16. Thromboseforum 2026

Stuttgart, 28. Februar 2026

Universitätsklinikum Deutsches Herzzentrum

Colchicine Reloaded: Was die Studien wirklich zeigen

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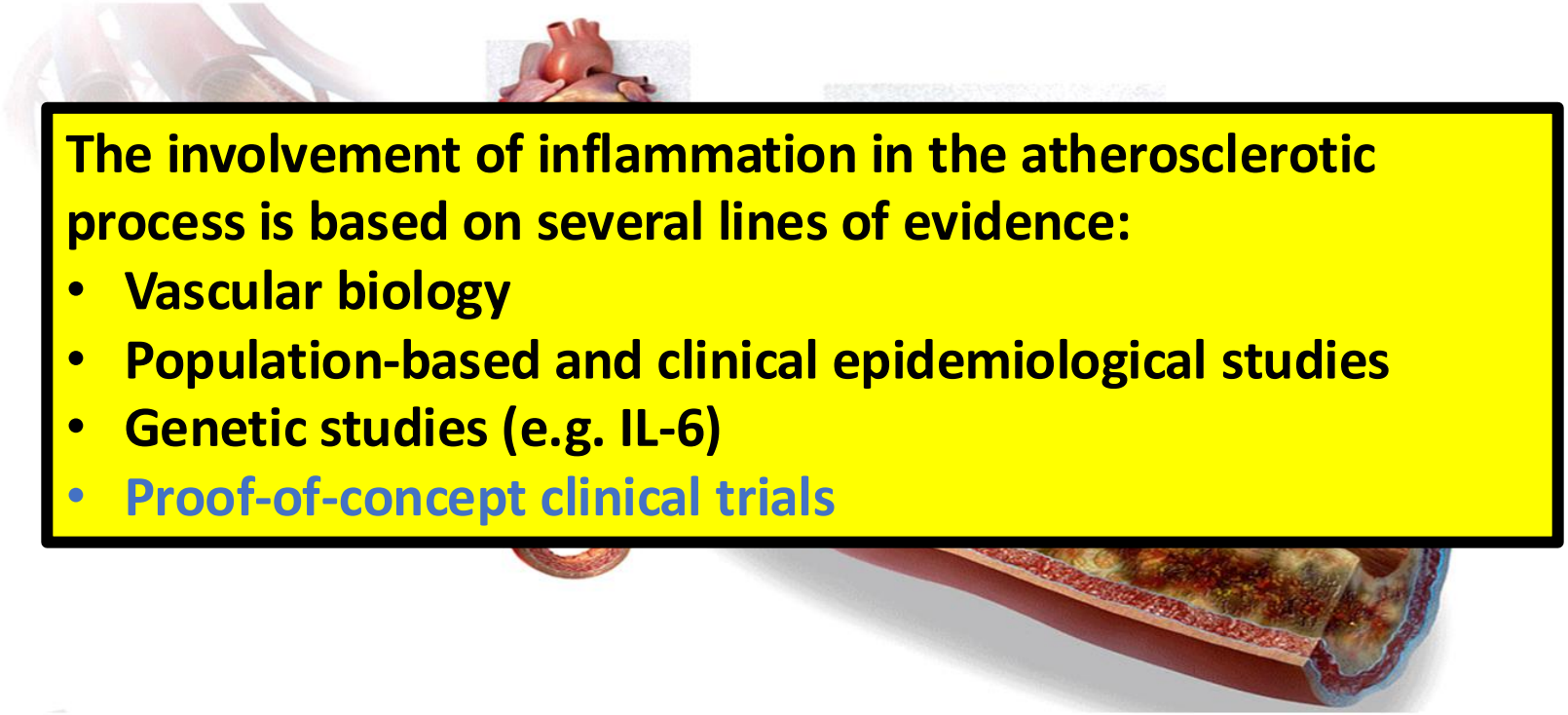
W. Koenig: Conflict of Interest (COI) - Disclosure

- ***Honorar für Vorträge***: AstraZeneca, Novartis, Amgen, Sanofi, Roche, Bristol-Myers Squibb, APONTIS
- ***Mitglied in Advisory Boards***: Novartis, Pfizer, Amgen, AstraZeneca, Kowa, Corvidia, DalCor, Genentech, Amarin, Daiichi-Sankyo, LIB Therapeutics, OMEICOS, Novo Nordisk, TenSixteen Bio, New Amsterdam Pharma, APONTIS
- ***Teilnahme an klinischen Studien***: CANTOS, HORIZON (Novartis), FOURIER, GLAGOV, VESALIUS, OCEAN(a) (Amgen), AZURE-LDL (AZ), OPTIONS I und II (Sanofi/Regeneron), SPIRE I und II (Pfizer), CAIN III (MHICC), PROMINENT (Kowa), DalGenE (DalCor), COLCOT (MHICC), ACCLAIM, MOVE (Lilly)
- ***Forschungsunterstützung***: Abbott Diagnostics, Roche Diagnostics, Beckmann, Singulex
- ***Aktienbesitz pharmazeutischer Unternehmen***: keine

Inflammation and Atherothrombosis

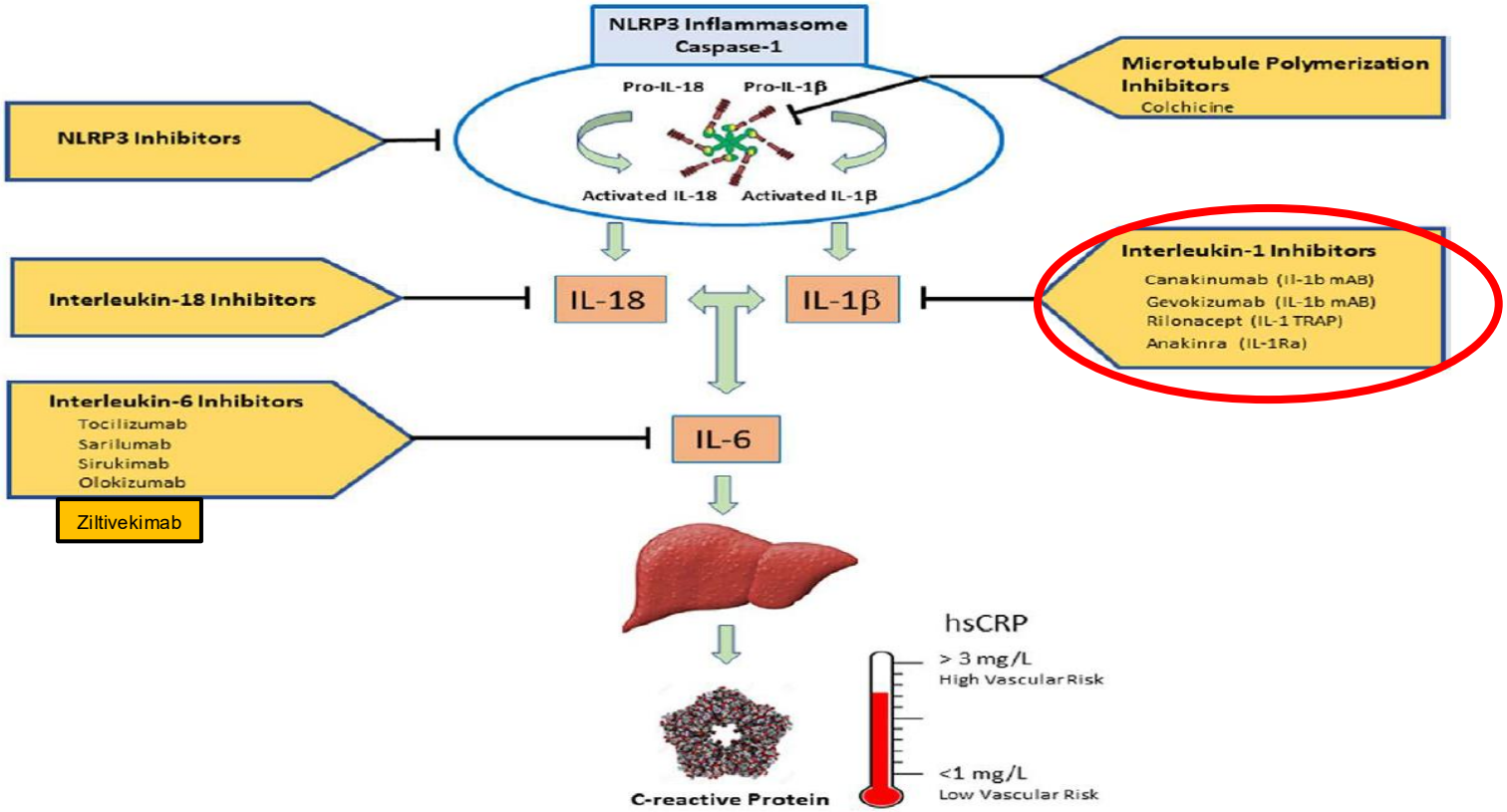


The involvement of inflammation in the atherosclerotic process is based on several lines of evidence:

