**SUPPLEMENTARY DATA**

**Detailed search strategy in PubMed:**

("colchicine") AND ("coronary artery disease" OR "coronary heart disease" OR "angina" OR "myocardial infarction" OR "acute myocardial infarct" OR "myocardial ischemia" OR "acute coronary syndrome" OR "ischemic heart disease" OR "percutaneous coronary intervention" OR "percutaneous transluminal coronary angioplasty" OR "myocardial revascularization"). Inception to Aug 23, 2021: 322 hits.

**Ovid Cochrane/Embase/MEDLINE:**

("colchicine" AND ("coronary artery disease" OR "coronary heart disease" OR "angina" OR "myocardial infarction" OR "acute myocardial infarct" OR "myocardial ischemia" OR "acute coronary syndrome" OR "ischemic heart disease" OR "percutaneous coronary intervention" OR "percutaneous transluminal coronary angioplasty" OR "myocardial revascularization")). mp. [mp = title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms].

Inception to August 23, 2021: 1533 hits Embase 1076

Cochrane 141

MEDLINE 316

**Web of Science**

Colchicine (All-fields) AND "coronary artery disease" OR "coronary heart disease" OR "angina" OR "myocardial infarction" OR "acute myocardial infarct" OR "myocardial ischemia" OR "acute coronary syndrome" OR "ischemic heart disease" OR "percutaneous coronary intervention" OR "percutaneous transluminal coronary angioplasty" OR "myocardial revascularization" (All-fields). Inception to Aug 23, 2021: 349 hits.

**ClinicalTrials.gov**

“colchicine” AND “percutaneous coronary revascularization.” Listed until August 23, 2021: 8

**Table 1 of the supplementary data.** Definition of endpoints as reported in each trial included

| Trial/Author | CV Death | MI | Stroke | Coronary revascularization |
|---|---|---|---|---|
| **COVERT-MI**[1] | NR | NR | NR | NR |
| **COPE-PCI**[2] | NR | Perioperative MI was defined by elevated post-PCI troponin levels > 5 × 99$^{th}$ upper reference limit when the pre-PCI troponin levels were normal or > 20% increase in post-PCI troponin when pre-PCI troponin levels raised but remained stable, and additional supporting evidence of new myocardial infarction. (Supporting evidence of new MI defined as<br>1. Evidence of prolonged ischemia (≥ 20 min) as demonstrated by prolonged chest pain or<br>2. Ischemic ST changes or new pathological Q waves or<br>3. Angiographic evidence of a flow-limiting complication like loss of patency in a<br>side branch, persistent slow-flow or no-reflow, embolization or<br>4. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. | NR | NR |
| **Colchicine-PCI**[3] | NR | PCI-related MI: Peak postoperative troponin I levels above the upper reference limit in subjects | NR | Target vessel revascularization at 30 days. |

| | | | | |
|---|---|---|---|---|
| | | with normal baseline cardiac biomarkers or > 20% from the most recent postoperative level in subjects with elevated but stable or falling baseline cardiac biomarkers.<br>Nonfatal MI was defined as PCI-related type 4a or type 1 MI according to the Third Universal Definition.<br>Another secondary outcome was PCI-related MI as defined by the Society for Cardiovascular Angiography and Interventions. | | |
| **COPS**[4] | Death resulting from myocardial infarction, sudden cardiac death, heart failure, and stroke. | ACS was defined as symptoms of acute myocardial ischemia associated with either elevated troponin levels or ECG changes, which included STEMI, NSTEMI, and unstable angina. | Ischemic stroke confirmed by computed tomography scan or magnetic resonance imaging interpreted as not due to atrial fibrillation or intracranial hemorrhage by the treating neurologist. | Unplanned hospitalization for percutaneous coronary interventions (PCI) or coronary artery bypass graft due to recurrent ischemic symptoms associated with objective features of ischemia like ECG changes or positive functional testing.<br>If a patient required emergency revascularization due to chest pain (without troponin elevation with symptoms of ischemia), this event was recorded as an emergency unplanned revascularization rather than an episode of unstable angina.<br>If a participant re-presented with STEMI/NSTEMI and required urgent |

| | | | | |
|---|---|---|---|---|
| | | | | revascularization, the primary endpoint was classified as STEMI/NSTEMI. |
| **LoDoCo-MI**[5] | NR | NR | NR | NR |
| **Talasaz**[6] | NR | NR | NR | NR |
| **COLCOT I**[7] | NR | NR | NR | NR |
| **Vaidya**[8] | NR | NR | NR | NR |
| **COLIN**[9] | NR | NR | NR | NR |
| **Defteros 2015**[10] | NR | NR | NR | NR |
| **Defteros 2013**[11] | NR | NR | NR | NR |
| **COOL**[12] | NR | NR | NR | NR |
| **O'Keefe**[13] | NR | NR | NR | NR |

