

Supplemental Material

Table S1. Inclusion and Exclusion Criteria of Studies.

Study	Inclusion Criteria	Exclusion Criteria
Yang et al. ¹	Patients with acute STEMI treated with primary PCI between January 2005 and December 2008, from the Database of Shanghai Rui Jin Hospital Percutaneous Coronary Intervention Outcomes Program. STEMI was diagnosed according to American Heart Association criteria including symptoms consistent with ongoing myocardial ischemia ≥ 30 min, ST-segment elevation ≥ 1 mm in two contiguous leads or more, new left bundle branch block, or true posterior infarction.	Nine patients were excluded from analysis as they died during hospital stay (n = 6) or were lost to follow-up (n = 3).
Shi et al. ²	Patients with acute STEMI treated with primary PCI between January 2005 to June 2009 admitted to Guangdong General Hospital. Acute STEMI was diagnosed according to American Heart Association criteria including symptoms consistent with ongoing myocardial ischemia ≥ 30 min, accompanied by an electrocardiogram with ST-segment elevation ≥ 1 mm(0.1mV) in two contiguous leads or more, new left bundle branch block, or true posterior infarction. Multivessel was defined as ≥ 1 stenosis $> 70\%$ of the coronary lumen diameter in > 1 of the noninfarct related epicardial arteries or left main stenosis $> 50\%$. A CTO was defined as a total occlusion in a non-IRA before PCI without antegrade flow or with antegrade or retrograde filling through collateral vessels.	Not available
Valenti et al. ³	Consecutive patients from the Florence PCI registry treated by successful primary PCI (Thrombolysis in Myocardial Infarction [TIMI] grade 3 flow and residual infarct artery stenosis $<30\%$). Coexisting none infarct-related artery (IRA) CTO. Evidence of viable myocardium in the territory supplied by the CTO vessel.	In-hospital death during the first week after primary PCI.
Watanabe et al. ⁴	STEMI patients enrolled in the Coronary Revascularization Demonstrating Outcome study in Kyoto (CREDO-Kyoto) AMI registry with multi-vessel disease who underwent primary PCI within 24 hours after the symptom. Presence of CTO in the non-IRA	Not available
Deng et al. ⁵	STEMI patients who underwent successful primary PCI from January 2006 to December 2014 at The General Hospital of Shenyang Military Region, China and had a non-IRA CTO lesion. CTO was defined as a flow vessel of Thrombolysis in Myocardial Infarction (TIMI) grade 0, and a complete obstruction of a native coronary artery over a period for more than 3 months.	Not available
Henriques et al. ⁶	STEMI patients with a non–infarct-related chronic total occlusion undergoing successful primary PCI for STEMI (within 12 hours of onset of symptoms) from November 2007 through April 2015 in 14 centers in Europe and Canada. Successful primary PCI was defined as a residual stenosis of the culprit lesion $<30\%$ and the TIMI flow of ≥ 2 . CTO was defined as a 100% luminal narrowing without antegrade flow or with antegrade or retrograde filling through collateral vessels. CTO located in a coronary vessel with a reference diameter of at least 2.5 mm.	Hemodynamic instability persisting for >48 h after primary PCI and factors precluding reliable CMR imaging such as persistent or permanent atrial fibrillation, severe renal insufficiency, and indications for pacemaker or implantable cardioverter-defibrillator insertion

Table S2. Risk of bias across individual observational studies.

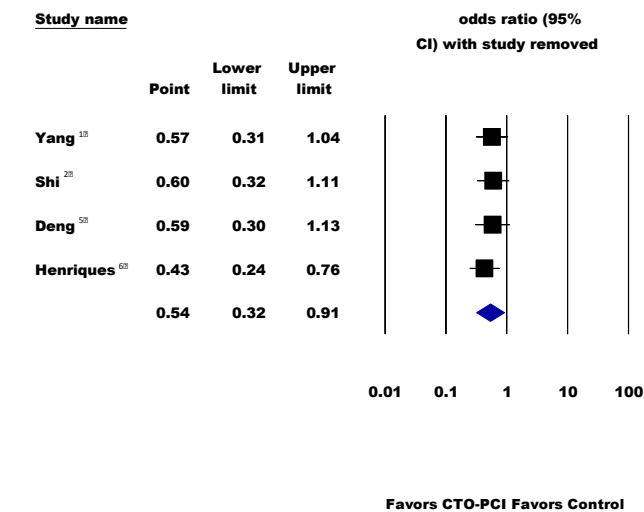
Author	Newcastle-Ottawa Scale
Yang ¹	7/9
Shi ²	7/9
Valenti ³	6/9
Watanabe ⁴	6/9
Deng ⁵	6/9

Table S3. Risk of bias across individual randomized control trials.

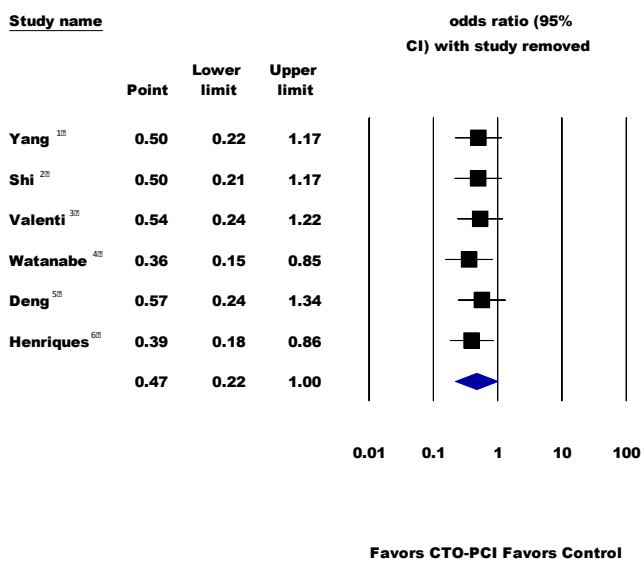
Study Name	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Baseline	Source of funding bias	Academic bias
Henriques ⁶	Low	Low	High	Moderate	Low	Low	Low	Low

