Pre-PCI Colchicine

Subodh Verma MD PhD FRCSC FAHA
Professor and Cardiac Surgeon
CRC Tier 1 Chair in CV Surgery
CardioLink Trials Co-Chair
University of Toronto

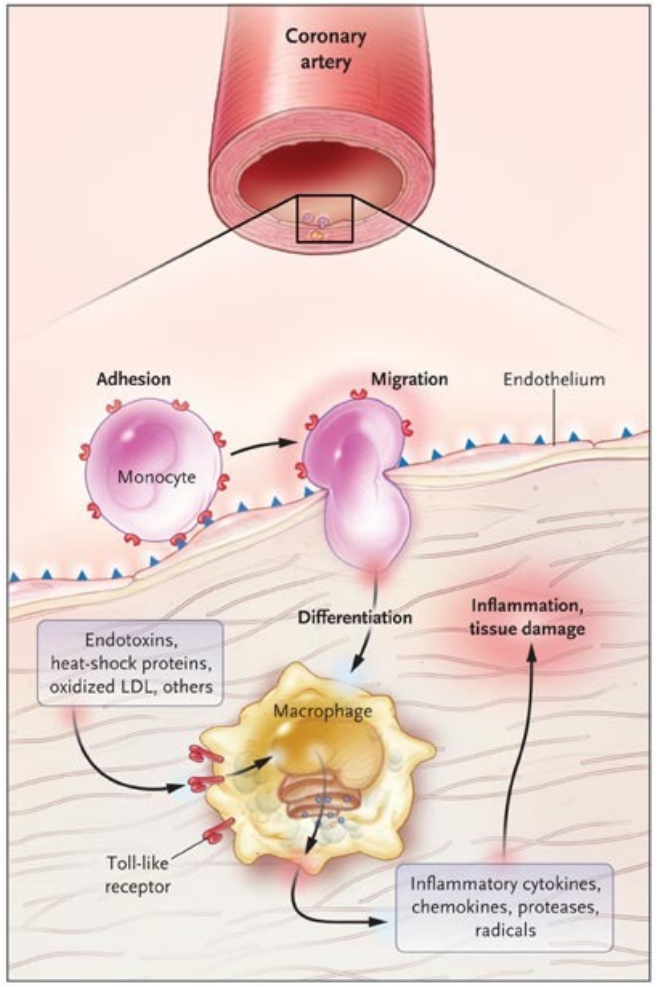
Disclosures

- Professor Subodh Verma has received speaking and/or research support from Amgen, Abbott, AstraZeneca, BI, Bayer, BMS, Merck, Janssen, Sanofi, Novartis, Lilly, Novonordisk, HLS
- NC for DAPA-HF, DELIVER-HFpEF, EMPEROR Trials, SOLOIST, SELECT
- SEC for EMPEROR-R and EMPEROR-P, DETERMINE-A and B
- PI/co-PI for NEWTON-CABG, ACE, SEARCH-AF, CAMRA, ENABLE-Chiropody, EMPA-HEART-1, EMPA-HEART-2
- Canadian Medical and Surgical Knowledge Translation Research Group
- SC CIRT, BELIEVE