- **Vascular biology**
- **Population-based and clinical epidemiological studies**
- **Genetic studies (e.g. IL-6)**
- **Proof-of-concept clinical trials**

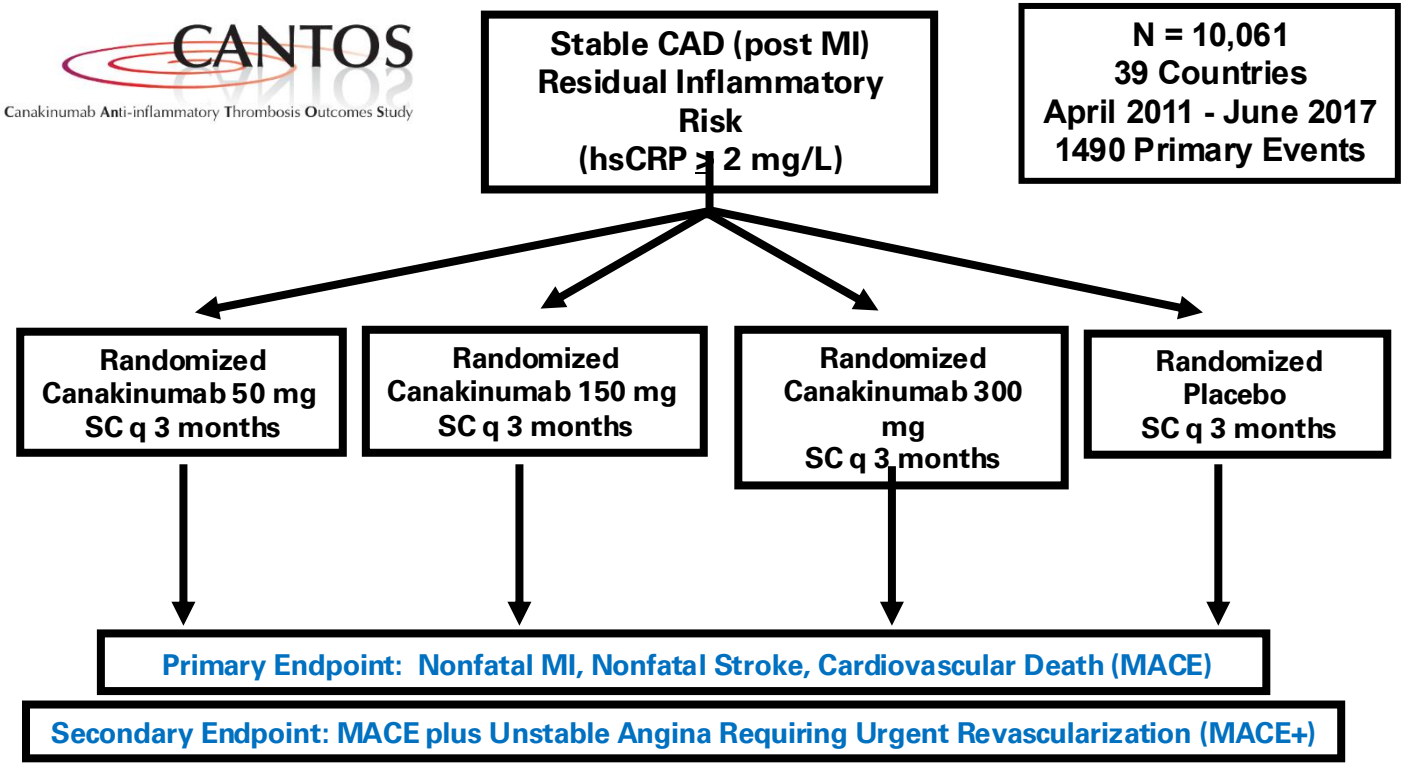
Peter Libby „A Fire Within“
Scientific American; May 2002

Potential Therapeutic Targets in the NLRP3 Inflammasome to IL-1 to IL-6 to CRP Signaling Pathway



Ridker et al Circulation. 2020;141:787–789

Canakinumab Anti-inflammatory Thrombosis Outcomes Study

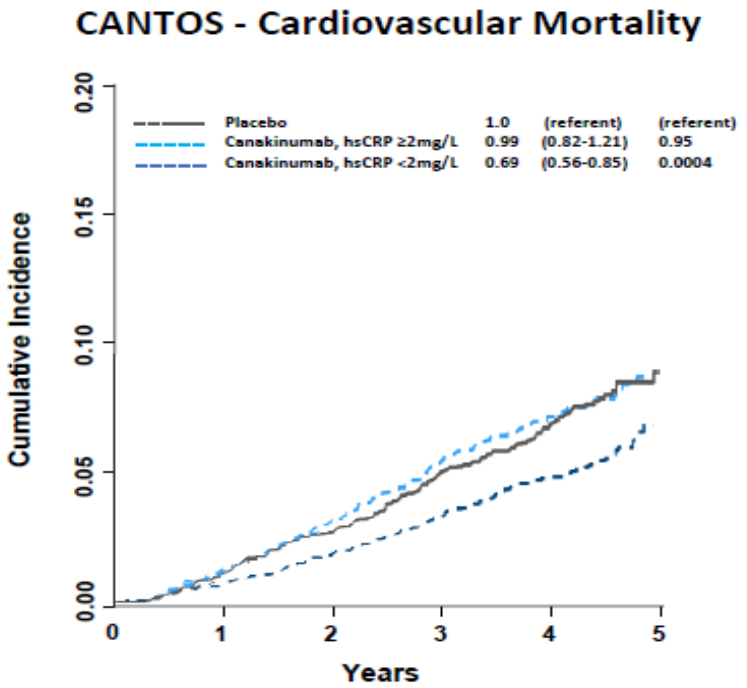


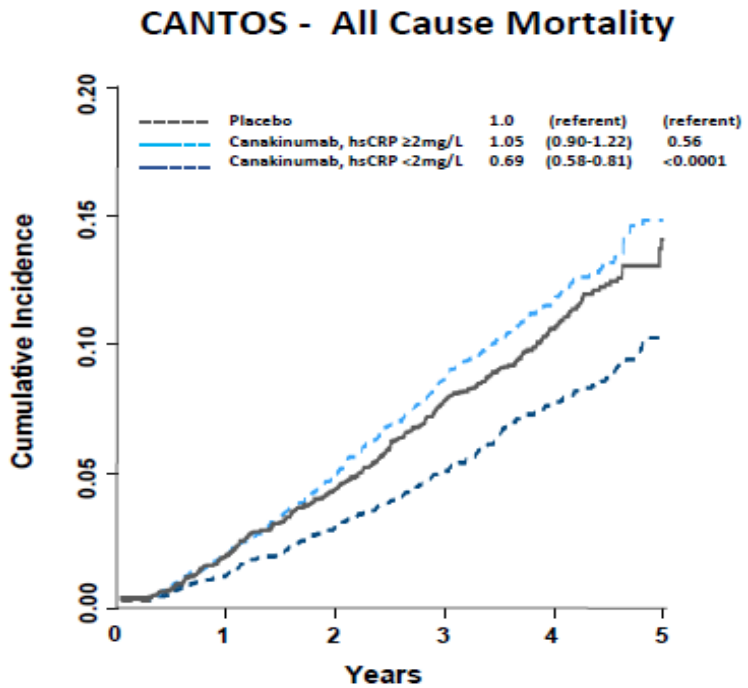
"Residual Inflammatory Risk"

