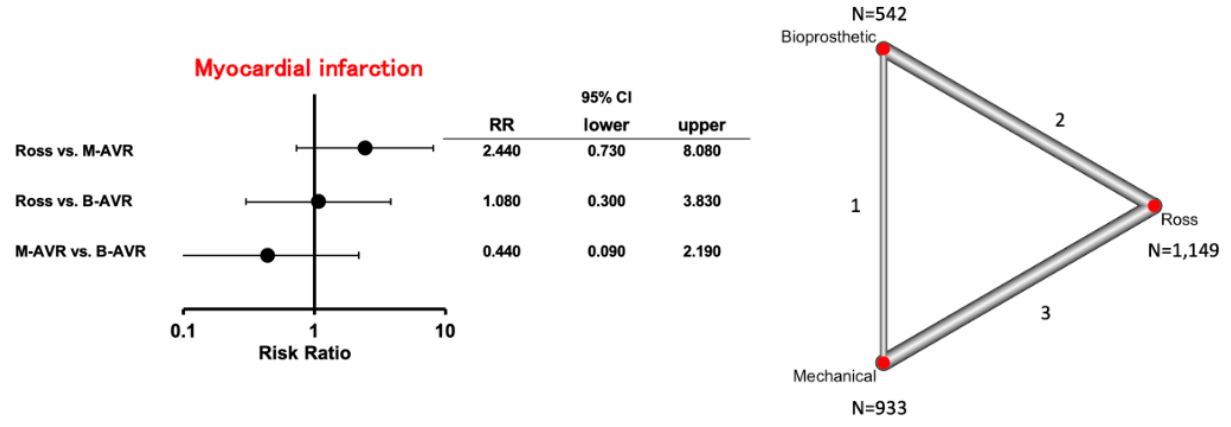


Figure S3. Forest plots of A) stroke, B) myocardial infarction, C) new onset atrial fibrillation, and D) reoperation for bleeding all-cause mortality among treatment strategies (random-effects model). The horizontal lines represent the values within the 95% confidence interval of the underlying effects. The vertical line indicates an incident hazard ratio of 1. B-AVR=bioprosthetic aortic valve replacement, CI=confidence interval, HR=hazard ratio, M-AVR=mechanical aortic valve replacement.

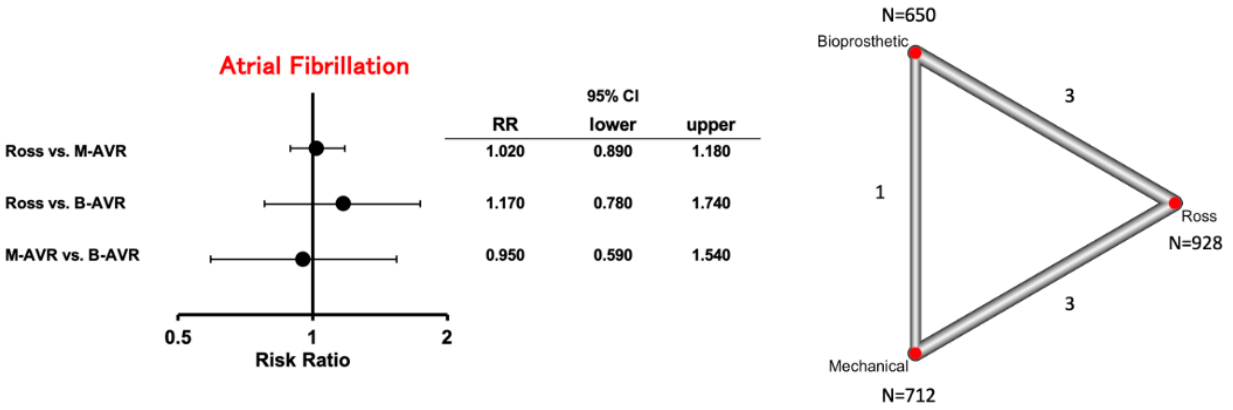
A)



B)



C)


Atrial Fibrillation
95% CI
RR lower upper
Ross vs. M-AVR 1.020 0.890 1.180
Ross vs. B-AVR 1.170 0.780 1.740
M-AVR vs. B-AVR 0.950 0.590 1.540
0.5
1
2
Risk Ratio
N=650
Bioprosthetic
3
1
Ross
N=928
3
Mechanical
N=712

D)

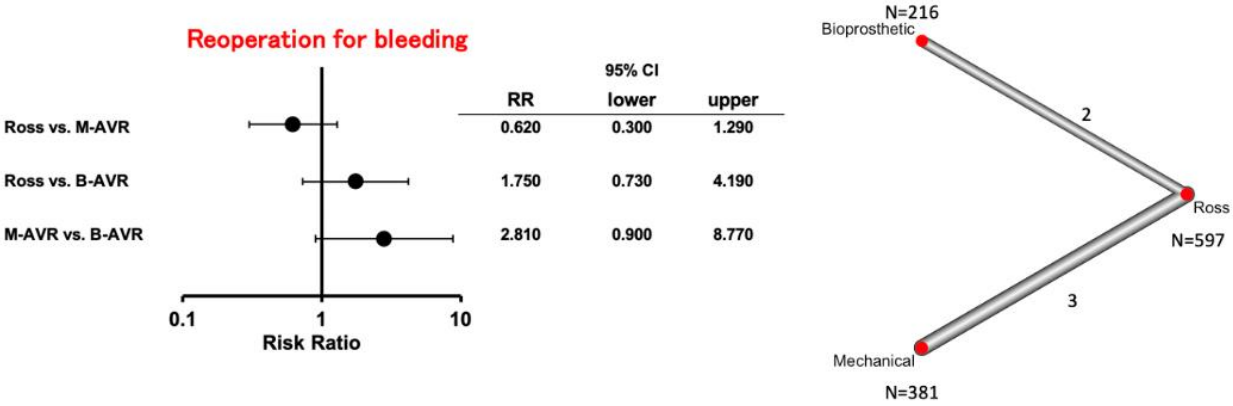
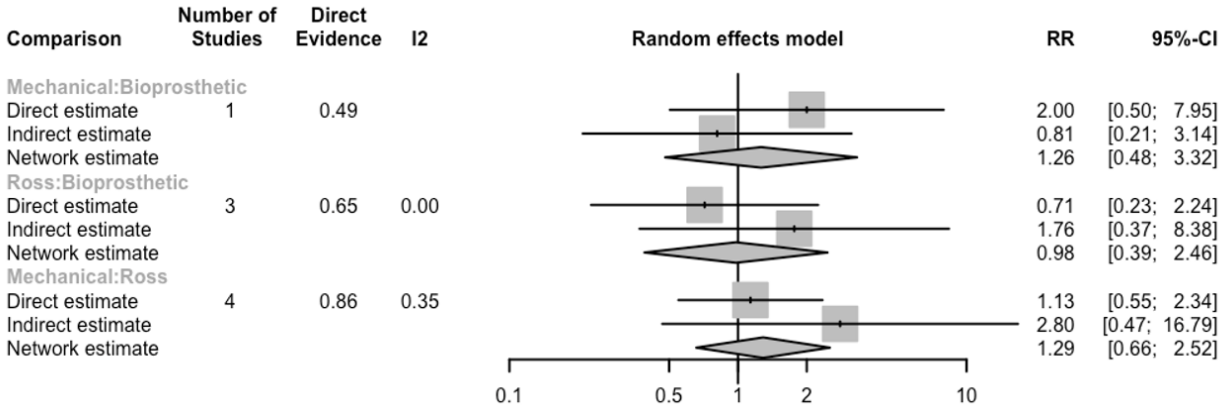
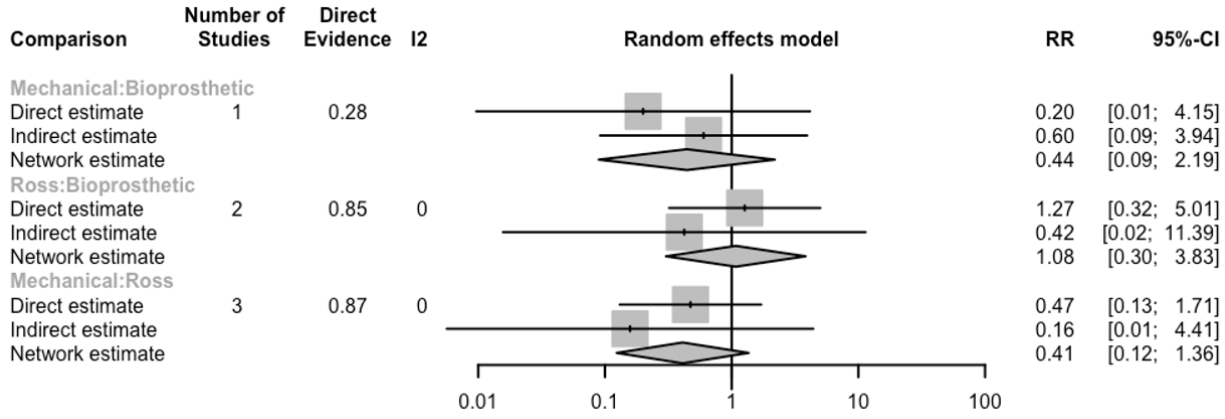

