

Supplementary Table 1- Full search strategy key

Medline	
#1	“Colchicine”[mh] OR “colchicine”[tw]
#2	“Cardiovascular outcome*” [tw] OR CVOT [tw] OR “MACE” [tw] OR “myocardial infarct*” [tw] OR “Heart infarct*” [tw] OR “Heart attack*”[tw] OR MI[tw] OR AMI[tw] OR “myocardial infarction”[mh] OR stroke[tw] OR “brain infarct*”[tw] OR “brain ischemia”[tw] OR “cerebrovascular accident*”[tw] OR Stroke[mh]
#3	#1 AND #2
#4	“randomized controlled trial”[pt]
#5	“controlled clinical trial”[pt]
#6	Randomized[tiab]
#7	Placebo[tiab]
#8	“drug therapy”[sh]
#9	Randomly[tiab]
#10	Trial[tiab]
#11	Groups[tiab]
#12	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13	Animals[mh] NOT humans[mh]
#14	#12 NOT #13
#15	#3 AND #14
Cochrane Central Register of Controlled Trials	
#1	“colchicine”
#2	MeSH descriptor: [colchicine] explode all trees
#3	#1 OR #2
#4	“Cardiovascular outcomes”
#5	MACE
#6	“Myocardial infarction”
#7	” Heart attack”
#8	MI
#9	AMI
#10	MeSH descriptor: [myocardial infarction] explode all trees
#11	Stroke
#12	“Cerebrovascular accident”
#13	MeSH descriptor: [stroke] explode all trees
#14	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
#15	“Randomized controlled trial”
#16	“Controlled clinical trial”
#17	MeSH descriptor: [Randomized Controlled Trials as Topic] explode all trees
#18	#16 OR #17
#19	#3 AND #14 AND #18

Supplementary Table 2 – Definitions used to report MACE by each study. MACE, major adverse cardiovascular event. NSTEMI, non-ST-segment elevation myocardial infarction. STEMI, ST-segment elevation myocardial infarction.

Trials	MACE or vascular events as reported by each study
Raju et al, 2012 [24]	Only one hospitalization for unstable angina and one stroke are reported.
LoDoCo, 2013 [19]	Composite of acute coronary syndrome, fatal or nonfatal out-of-hospital cardiac arrest or noncardioembolic ischemic stroke.
COLIN, 2017 [20]	Only one myocardial infarction and one hospitalization for heart failure are reported.
LoDoCo-MI, 2019 [22]	All-cause hospitalizations
COLCOT, 2019 [7]	Composite of death from cardiovascular causes, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina leading to coronary revascularization
LoDoCo2, 2020 [8]	Composite of cardiovascular death, spontaneous (nonprocedural) myocardial infarction, ischemic stroke, or ischemia-driven coronary revascularization
COPS, 2020 [23]	Composite of death from any cause, acute coronary syndrome (STEMI/non-STEMI/stable angina), ischemia- driven urgent revascularization and noncardioembolic ischemic stroke
AKRAMI, 2021 [21]	Death from any cause, non-cardio-embolic ischemic stroke, hospital admission due to typical chest pain (unstable angina, STEMI/NSTEMI), urgent need for revascularization and decompensated heart failure.
CONVINCE, 2024 [13]	Composite of first recurrent non-fatal ischaemic stroke, myocardial infarction, cardiac arrest, or hospitalisation for unstable angina or vascular death
CHANCE-3, 2024 [14]	Composite of ischaemic stroke, haemorrhagic stroke, transient ischemic attack, myocardial infarction, or death from vascular causes.
CLEAR, 2024 [15]	Composite of death from cardiovascular causes, recurrent myocardial infarction, stroke, or unplanned ischemia- driven coronary revascularization

Supplementary Table 3- Articles Excluded After Full-Text Review

N	Title	Year	Author	Journal	Exclusion criteria
1	Anti-Inflammatory Treatment With Colchicine in Acute Myocardial Infarction: A Pilot Study.	2015	Deftereos, S	Circulation	Duration of treatment <30 days
2	Colchicine's effects on metabolic and inflammatory molecules in adults with obesity and metabolic syndrome: results from a pilot randomized controlled trial	2020	Demidowicz, A. P.	Int J Obes	No established atherosclerosis
3	Effects of Acute Colchicine Administration Prior to Percutaneous Coronary Intervention: COLCHICINE-PCI Randomized Trial	2020	Shah	Circ. Cardiovasc. Interv.	Duration of treatment <30 days
4	Colchicine prevents stroke in patients with coronary artery disease - a trial sequential analysis.	2020	Chan, J. S. K	Eur J Neurol	No RCT
5	Colchicine in Patients With Chronic Coronary Disease in Relation to Prior Acute Coronary Syndrome.	2021	Opstal, T. S. J.	J Am Coll Cardiol	Overlapping data
6	Effect of Colchicine on Myocardial Injury in Acute Myocardial Infarction	2021	Mewton, N.	Circulation	Duration of treatment <30 days

