

Supplementary Table S1 Definition of outcomes.

| Study | Definitions |
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| Aoki 2005 | <p>All-cause death: Deaths from all causes were reported.</p> <p>Myocardial infarction: In the first 7 days after the intervention, a definite diagnosis of myocardial infarction was made if there was documentation of new abnormal Q waves and either cardiac enzymes greater than five times the upper limit of normal or a ratio of peak serum creatinine kinase-myocardial band to creatinine kinase greater than 0.1. From the eighth day onwards, either abnormal Q waves or enzymatic changes were sufficient for a diagnosis of myocardial infarction.</p> |
| Chang 2012 | Not reported. |
| Chang 2013 | <p>All-cause death: Death from any cause.</p> <p>Acute coronary syndrome: Either acute myocardial infarction or unstable angina.</p> <p>Repeat revascularization: Coronary artery bypass grafting procedures occurring within 14 days of the initial revascularization and percutaneous coronary interventions occurring within 3 days of the initial revascularization were considered part of the index procedure and not as repeat revascularizations.</p> |
| Bangalore 2015 | <p>Myocardial infarction: Myocardial infarction included both procedural myocardial infarction (defined as new Q waves in both the Percutaneous Coronary Intervention Reporting System and the Cardiac Surgery Reporting System) and spontaneous myocardial infarction (defined as an emergency admission with a principal diagnosis of myocardial infarction or a principal diagnosis of cardiogenic shock with a secondary diagnosis of myocardial infarction).</p> <p>Stroke: Stroke was identified either as a complication at the time of the index procedure or at readmission (principal diagnosis of stroke).</p> <p>Repeat revascularization: Repeat revascularization was identified as any unstaged revascularization after the index procedure.</p> |

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| | <p>Staged revascularization was defined as a nontarget vessel revascularization within 90 days of the index procedure that was coded as intended to be staged in the index procedure and at the time of the staged procedure.</p> |
| Chan 2015 | <p>Not reported.</p> |
| Komiya 2015 | <p>All-cause death: Death from any cause. Death was regarded as cardiac in origin unless obvious non-cardiac causes could be identified.</p> <p>Myocardial infarction: In the first 7 days after the intervention, a definite diagnosis of myocardial infarction was made if there was documentation of new abnormal Q waves and either cardiac enzymes greater than five times the upper limit of normal or a ratio of peak serum creatinine kinase-myocardial band to creatinine kinase greater than 0.1. From the eighth day onwards, either abnormal Q waves or enzymatic changes were sufficient for a diagnosis of myocardial infarction.</p> <p>Stroke: Stroke was defined as an ischemic or hemorrhagic stroke with symptoms lasting more than 24 h either during the index hospitalization for the initial coronary revascularization or requiring hospitalization during follow-up.</p> <p>Repeat revascularization: Any revascularization performed after 3 months of the initial procedure.</p> |
| Baber 2016 | <p>Myocardial infarction: Spontaneous myocardial infarction was defined as a typical increase in the troponin level or a more rapid rise and fall in the myocardial band fraction of creatine kinase with the presence of one or more of the following factors: ischemic symptoms, development of pathologic Q waves on electrocardiography, changes indicative of ischemia on electrocardiography, the need for repeated coronary artery intervention, or pathologic findings of an acute myocardial infarction. Periprocedural myocardial infarction was defined as the presence of new Q waves in at least 2 or more contiguous leads when compared to baseline within 30 days of any revascularization procedure. Analyses for the outcome of myocardial infarction were repeated after excluding periprocedural events.</p> <p>Stroke: A focal neurological deficit of central origin lasting more than 72 hours; or A focal neurological deficit of central origin</p> |