Baseline LDL-C 82mg/dL (2.1mmol/L) but hsCRP 4.1 mg/L

Ridker PM et al. N Engl J Med. 2017;377:1119-31

CANTOS: 31% RRR in Mortality Among Participants with Robust Inhibition of the Inflammatory Response

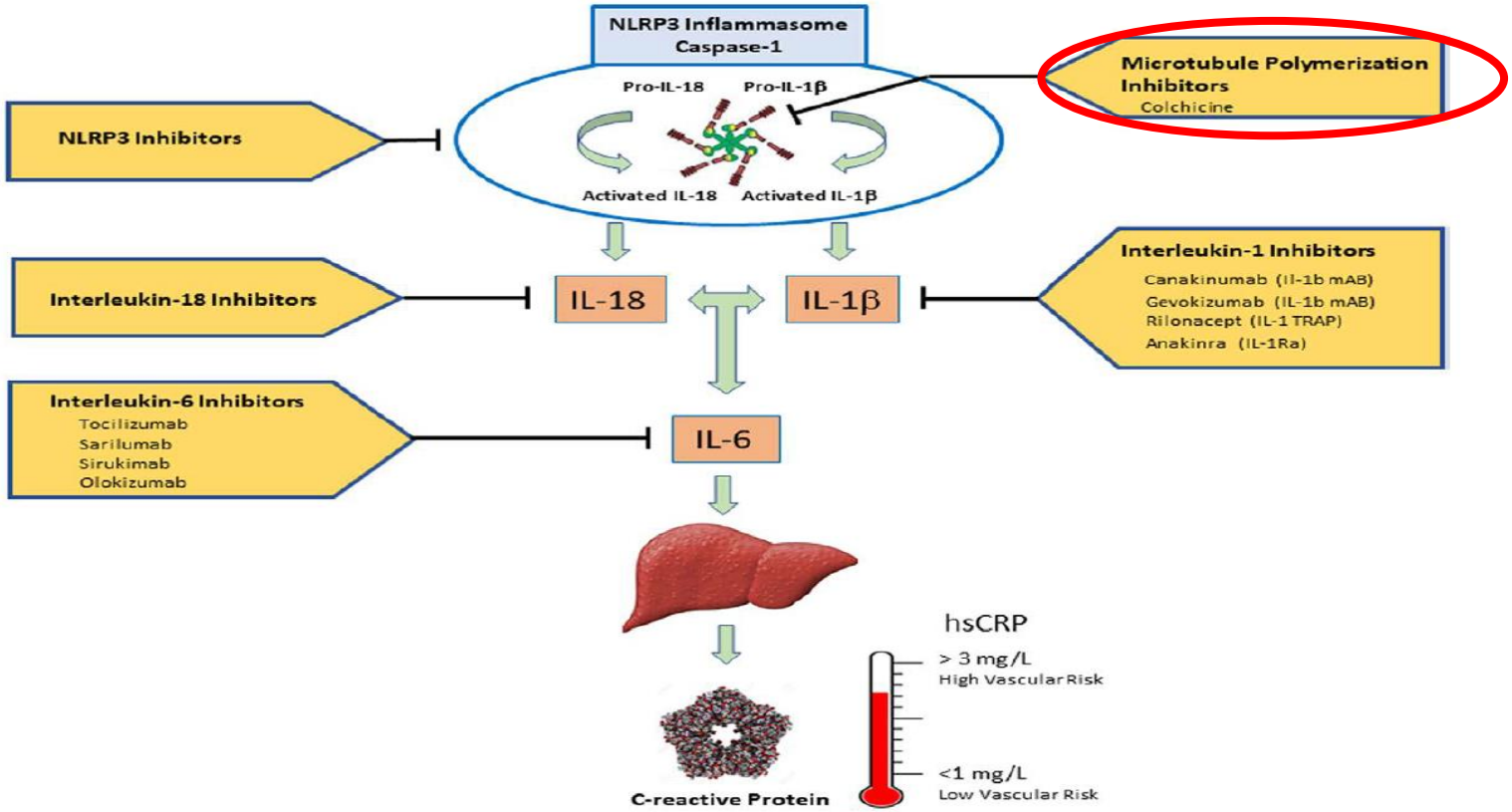




35 - 40% reductions in hsCRP and IL-6
No change in LDLC

Ridker PM et al. Circulation 2018;137:1763-1766

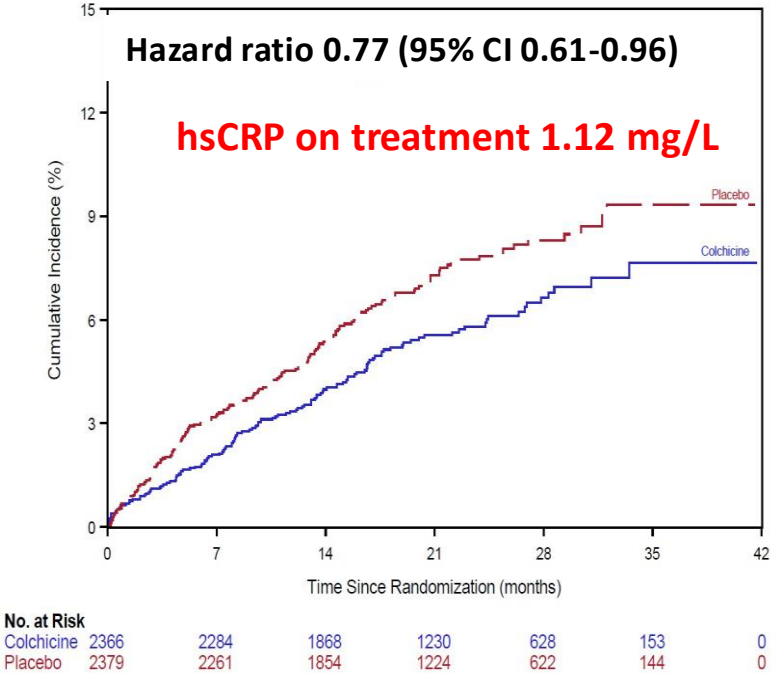
Potential Therapeutic Targets in the NLRP3 Inflammasome to IL-1 to IL-6 to CRP Signaling Pathway



Ridker et al Circulation. 2020;141:787–789

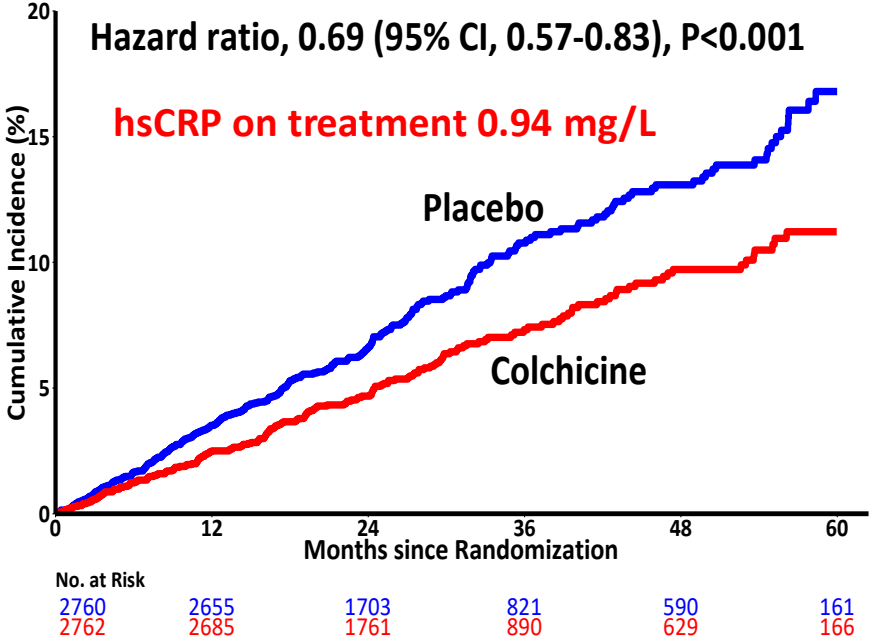
Two Recent Trial Showing Benefit for Colchicine in CAD