7	Colchicine effectively attenuates inflammatory biomarker high-sensitivity C-reactive protein (hs-CRP) in patients with non-ST-segment elevation myocardial infarction: a randomised, double-blind, placebo-controlled clinical trial	2021	Gholoobi, A	Inflammopharmacology	No eligible outcomes
8	Low-dose colchicine in type 2 diabetes with microalbuminuria: a double-blind randomized clinical trial.	2021	Wang, Y.	JJ. Diabetes	No established atherosclerosis
9	Colchicine Use and Risks of Stroke Recurrence in Acute Non-Cardiogenic Ischemic Stroke Patients: A Population-Based Cohort Study	2021	Liu, C. H.	J. Pers. Med	No RCT
10	Preprocedural Colchicine in Patients With Acute ST-elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention: A Randomized Controlled Trial (PodCAST-PCI)	2022	Hosseini, S. H	J. Cardiovasc. Pharmacol.	Duration of treatment <30 days
11	Effect of different doses of colchicine on high sensitivity C-reactive protein in patients with acute minor stroke or transient ischemic attack: a pilot randomized controlled trial	2022	Yuan, B.	Eur. J. Pharm. Sci	Duration of treatment <30 days
12	Colchicine to Prevent Periprocedural Myocardial Injury in Percutaneous Coronary Intervention (COPE-PCI): coronary Microvascular Physiology Pilot Substudy.	2022	Cole, J.,	J. Interv. Cardiol.	Duration of treatment <30 days
13	Colchicine in Cardiac Surgery: The COCS Randomized Clinical Trial.	2022	Shvartz, V.	J. Cardiovasc. Dev. Dis.	Duration of treatment <30 days
14	Effect of Colchicine in reducing MMP-9, NOX2, and TGF- β 1 after myocardial infarction	2023	Suryono, S	BMC Cardiovasc Disord	No eligible outcomes
15	Individual lifetime benefit from low-dose colchicine in patients with chronic coronary artery disease	2023	Burger, P. M.	Eur J Prev Cardiol	No RCT
16	Role of colchicine to reduce NLRP3 marker in STEMI patients undergo primary PCI: A randomised controlled clinical trial	2024	Karim, B.	Med J Malaysia	No eligible outcomes
17	Colchicine in acute myocardial infarction: cardiovascular events at 1-year follow up	2024	Bouleti, C	Open Heart	Overlapping data
18	In patients with type 2 diabetes and recent MI, colchicine reduced a composite CV outcome at 23 mo	2024	Bates, E. R.	Ann Intern Med	No RCT
19	Colchicine to prevent sympathetic denervation after acute myocardial infarction: the COLD-MI trial.	2024	Huet, F.	Eur. Heart J.	No eligible outcomes

References of excluded articles

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Supplementary Table 4 – Discontinuation of colchicine or placebo

Trials	Run-In-Period	Colchicine group (%)	Placebo group (%)
Raju et al, 2012 [24]	No	12.5	5.0
LoDoCo, 2013 [19]	Yes	11.3	-
COLIN, 2017 [20]	No	0	-
LoDoCo-MI, 2019 [22]	No	2	4
COLCOT, 2019 [7]	No	18.4	18.7
LoDoCo2, 2020 [8]	Yes	10.5	10.5
COPS, 2020 [23]	No	15.0	8.0
AKRAMI, 2021 [21]	No	2	0
CONVINCE, 2024 [13]	No	20.5	-
CHANCE-3, 2024 [14]	No	4.7	4.9
CLEAR, 2024 [15]	No	25.9	25.5

Supplementary Table 5 – Sensitivity analysis including only major trials (n > 1 000)

Outcome	OR	95% CI	I ²	p value
Primary outcome	0.87	0.77-0.99	45%	0.03
RCTs' MACE definition	0.84	0.73-0.97	63%	0.02
Myocardial infarction	0.84	0.72-0.97	0%	0.02
Unstable angina	0.77	0.58-1.02	60%	0.07
Stroke	0.84	0.64-1.09	61%	0.19
Cardiovascular mortality	0.93	0.76-1.14	0%	0.49
All-cause mortality	0.97	0.84-1.12	0%	0.65
Non-cardiovascular mortality	1.02	0.75-1.40	52%	0.90
Gastrointestinal symptoms	1.55	1.05-2.30	95%	0.03
Hematologic effects	0.90	0.41-1.98	58%	0.80
Infections	0.98	0.74-1.31	55%	0.89

Supplementary Table 6 – Sensitivity analysis using Peto's fixed-effect method

Outcome	OR	95% CI	I ²	p value
Primary outcome	0.86	0.78-0.94	62%	<0.001
RCTs' MACE definition	0.82	0.75-0.88	73%	<0.001
Myocardial infarction	0.79	0.68-0.91	40%	0.001
Unstable angina	0.76	0.66-0.88	69%	<0.001
Stroke	0.88	0.77-1.0	54%	0.05
Cardiovascular mortality	0.93	0.76-1.13	26%	0.46
All-cause mortality	0.97	0.85-1.12	48%	0.72
Non-cardiovascular mortality	1.03	0.84-1.26	56%	0.80
Gastrointestinal symptoms	1.40	1.30-1.50	92%	<0.001
Hematologic effects	1.07	0.75-1.53	76%	0.71

Infections	0.99	0.84-1.16	56%	0.89
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