Figure S1. Sensitivity Analysis with removal of each study one at a time

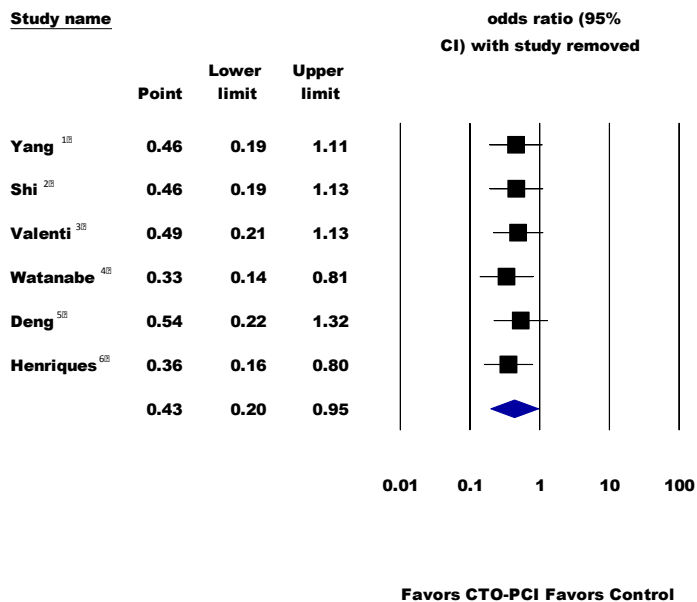
A. Major Adverse Cardiovascular Events



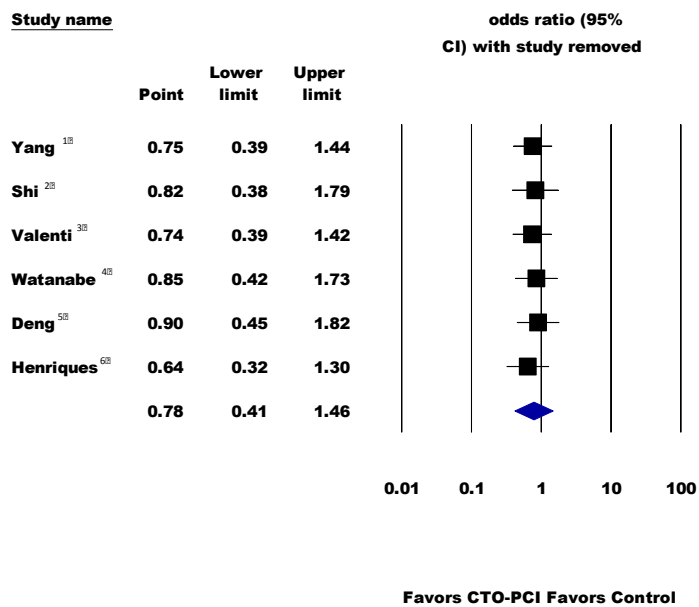
B. All-Cause Mortality



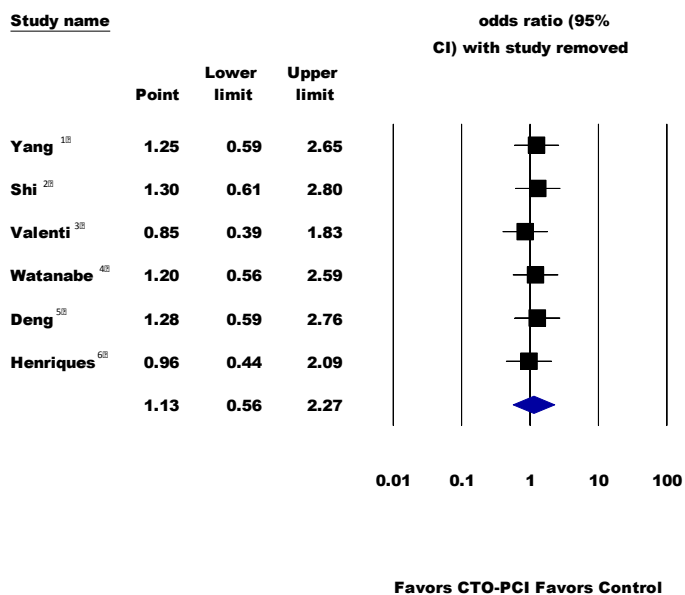
C. Cardiovascular Mortality



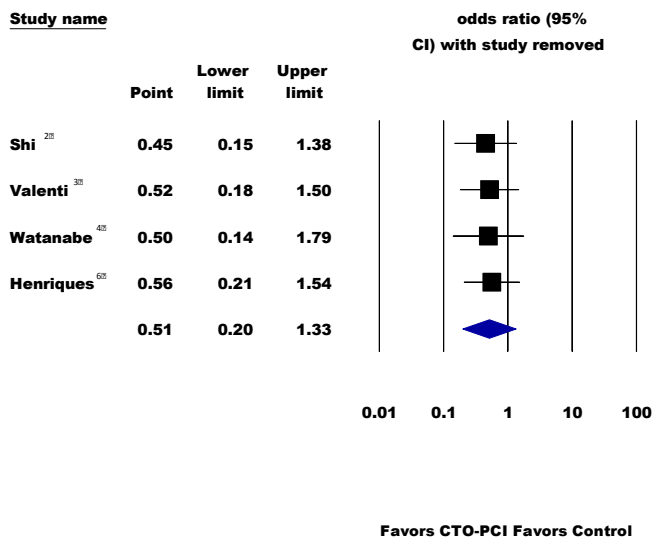
D. Myocardial Infarction



E. Repeat Revascularization



F. Stroke



G. Heart Failure

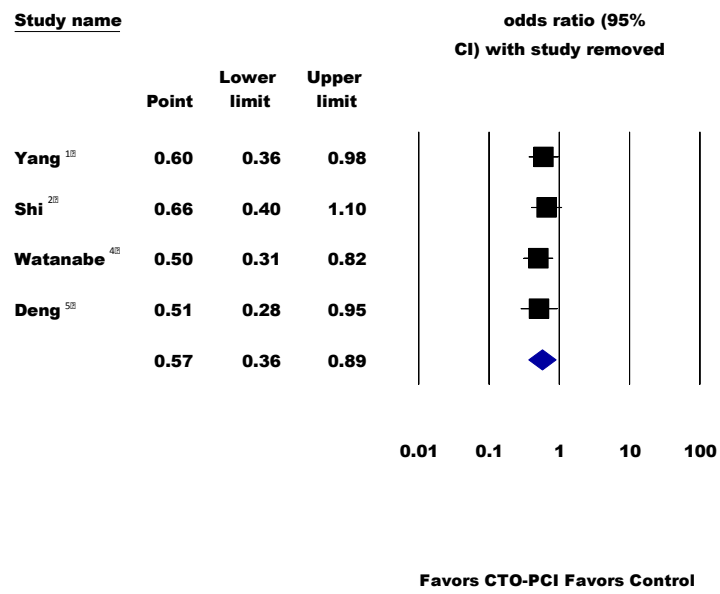
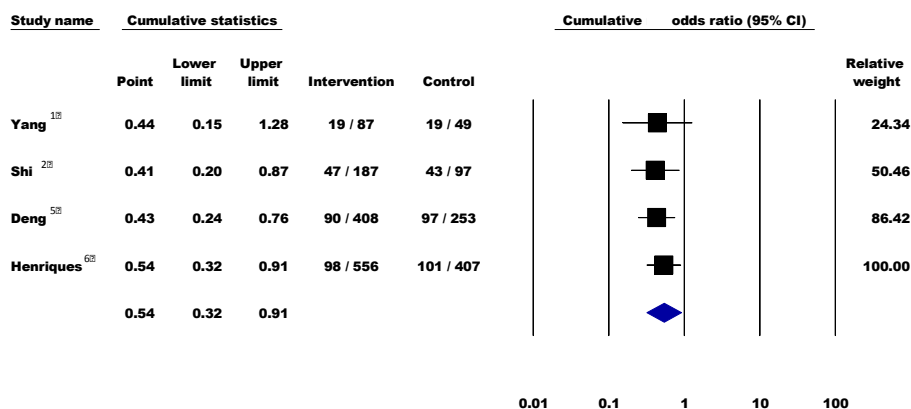


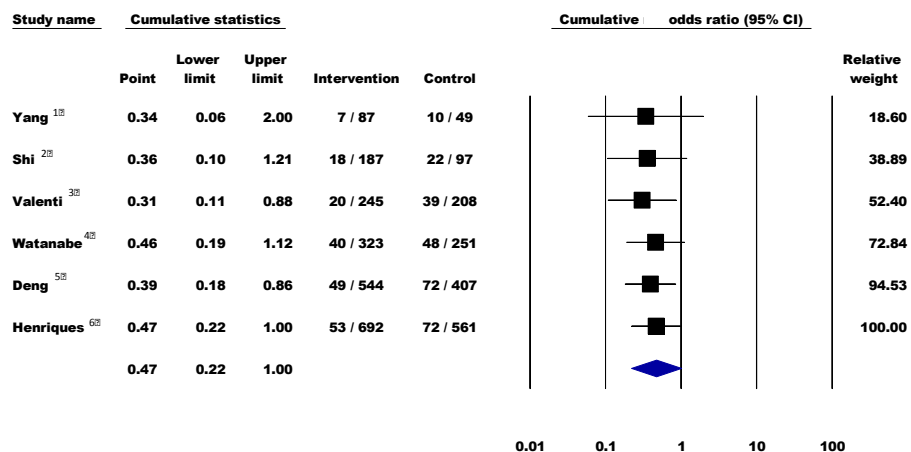
Figure S2. Cumulative analysis for Each Outcome.