ACS, acute coronary syndrome; ECG, electrocardiogram; MI, myocardial infarction; NR, not reported; NSTEMI, non-ST-elevation acute myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

**Table 2 of the supplementary data.** Risk of bias for the 12 RCTs included

| Trial/Author | Year of publication | Bias from the randomization process | Bias due to deviations from the procedures intended | Bias due to missing outcome data | Bias in outcome measurement | Bias in selection of results reported | Overall bias |
|---|---|---|---|---|---|---|---|
| **COVERT-MI**[1] | 2021 | Low | Low | Low | Low | Low | Low |
| **COPE-PCI**[2] | 2021 | Moderate | Low | Low | Low | Low | Moderate |
| **Colchicine-PCI**[3] | 2020 | Low | Low | Low | Low | Low | Low |
| **COPS**[4] | 2020 | Low | Low | Low | Low | Low | Low |
| **LoDoCo-MI**[5] | 2019 | Low | Low | Low | Low | Low | Low |
| **Talasaz**[6] | 2019 | Low | High | Low | Low | Moderate | High |
| **COLCOT I**[7] | 2019 | Low | Low | Low | Low | Low | Low |
| **COLIN**[9] | 2017 | Low | Low | Low | Low | Low | Low |
| **Defteros 2015**[10] | 2015 | Low | Low | Low | Low | Low | Low |
| **Defteros 2013**[11] | 2013 | Low | Low | Low | Low | Low | Low |
| **COOL**[12] | 2012 | Low | Low | Low | Low | Low | Low |
| **O'Keefe**[13] | 1992 | Low | Low | Low | Low | Low | Low |

**Table 3 of the supplementary.** Risk of bias for the observational trial included

| Trial/Author | Year of publication | Bias due to confounding | Bias in participant selection | Bias in classification of procedures | Bias due to deviations from the procedures intended | Bias in missing outcome data | Bias in outcome measurement | Bias in selection of results reported | Overall bias |
|---|---|---|---|---|---|---|---|---|---|
| **Vaidya[8]** | 2018 | Low | Low | Low | Low | Low | Low | Low | Low |

**Table 4 of the supplementary data.** Leave-one-out sensitivity analysis for all-cause mortality

| Study omitted | OR | 95%CI |
|---|---|---|
| **COLCOT I**[7] | 1.47 | 0.60 - 3.58 |
| **COPS**[4] | 0.98 | 0.66 - 1.45 |
| **COLCHICINE-PCI**[3] | 1.06 | 0.72 - 1.56 |
| **COOL**[12] | 1.06 | 0.72 - 1.55 |
| **Vaidya et al.**[8] | 1.06 | 0.72 - 1.55 |
| **Defteros 2015**[10] | 1.06 | 0.72 - 1.56 |
| **Talasaz**[6] | 1.02 | 0.68 - 1.51 |
| **Defteros 2013**[11] | 1.06 | 0.72 - 1.56 |
| **O`Keefe**[13] | 1.1 | 0.74 - 1.62 |
| **COLIN**[9] | 1.06 | 0.72 - 1.55 |
| **LoDoCo-MI**[5] | 1.06 | 0.72 - 1.55 |
| **COVERT-MI**[1] | 1.06 | 0.72 - 1.55 |

95%CI, 95% confidence interval; OR, odds ratio.

**Table 5 of the supplementary data.** Leave-one-out sensitivity analysis for cardiovascular death

| Study omitted | OR | 95%CI |
|---|---|---|
| **COLCOT I**[7] | 3.03 | 0.31 - 9.33 |
| **COPS**[4] | 0.83 | 0.46 - 1.51 |
| **Vaidya**[8] | 0.98 | 0.42 - 2.28 |
| **Defteros 2013**[11] | 0.98 | 0.42 - 2.28 |
| **COLIN**[9] | 0.98 | 0.42 - 2.28 |
| **LoDoCo-MI**[5] | 0.98 | 0.42 - 2.28 |
| **COVERT-MI**[1] | 0.98 | 0.42 - 2.28 |

95%CI, 95% confidence interval; OR, odds ratio.