COLCOT- Acute MI (N=4745, 301 events)



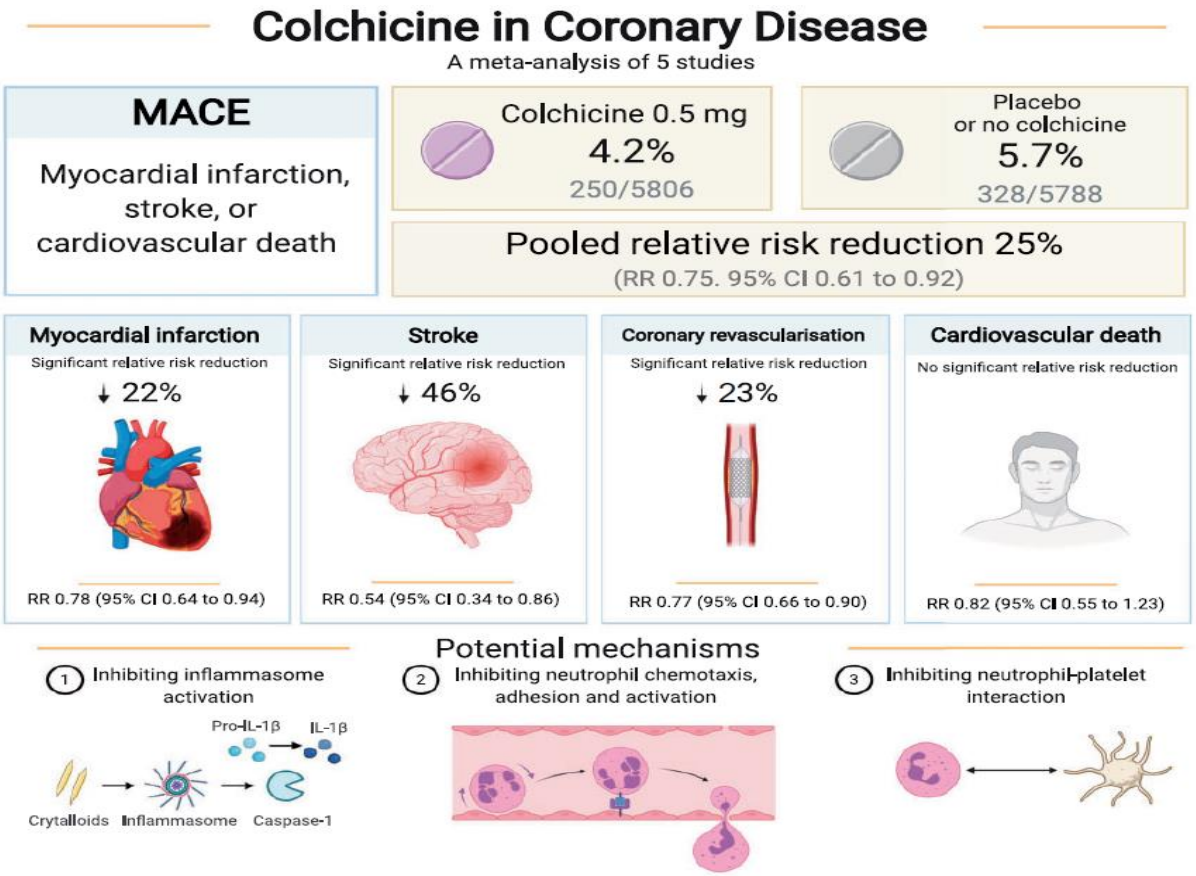
Tardif JC, et al. NEJM. 2019;381:2497-2505.

LODOCO2- stable CAD (N=5522, 451 events)



Nidorf M, et al. NEJM 2020; 5;383:1838-1847.

Colchicine in Coronary Disease



Trials included:

- LoDoCo
- COLCOT
- COPS
- Deftereos
- LoDoCo2

Fiolet et al. EHJ 2021;42;2765-2775

Serious Adverse Events

		Colchicine (N = 2762)	Placebo (N = 2760)
Non-cardiovascular death	1.51 (0.99–2.31)	53(1.9)	35(1.3)
Diagnosis of new cancer		120(4.3)	122(4.4)
Hospitalization for infection		137(5.0)	144(5.2)
Hospitalization for pneumonia		46(1.7)	55(2.0)
Hospitalization for gastro-intestinal reason		53(1.9)	50(1.8)
Neutropenia		3(0.1)	3(0.1)
Myotoxicity		4(0.1)	3(0.1)

Nidorf SM et al. N Engl J Med 2020 Aug 31

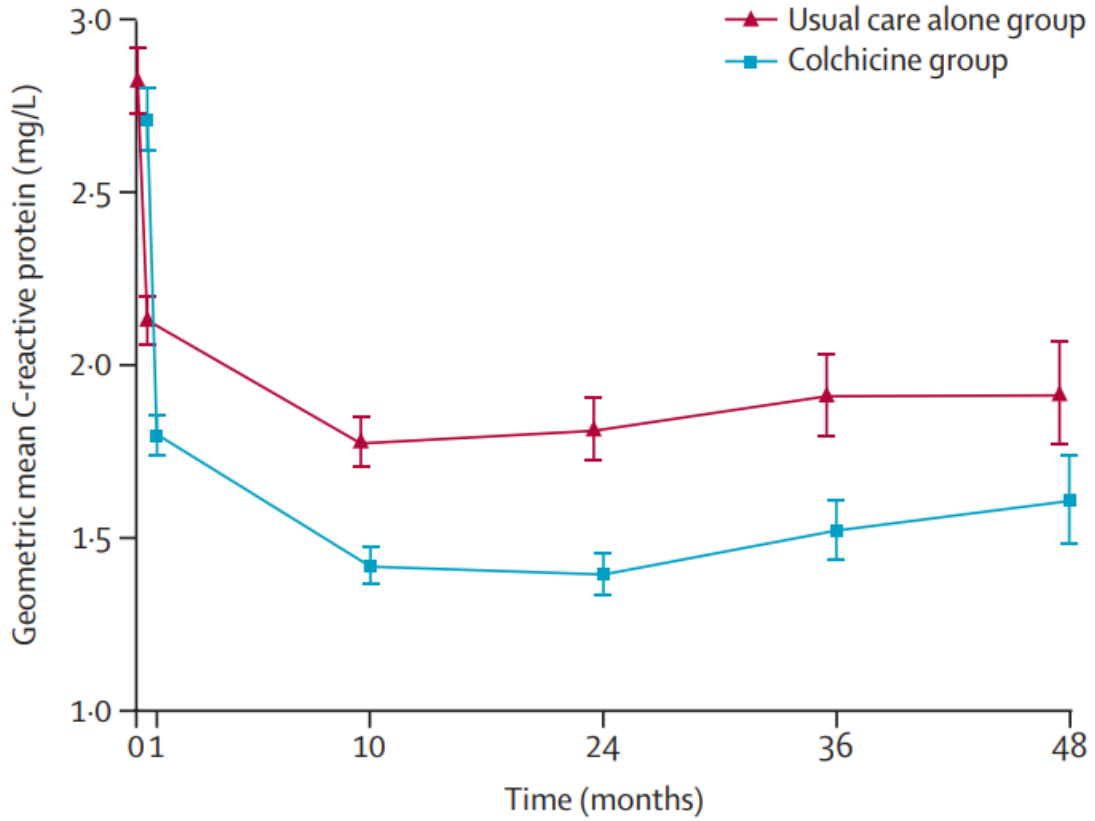
Long-term colchicine for the prevention of vascular recurrent events in non-cardioembolic stroke (CONVINCE): a randomised controlled trial

