The COLchicine Cardiovascular Outcomes Trial

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on behalf of the COLCOT Investigators

Montreal Health Innovations Coordinating Center
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Background

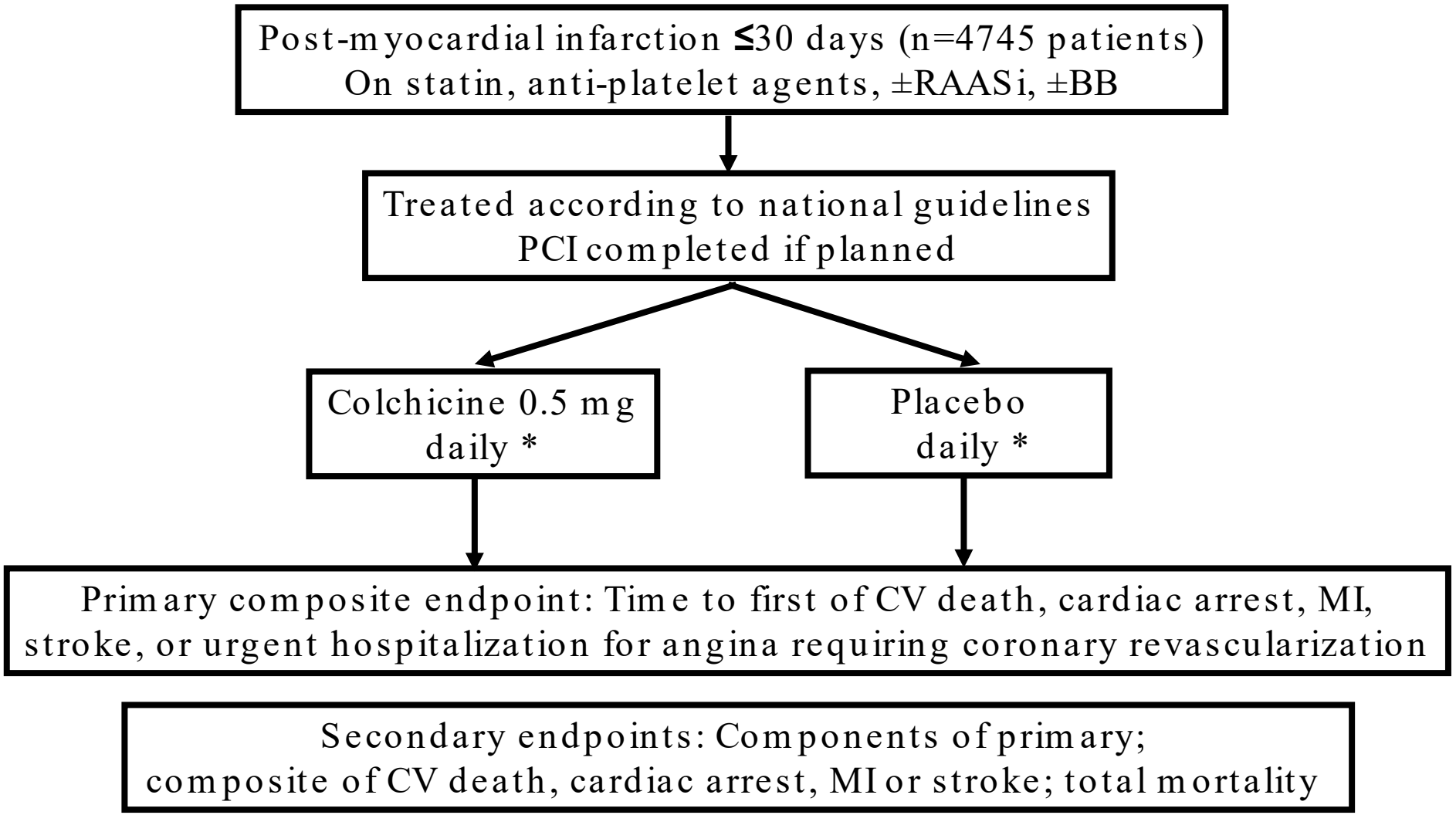
- **Experimental and clinical evidence support the role of inflammation in atherosclerosis and its complications.**

- **The search for a widely used anti-inflammatory treatment that may reduce the risk of atherosclerotic events in patients with coronary artery disease continues.**

- **Colchicine is an orally administered, potent anti-inflammatory medication currently indicated for gout and pericarditis.**

- **COLCOT was conducted in patients with a recent myocardial infarction to evaluate the effects of colchicine on cardiovascular outcomes and its long-term safety and tolerability.**