A. Major Adverse Cardiovascular Events



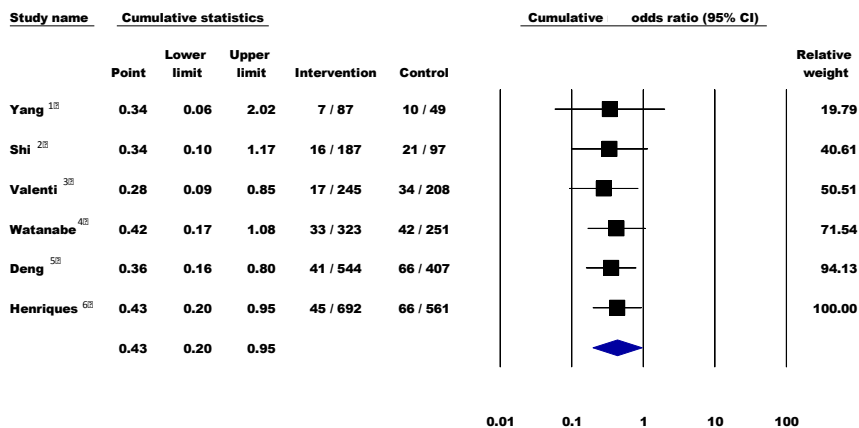
Favors CTO-PCI Favours Control

B. All-Cause Mortality



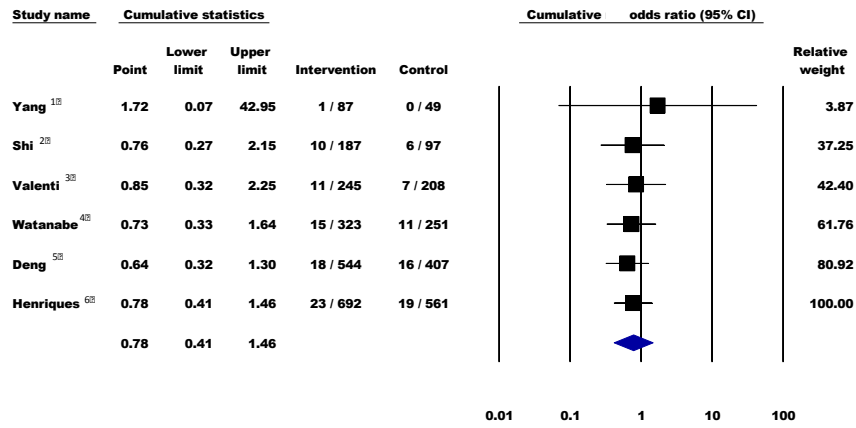
Favors CTO-PCI Favours Control

C. Cardiovascular Mortality



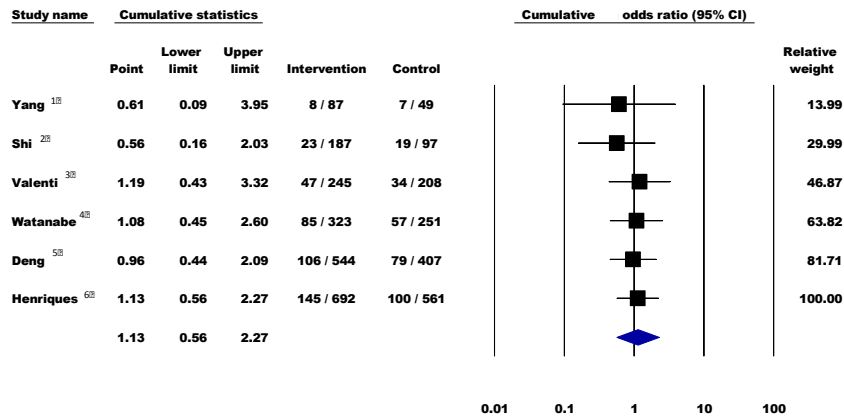
Favors CTO-PCI Favours Control

D. Myocardial Infarction



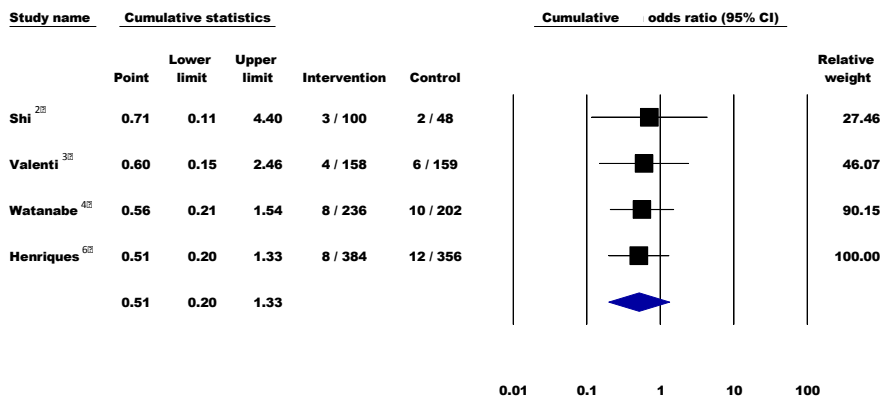
Favors CTO-PCI Favours Control

E. Repeat Revascularization



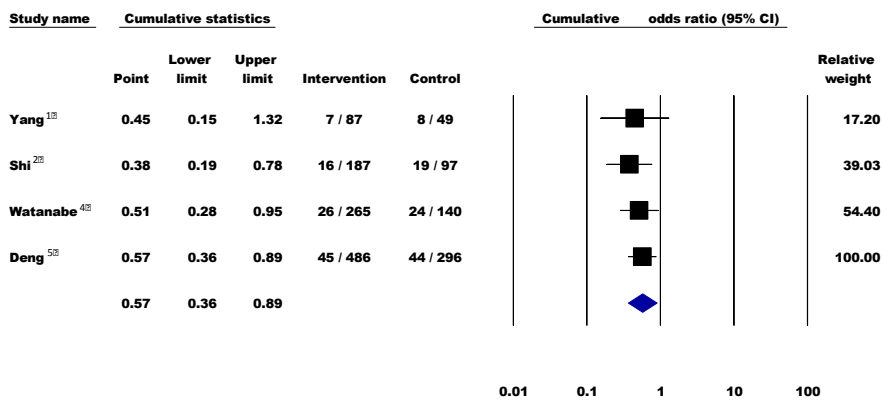
Favors CTO-PCI Favours Control

F. Stroke



Favors CTO-PCI Favours Control

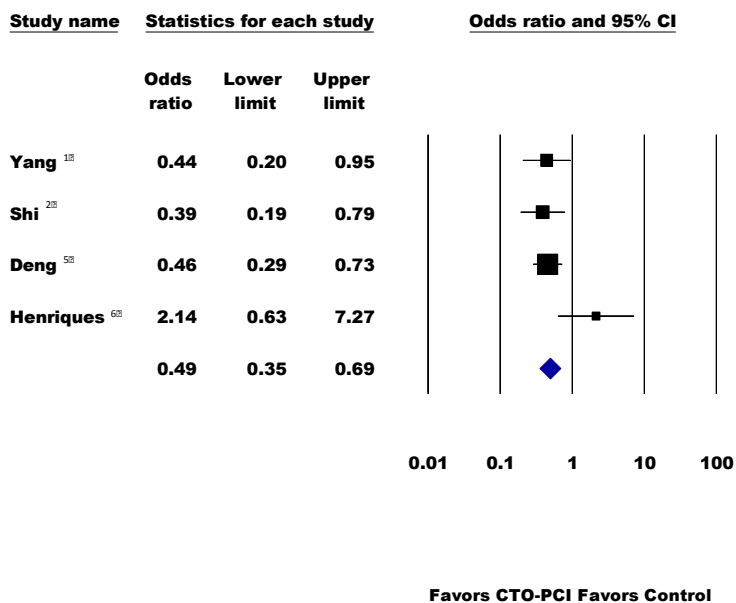
G. Heart Failure



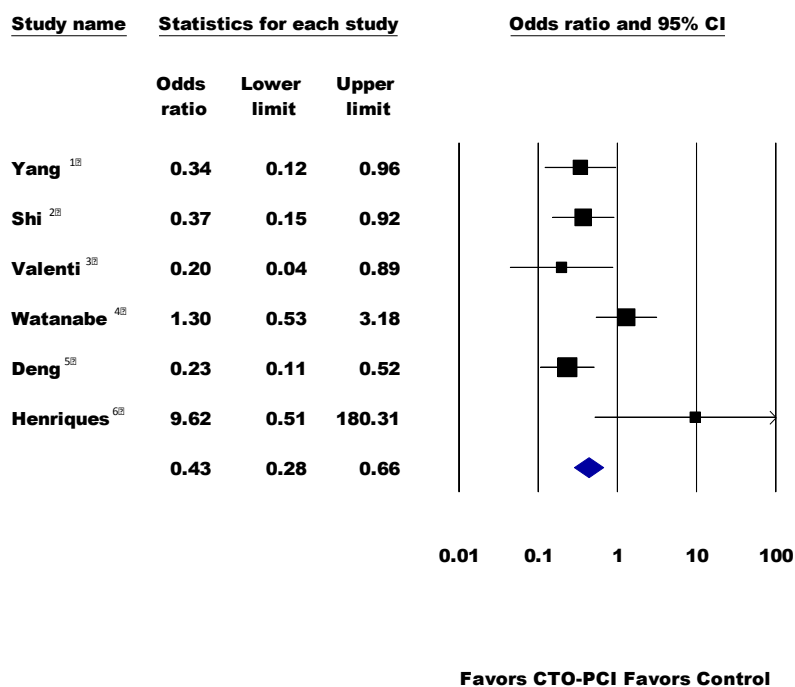
Favors CTO-PCI Favors Control

Figure S3. Sensitivity Analysis with fixed effect model.