Reoperation for bleeding
95% CI
RR lower upper
Ross vs. M-AVR 0.620 0.300 1.290
Ross vs. B-AVR 1.750 0.730 4.190
M-AVR vs. B-AVR 2.810 0.900 8.770
0.1
1
10
Risk Ratio
N=216
Bioprosthetic
2
Ross
N=597
3
Mechanical
N=381

Figure S4. Direct and indirect comparisons for A) stroke, B) myocardial infarction, C) permanent pacemaker implantation, D) new onset atrial fibrillation, E) reoperation for bleeding, F) all-cause mortality, G) reintervention, H) major bleeding, I) long-term stroke, and J) infectious endocarditis.

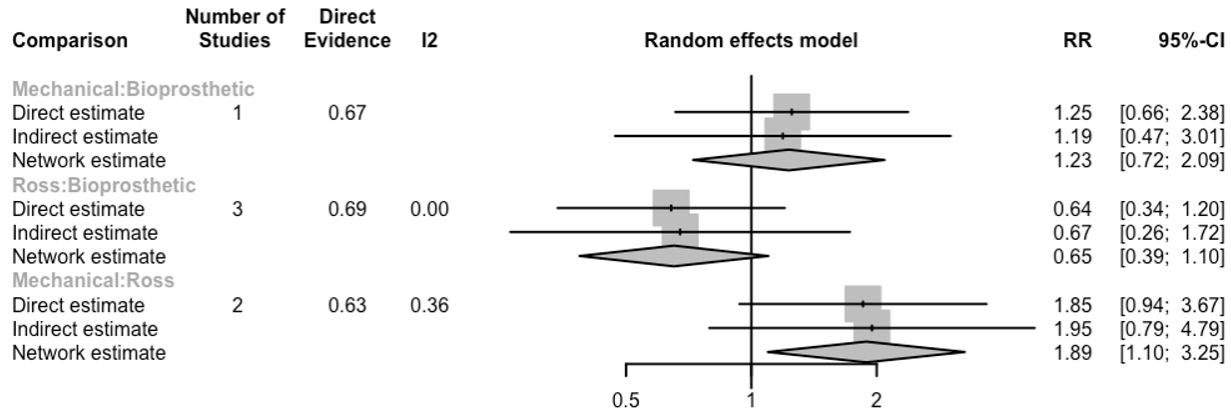
A)



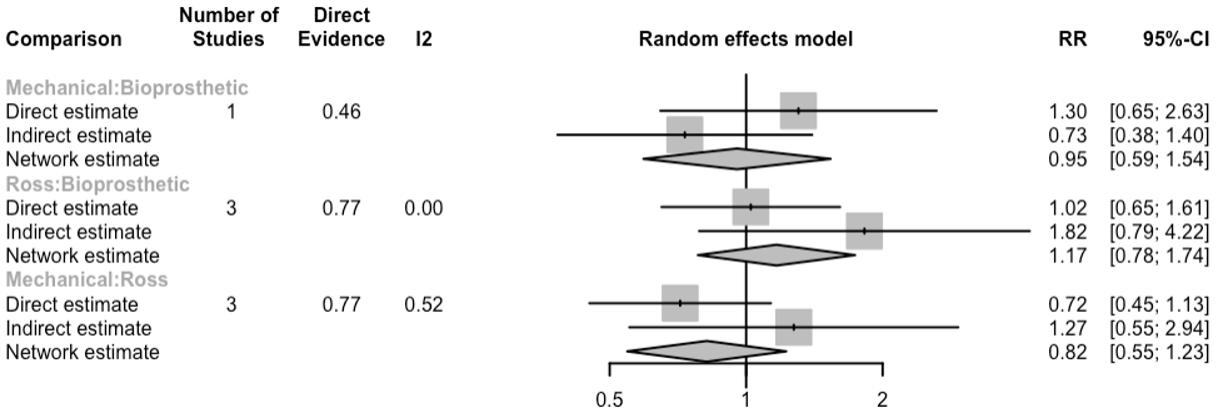
B)



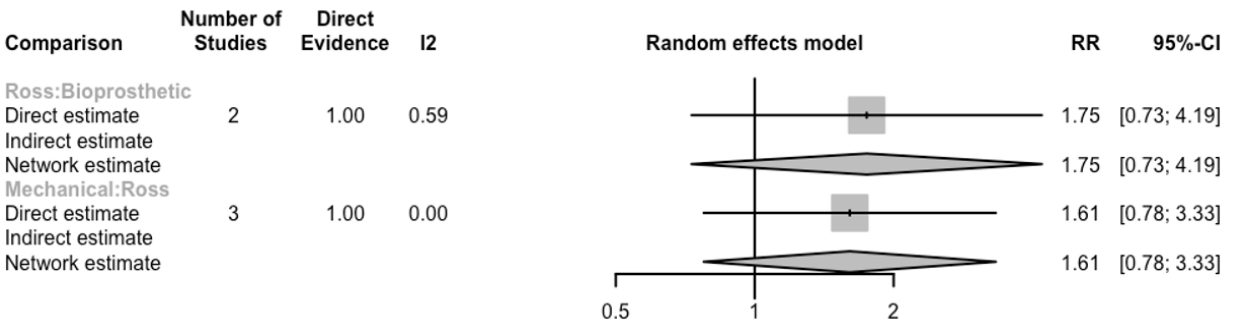
C)


Comparison
Number of Studies
Direct Evidence
I2
Random effects model
RR
95%-CI
Mechanical:Bioprosthetic
Direct estimate 1 0.67 1.25 [0.66; 2.38]
Indirect estimate 1.19 [0.47; 3.01]
Network estimate 1.23 [0.72; 2.09]
Ross:Bioprosthetic
Direct estimate 3 0.69 0.00 0.64 [0.34; 1.20]
Indirect estimate 0.67 [0.26; 1.72]
Network estimate 0.65 [0.39; 1.10]
Mechanical:Ross
Direct estimate 2 0.63 0.36 1.85 [0.94; 3.67]
Indirect estimate 1.95 [0.79; 4.79]
Network estimate 1.89 [1.10; 3.25]
0.5
1
2

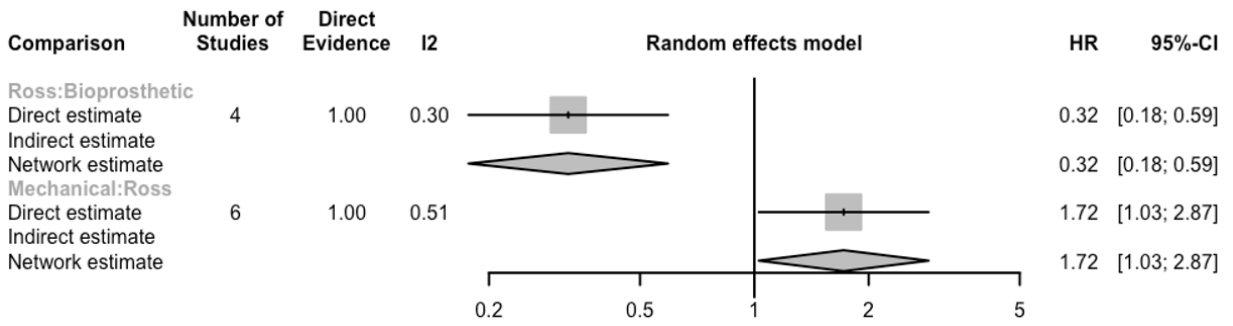
D)