Study design



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*provided by Pharmascience (Montreal)

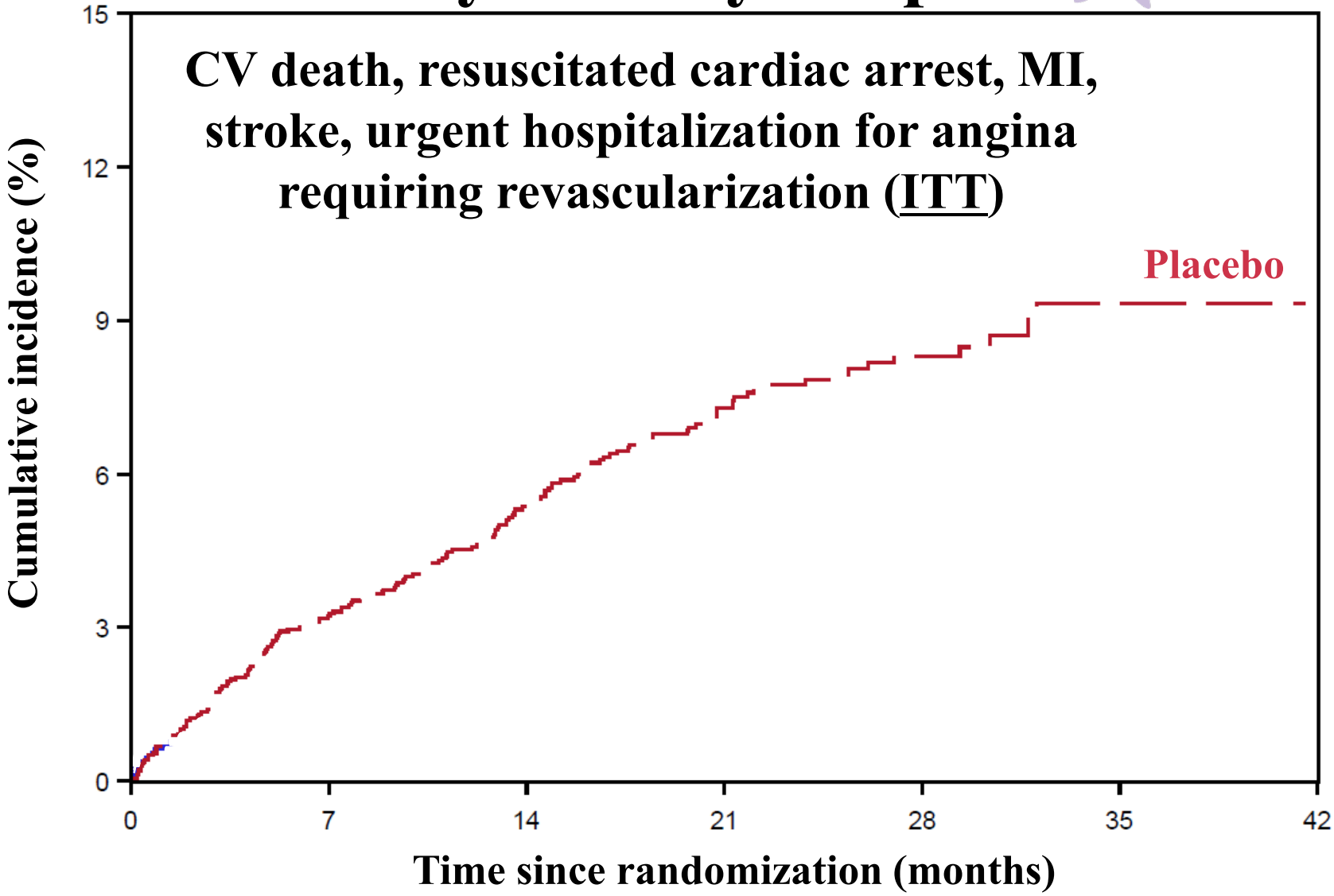
Patient characteristics

	Colchicine (N=2366)	Placebo (N=2379)
Age - years	60.6±10.7	60.5±10.6
Female sex - no. (%)	472 (19.9%)	437 (18.4%)
Caucasian - no. (%)	1350/1850 (73.0%)	1329/1844 (72.1%)
Body-mass index - kg/m^2	28.2±4.8	28.4±4.7
Smoking - no. (%)	708 (29.9%)	708 (29.8%)
Hypertension - no. (%)	1185 (50.1%)	1236 (52.0%)
Diabetes - no. (%)	462 (19.5%)	497 (20.9%)
Prior MI - no. (%)	370 (15.6%)	397 (16.7%)
Prior PCI - no. (%)	392 (16.6%)	406 (17.1%)
Prior CABG - no. (%)	69 (2.9%)	81 (3.4%)
Prior HF - no. (%)	48 (2.0%)	42 (1.8%)
Prior stroke/TIA - no. (%)	55 (2.3%)	67 (2.8%)