**Table 6 of the supplementary data.** Leave-one-out sensitivity analysis for coronary revascularization

| Study omitted | OR | 95%CI |
|---|---|---|
| **COLCOT I**[7] | 0.75 | 0.21 - 2.66 |
| **COPS**[4] | 0.83 | 0.33 - 2.12 |
| **Colchicine-PCI**[3] | 0.64 | 0.29 - 1.40 |
| **Vaidya et al.**[8] | 0.64 | 0.29 - 1.40 |
| **Talasaz et al.**[6] | 0.68 | 0.28 - 1.62 |
| **Defteros 2013**[11] | 0.64 | 0.29 - 1.40 |

95%CI, 95% confidence interval; OR, odds ratio.

**Table 7 of the supplementary data.** Leave-one-out sensitivity analysis for stroke

| Study omitted | OR | 95%CI |
|---|---|---|
| **COLCOT I**[7] | 0.65 | 0.20 - 2.05 |
| **COPS**[4] | 0.50 | 0.16 - 1.56 |
| **COOL**[12] | 0.38 | 0.18 - 0.81 |
| **Defteros 2013**[11] | 0.44 | 0.17 - 1.15 |
| **COVERT-MI**[1] | 0.38 | 0.18 - 0.81 |

95%CI, 95% confidence interval; OR, odds ratio.

**Table 8 of the supplementary data.** Leave-one-out sensitivity analysis for myocardial infarction

| Study omitted | OR | 95%CI |
|---|---|---|
| **COLCOT I**[7] | 0.69 | 0.45 - 1.07 |
| **COPS**[4] | 0.89 | 0.69 - 1.15 |
| **COLCHICINE-PCI**[3] | 0.81 | 0.60 - 1.09 |
| **Vaidya et al.**[8] | 0.84 | 0.66 - 1.07 |
| **Talasaz**[6] | 0.84 | 0.66 - 1.07 |
| **COLIN**[9] | 0.84 | 0.66 - 1.07 |
| **LoDoCo-MI**[5] | 0.83 | 0.65 - 1.05 |
| **COPE-PCI**[2] | 0.84 | 0.66 - 1.07 |
| **COVERT-MI**[1] | 0.84 | 0.66 - 1.07 |

95%CI, 95% confidence interval; OR, odds ratio.

**Table 9 of the supplementary data.** Sensitivity analysis reporting incidence rate ratios of events based on the longest follow-up available

| **Endpoint** | **IRR** | **95%CI** | ***P*** |
|---|---|---|---|
| All-cause mortality | 1.13 | 0.78 - 1.63 | .510 |
| Cardiovascular mortality | 0.92 | 0.52 - 1.62 | .773 |
| Myocardial infarction | 0.85 | 0.67 - 1.07 | .169 |
| Stroke | 0.37 | 0.18 - 0.76 | .007 |
| Any revascularization | 0.28 | 0.23 - 1.53 | .285 |

95%CI, 95% confidence interval; IRR, incidence rate ratio; OR, odds ratio.

**Table 10 of the supplementary data.** Pooled analysis according to random-effects model for clinical endpoints

| **Endpoint** | **RR** | **95%CI** | ***P*** |
|---|---|---|---|
| | Random-effects | | |
| All-cause mortality | 1.06 | 0.72 - 1.54 | .77 |
| Cardiovascular mortality | 0.98 | 0.43 - 2.26 | .97 |
| Myocardial infarction | 0.85 | 0.67 - 1.06 | .15 |
| Stroke | 0.38 | 0.18 - 0.82 | .013 |
| Any revascularization | 0.64 | 0.29 - 1.4 | .26 |

95%CI, 95% confidence interval; OR, odds ratio; RR, relative risk.

**Table 11 of the supplementary data.** Meta-regression outcomes

| **Outcome** | **Variable** | **Coefficient** | ***P*** |
|---|---|---|---|
| All-cause mortality | Use of colchicine | -1.68 | .337 |
| All-cause mortality | Follow-up duration | -0.005 | .886 |
| All-cause mortality | Acute coronary syndrome | 0.014 | .373 |
| All-cause mortality | Diabetes mellitus | 0.0007 | .967 |