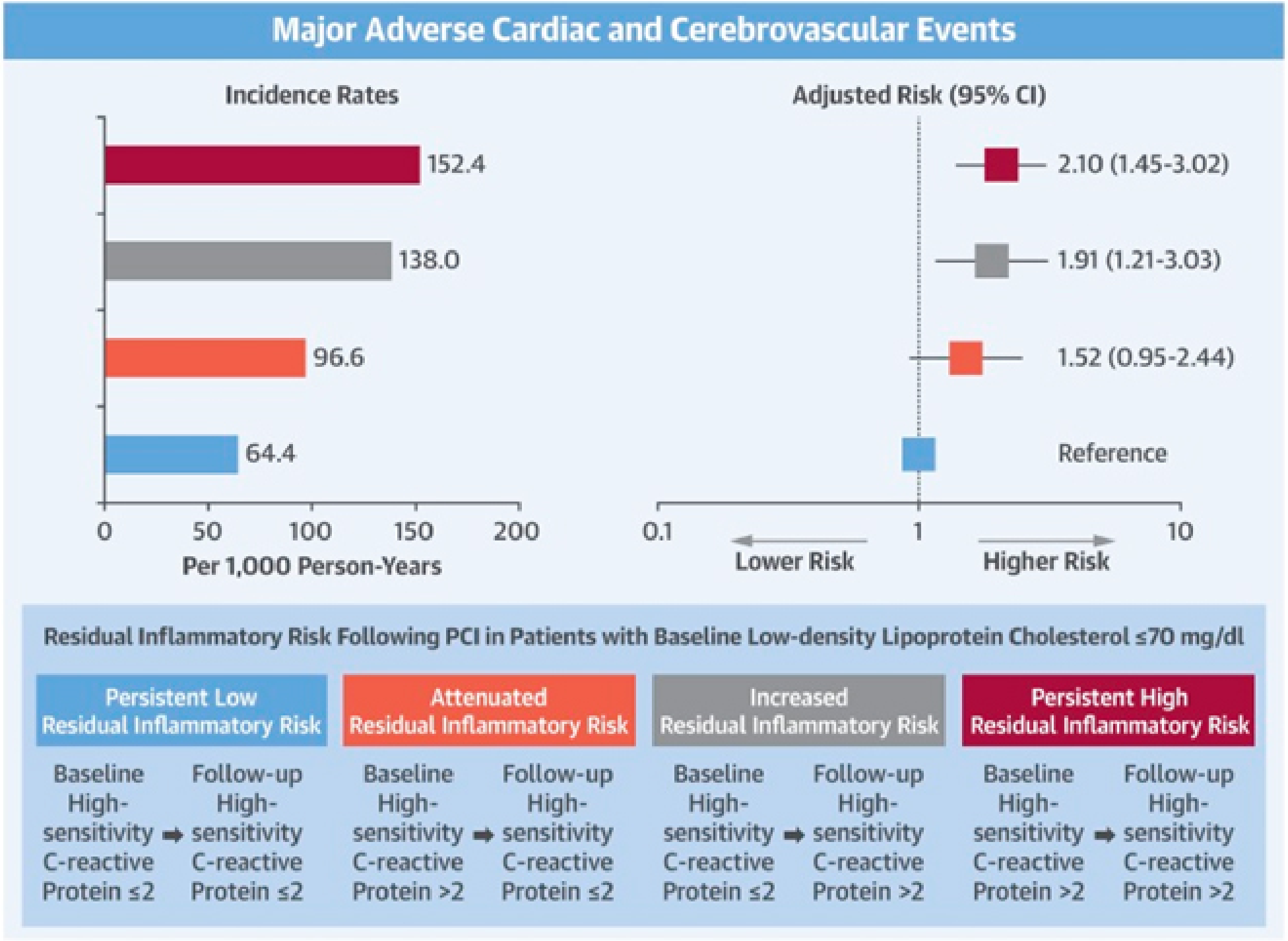
The Importance of Peri-PCI Inflammation

- Peri-PCI vascular inflammation (either primary or secondary) has been independently associated with atherothrombotic outcomes.

- Activation of both the innate and adaptive immune systems can lead to aberrant vessel repair, re-endothelialization, restenosis and recurrent events.