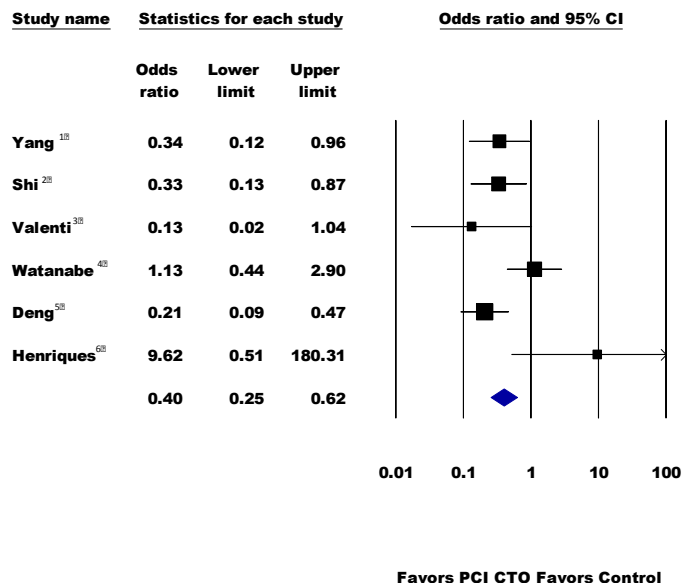
A. Major Adverse Cardiovascular Events



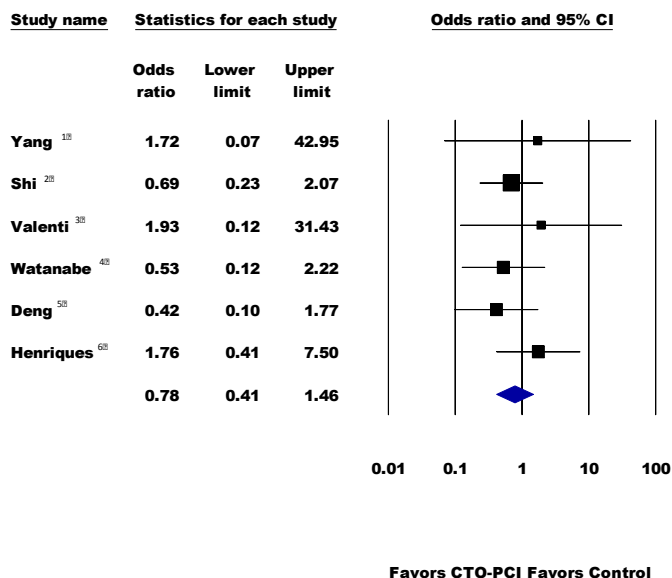
B. All-Cause Mortality



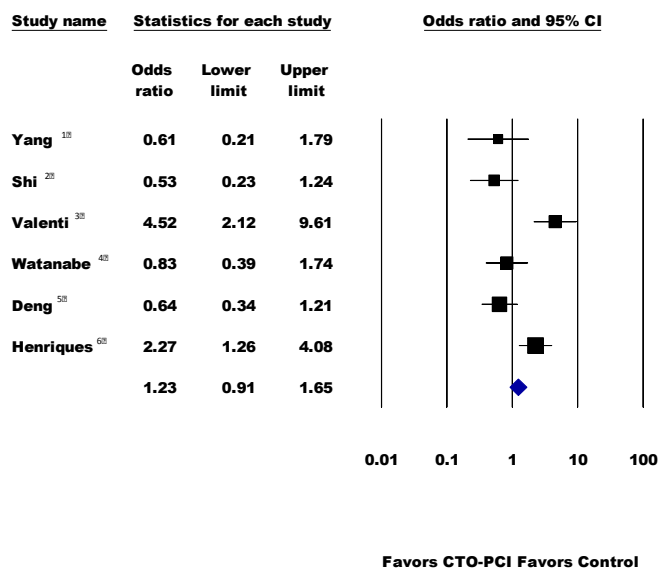
C. Cardiovascular Mortality



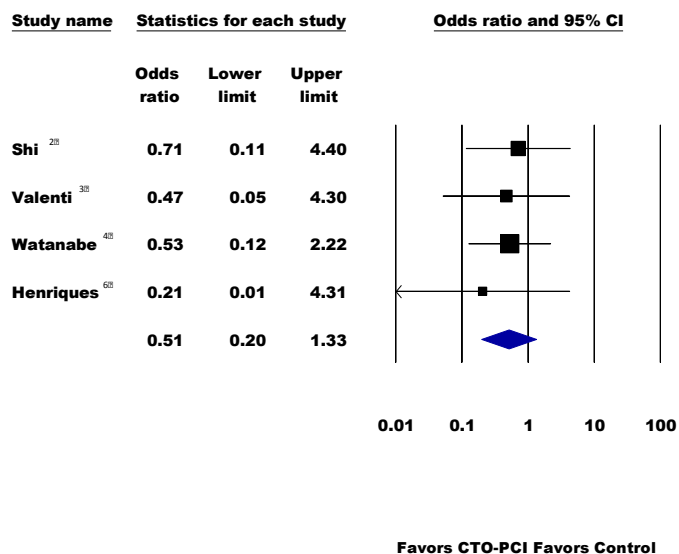
D. Myocardial Infarction



E. Repeat Revascularization



F. Stroke



G. Heart Failure

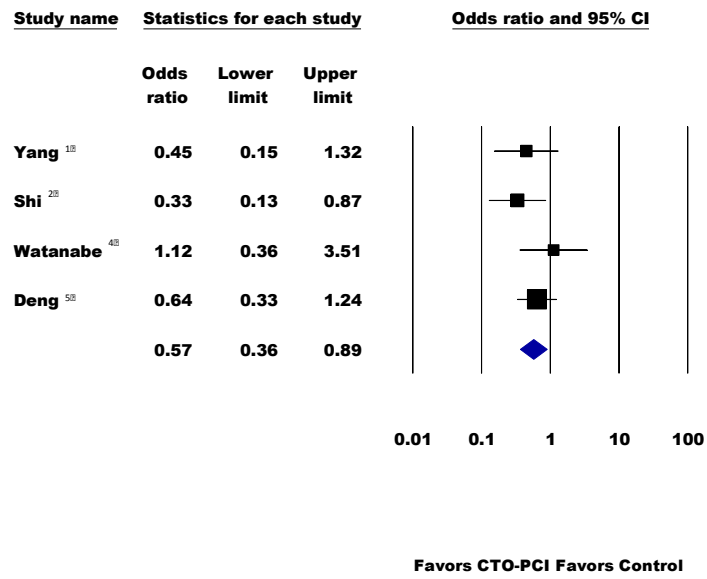
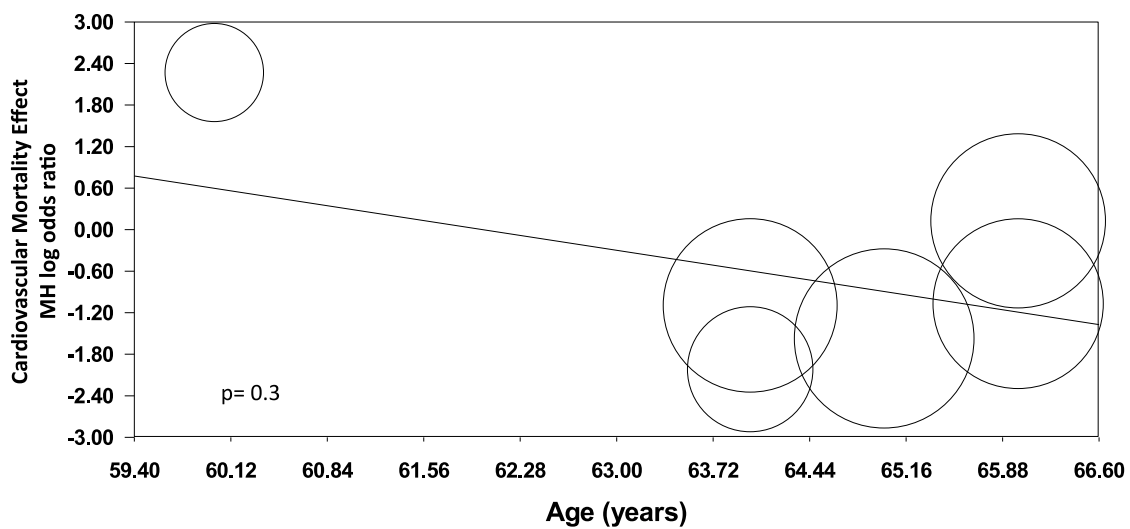
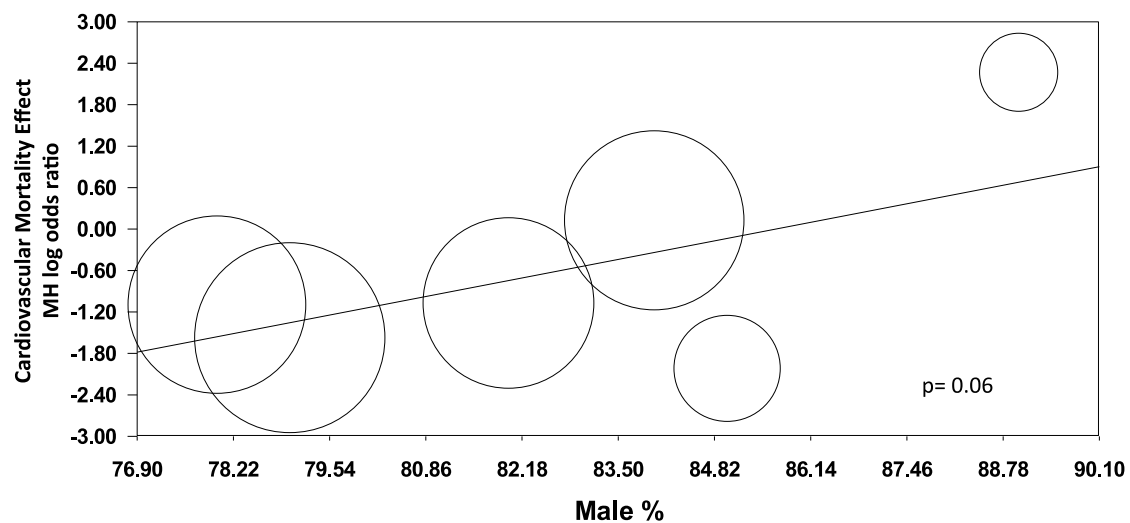


Figure S4. Meta-regression analysis by representative plots.