Comparison
Number of Studies
Direct Evidence
I2
Random effects model
RR
95%-CI
Mechanical:Bioprosthetic
Direct estimate 1 0.46 1.30 [0.65; 2.63]
Indirect estimate 0.73 [0.38; 1.40]
Network estimate 0.95 [0.59; 1.54]
Ross:Bioprosthetic
Direct estimate 3 0.77 0.00 1.02 [0.65; 1.61]
Indirect estimate 1.82 [0.79; 4.22]
Network estimate 1.17 [0.78; 1.74]
Mechanical:Ross
Direct estimate 3 0.77 0.52 0.72 [0.45; 1.13]
Indirect estimate 1.27 [0.55; 2.94]
Network estimate 0.82 [0.55; 1.23]
0.5
1
2

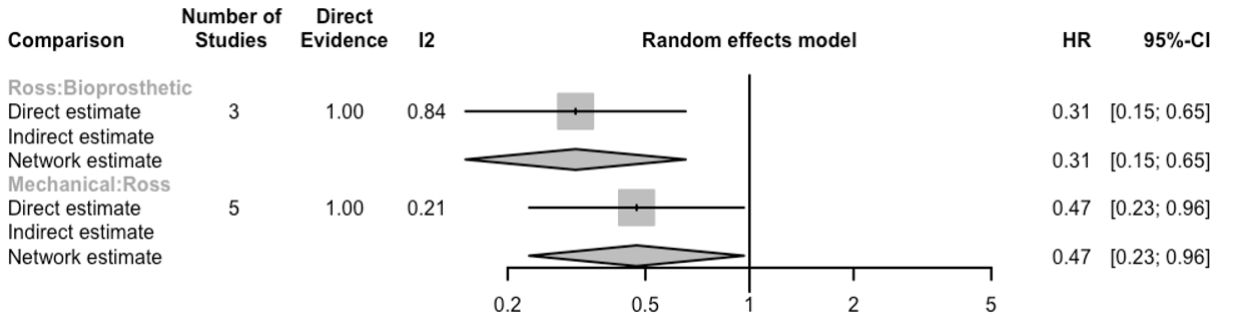
E)


Comparison
Number of Studies
Direct Evidence
I2
Random effects model
RR
95%-CI
Ross:Bioprosthetic
Direct estimate 2 1.00 0.59 1.75 [0.73; 4.19]
Indirect estimate
Network estimate 1.75 [0.73; 4.19]
Mechanical:Ross
Direct estimate 3 1.00 0.00 1.61 [0.78; 3.33]
Indirect estimate
Network estimate 1.61 [0.78; 3.33]
0.5
1
2

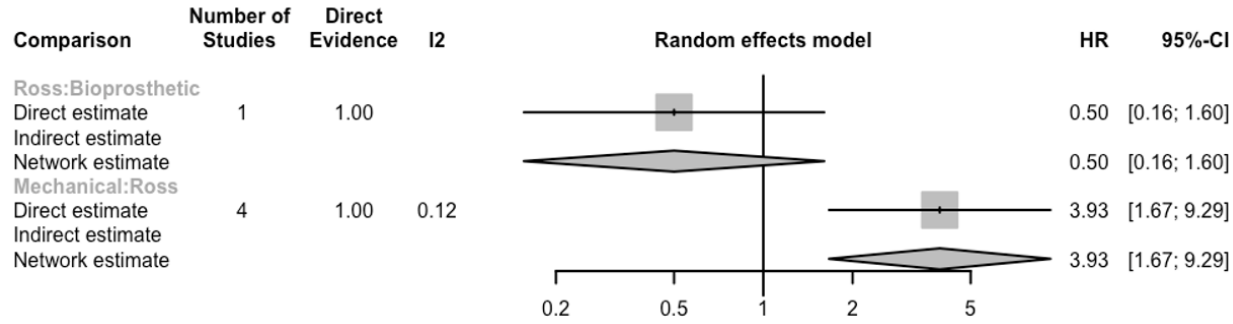
F)


Comparison
Number of Studies
Direct Evidence
I2
Random effects model
HR
95%-CI
Ross:Bioprosthetic
Direct estimate 4 1.00 0.30 0.32 [0.18; 0.59]
Indirect estimate
Network estimate 0.32 [0.18; 0.59]
Mechanical:Ross
Direct estimate 6 1.00 0.51 1.72 [1.03; 2.87]
Indirect estimate
Network estimate 1.72 [1.03; 2.87]
0.2
0.5
1
2
5

G)


Comparison
Number of Studies
Direct Evidence
I2
Random effects model
HR
95%-CI
Ross:Bioprosthetic
Direct estimate 3 1.00 0.84 0.31 [0.15; 0.65]
Indirect estimate
Network estimate 0.31 [0.15; 0.65]
Mechanical:Ross
Direct estimate 5 1.00 0.21 0.47 [0.23; 0.96]
Indirect estimate
Network estimate 0.47 [0.23; 0.96]
0.2
0.5
1
2
5

H)


Comparison
Number of Studies
Direct Evidence
I2
Random effects model
HR
95%-CI
Ross:Bioprosthetic
Direct estimate 1 1.00 0.50 [0.16; 1.60]
Indirect estimate
Network estimate 0.50 [0.16; 1.60]
Mechanical:Ross
Direct estimate 4 1.00 0.12 3.93 [1.67; 9.29]
Indirect estimate
Network estimate 3.93 [1.67; 9.29]
0.2
0.5
1
2
5

I)