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| | <p>lasting more than 24 hours with imaging evidence of cerebral infarction or intracerebral hemorrhage; or A non-focal encephalopathy lasting more than 24 hours with imaging evidence of cerebral infarction or hemorrhage adequate to account for the clinical state.</p> |
| Giustino 2018 | <p>All-cause death: Death from any cause. The cause of death will be adjudicated as being due to cardiovascular causes, non-cardiovascular causes, or undetermined causes.</p> <p>Myocardial infarction: Myocardial infarction included both post-procedure myocardial infarction and spontaneous myocardial infarction. Post-procedure myocardial infarction: Defined as the occurrence within 72 hours after either percutaneous coronary intervention or coronary artery bypass grafting of either: creatinine kinase-myocardial band >10x upper reference limit, or creatinine kinase-myocardial band >5x upper reference limit, plus new pathological Q waves in at least 2 contiguous leads or new persistent non-rate related left bundle branch block, or angiographically documented graft or native coronary artery occlusion or new severe stenosis with thrombosis and/or diminished epicardial flow, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. Spontaneous myocardial infarction: Defined as the occurrence >72 hours after any percutaneous coronary intervention or coronary artery bypass grafting of: The rise and/or fall of cardiac biomarkers (creatinine kinase-myocardial band or troponin) >1x upper reference limit, plus: electrocardiogram changes indicative of new ischemia [ST-segment elevation or depression, in the absence of other causes of ST-segment changes such as left ventricular hypertrophy or bundle branch block], or development of pathological Q waves (≥ 0.04 seconds in duration and ≥ 1 mm in depth) in ≥ 2 contiguous precordial leads or ≥ 2 adjacent limb leads) of the electrocardiogram, or angiographically documented graft or native coronary artery occlusion or new severe stenosis with thrombosis and/or diminished epicardial flow, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.</p> <p>Stroke: Strokes will be classified as ischemic, hemorrhagic, or unknown. Four criteria must be fulfilled to diagnosis stroke:</p> |

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| | <p>1. Rapid onset of a focal/global neurological deficit with at least one of the following: change in level of consciousness, hemiplegia, hemiparesis, numbness or sensory loss affecting one side of the body, dysphasia/aphasia, hemianopia, amaurosis fugax, other new neurological sign(s)/symptom(s) consistent with stroke; and</p> <p>2. Duration of a focal/global neurological deficit ≥ 24 hours or < 24 hours if any of the following conditions exist: i. At least one of the following therapeutic interventions: a. Pharmacologic (i.e., thrombolytic drug administration) b. Non-pharmacologic (i.e., neurointerventional procedure such as intracranial angioplasty) ii. Available brain imaging clearly documents a new hemorrhage or infarct iii. The neurological deficit results in death</p> <p>3. No other readily identifiable non-stroke cause for the clinical presentation (e.g., brain tumor, trauma, infection, hypoglycemia, other metabolic abnormality, peripheral lesion, or drug side effect). Patients with non-focal global encephalopathy will not be reported as a stroke without unequivocal evidence based upon neuroimaging studies.</p> <p>4. Confirmation of the diagnosis by a neurology or neurosurgical specialist and at least one of the following: a. Brain imaging procedure (at least one of the following): i. computerized tomography scan ii. magnetic resonance imaging scan iii. Cerebral vessel angiography b. Lumbar puncture (i.e. spinal fluid analysis diagnostic of intracranial hemorrhage).</p> <p>All strokes with stroke disability of modified Rankin Scale ≥ 1 (increase from baseline assessment) will be included in the primary endpoint. All diagnosed strokes (even with modified Rankin Scale 0) will also be tabulated.</p> <p>Ischemia-driven revascularization: A coronary revascularization procedure may be either a coronary artery bypass grafting or a percutaneous coronary intervention.</p> |
| Lima 2018 | <p>Myocardial infarction: Myocardial infarction was blindly adjudicated and defined as the presence of significant new Q waves in at least two electrocardiographic leads or symptoms compatible with myocardial infarction associated with creatine kinase-myocardial band fraction concentrations that were more than three times the upper limit of the reference range.</p> |