Peter Kelly, Robin Lemmens, Christian Weimar, Cathal Walsh, Francisco Purroy, Mark Barber, Ronan Collins, Simon Cronin, Anna Czlonkowska, Philippe Desfontaines, Adinda De Pauw, Nicholas Richard Evans, Urs Fischer, Catarina Fonseca, John Forbes, Michael D Hill, Dalius Jatuzis, Janika Kõrv, Peter Kraft, Christina Kruuse, Catherine Lynch, Dominick McCabe, Robert Mikulik, Sean Murphy, Paul Nederkoorn, Martin O'Donnell, Peter Sandercock, Bernadette Schroeder, Gek Shim, Katrina Tobin, David J Williams, Christopher Price

- 3154 patients with non-severe ischemic stroke were randomized in a parallel-group, open label (*not placebo controlled*) trial. First patient in Dec. 19, 2016
- PEP: Composite of first fatal or non-fatal recurrent ischemic stroke, MI, cardiac arrest or hospitalisation for unstable angina.
- Trial was paused for 3 months in 2020 followed by slower recruitment than expected
- Median follow-up appr. 3 years
- ***The trial finished before the anticipated number of outcomes was accrued due to budgetary constraints attributable to the COVID-19 pandemic***

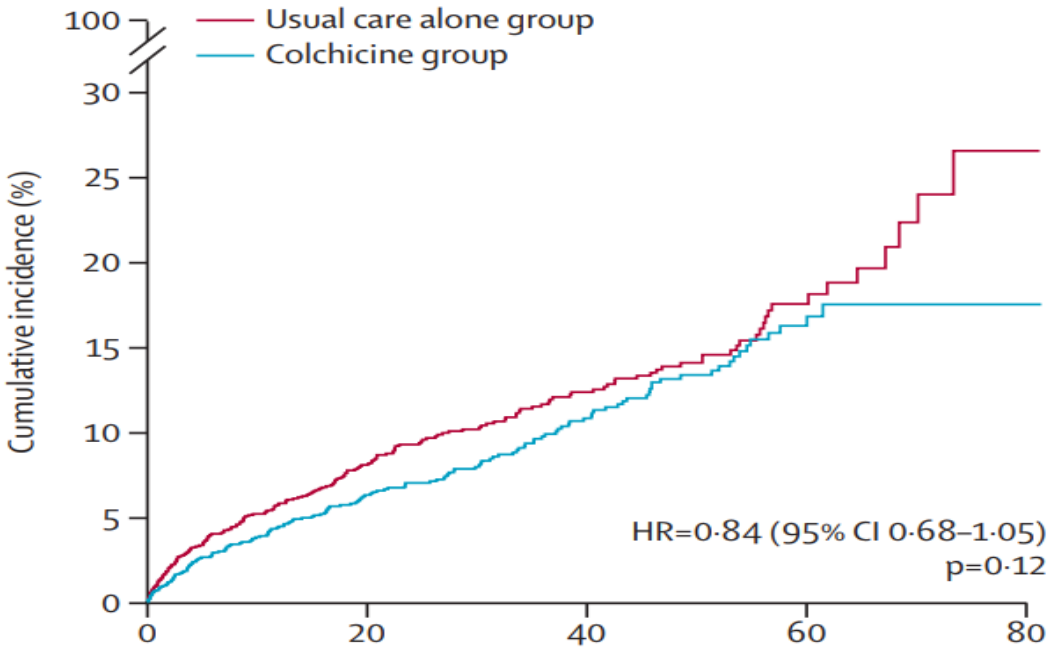
Kelly et al. Lancet 2024;404:125-133

CONVINCE: Geometric Mean C-reactive Protein Over Time



Kelly et al. Lancet 2024;404:125-133

CONVINCE: Cumulative Incidence of CV Events in the Primary Outcome, Intention-to-Treat Population



Kelly et al. Lancet 2024;404:125-133

CONVINCE: AEs for the Intention-to-Treat Population

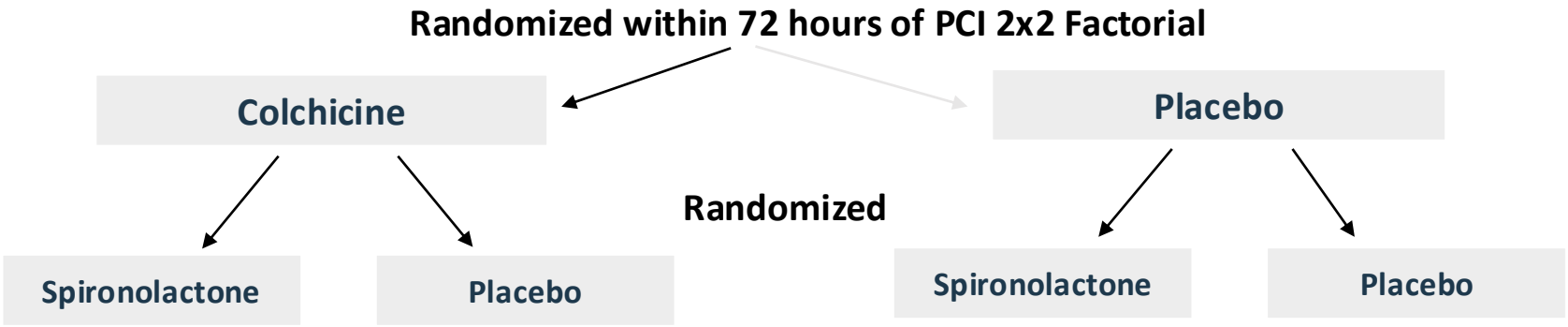
	Colchicine and usual care (n=1569)	Usual care alone (n=1575)	Relative risk (95% CI)
Serious adverse events			
All serious adverse events	1096 (69·9%)	1115 (70·8%)	0·99 (0·94–1·03)
Non-cardiovascular deaths	45 (2·9%)	41 (2·6%)	1·10 (0·73–1·67)
Non-outcome deaths	55 (3·5%)	49 (3·1%)	1·13 (0·77–1·65)
Serious adverse events due to cancer	81 (5·2%)	86 (5·5%)	0·95 (0·71–1·27)
Fatal cancer	13 (0·8%)	10 (0·6%)	1·30 (0·57–2·96)
Serious adverse events due to infection	313 (19·9%)	325 (20·6%)	0·97 (0·84–1·12)
Fatal infections	7 (0·4%)	14 (0·9%)	0·5 (0·20–1·25)
Serious adverse events due to haemorrhage			
All	28 (1·8%)	31 (2·0%)	0·91 (0·55–1·51)
Intracranial	12 (0·8%)	14 (0·9%)	0·86 (0·40–1·86)
Gastrointestinal	13 (0·8%)	14 (0·9%)	0·93 (0·44–1·98)
Other	3 (0·2%)	3 (0·2%)	1·0 (0·20–4·97)

Kelly et al. Lancet 2024;404:125-133

CLEAR SYNERGY Trial

7062 patients diagnosed with Acute Myocardial Infarction (MI) referred for PCI

SYNERGY stent recommended for use when available*



Primary Outcome

Colchicine vs. placebo: Composite of CV death, MI, stroke or ischemia driven revascularization over duration of follow-up