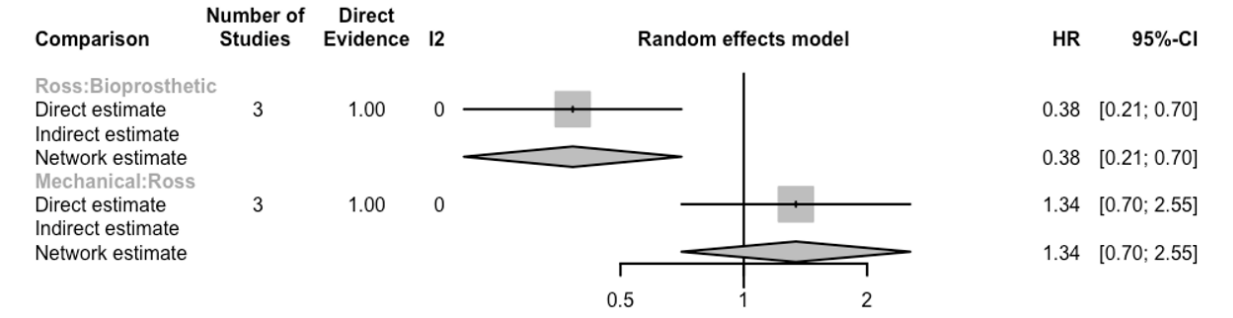
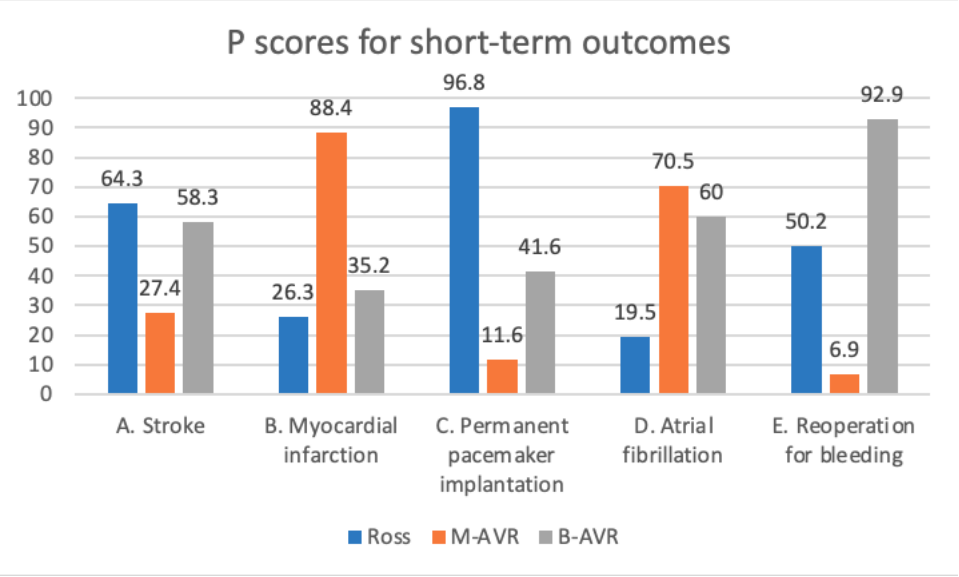
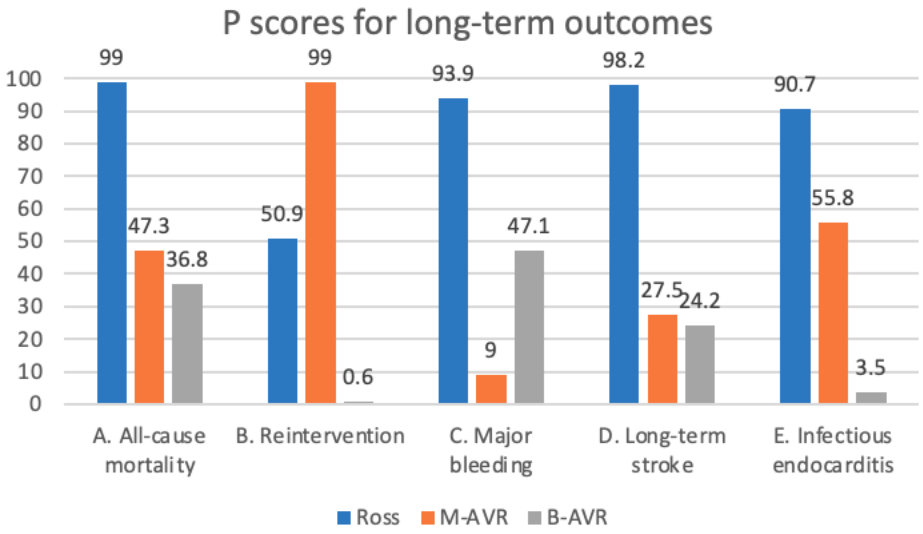

Comparison
Number of Studies
Direct Evidence
I2
Random effects model
HR
95%-CI
Ross:Bioprosthetic
Direct estimate 3 1.00 0 0.38 [0.21; 0.70]
Indirect estimate
Network estimate 0.38 [0.21; 0.70]
Mechanical:Ross
Direct estimate 3 1.00 0 1.34 [0.70; 2.55]
Indirect estimate
Network estimate 1.34 [0.70; 2.55]
0.5
1
2

Figure S5. P scores for short-term outcomes.



B-AVR, bioprosthetic aortic valve replacement; M-AVR, mechanical aortic valve replacement

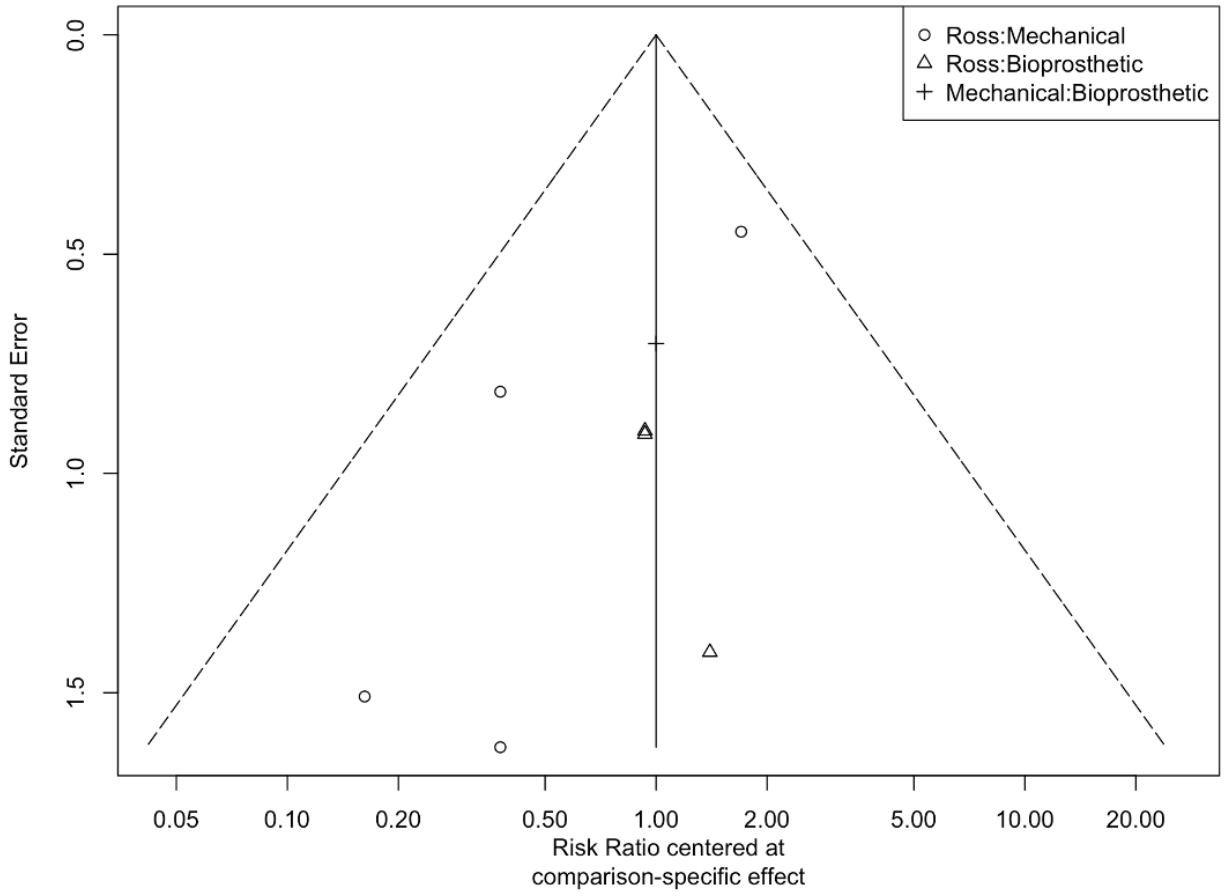
Figure S6. P scores for long-term outcomes.