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| Milojevic 2018 | <p>All-cause death: Death from any cause. Deaths were considered cardiac unless an unequivocal, noncardiac cause was established.</p> <p>Myocardial infarction: Myocardial infarction was defined in relation to intervention status as follows: i) after allocation but before treatment: Q-wave (new pathological Q-waves in ≥ 2 leads lasting ≥ 0.04 seconds with creatine kinase-myocardial band levels elevated above normal), and non-Q wave myocardial infarction (elevation of creatine kinase levels > 2 times the upper limit of normal with positive creatine kinase-myocardial band or elevation of creatine kinase levels to > 2 times the upper limit of normal without new Q-waves if no baseline creatine kinase-myocardial band was available); ii) < 7d after intervention: new Q-waves and either peak creatine kinase-myocardial band /total creatine kinase $> 10\%$ or plasma level of creatine kinase-myocardial band $5x$ the upper limit of normal; iii) ≥ 7d after intervention: new Q waves or peak creatine kinase-myocardial band /total creatine kinase $> 10\%$ or plasma level of creatine kinase-myocardial band $5x$ the upper limit of normal or plasma level of creatine kinase $5x$ the upper limit of normal.</p> <p>Stroke: Stroke was defined as a focal, central neurological deficit lasting > 72 hours which resulted in irreversible brain damage or body impairment.</p> <p>Repeat revascularization: Repeat revascularization was defined as any repeat percutaneous coronary intervention or coronary artery bypass grafting.</p> |
| Gaipov 2019 | Not reported. |

Supplementary Table S2 Quality assessment of observational studies using the Newcastle–Ottawa scale.

| Study | Selection | Comparability | Outcome | Total Score |
|----------------|-----------|---------------|---------|-------------|
| Chang 2012 | 4 | 2 | 3 | 9 |
| Chang 2013 | 4 | 2 | 3 | 9 |
| Bangalore 2015 | 4 | 2 | 3 | 9 |
| Chan 2015 | 4 | 2 | 3 | 9 |
| Komiya 2015 | 4 | 2 | 3 | 9 |
| Gaipov 2019 | 4 | 2 | 3 | 9 |

Supplementary Table S3 Quality assessment of randomized controlled trials.

| Study | Sequence generation | Concealment of allocation | Blinding of participants, personnel and outcome assessors | Incomplete outcome data addressed | Free of selective reporting | Free of other bias |
|----------------|---------------------|---------------------------|---|-----------------------------------|-----------------------------|--------------------|
| Aoki 2005 | Low | Low | Moderate | Low | Low | Low |
| Baber 2016 | Low | Low | Moderate | Low | Low | Low |
| Giustino 2018 | Low | Low | Moderate | Low | Low | Low |
| Lima 2018 | Low | Low | Moderate | Low | Low | Low |
| Milojevic 2018 | Low | Low | Moderate | Low | Low | Low |

Supplementary Table S4 Publication bias.

| Outcomes | p Egger test | p Begg test |
|---------------------------|--------------|-------------|
| Long-term all-cause death | 0.196 | 1.000 |
| Short-term death | 0.505 | 0.734 |
| Myocardial infarction | 0.839 | 0.754 |
| Stroke | 0.113 | 0.133 |
| Repeat revascularization | 0.237 | 0.902 |