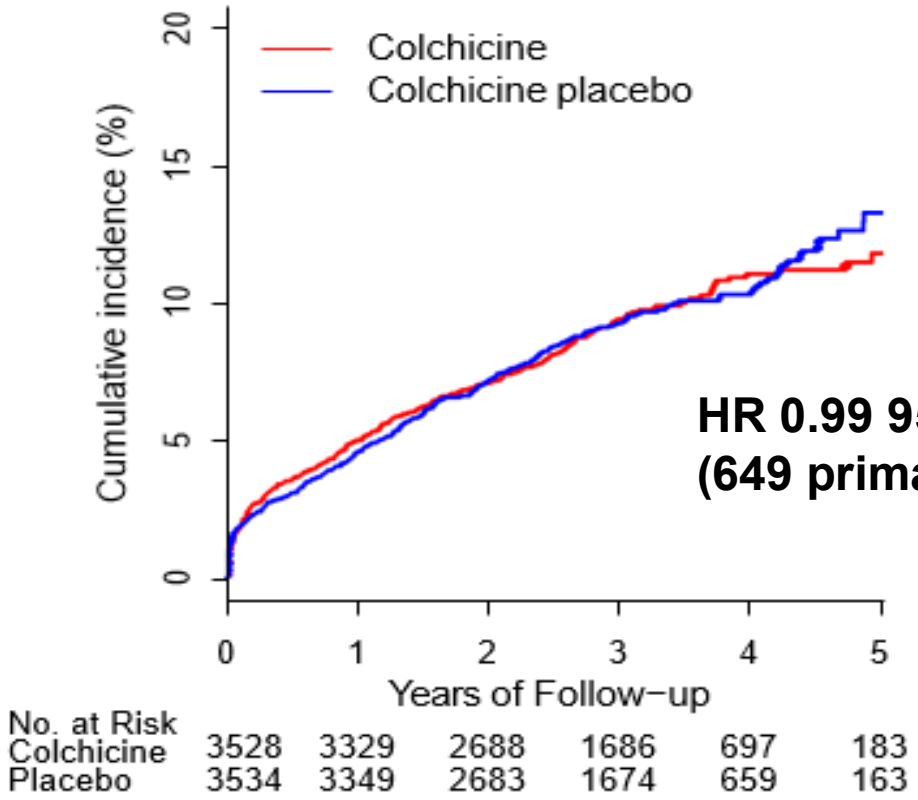
Jolly et al NEJM 2025;13:633-642.

CLEAR SYNERGY: Baseline Characteristics

	Colchicine N=3528	Placebo N=3534
Mean Age	60.6	60.7
Female	20.5%	20.2%
STEMI	95.3%	94.8%
NSTEMI	4.7%	5.2%
Diabetes	18.7%	18.3%
Prior MI	8.8%	9.2%

Jolly et al NEJM 2025;13:633-642.

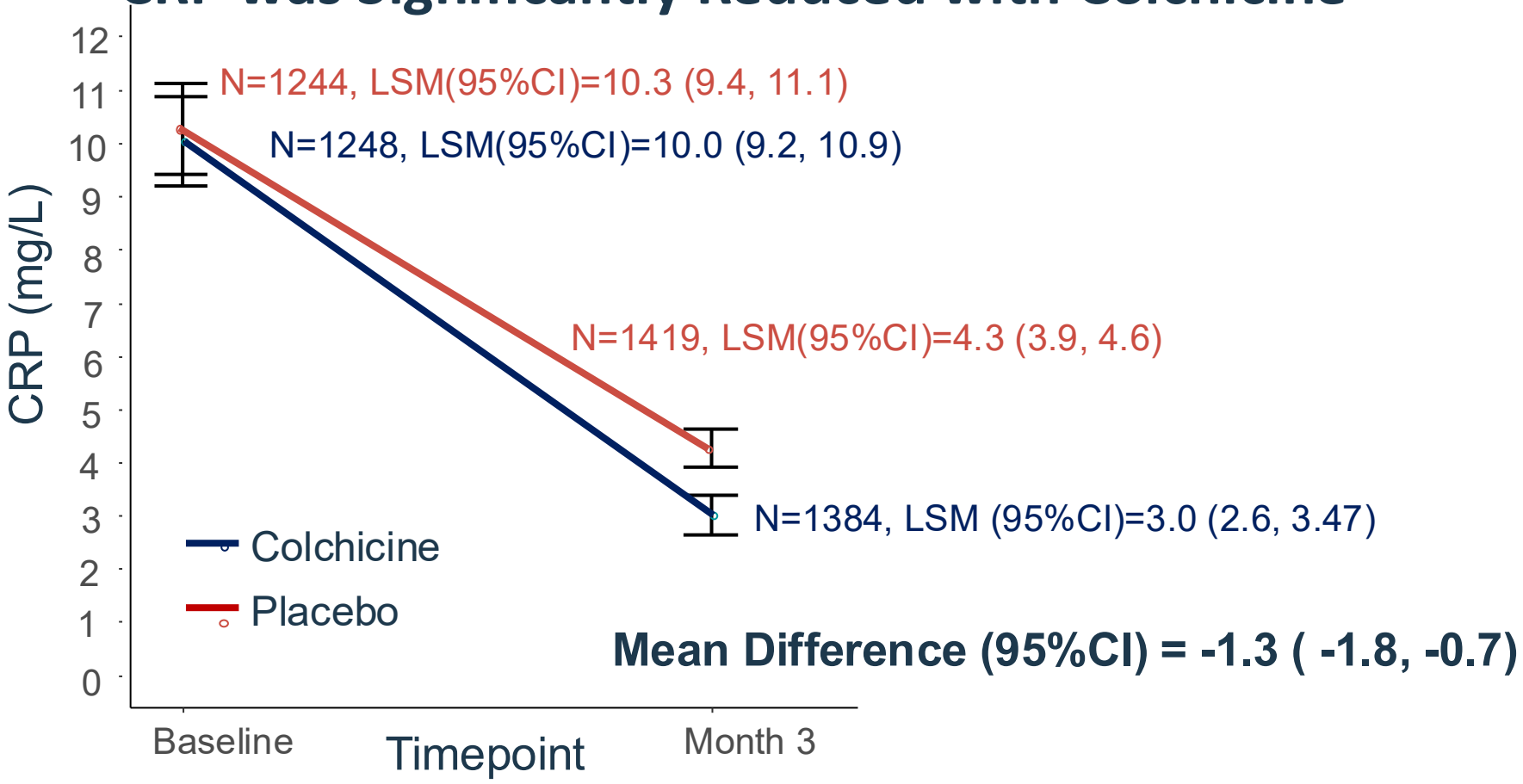
Primary Outcome of CV Death, MI, Stroke or Ischemia Driven Revascularization: CLEAR SYNERGY



HR 0.99 95% CI 0.85-1.16, p=0.93
(649 primary outcome events)

Jolly et al NEJM 2025;13:633-642.

CRP was Significantly Reduced with Colchicine



Jolly et al NEJM 2025;13:633-642.

CLEAR SYNERGY: On Treatment Analysis

	Colchicine (N=3488) (%)	Placebo (N=3492) (%)	HR	95% CI	p
CV death, MI, stroke or ischemia driven revascularization	7.5%	7.5%	0.99	0.85-1.16	0.93
CV death	2.7%	2.5%	1.04	0.80-1.35	
MI	2.3%	2.4%	0.89	0.67-1.18	
Stroke	1.1%	1.0%	1.09	0.68-1.75	
Ischemia driven revascularization	3.9%	3.8%	1.03	0.82-1.29	
CV death, MI or stroke	5.5%	5.7%	0.97	0.81-1.16	
All cause death	3.4%	3.8%	0.90	0.70-1.15	
Non-CV death	0.7%	1.3%	0.71	0.49-1.04	

Jolly et al NEJM 2025;13:633-642.

CLEAR SYNERGY - Critical Issues

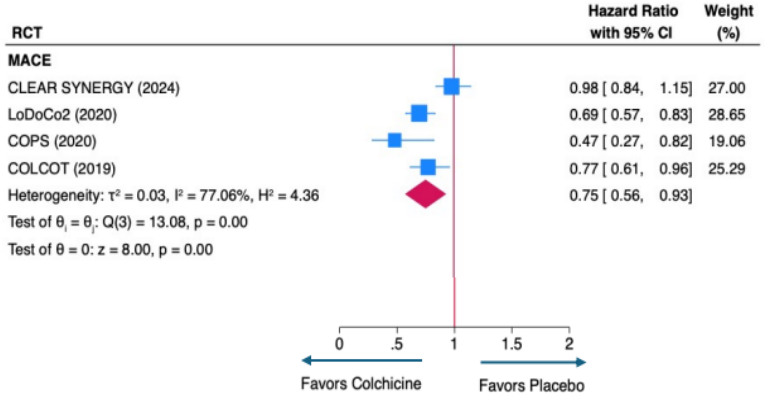
1- Initially RRR of 22%, lost during COVID
2- Low recruitment numbers of STEMI patients (95%)
3- Modification of protocol to enrol large NSTEMI + LVEF <45%
4- HsCRP 3.0 mg/L in the colchicine group at 3 months.
5- High discontinuation rate of 26%
6- In interim analysis low incidence of events: increase in sample size from 4000 to 7000
7- lack of benefit of colchicine on pericarditis
8- Incidence of gout not reported
9- Adherence has not been controlled for
10- Spironolactone did not show an effect

Long-term Trials of Colchicine for Secondary Prevention of Vascular Events: A Meta-analysis

European Society of Cardiology guidelines (2024) recommend daily low-dose colchicine (0.5 mg/day), in addition to guideline-directed therapy, to patients with coronary artery disease with a class IIa recommendation.