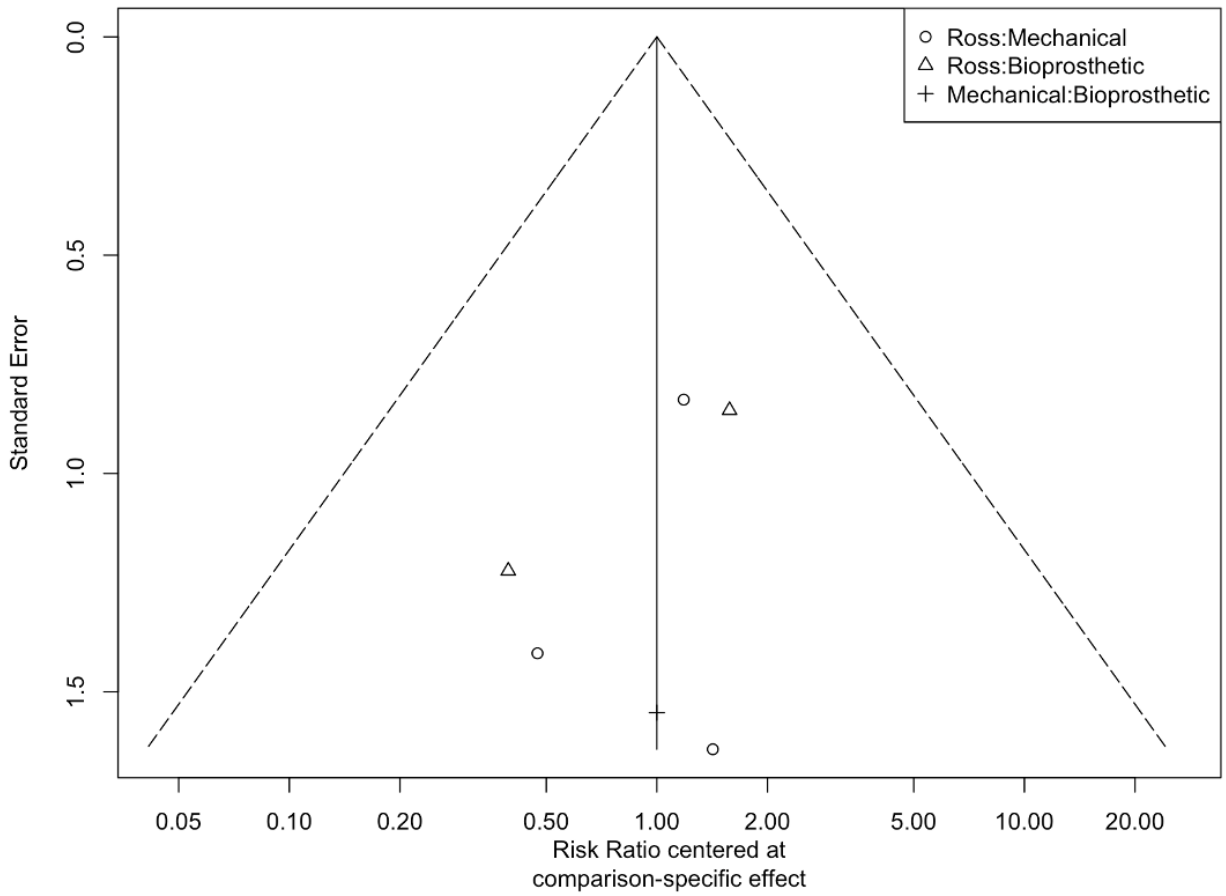
B-AVR, bioprosthetic aortic valve replacement; M-AVR, mechanical aortic valve replacement

Figure S7. Publication bias assessment using Funnel plot for A) stroke, B) myocardial infarction, C) permanent pacemaker implantation, D) new onset atrial fibrillation, E) reoperation for bleeding, F) all-cause mortality, G) reintervention, H) major bleeding, I) long-term stroke, and J) infectious endocarditis.

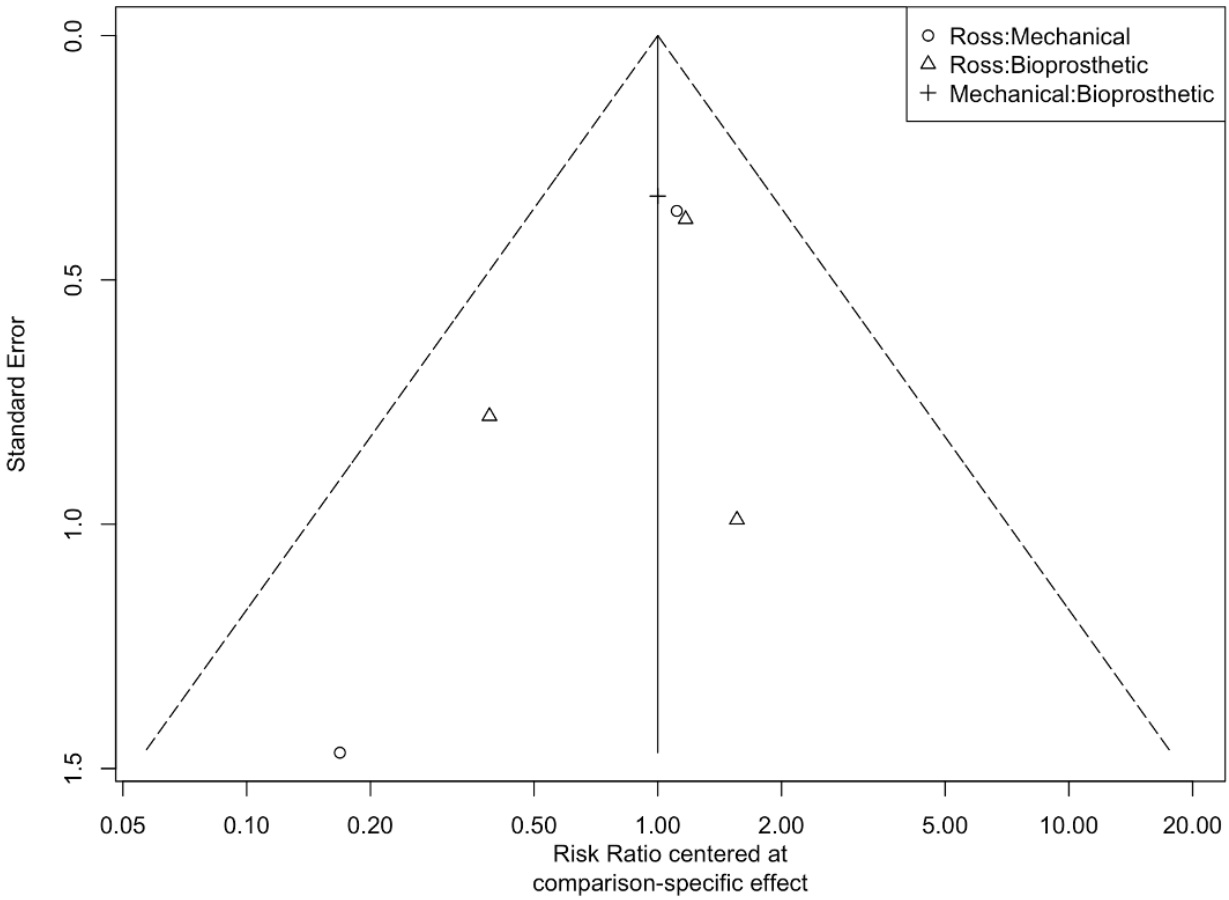
A)



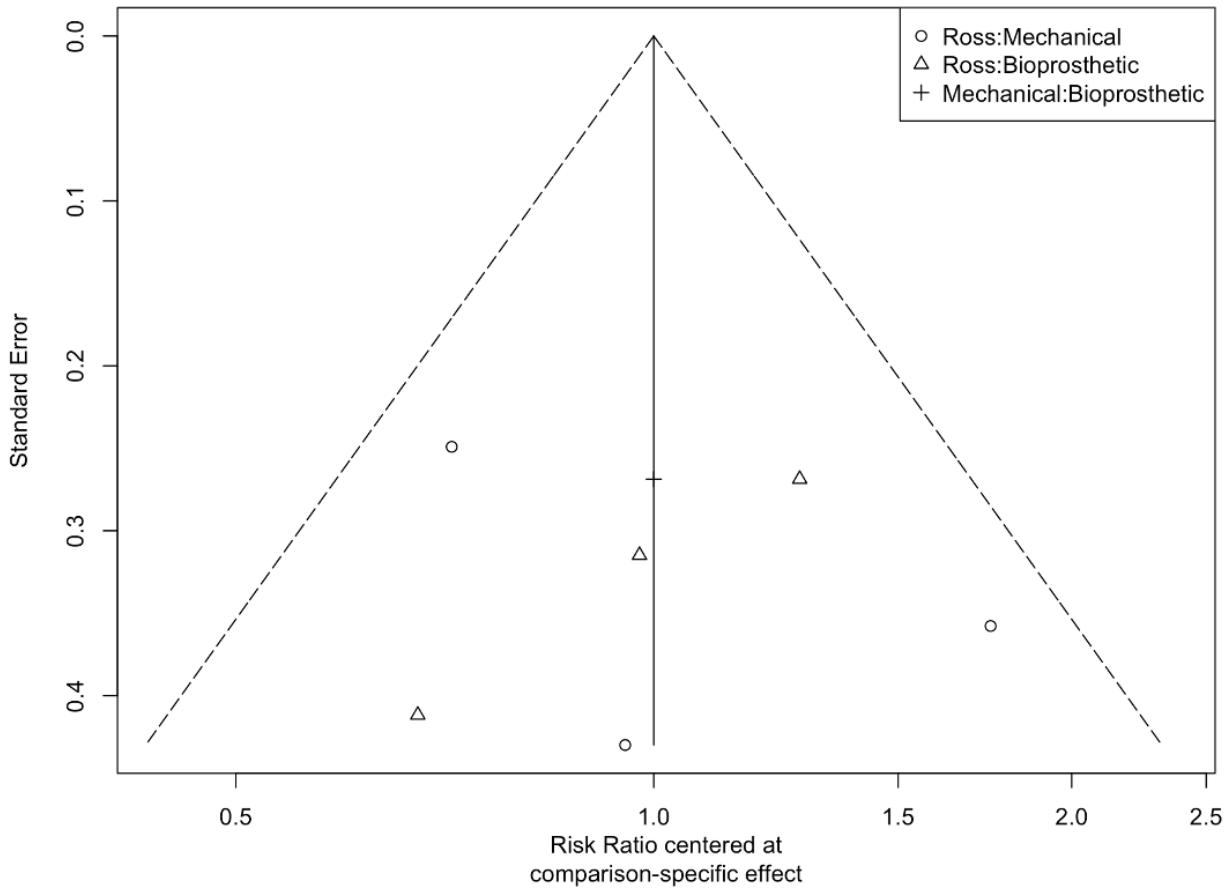
B)