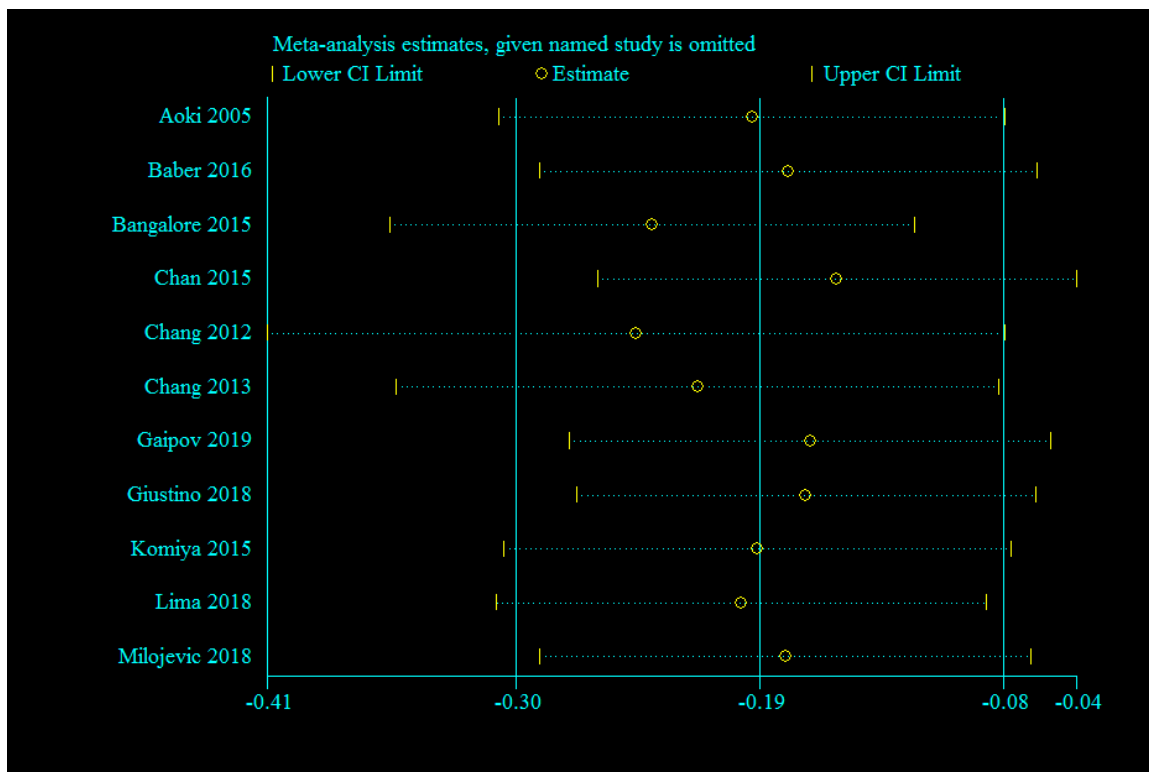
Supplementary Table S5 Meta-regression analysis.

| Outcome | Patient characteristics | Regression coefficient (95% CI) | P value |
|-----------------------|-----------------------------|----------------------------------|--------------|
| Long-term death | Age | -0.021 (-0.071 to 0.028) | 0.346 |
| | Gender | 0.002 (-0.033 to 0.036) | 0.912 |
| | Diabetes | -0.0004 (-0.010 to 0.010) | 0.928 |
| | Hypertension | -0.015 (-0.037 to 0.006) | 0.137 |
| | Dyslipidemia | -0.003 (-0.011 to 0.006) | 0.456 |
| | Prior myocardial infarction | -0.004 (-0.034 to 0.025) | 0.723 |
| Short-term death | Age | -0.119 (-0.186 to 0.424) | 0.235 |
| | Gender | 0.0004 (-0.301 to 0.302) | 0.996 |
| | Diabetes | -0.107 (-0.324 to 0.110) | 0.168 |
| | Hypertension | 0.105 (-0.121 to 0.331) | 0.184 |
| | Dyslipidemia | 0.057 (-0.062 to 0.176) | 0.176 |
| | Prior myocardial infarction | 0.153 (-1.004 to 1.310) | 0.342 |
| Myocardial infarction | Age | -0.070 (-0.333 to 0.194) | 0.542 |
| | Gender | 0.046 (-0.055 to 0.148) | 0.306 |
| | Diabetes | -0.011 (-0.037 to 0.014) | 0.309 |
| | Hypertension | -0.030 (-0.077 to 0.017) | 0.168 |
| | Dyslipidemia | -0.031 (-0.071 to 0.008) | 0.103 |
| | Prior myocardial infarction | -0.045 (-0.089 to -0.001) | 0.047 |
| Stroke | Age | -0.087 (-0.232 to 0.058) | 0.184 |
| | Gender | -0.010 (-0.107 to 0.087) | 0.803 |