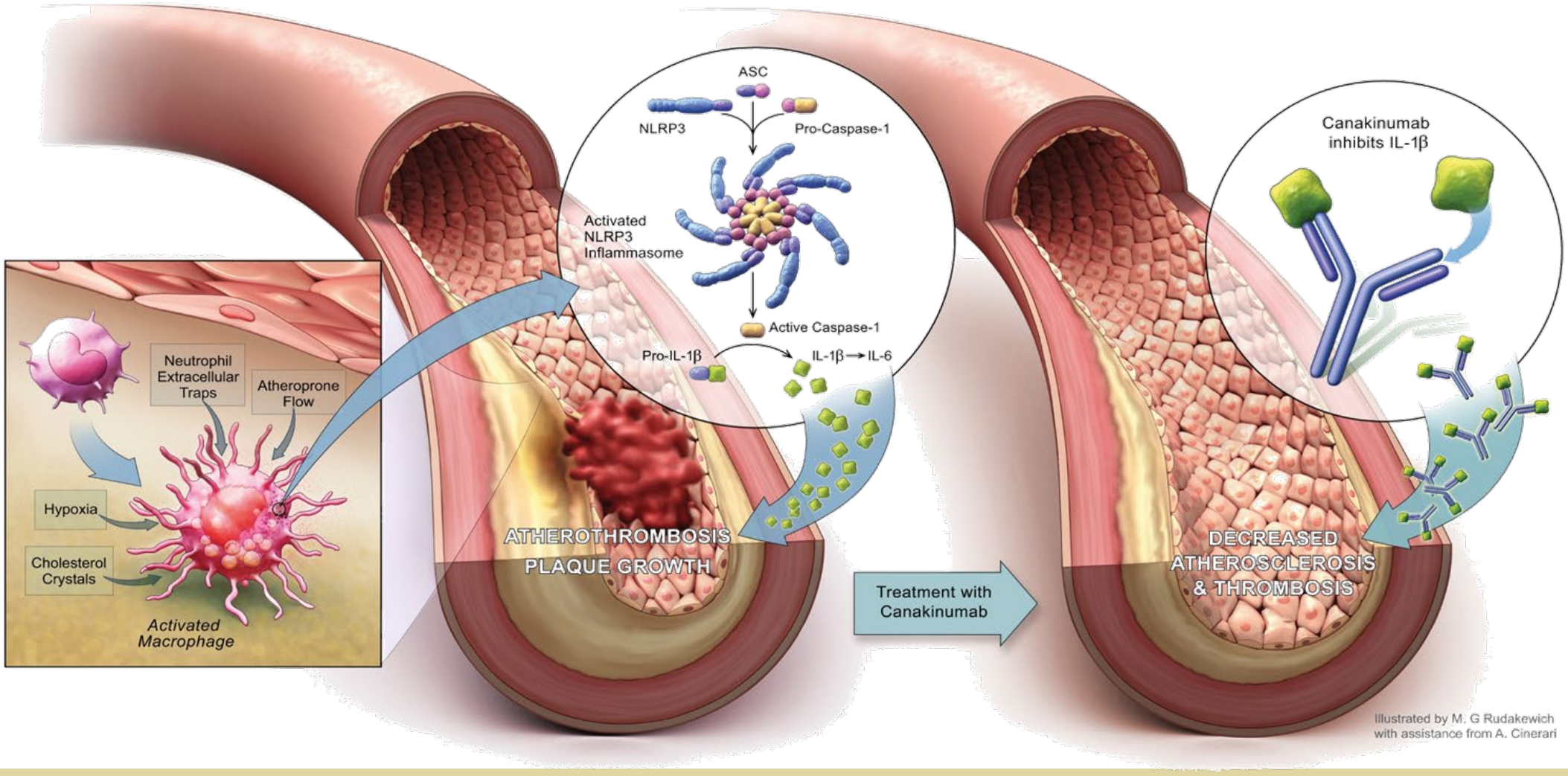


1-Year Impact of Residual Inflammatory Risk in Patients Undergoing PCI with Baseline LDL-C ≤70 mg/dL