**Table 12 of the supplementary data.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist

| **Section and Topic** | **Item #** | **Checklist item** | **Location where item is reported** |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | 1 |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | 2, 3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | 4, 5 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) addressed by the review. | 5 |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify inclusion and exclusion criteria of the review and how studies were grouped for the syntheses. | 5, 6, 7 |
| Information sources | 6 | Specify all databases, registers, websites, organizations, reference lists, and other | 6 |

| | | | |
|---|---|---|---|
| | | sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | |
| Search strategy | 7 | Present the full search strategies for all databases, registers, and websites, including all filters and limits used. | 6, 7 & supplementary data |
| Selection process | 8 | Specify the methods used to decide whether a study met the review inclusion criteria including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, all details on automation tools used in the process. | 6, 7 |
| Data collection process | 9 | Specify the methods used to collect data from reports including how many reviewers collected data from each report, whether they worked independently, all the processes used to obtain or confirm data from study investigators, and if applicable, all details of automation tools used in the process. | 7 |

| | | | |
|---|---|---|---|
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results compatible with each outcome domain in each study were sought (eg, for all measures, time points, analyses). If not, the methods used to decide which results should be collected instead. | 7 |
| | 10b | List and define all other variables for which data were sought (eg, participant and procedural characteristics, funding sources). Describe any assumptions made on missing or unclear information. | 7 |
| Study risk of bias assessment | 11 | Specify the methods used to assess the risk of bias of studies including details of tool(s) used, how many reviewers assessed each study, and whether they worked independently, and if applicable, all details of automation tools used in the process. | 7, 8 |
| Effect measures | 12 | Specify the effect measure(s) (eg, risk ratio, mean difference) used in the synthesis or presentation of results for each outcome. | 8, 9 |

| | | | |
|---|---|---|---|
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (eg, tabulating the study procedural characteristics and comparing it to the planned groups for each synthesis (item #5)). | 7, 8 |
| | 13b | Describe all methods required to prepare the data for presentation or synthesis like handling missing summary statistics or data conversions. | 7, 8, 9 |
| | 13c | Describe all methods used to tabulate or visually display results of each individual study and synthesis. | 7, 8, 9 |
| | 13d | Describe all methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was conducted, describe the model(s), method(s) used to identify the presence and extent of statistical heterogeneity, and software package(s) used. | 7, 8, 9 |
| | 13e | Describe all methods used to explore possible causes of heterogeneity among | 7, 8, 9 |

| | | | |
|---|---|---|---|
| | | study results (eg, subgroup analysis, meta-regression). | |
| | 13f | Describe all sensitivity analyses conducted to assess robustness of synthesized results. | 7, 8, 9 |
| Reporting bias assessment | 14 | Describe all methods used to assess risk of bias due to missing results in a synthesis (from reporting biases). | 7, 8 |
| Certainty assessment | 15 | Describe all methods used to assess certainty (or confidence) in the body of evidence for each outcome. | 7, 8, 9 |
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process from the number of records identified in the search to the number of studies included in the review, ideally using a flowchart. | 9, 10 & supplementary data |
| | 16b | Cite studies that, although appear to meet the inclusion criteria, ended up being excluded. Also, explain why they were excluded. | Figure 1 |