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| | Diabetes | 0.012 (-0.008 to 0.033) | 0.187 |
| | Hypertension | 0.022 (-0.022 to 0.065) | 0.256 |
| | Dyslipidemia | 0.002 (-0.040 to 0.045) | 0.899 |
| | Prior myocardial infarction | -0.045 (-0.187 to 0.098) | 0.393 |
| Repeat | Age | -0.180 (-0.420 to 0.060) | 0.116 |
| revascularization | Gender | 0.078 (-0.022 to 0.179) | 0.106 |
| | Diabetes | -0.0004 (-0.028 to 0.027) | 0.972 |
| | Hypertension | -0.003 (-0.054 to 0.047) | 0.880 |
| | Dyslipidemia | -0.001 (-0.050 to 0.048) | 0.957 |
| | Prior myocardial infarction | -0.042 (-0.068 to -0.016) | 0.011 |

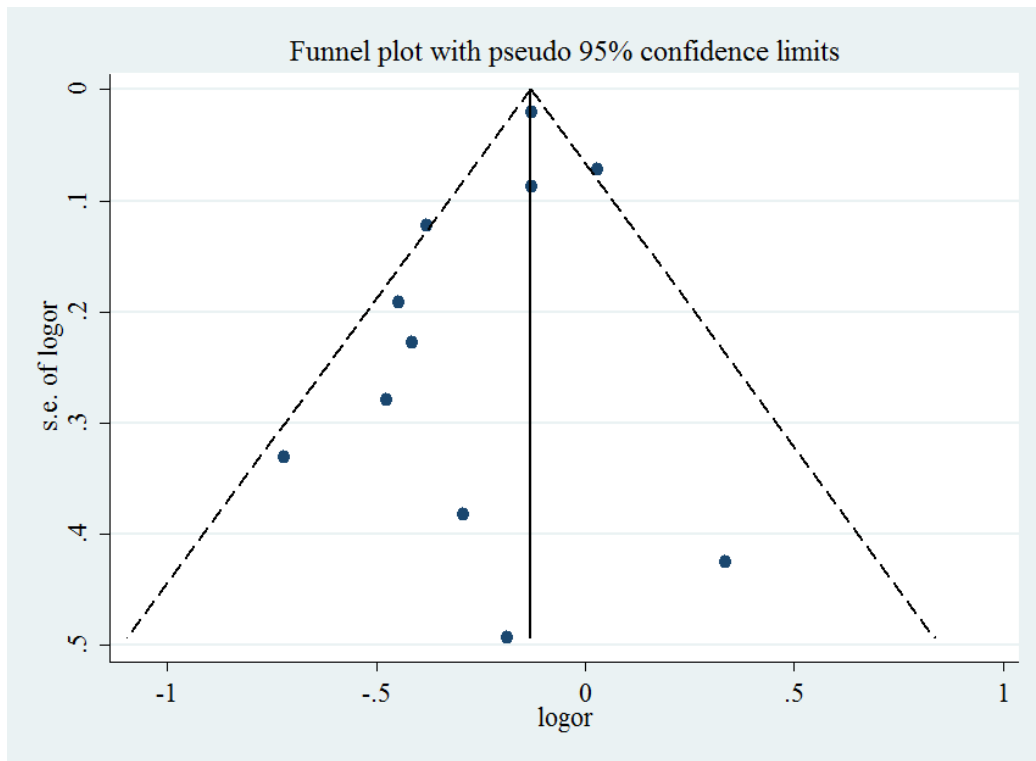
CI, confidence interval.

Supplementary Figure S1 Sensitivity analysis. CI, confidence interval.