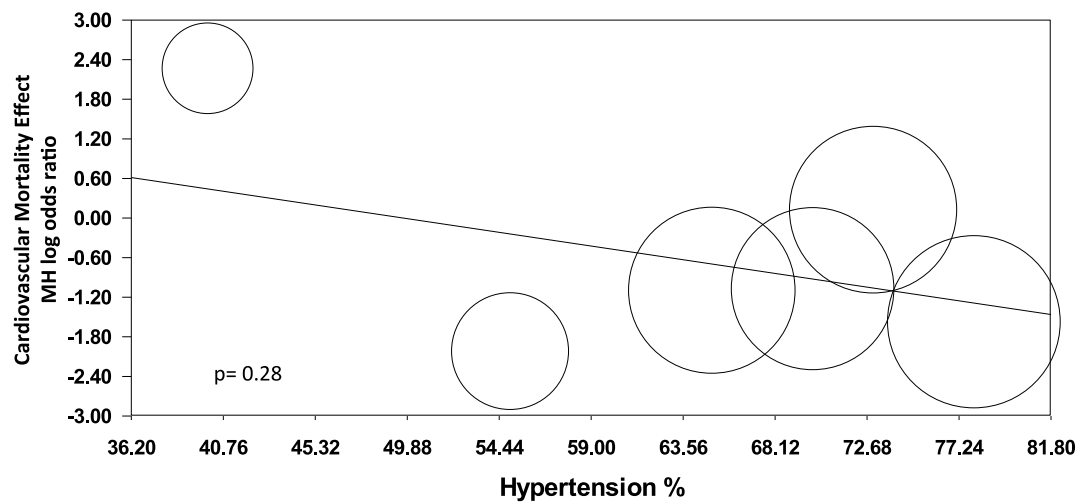
A. Age



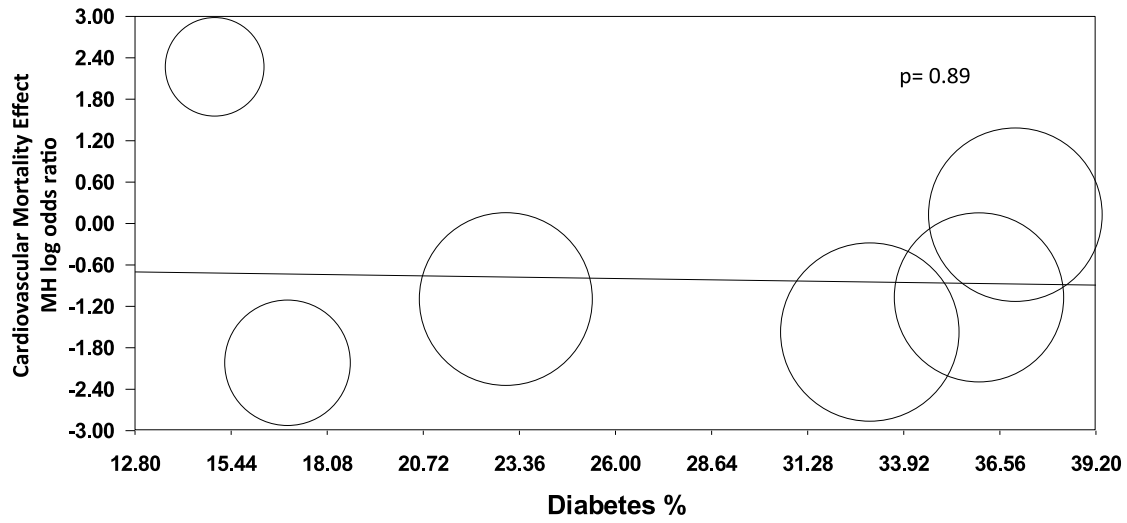
B. Male sex



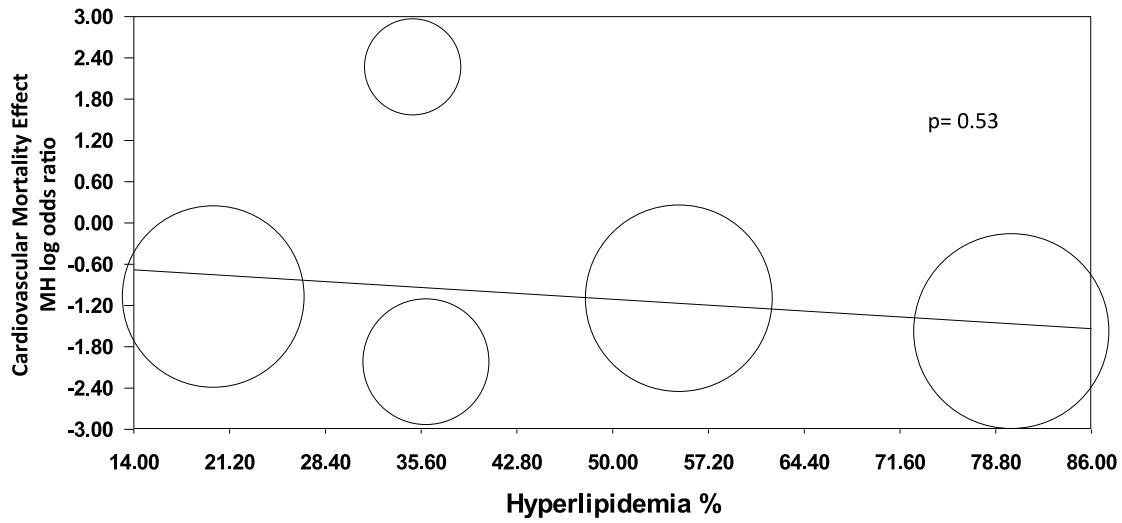
C. Hypertension



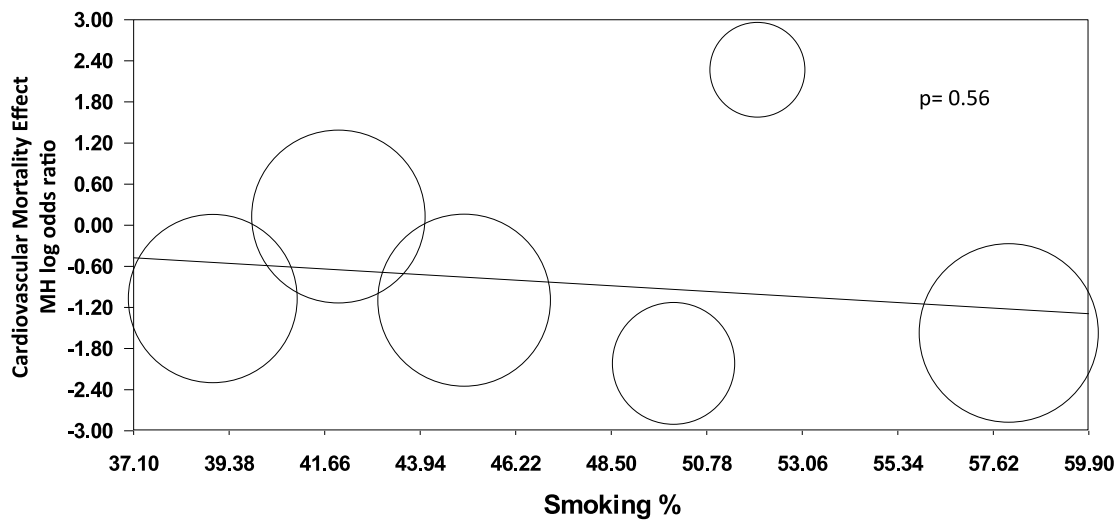
D. Diabetes Mellitus



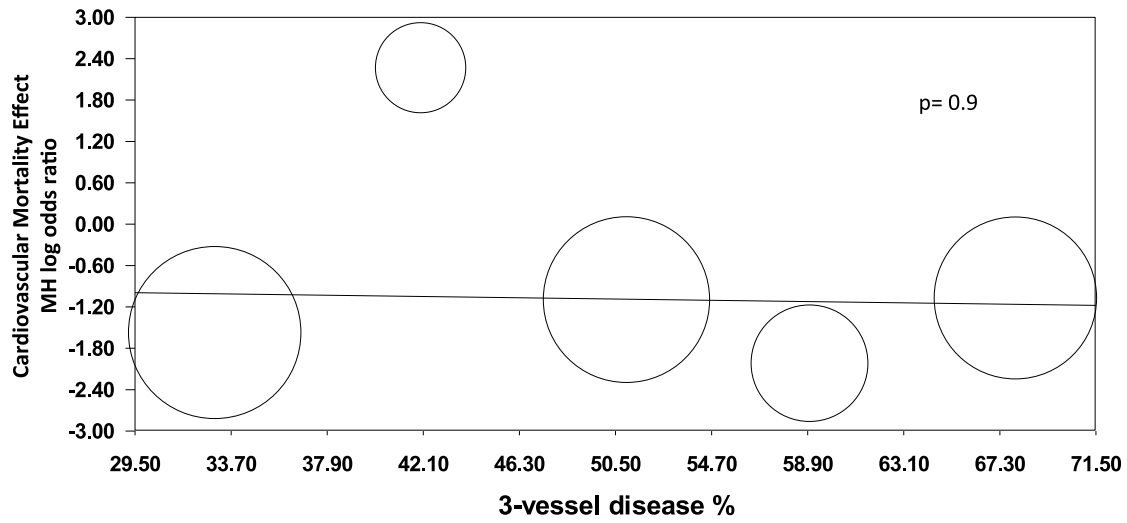
E. Hyperlipidemia