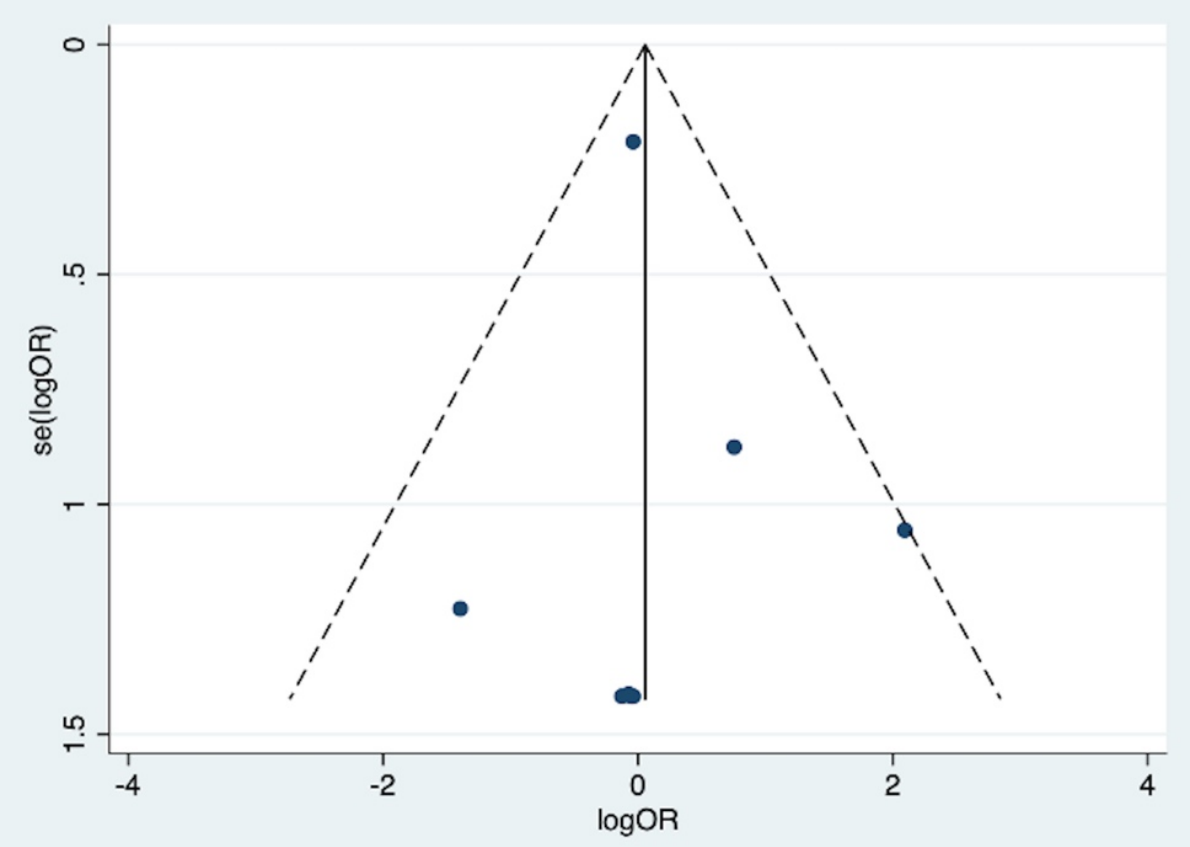
| | | | |
|---|---|---|---|
| Study characteristics | 17 | Cite each study included and present its characteristics. | 9, 10 & supplementary data |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each study included. | Supplementary data |
| Results of each particular study | 19 | Regarding all outcomes, present for each particular study (a) the summary statistics of each group (when appropriate) and (b) an effect estimate and its precision (eg, confidence/credible interval), ideally using structured tables or plots. | 10, 11 |
| Results of syntheses | 20a | For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies. | 10, 11 |
| | 20b | Present the results of all statistical syntheses conducted. If meta-analysis was conducted, present for each the summary estimate and its precision (eg, confidence/credible interval), as well as measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | 10, 11 |

| | | | |
|---|---|---|---|
| | 20c | Present the results of all investigations of possible causes of heterogeneity among the study results. | 10, 11 & supplementary data |
| | 20d | Present the results of all sensitivity analyses conducted to assess the robustness of synthesized results. | 11 & supplementary data |
| Reporting biases | 21 | Present the assessments of risk of bias due to missing results (from reporting biases) for each synthesis assessed. | 11 & supplementary data |
| Certainty of evidence | 22 | Present the assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | 11 & supplementary data |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of results in the context of other evidence. | 12, 13, 14 |
| | 23b | Discuss all limitations of the evidence included in the review. | 14 |
| | 23c | Discuss all limitations of the review processes used. | 14 |
| | 23d | Discuss implications of the results regarding practice, policy, and future research. | 12, 13, 14 |
| **OTHER INFORMATION** | | | |

| | | | |
|---|---|---|---|
| Registration and protocol | 24a | Provide registration information for the review including register name and registration number or say if the review was not registered. | 5 |
| | 24b | Indicate where the review protocol can be accessed or state that a protocol was not prepared. | 5 |
| | 24c | Describe and explain all amendments made to the information provided at registration or in the protocol. | Not applicable |
| Support | 25 | Describe the sources of financial or non-financial support for the review, and the role of funders or sponsors in the review. | 1 |
| Competing interests | 26 | Declare all competing interests from the authors of the review. | 1 |
| Availability of data, code, and other materials | 27 | Report which of the following are publicly available and where can be found: template data collection forms, data drawn from studies included, data used for all analyses, analytical code, any other materials used in the review. | 5 |