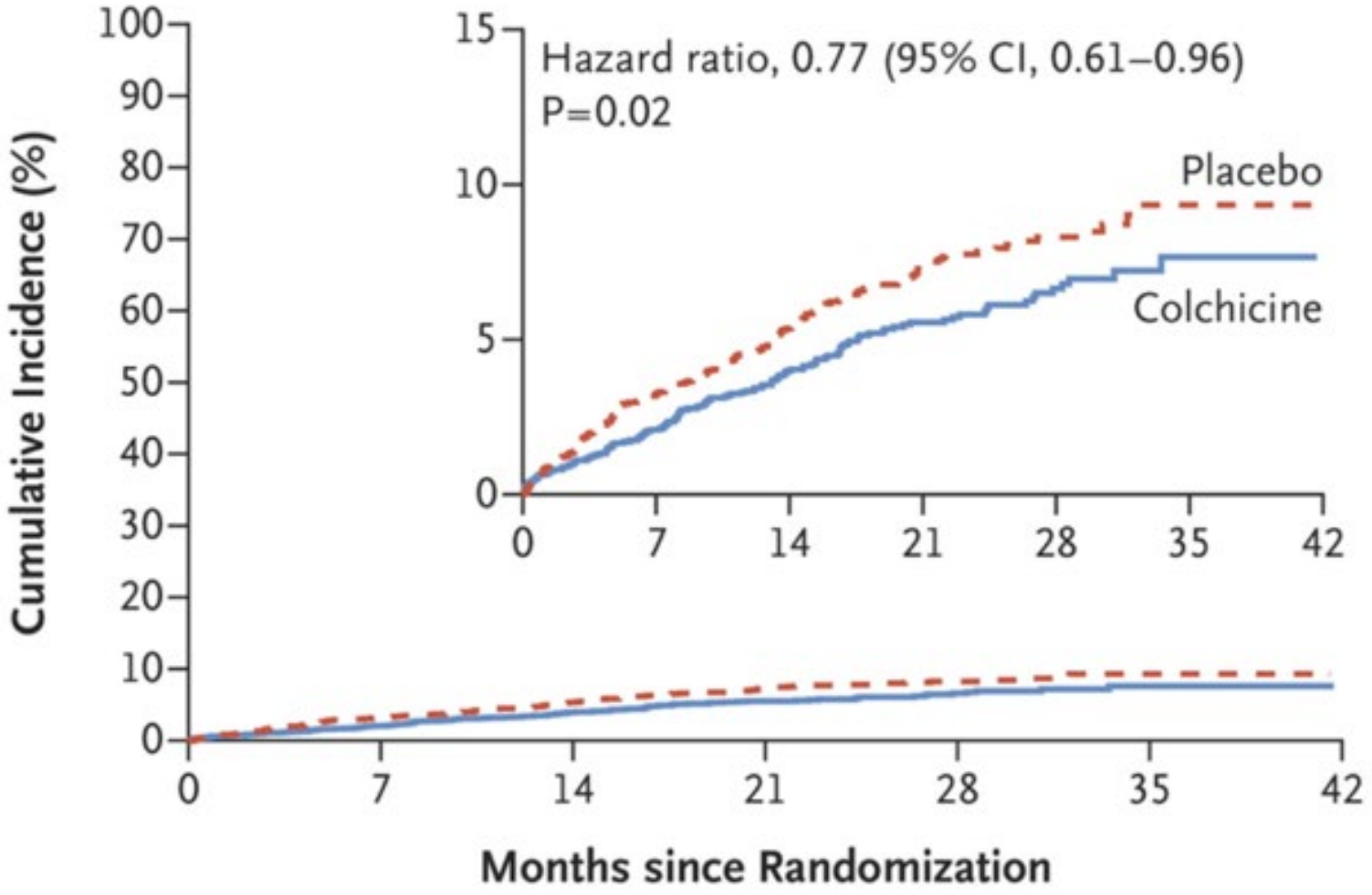
Guedeney P et al.
J Am Coll Cardiol. 2019;73:2401-2409.

CANTOS: A Critical Proof of Concept in patients with a history of myocardial infarction



Verma S, Leiter LA, Bhatt DL. Cell Metab. 2017;26:703-705.