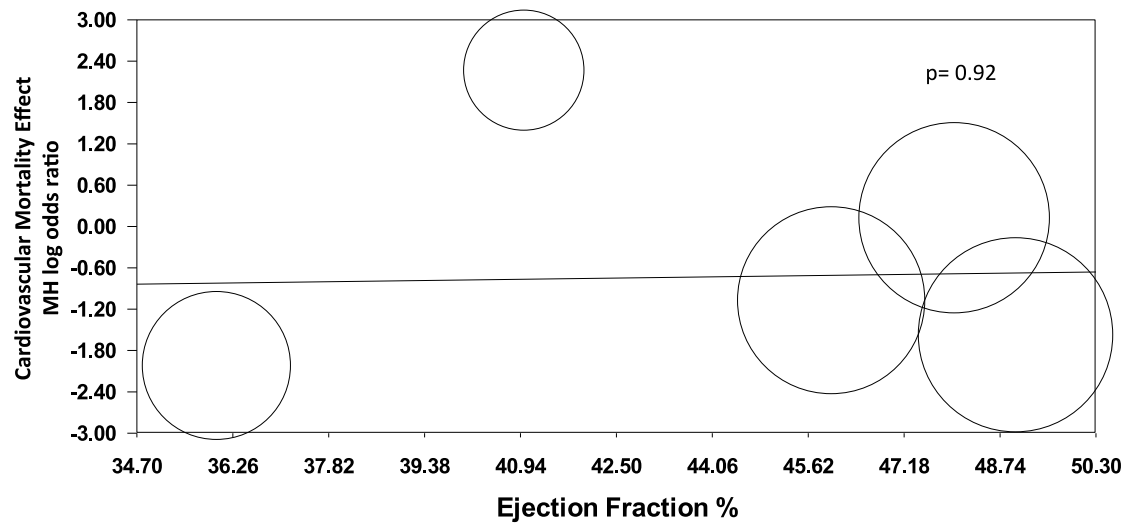
F. Smoking



G. 3-vessel disease



H. Ejection Fraction



I. CTO of the left anterior descending artery

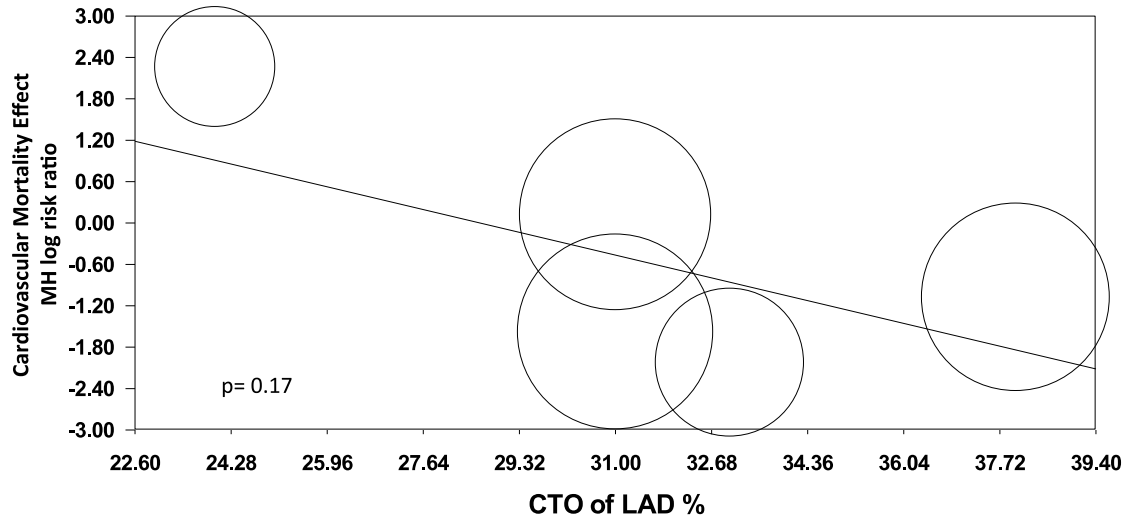
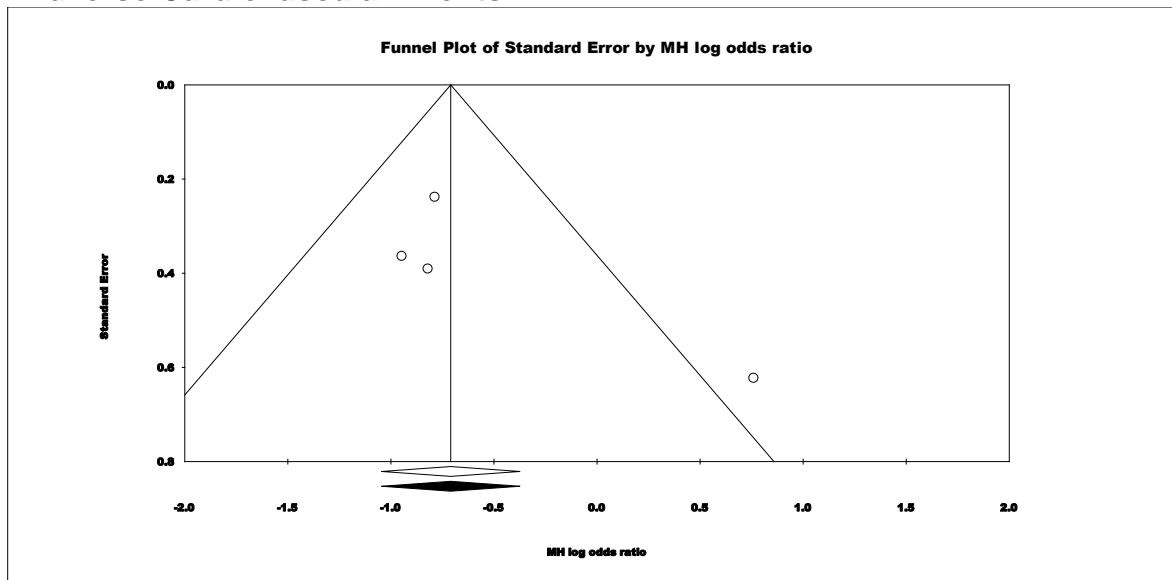
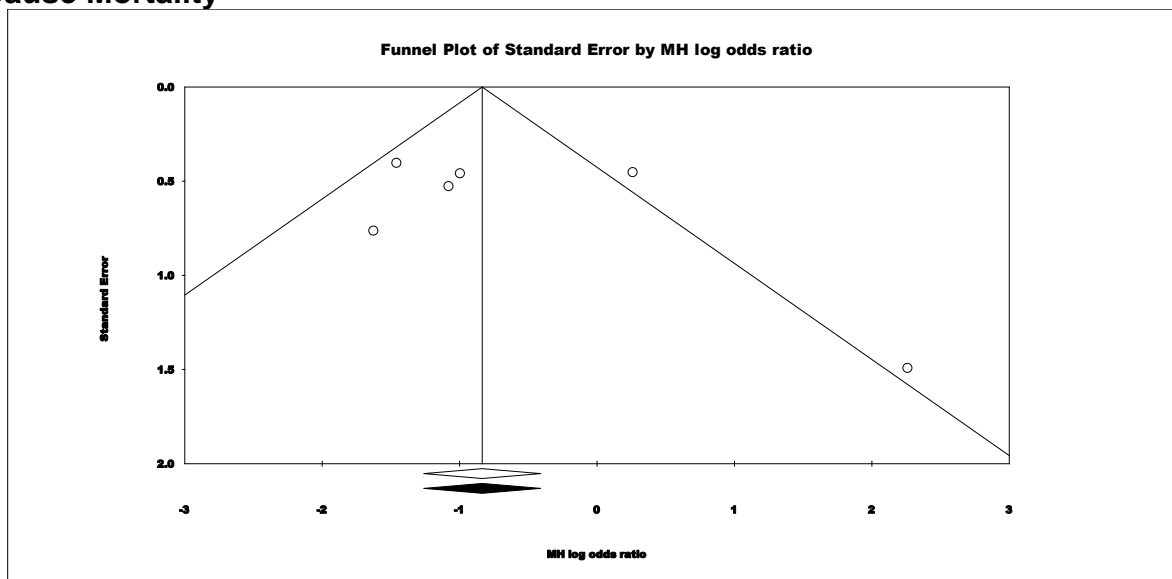


Figure S5. Funnel Plots for each outcome.