Ross:Mechanical
Ross:Bioprosthetic
Mechanical:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Risk Ratio centered at
comparison-specific effect

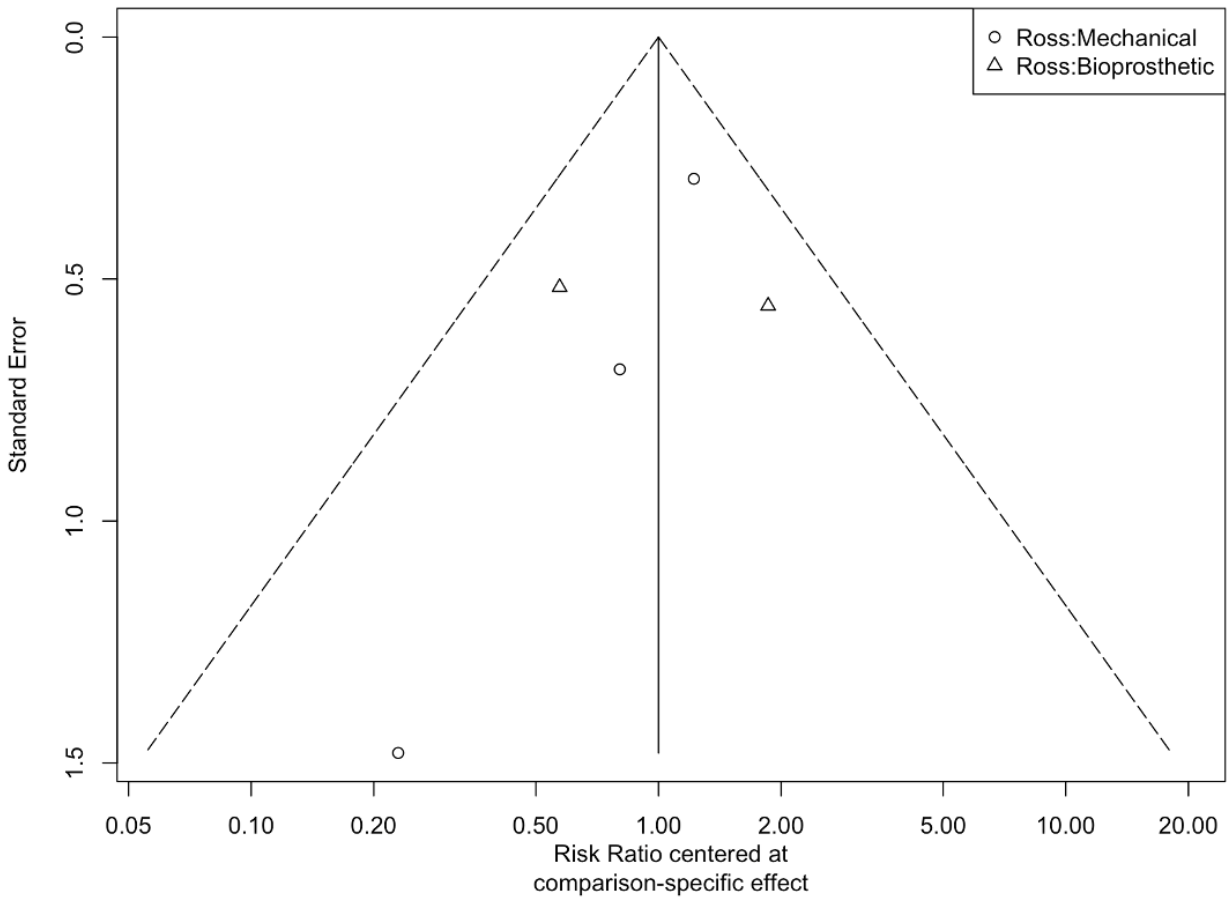
C)


Ross:Mechanical
Ross:Bioprosthetic
Mechanical:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Risk Ratio centered at
comparison-specific effect

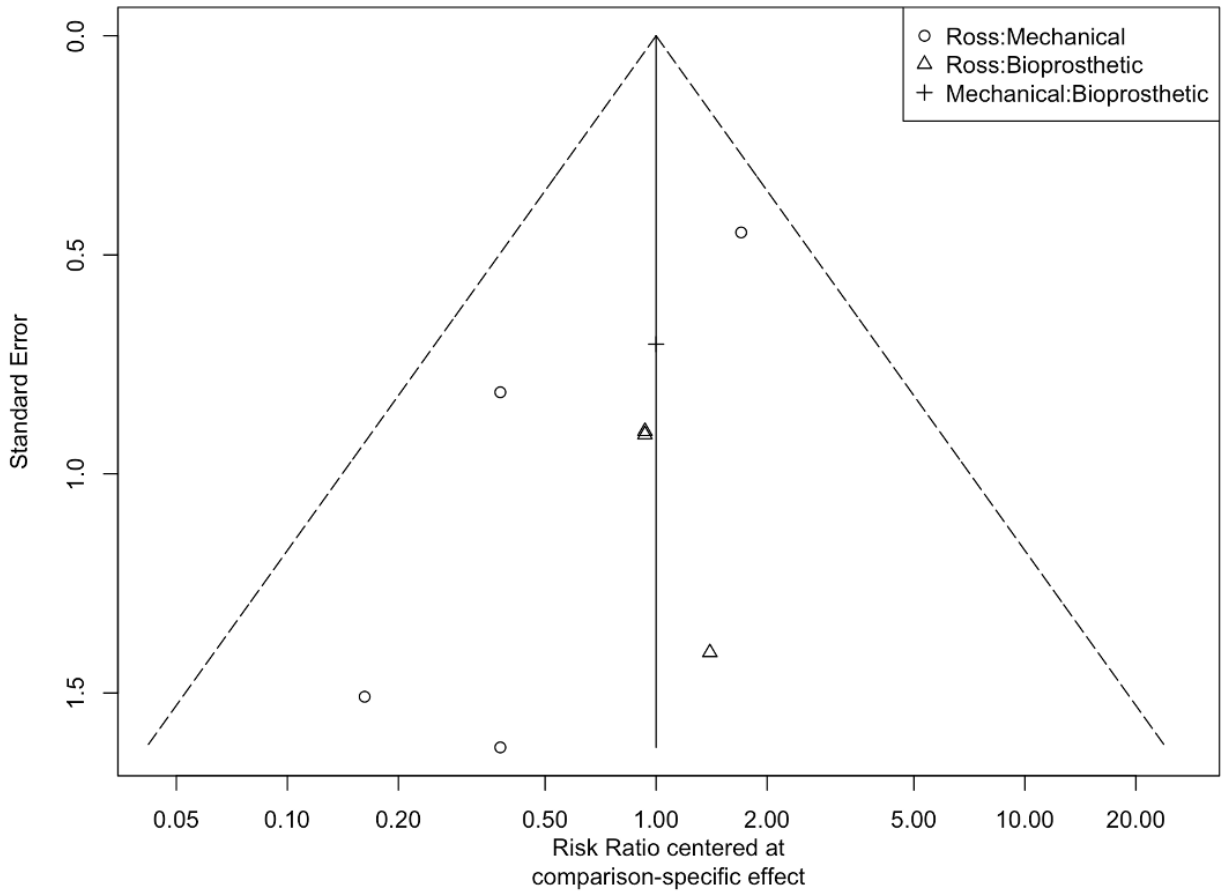
D)