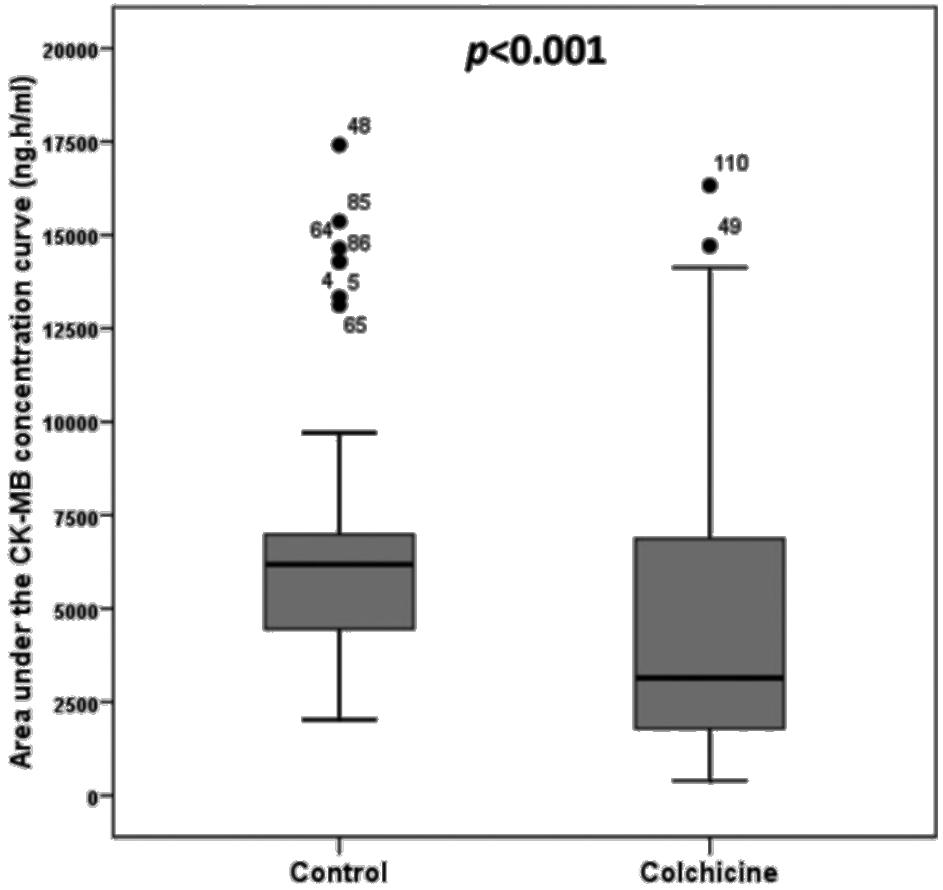
COLCOT – Colchicine for post MI



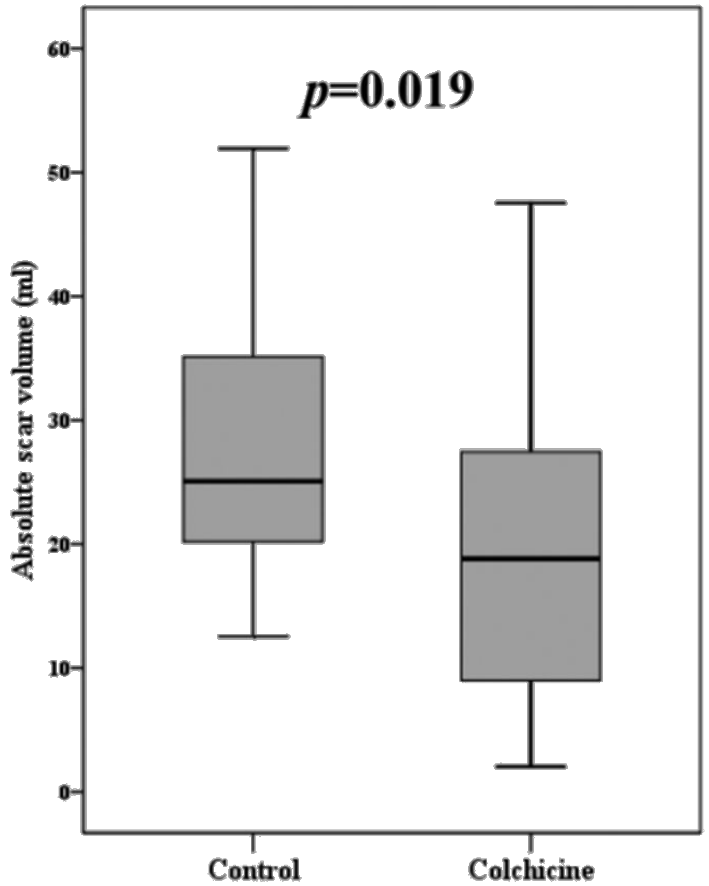
Tardif JC et al. NEJM 2019

Colchicine reduced infarct size in patients with STEMI undergoing primary PCI

Creatine kinase-myocardial brain fraction (CK-MB)



MRI with late gadolinium enhancement (MRI-LGE)



Deftereos S et al. Circulation. 2015;132:1395-403.