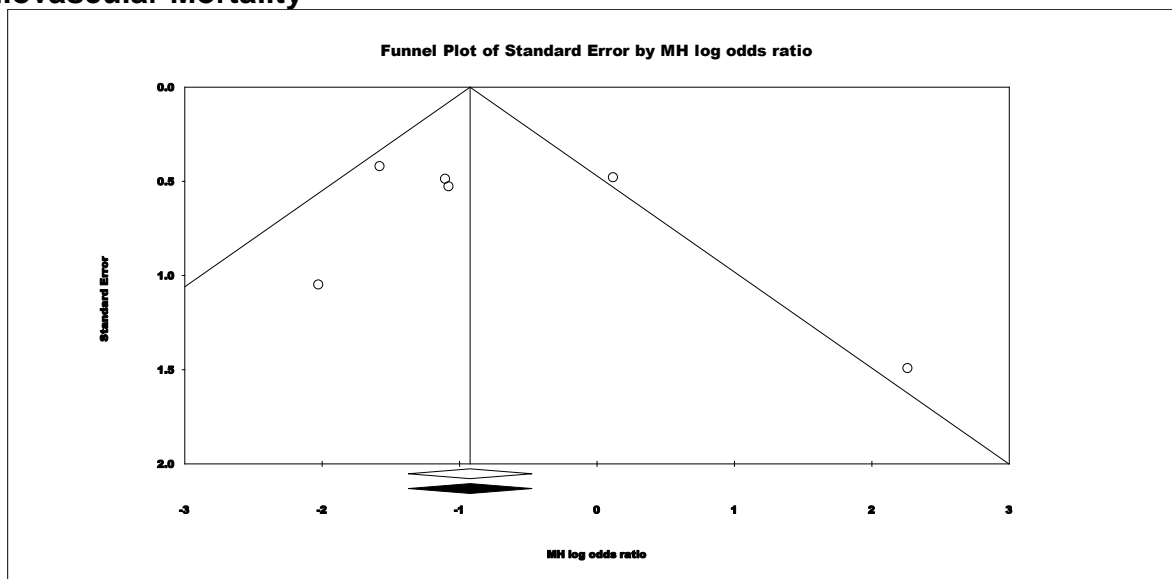
A. Major Adverse Cardiovascular Events



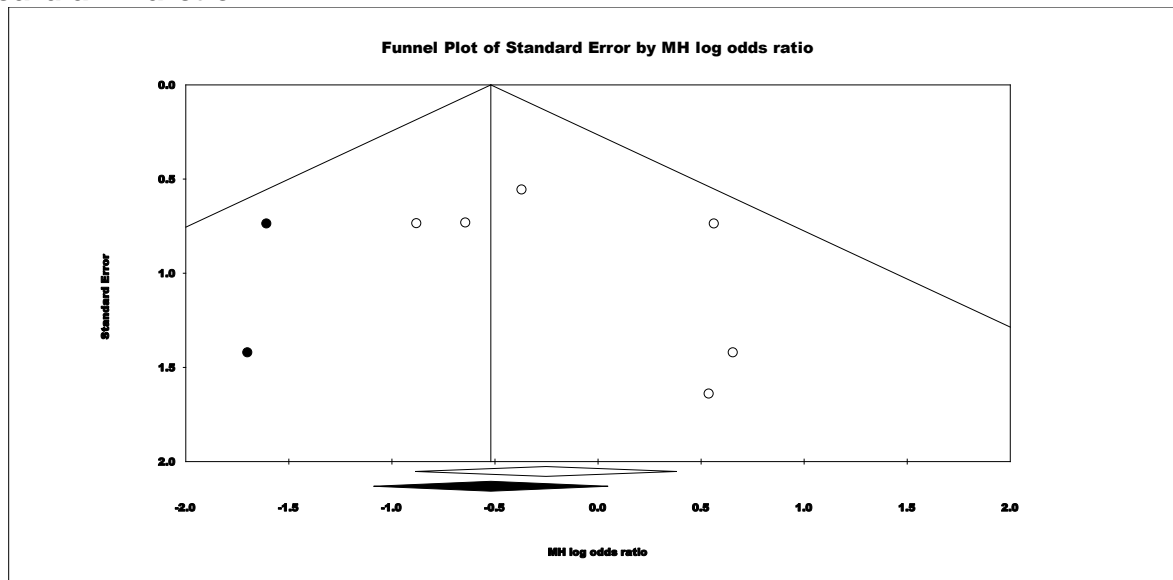
B. All-Cause Mortality



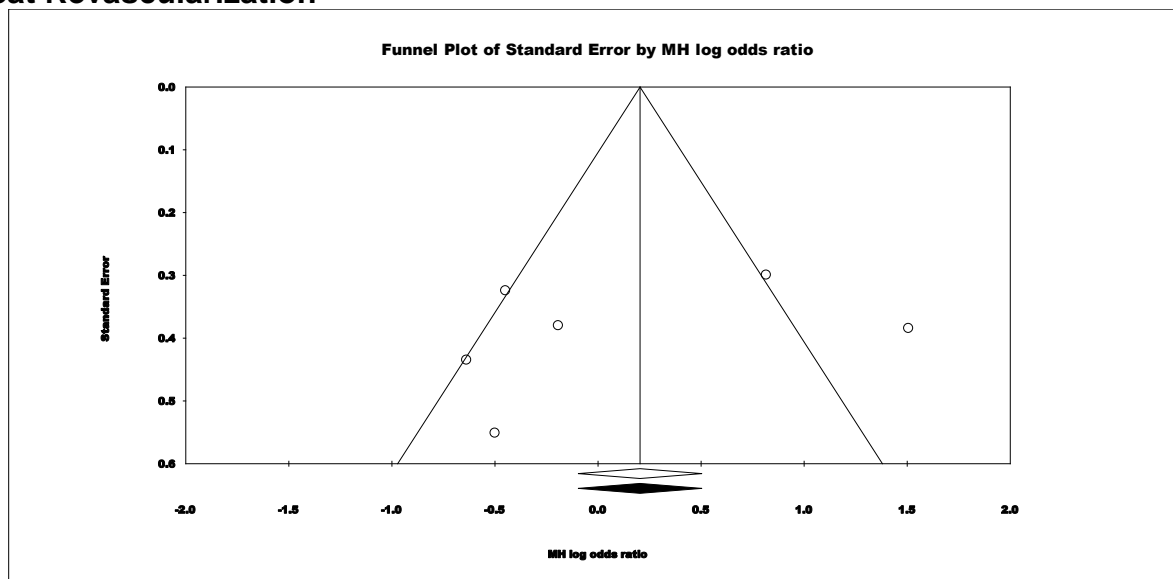
C. Cardiovascular Mortality



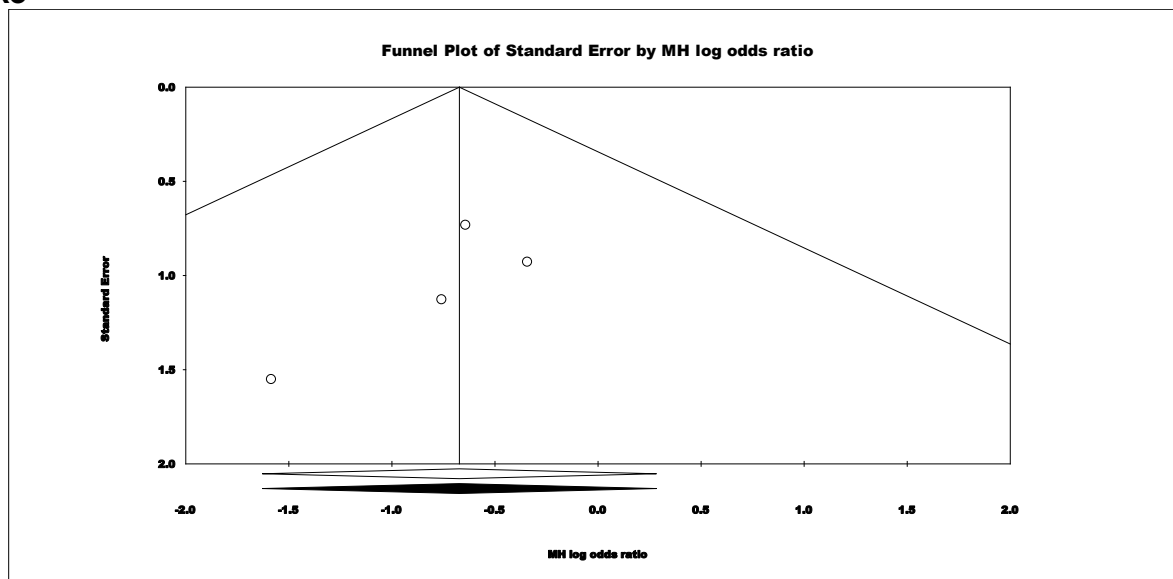
D. Myocardial Infarction



E. Repeat Revascularization



F. Stroke



G. Heart Failure

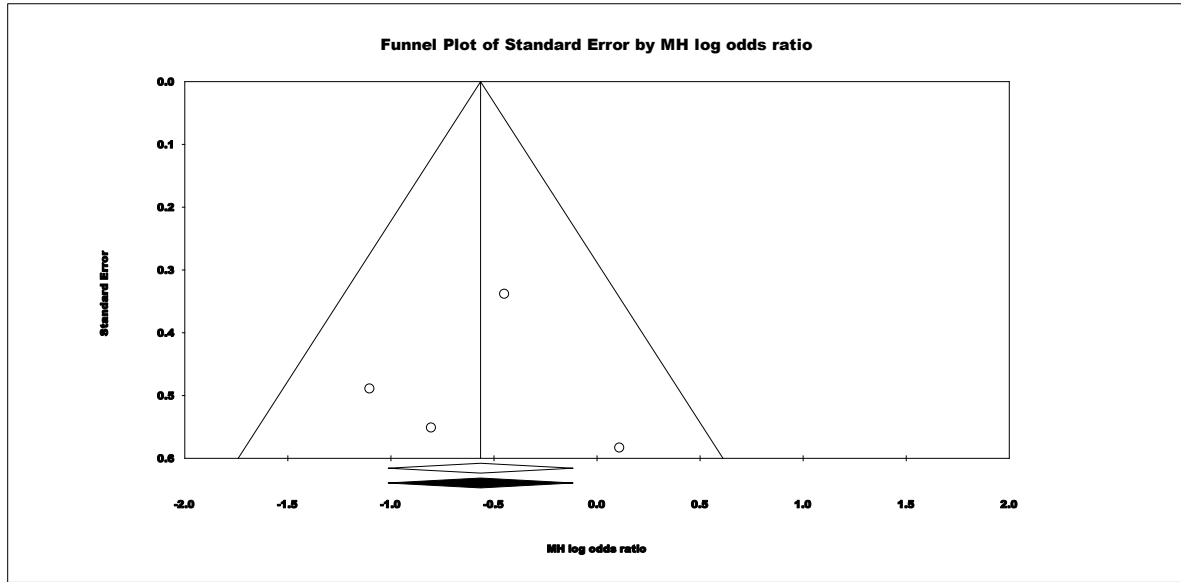


Figure S6. Quantification of Bias for each outcome using Begg and Mazumbar rank correlation, Egger's regression intercept, Duval and Tweedie's trim and fill test.