Ross:Mechanical
Ross:Bioprosthetic
Mechanical:Bioprosthetic
Standard Error
0.0
0.1
0.2
0.3
0.4
0.5
1.0
1.5
2.0
2.5
Risk Ratio centered at
comparison-specific effect

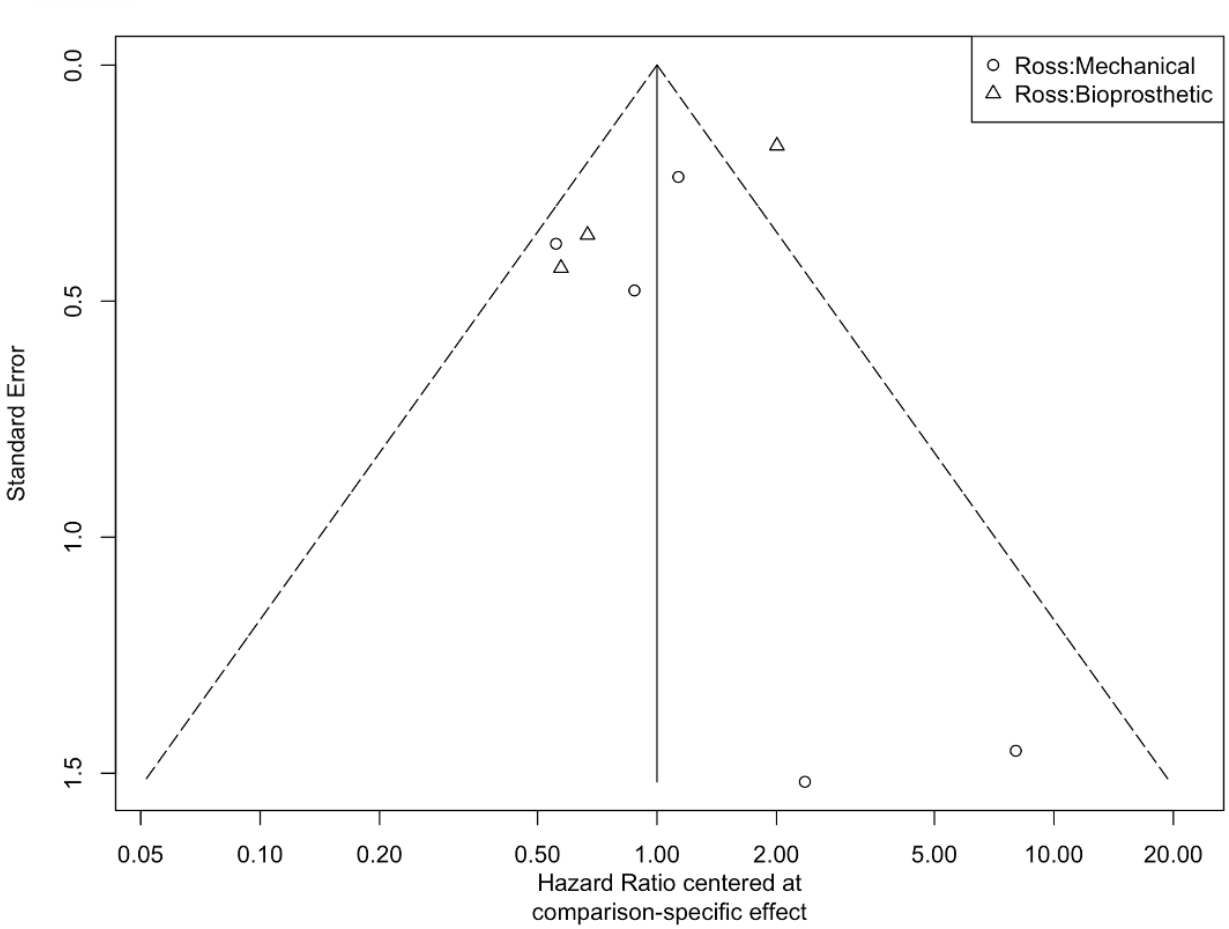
E)


Ross:Mechanical
Ross:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Risk Ratio centered at
comparison-specific effect

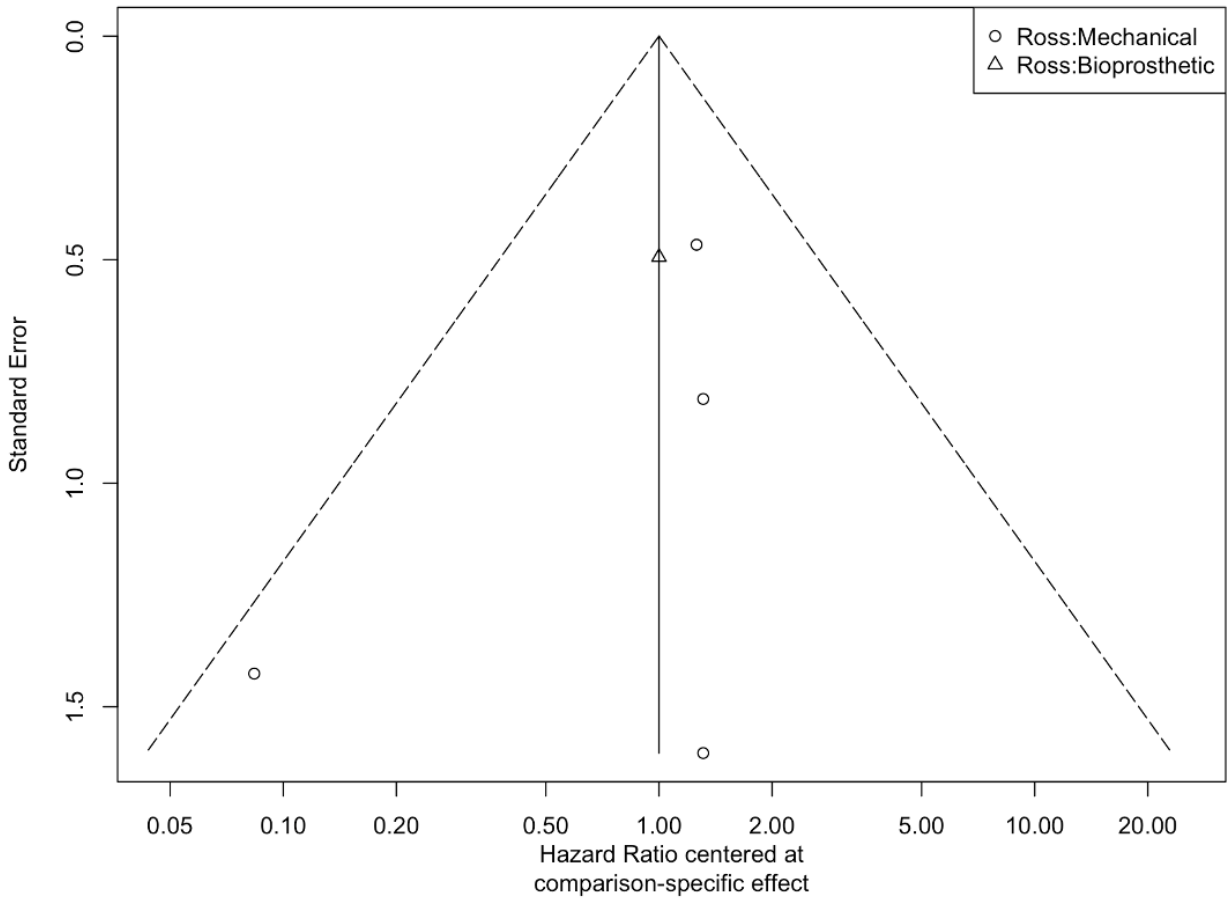
F)