This updated systematic review and meta-analysis of 6 randomized controlled trials in 21,800 patients with vascular disease (post- myocardial infarction, stroke, and stable CAD) demonstrated that colchicine (compared to medical therapy only) reduced:

- 25% ↓ **MACE**
- 29% ↓ Myocardial Infarction
- 37% ↓ Ischemic Stroke
- 33% ↓ Urgent Coronary Revascularization



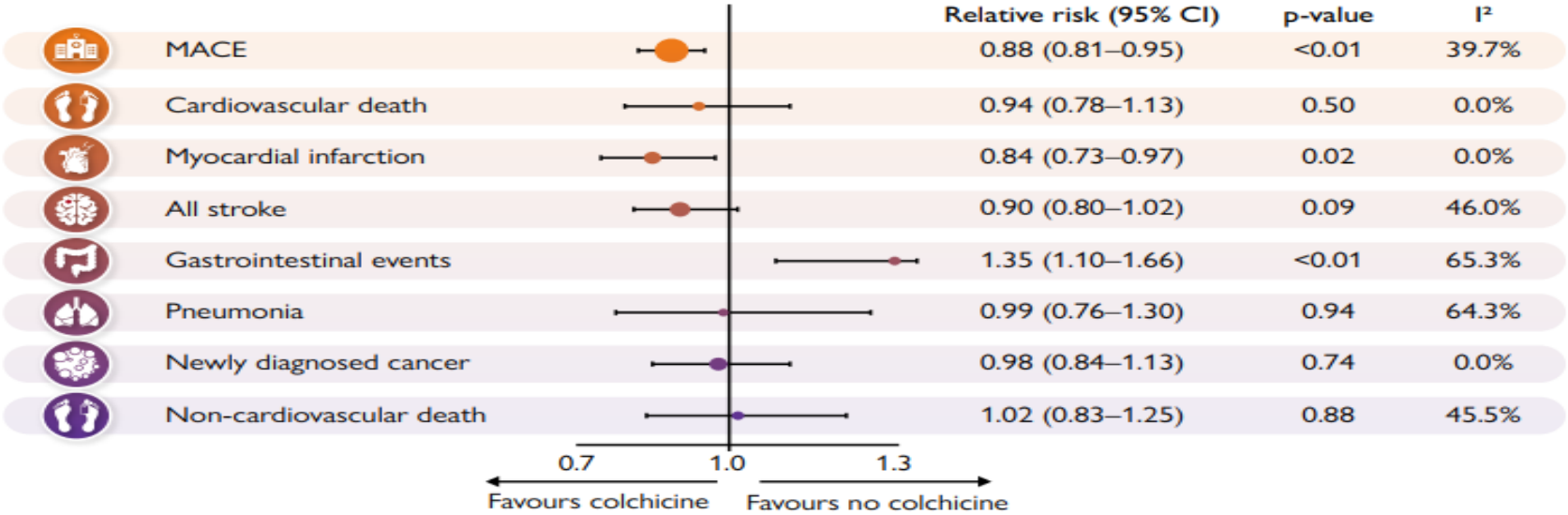
Samuel M….Koenig W……Tardif JC Eur Heart J 2025; 46:2552-2563.

Colchicine for Secondary Prevention of Vascular Events: A Meta-analysis of Trials

9 trials, including 30 659 patients in a secondary prevention ASCVD population

15 255 Patients who received colchicine

15 404 Patients who received placebo, or no colchicine



Included CHANCE 3 with 8343 pts after stroke followed for 90 days

d`Entremont et al. Eur Heart J 2025;46:2564-2575

Approval of Low Dose Colchicine for Secondary Prevention by FDA

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LODOCO safely and effectively. See full prescribing information for LODOCO.

LODOCO (colchicine) tablets, for oral use
Initial U.S. Approval: 1961

----------INDICATIONS AND USAGE----------
LODOCO is an alkaloid indicated:

- to reduce the risk of myocardial infarction (MI), stroke, coronary revascularization, and cardiovascular death in adult patients with established atherosclerotic disease or with multiple risk factors for cardiovascular disease (1).

----------DOSAGE AND ADMINISTRATION----------
The recommended dosage is 0.5 mg orally once daily. (2.1).

----------DOSAGE FORMS AND STRENGTHS----------
Tablets: 0.5 mg (3).

----------CONTRAINDICATIONS----------

- Concurrent use of strong CYP3A4 inhibitors or P-gp inhibitors with LODOCO is contraindicated, including in patients with hepatic or renal impairment (4).
- LODOCO is contraindicated in patients with pre-existing blood dyscrasias, renal failure, and severe hepatic impairment (4).

----------WARNINGS AND PRECAUTIONS----------

- *Blood dyscrasias*: myelosuppression, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, and aplastic anemia have been reported (5.1).
- *Neuromuscular toxicity*: Myotoxicity including rhabdomyolysis may occur, especially in combination with other drugs known to cause this effect. Consider temporary interruption or discontinuation of LODOCO (5.2).

----------ADVERSE REACTIONS----------
The common side-effects reported in published clinical studies and literature with the use of colchicine are gastrointestinal symptoms (diarrhea; vomiting; abdominal cramping) and myalgia (6).

To report SUSPECTED ADVERSE REACTIONS, contact AGEPHA Pharma FZ LLC at 1 (800) 963-0353 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
Coadministration of P-gp and/or CYP3A4 inhibitors (e.g., cyclosporine or clarithromycin) have been demonstrated to alter the concentration of colchicine. The potential for drug-drug interactions must be considered prior to and during therapy. See FPI for a complete list of reported and potential interactions (7).

----------USE IN SPECIFIC POPULATIONS----------

- Females and Males of Reproductive Potential: Advise males that LODOCO may rarely and transiently impair fertility (8.3)
- Patients with renal or hepatic impairment should be monitored closely for adverse effects of colchicine (8.6, 8.7).

New recommendations (14)

Recommendations	Class	Level
Sodium–glucose cotransporter 2 inhibitors and/or glucagon-like peptide-1 receptor agonists in patients with chronic coronary syndrome		
SGLT2 inhibitors with proven CV benefit are recommended in patients with T2DM and CCS to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication.	I	A
The GLP-1 receptor agonist semaglutide should be considered in CCS patients without diabetes, but with overweight or obesity (BMI >27 kg/m^2), to reduce CV mortality, MI, or stroke.	IIa	B
Anti-inflammatory drugs in patients with chronic coronary syndrome		
In CCS patients with atherosclerotic CAD, low-dose colchicine (0.5 mg daily) should be considered to reduce myocardial infarction, stroke, and need for revascularization.	IIa	A

Summary and Conclusions

- Inflammatory processes in the vascular wall are present during all stages of atherogenesis and are accompanied by a low-grade systemic inflammation
- CANTOS, a proof of concept trial, has demonstrated that targeting inflammation without interfering with lipid metabolisms can reduce important clinical endpoints in ASCVD patients with hsCRP > 2mg/L at baseline and achieving a hsCRP level < 2mg/L
- The NLRP3/IL-1ß/IL-6 pathway at present seems to be the most relevant one targeting inflammation in the context of atherosclerosis
- Treatment with colchicine may be considered in very high risk patients on optimal established medication (class IIa recommendation).

Thank You for Your Attention!