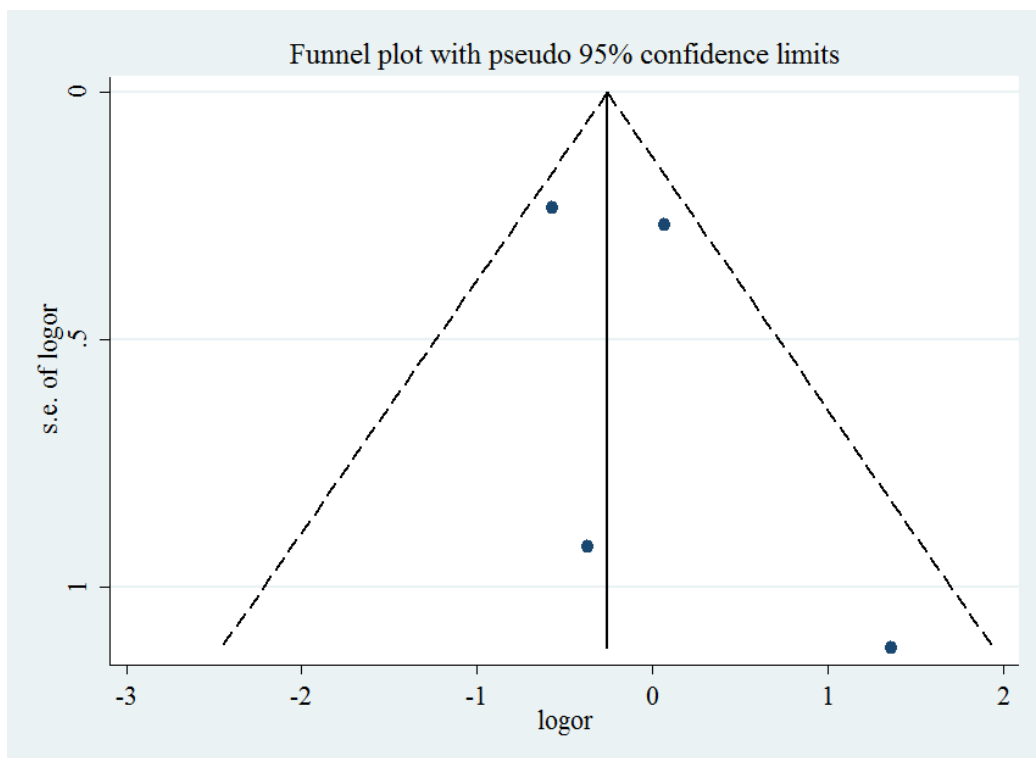


Supplementary Figure S2 Publication bias. OR, odds ratio.