Ross:Mechanical
Ross:Bioprosthetic
Mechanical:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Risk Ratio centered at
comparison-specific effect

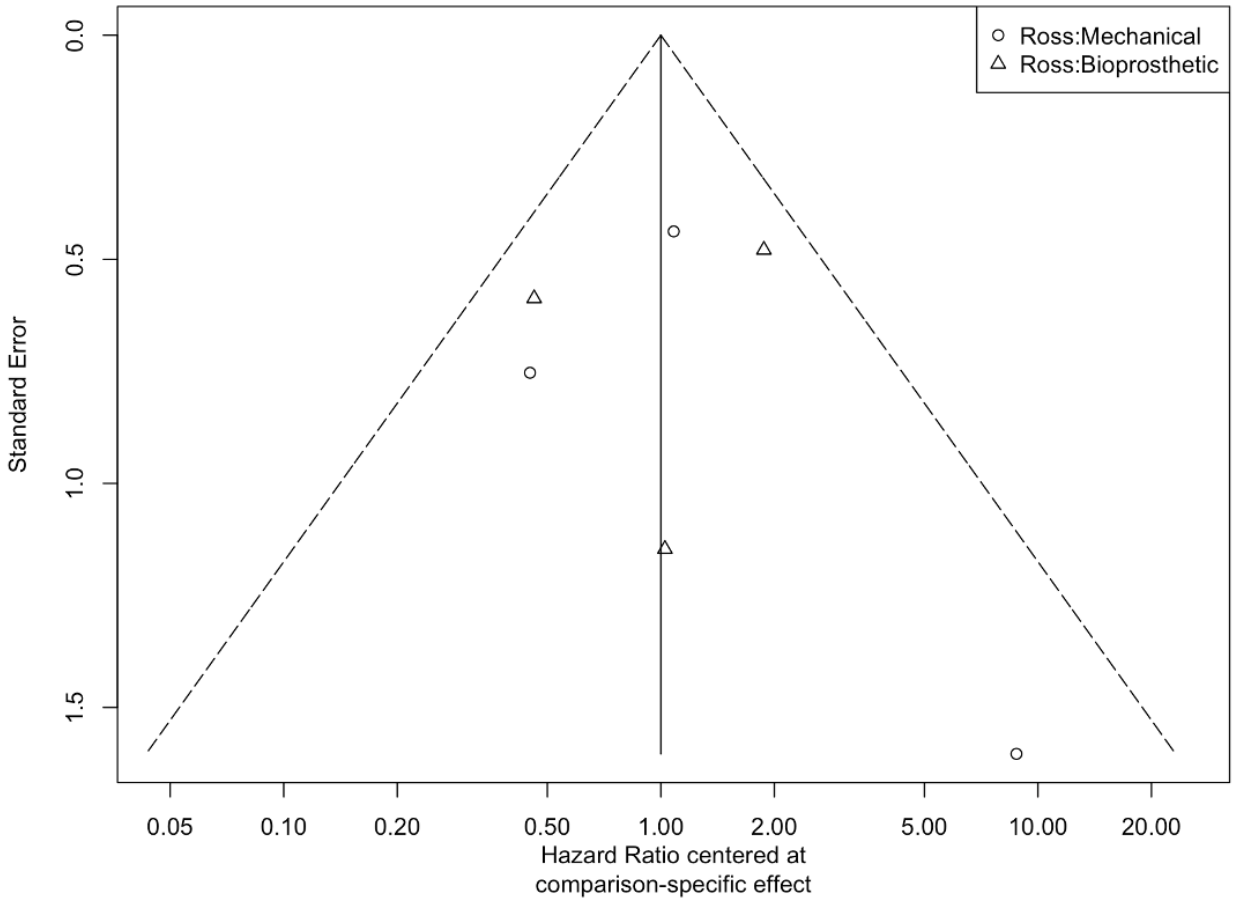
G)


Ross:Mechanical
Ross:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Hazard Ratio centered at
comparison-specific effect

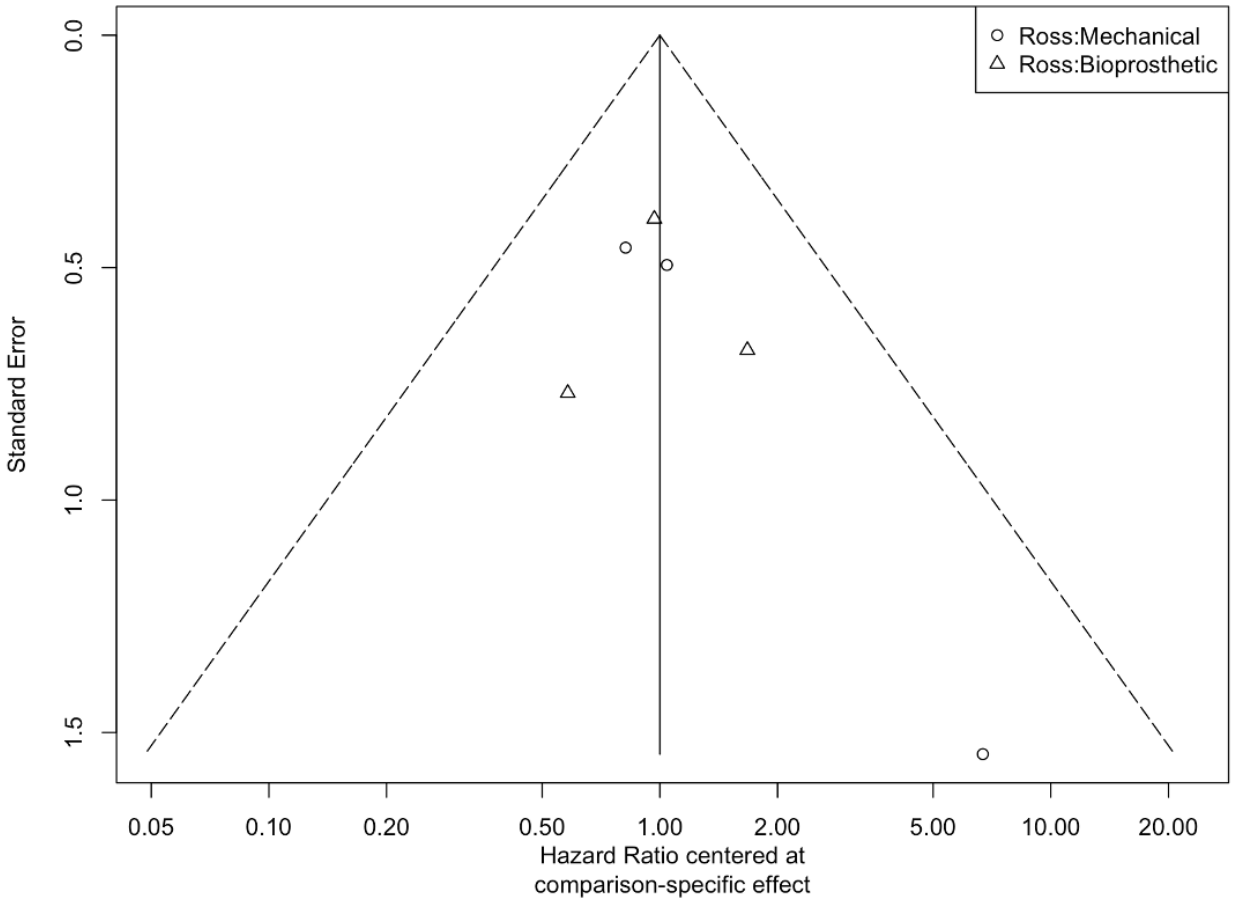
H)


Ross:Mechanical
Ross:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Hazard Ratio centered at
comparison-specific effect

I)


Ross:Mechanical
Ross:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Hazard Ratio centered at
comparison-specific effect

J)


Ross:Mechanical
Ross:Bioprosthetic
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Hazard Ratio centered at
comparison-specific effect