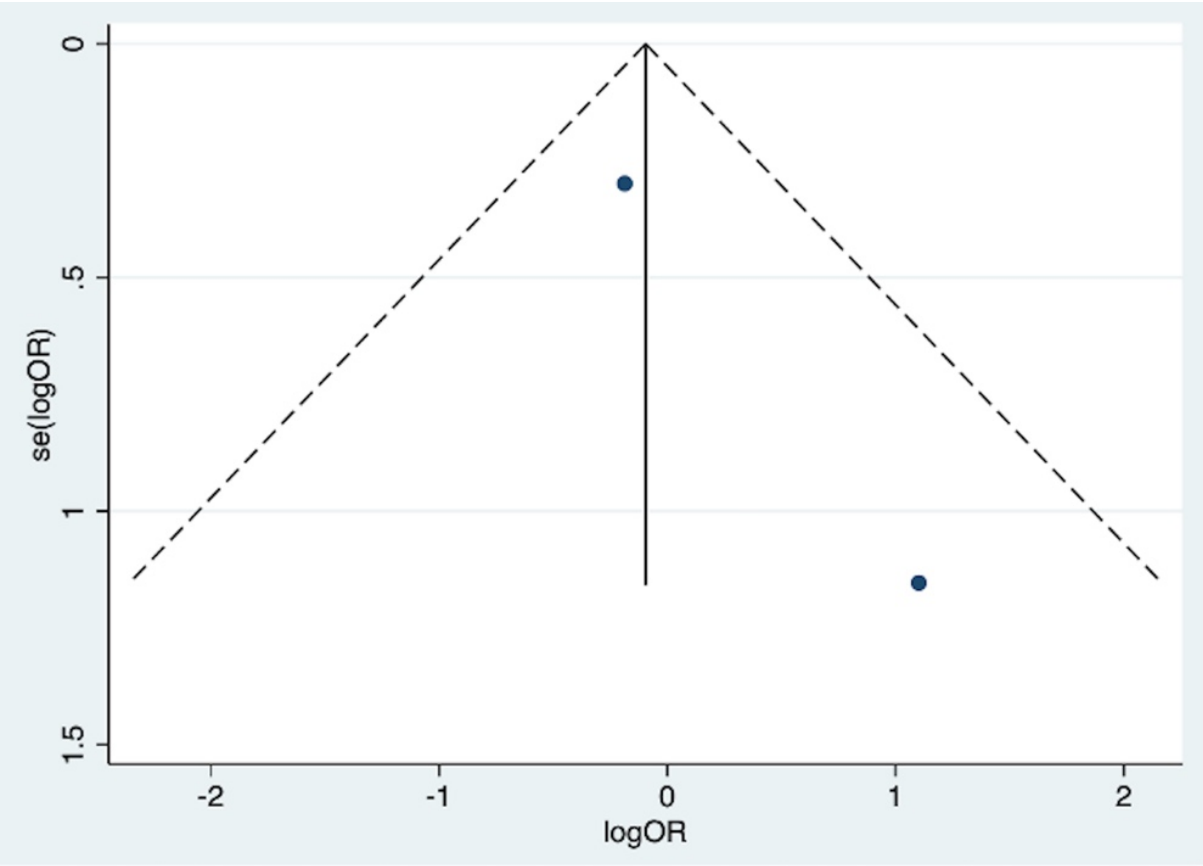
**Figure 1 of the supplementary data.** Funnel plot for all-cause mortality

(Harbord test; *P* = .794).