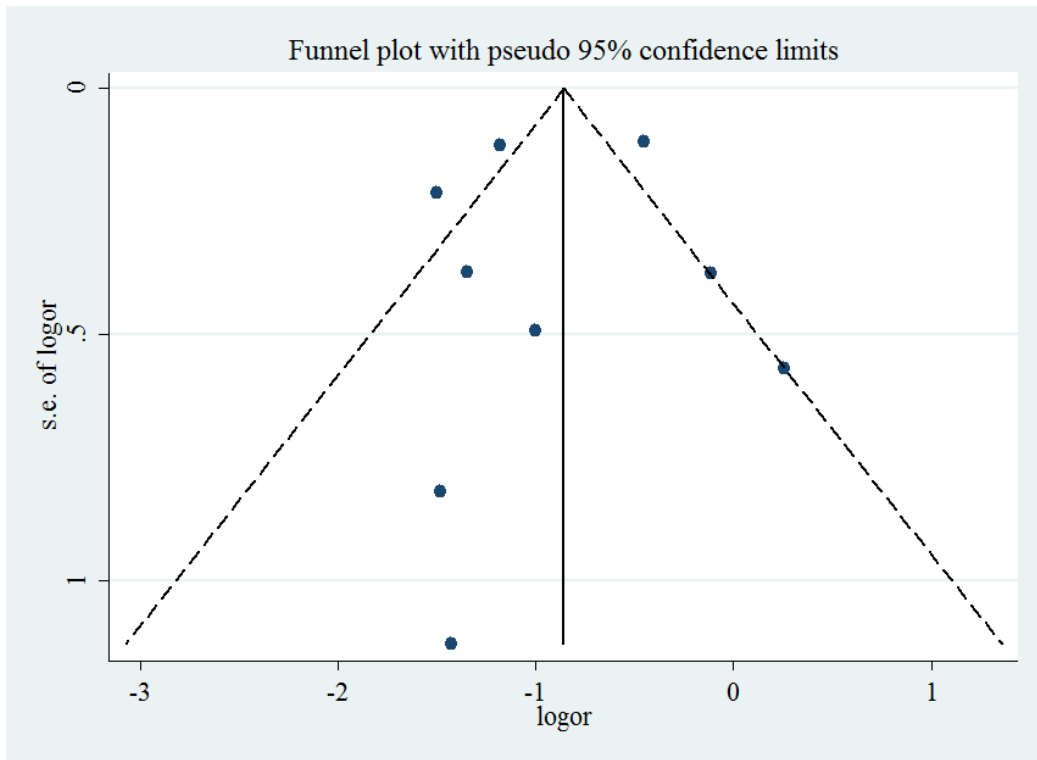
A. Long-term all-cause mortality



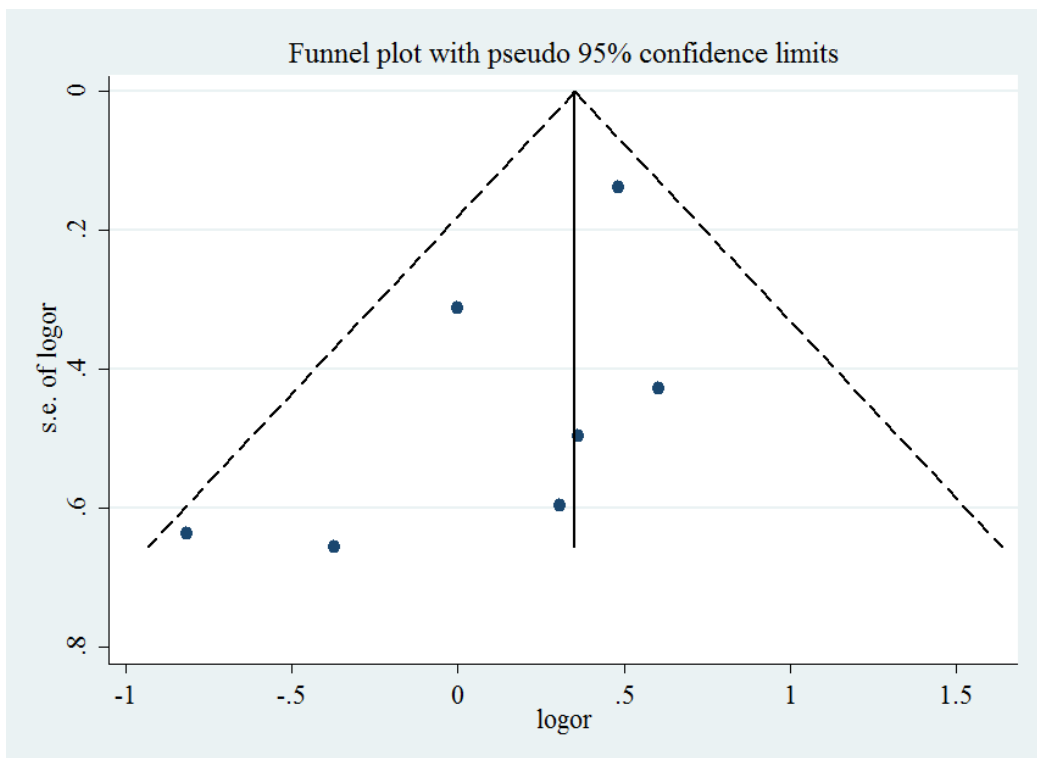
B. Short-term mortality



C. Myocardial infarction



D. Stroke



E. Repeat revascularization