A. Major Adverse Cardiovascular Events

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) 4.00000

Kendall's tau without continuity correction

Tau 0.66667
 z-value for tau 1.35873
 P-value (1-tailed) 0.08712
 P-value (2-tailed) 0.17423

Kendall's tau with continuity correction

Tau 0.50000
 z-value for tau 1.01905
 P-value (1-tailed) 0.15409
 P-value (2-tailed) 0.30818

Egger's regression intercept

Intercept 2.82248
 Standard error 1.93455
 95% lower limit (2-tailed) -5.50120
 95% upper limit (2-tailed) 11.14615
 t-value 1.45899
 df 2.00000
 P-value (1-tailed) 0.14098
 P-value (2-tailed) 0.28196

Duval and Tweedie's trim and fill

	Fixed Effects			Random Effects			Q Value	
	Studies Trimmed	Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit		Upper Limit
Observed values		0.49182	0.35159	0.68797	0.53540	0.31619	0.90657	6.16125
Adjusted values	0	0.49182	0.35159	0.68797	0.53540	0.31619	0.90657	6.16125

B. All-Cause Mortality

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) 1.00000

Kendall's tau without continuity correction

Tau 0.06667
 z-value for tau 0.18787
 P-value (1-tailed) 0.42549
 P-value (2-tailed) 0.85098

Kendall's tau with continuity correction

Tau 0.00000
 z-value for tau 0.00000
 P-value (1-tailed) 0.50000
 P-value (2-tailed) 1.00000

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) 1.00000

Kendall's tau without continuity correction

Tau 0.06667
 z-value for tau 0.18787
 P-value (1-tailed) 0.42549
 P-value (2-tailed) 0.85098

Kendall's tau with continuity correction

Tau 0.00000
 z-value for tau 0.00000
 P-value (1-tailed) 0.50000
 P-value (2-tailed) 1.00000

Duval and Tweedie's trim and fill

	Fixed Effects				Random Effects			Q Value
	Studies Trimmed	Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit	Upper Limit	
Observed values		0.43373	0.28356	0.66342	0.46831	0.21889	1.00193	13.81572
Adjusted values	0	0.43373	0.28356	0.66342	0.46831	0.21889	1.00193	13.81572

C. Cardiovascular Mortality

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) 3.00000

Kendall's tau without continuity correction

Tau 0.20000
 z-value for tau 0.56360
 P-value (1-tailed) 0.28651
 P-value (2-tailed) 0.57303

Kendall's tau with continuity correction

Tau 0.13333
 z-value for tau 0.37573
 P-value (1-tailed) 0.35356
 P-value (2-tailed) 0.70711

Egger's regression intercept

Intercept 1.42876
 Standard error 1.96083
 95% lower limit (2-tailed) -4.01539
 95% upper limit (2-tailed) 6.87291
 t-value 0.72865
 df 4.00000
 P-value (1-tailed) 0.25329
 P-value (2-tailed) 0.50658

Duval and Tweedie's trim and fill

	Studies Trimmed	Fixed Effects			Random Effects			Q Value
		Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit	Upper Limit	
Observed values		0.39713	0.25323	0.62281	0.43158	0.19588	0.95089	12.941
Adjusted values	0	0.39713	0.25323	0.62281	0.43158	0.19588	0.95089	12.941

D. Myocardial Infarction

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) 3.00000

Kendall's tau without continuity correction

Tau 0.20000
 z-value for tau 0.56360
 P-value (1-tailed) 0.28651
 P-value (2-tailed) 0.57303

Kendall's tau with continuity correction

Tau 0.13333
 z-value for tau 0.37573
 P-value (1-tailed) 0.35356
 P-value (2-tailed) 0.70711

Egger's regression intercept

Intercept 1.01257
 Standard error 0.94028
 95% lower limit (2-tailed) -1.59806
 95% upper limit (2-tailed) 3.62320
 t-value 1.07689
 df 4.00000
 P-value (1-tailed) 0.17107
 P-value (2-tailed) 0.34215

Duval and Tweedie's trim and fill

	Fixed Effects				Random Effects			Q Value
	Studies Trimmed	Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit	Upper Limit	
Observed values		0.77693	0.41248	1.46339	0.77693	0.41248	1.46339	2.90450
Adjusted values	2	0.59445	0.33683	1.04912	0.59445	0.33683	1.04912	6.42938

E. Repeat Revascularization

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) -1.00000

Kendall's tau without continuity correction

Tau -0.06667
 z-value for tau 0.18787
 P-value (1-tailed) 0.42549
 P-value (2-tailed) 0.85098

Kendall's tau with continuity correction

Tau 0.00000
 z-value for tau 0.00000
 P-value (1-tailed) 0.50000
 P-value (2-tailed) 1.00000

Egger's regression intercept

Intercept -3.89586
 Standard error 5.26703
 95% lower limit (2-tailed) -18.51948
 95% upper limit (2-tailed) 10.72775
 t-value 0.73967
 df 4.00000
 P-value (1-tailed) 0.25028
 P-value (2-tailed) 0.50056

Duval and Tweedie's trim and fill

	Studies Trimmed	Fixed Effects			Random Effects			Q Value
		Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit	Upper Limit	
Observed values		1.22605	0.90868	1.65426	1.12785	0.56010	2.27111	26.10472
Adjusted values	0	1.22605	0.90868	1.65426	1.12785	0.56010	2.27111	26.10472

F. Stroke

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) -4.00000

Kendall's tau without continuity correction

Tau -0.66667
z-value for tau 1.35873
P-value (1-tailed) 0.08712
P-value (2-tailed) 0.17423

Kendall's tau with continuity correction

Tau -0.50000
z-value for tau 1.01905
P-value (1-tailed) 0.15409
P-value (2-tailed) 0.30818

Egger's regression intercept

Intercept -0.98881
Standard error 0.64868
95% lower limit (2-tailed) -3.77985
95% upper limit (2-tailed) 1.80224
t-value 1.52434
df 2.00000
P-value (1-tailed) 0.13345
P-value (2-tailed) 0.26691

Duval and Tweedie's trim and fill

	Studies Trimmed	Fixed Effects			Random Effects			Q Value
		Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit	Upper Limit	
Observed values		0.51041	0.19632	1.32704	0.51041	0.19632	1.32704	0.47813
Adjusted values	0	0.51041	0.19632	1.32704	0.51041	0.19632	1.32704	0.47813

G. Heart Failure

Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q) 2.00000

Kendall's tau without continuity correction

Tau 0.33333
z-value for tau 0.67937
P-value (1-tailed) 0.24845
P-value (2-tailed) 0.49691

Kendall's tau with continuity correction

Tau 0.16667
z-value for tau 0.33968
P-value (1-tailed) 0.36705
P-value (2-tailed) 0.73410

Egger's regression intercept

Intercept -0.08401
Standard error 2.66251
95% lower limit (2-tailed) -11.53985
95% upper limit (2-tailed) 11.37184
t-value 0.03155
df 2.00000
P-value (1-tailed) 0.48885
P-value (2-tailed) 0.97770

Duval and Tweedie's trim and fill

	Studies Trimmed	Fixed Effects			Random Effects			Q Value
		Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit	Upper Limit	
Observed values		0.56840	0.36290	0.89028	0.56840	0.36290	0.89028	2.84170
Adjusted values	0	0.56840	0.36290	0.89028	0.56840	0.36290	0.89028	2.84170

Supplemental References:

1. Yang ZK, Zhang RY, Hu J, Zhang Q, Ding FH, Shen WF. Impact of successful staged revascularization of a chronic total occlusion in the non-infarct-related artery on long-term outcome in patients with acute st-segment elevation myocardial infarction. *Int J Cardiol.* 2013;165:76-79.
2. Shi G, He P, Liu Y, Lin Y, Yang X, Chen J, Zhou Y, Tan N. Evaluation of the effect of concurrent chronic total occlusion and successful staged revascularization on long-term mortality in patients with st-elevation myocardial infarction. *ScientificWorldJournal.* 2014;2014:756080.
3. Valenti R, Marrani M, Cantini G, Migliorini A, Carrabba N, Vergara R, Cerisano G, Parodi G, Antoniucci D. Impact of chronic total occlusion revascularization in patients with acute myocardial infarction treated by primary percutaneous coronary intervention. *The American journal of cardiology.* 2014;114:1794-1800.
4. Watanabe H, Morimoto T, Shiomi H, Furukawa Y, Nakagawa Y, Ando K, Kadota K, Kimura T. Chronic total occlusion in a non-infarct-related artery is closely associated with increased five-year mortality in patients with st-segment elevation acute myocardial infarction undergoing primary percutaneous coronary intervention (from the credo-kyoto ami registry). *EuroIntervention.* 2017;12:e1874-e1882.
5. Deng J, Wang X, Shi Y, Zhao X, Han Y. Prognostic value of the age, creatinine, and ejection fraction score for non-infarct-related chronic total occlusion revascularization after primary percutaneous intervention in acute st-elevation myocardial infarction patients: A retrospective study. *J Interv Cardiol.* 2018;31:33-40.
6. Henriques JP, Hoebbers LP, Ramunddal T, Laanmets P, Eriksen E, Bax M, Ioanes D, Suttorp MJ, Strauss BH, Barbato E, Nijveldt R, van Rossum AC, Marques KM, Elias J, van Dongen IM, Claessen BE, Tijssen JG, van der Schaaf RJ, Investigators ET. Percutaneous intervention for concurrent chronic total occlusions in patients with stemi: The explore trial. *Journal of the American College of Cardiology.* 2016;68:1622-1632.