Prof. Wolfgang Koenig
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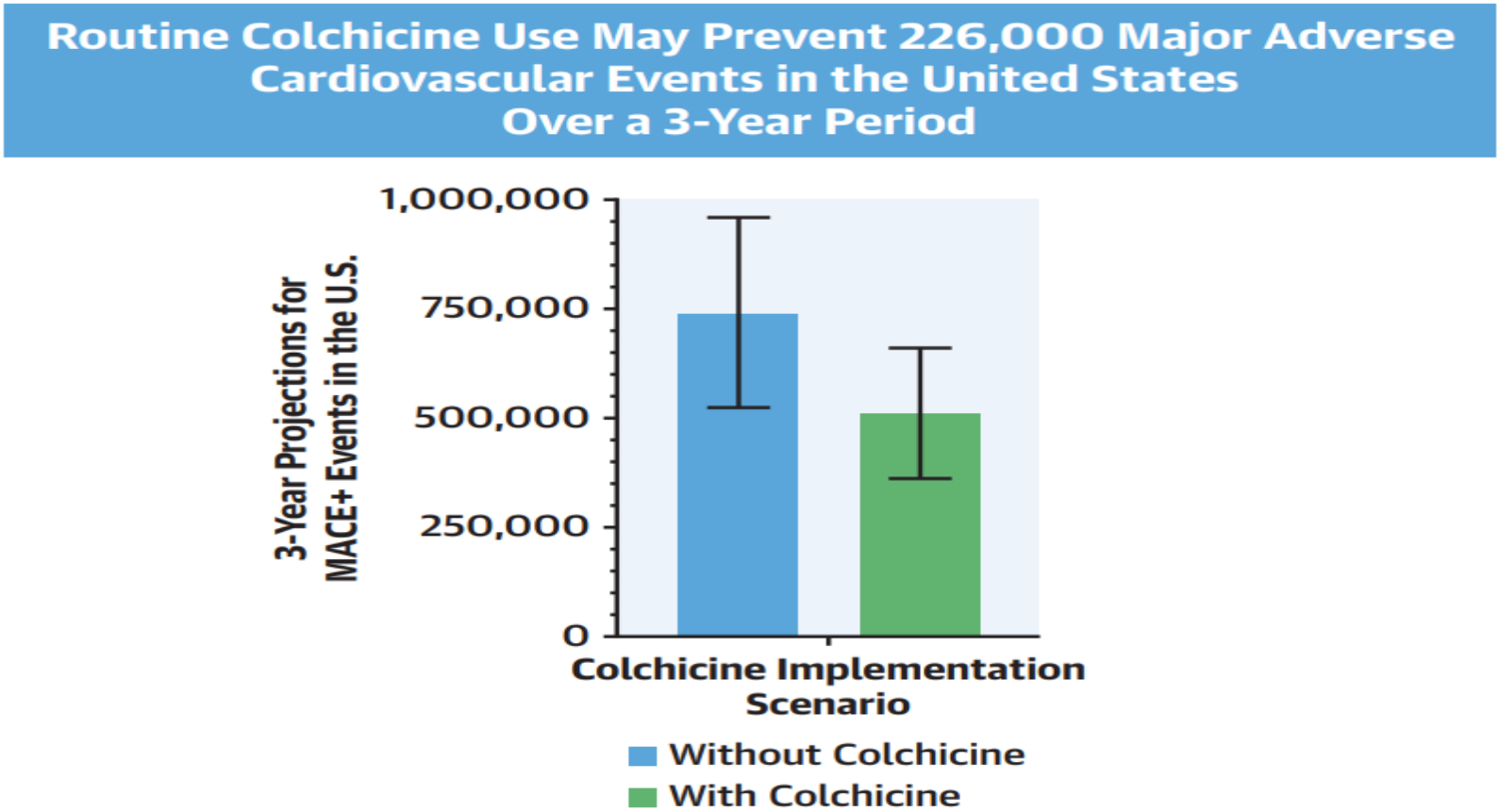
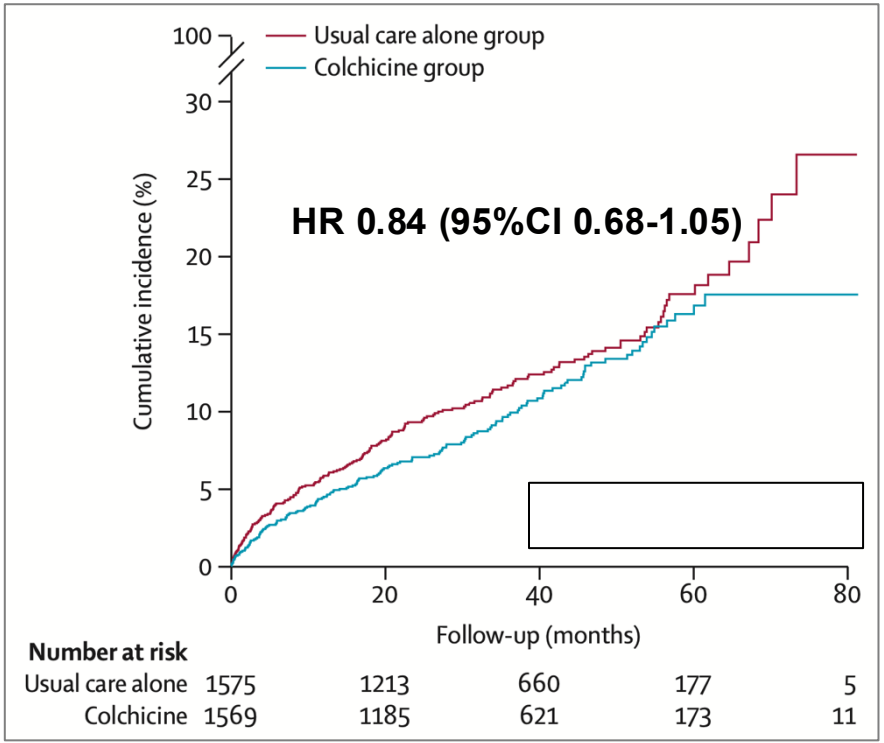
Potential Impact of Colchicine on CAD in the United States



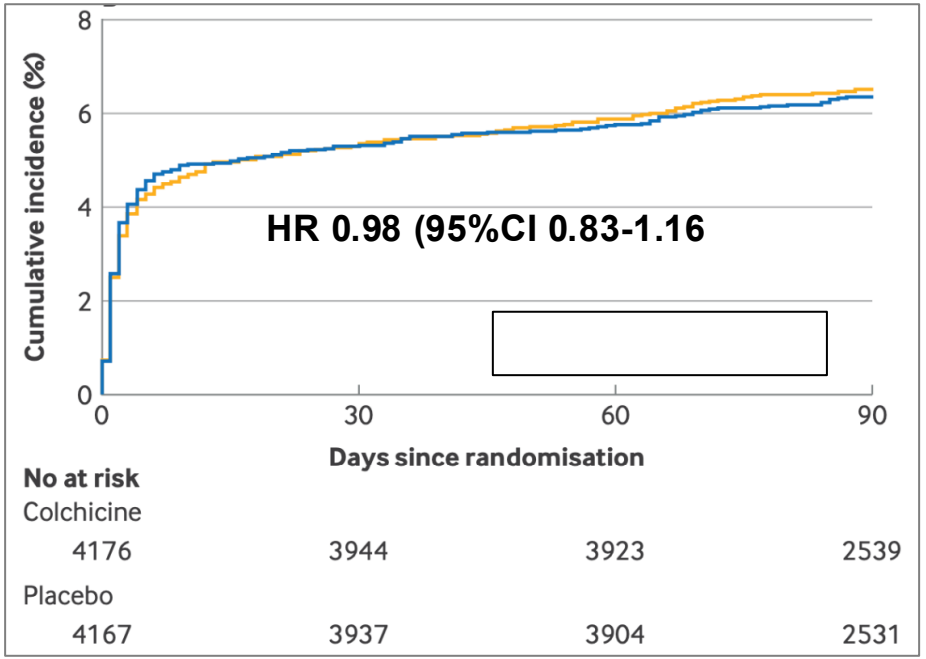
Buckley et al. JACC Adv. 2025;4:101622

Cerebrovascular Disease: No Difference

CONVINCE (N = 3154, MACE+, 338 events)



CHANCE3 (N = 8343, all stroke, 534 events)



16. Thromboseforum

Stuttgart, 28. Februar 2026

Ist eine Disussion bei formalem Vorliegen einer IA Indikation und Fehlen ernsthafter Nebenwirkungen noch notwendig?

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