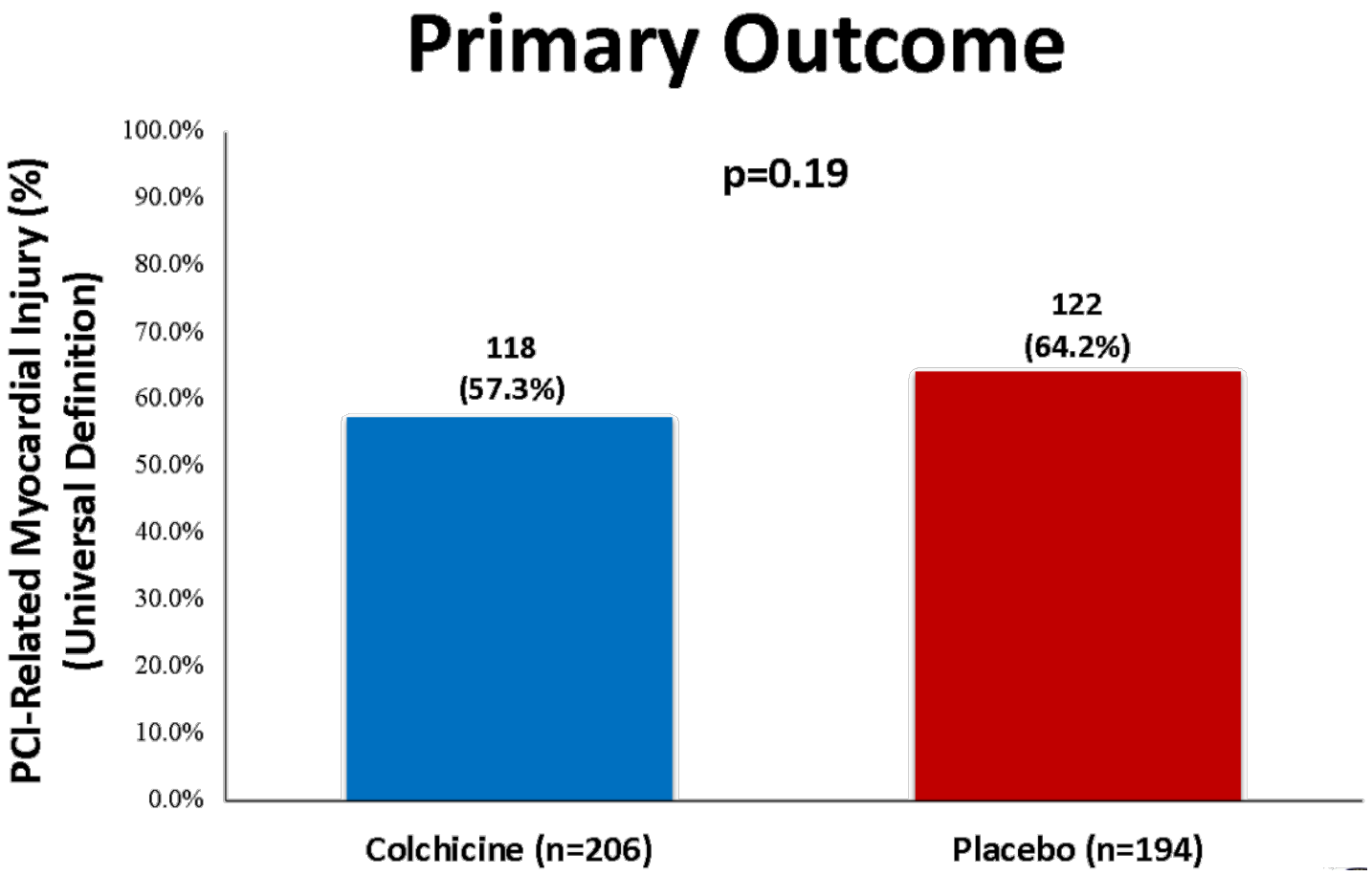
An important question was asked

Does pre-procedural colchicine reduce