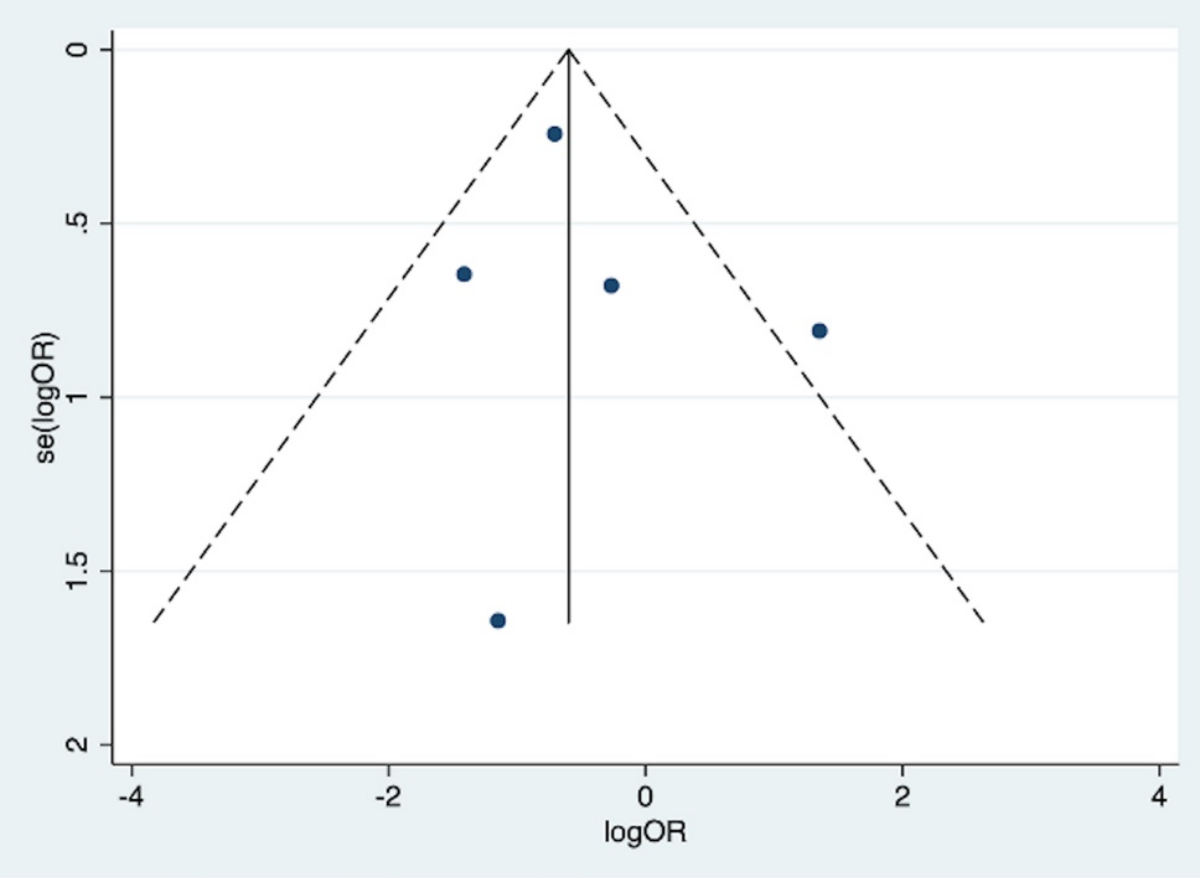

SE, standard error; OR, odds ratio.

**Figure 2 of the supplementary data.** Funnel plot for cardiovascular death.



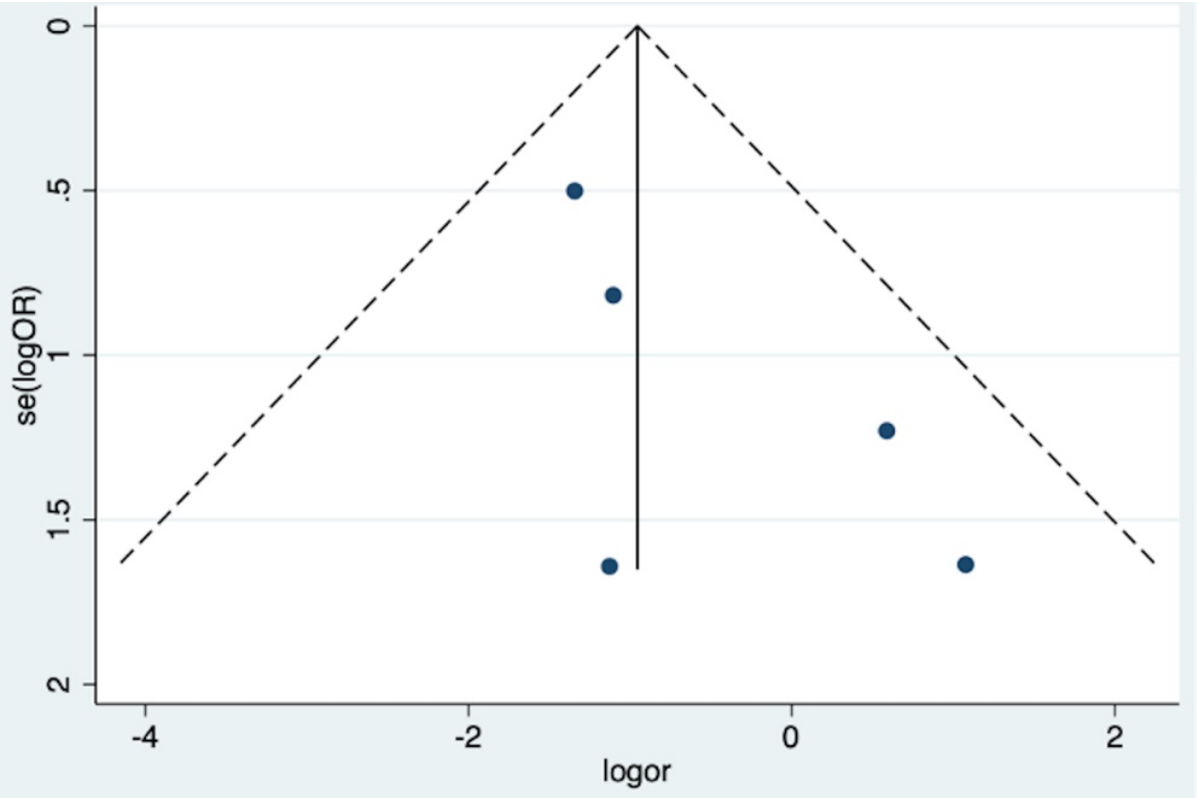

SE, standard error; OR, odds ratio.