inflammation and myocardial injury?

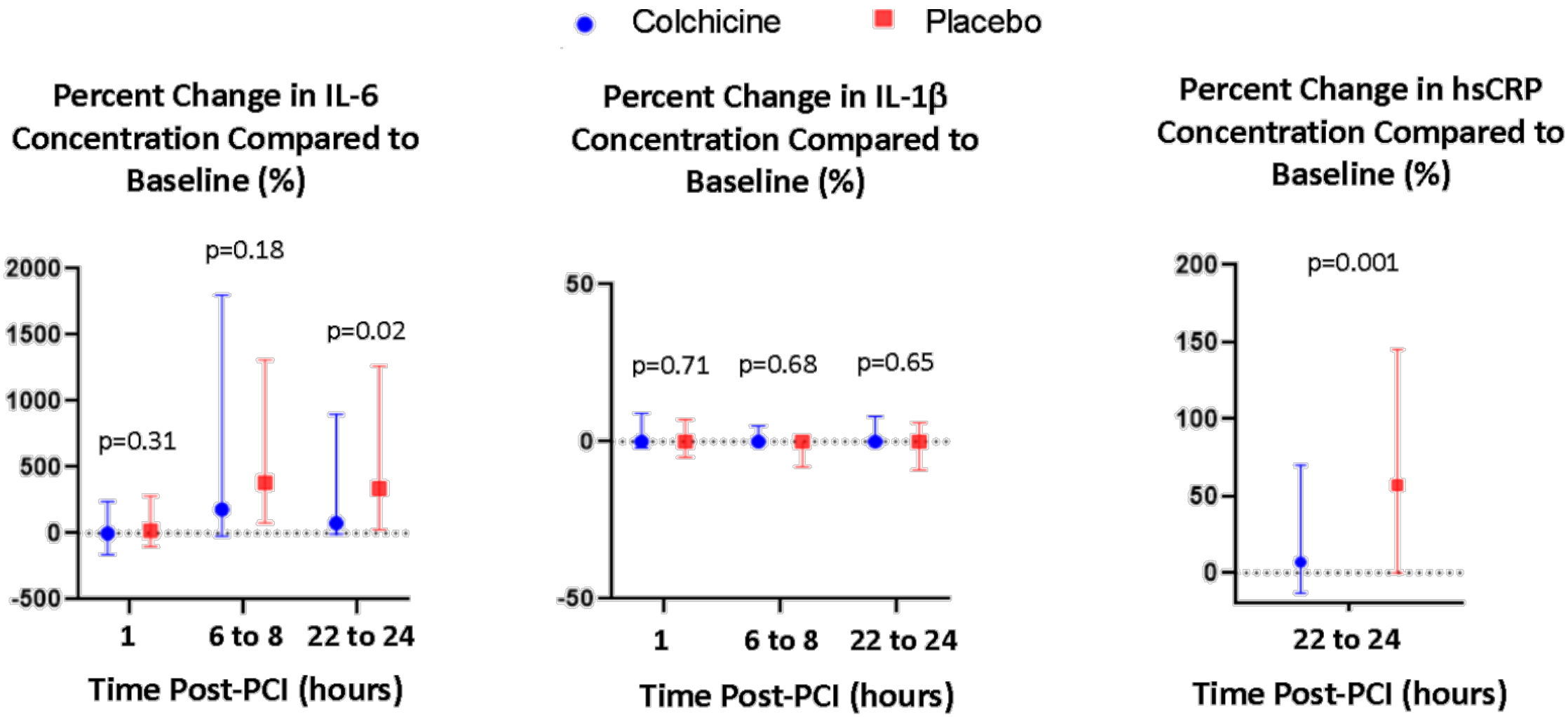
How was the question addressed?

Population	Intervention	1º Outcomes	Follow-up
Patients undergoing diagnostic coronary angiography (with or without possible PCI)	Pre-cath 1.8 mg colchicine single dose	• Change in IL-6 (baseline to 1h post PCI) • PCI-related myocardial injury (troponin I)	• 1h • 6-8h • 22-24h • 30-day

What did they find?



What did they find?



Study Analysis and Implications (1)

- Well conducted and executed study
- Single center experience
- Mixed population of patients undergoing diagnostic angiography or ACS
- Inflammatory biomarkers during ACS are highly variable (acute phase reactant)
- Baseline levels of inflammatory markers not reported
- Do patients with increased baseline inflammation have greater benefit (analogous to CANTOS)?
- Study was powered to detect a 40% RRR in primary outcome and 35% RRR in IL-6
- Single dose
- Excluded patients on high intensity statin within preceding 24 hours

Study Analysis and Implications (2)

- Local changes in inflammatory biomarkers may be missed (coronary sinus effluent)
- Lack of changes in circulating IL-6 and IL-1β may be an issue of sensitivity, variability and confounded by the milieu of ACS
- Reassuring to see lower hsCRP at 24 hours post-PCI ($p<0.001$)
- 93.7% were men
- Background medical therapy and lipid levels?
- Excluded patients without CAD what were the results?
- Good safety profile

CLEAR SYNERGY (OASIS 9)

CoLchicine and spironolactonE in patients with ST elevation myocARdial infarction – OASIS 9 Trial/SYNERGY Stent Registry

Sanjit S. Jolly MD, MSc.
PHRI, McMaster University,
Hamilton Health Sciences

CLEAR SYNERGY (OASIS 9) Study Design

4000 patients diagnosed with STEMI referred for PCI

Initial 800 patients
SYNERGY Stent REQUIRED where commercially available

Within **48 hours** of successful PCI and during initial hospitalization,
RANDOMIZED to (2 x 2 factorial):

Colchicine **Placebo** + Spironolactone **Placebo**	Colchicine **ACTIVE** + Spironolactone **Placebo**	Colchicine **Placebo** + Spironolactone **ACTIVE**	Colchicine **ACTIVE** + Spironolactone **ACTIVE**

Follow-up: Discharge, 3, 6, 12 months; 24, and 36 months, or Common Study End Date

Primary Outcomes

SYNERGY Stent: Major adverse cardiac events (MACE) compared to performance goal within 1 year
Colchicine vs. placebo: Composite of CV death, recurrent MI, or stroke over duration of follow-up
Spironolactone vs. placebo: Composite of CV death or new or worsening HF over duration of follow-up

MACE was defined as the composite of death, recurrent target vessel MI, stroke or ischemia driven target vessel revascularization.

So what's the bottom line for colchicine?

Recent MI	YES - COLCOT
Acute peri-STEMI	? CLEAR SYNERGY
Pre-PCI	? Not yet

More studies targeting patients with RIR with acute + chronic Rx
High risk primary prevention patients (COLCOT-2) (TDM)