**Figure 3 of the supplementary data.** Funnel plot for coronary revascularization (Harbord test; *P* = .753).



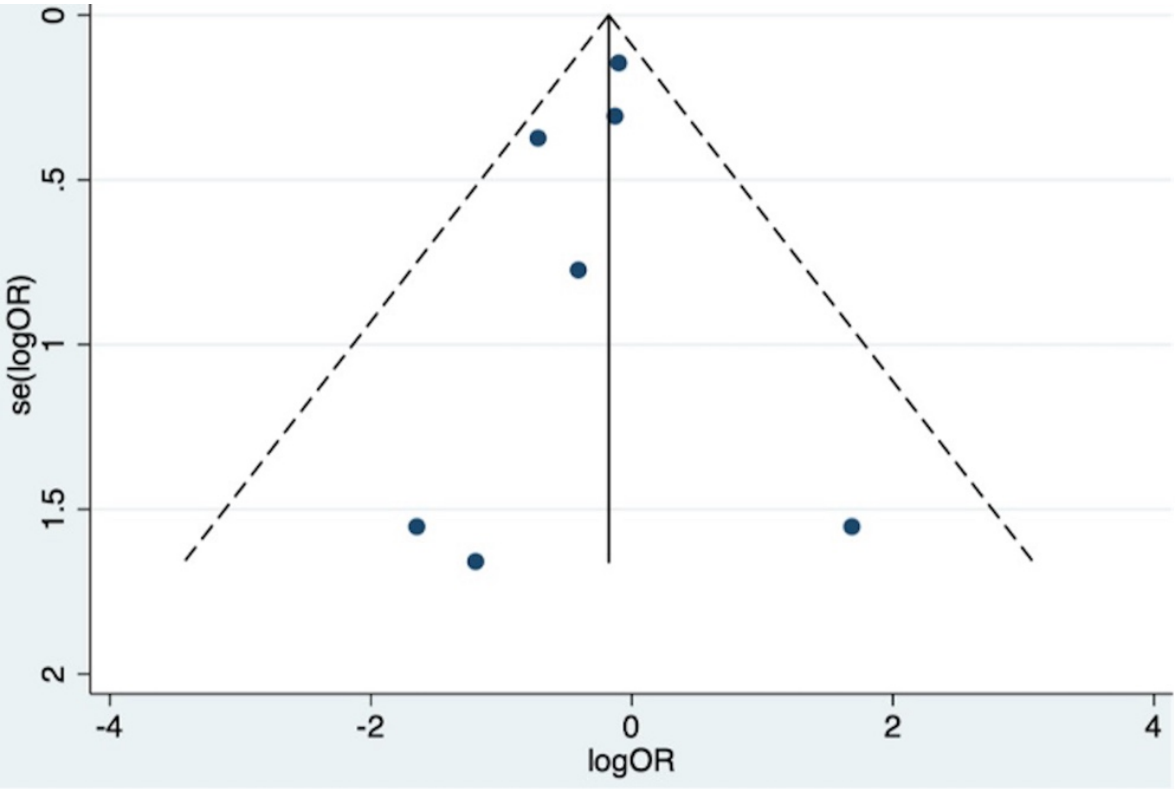

SE, standard error; OR, odds ratio.

**Figure 4 of the supplementary data.** Funnel plot for stroke (Harbord test; *P* = .283).




SE, standard error; OR, odds ratio.

**Figure 5 of the supplementary data.** Funnel plot for myocardial infarction (Harbord test; *P* = .490).




SE, standard error; OR, odds ratio.

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2. Cole J, Htun N, Lew R, Freilich M, Quinn S, Layland J. Colchicine to Prevent Periprocedural Myocardial Injury in Percutaneous Coronary Intervention: The COPE-PCI Pilot Trial. *Circ Cardiovasc Interv.* 2021. https://doi.org/10.1161/CIRCINTERVENTIONS.120.009992.

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11. Deftereos S, Giannopoulos G, Raisakis K, et al. Colchicine treatment for the prevention of bare-metal stent restenosis in diabetic patients. *J Am Coll Cardiol.* 2013;61:1679-1685.

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