Patient characteristics

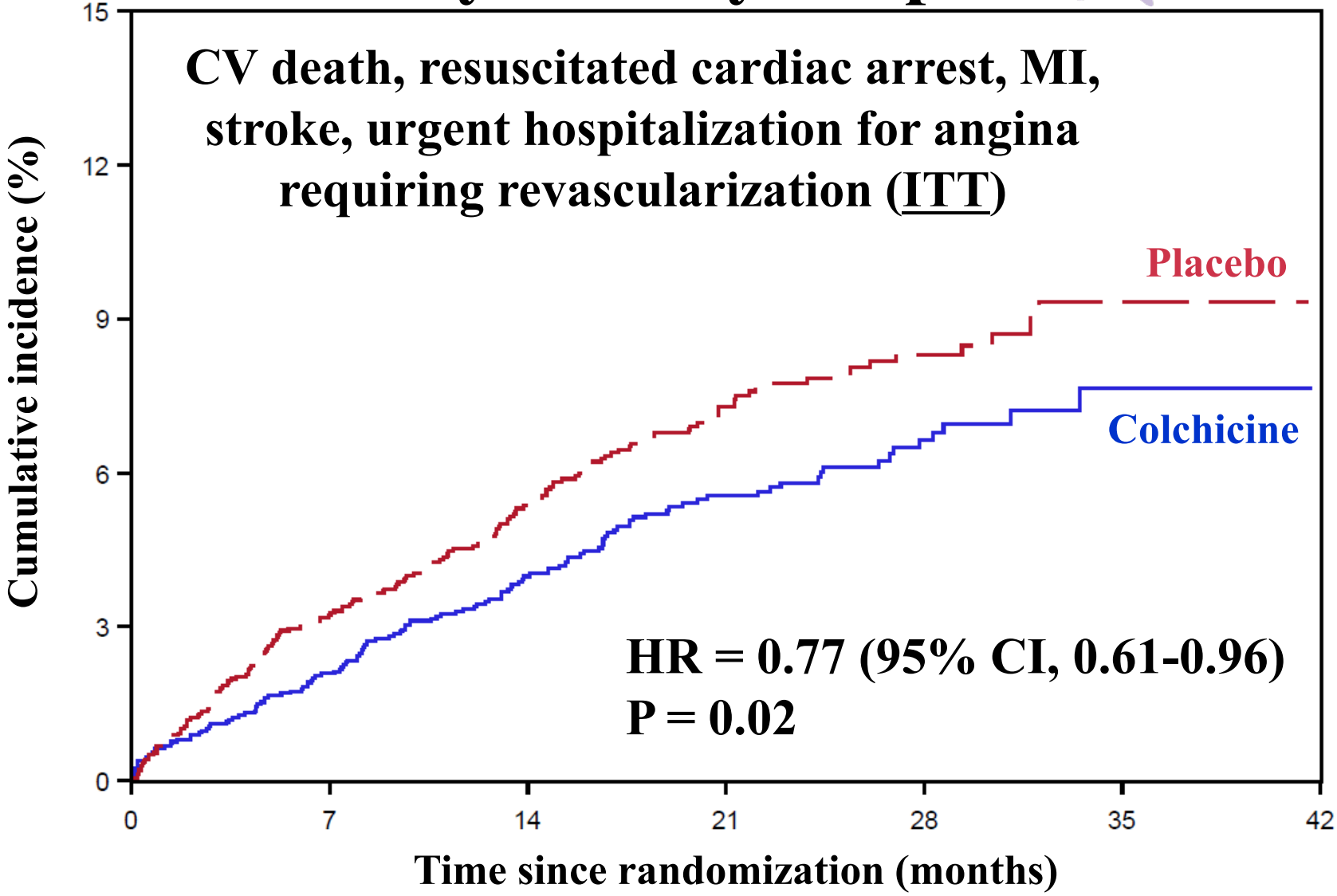
	Colchicine (N=2366)	Placebo (N=2379)
Index MI to randomization - days	13.4 ± 10.2	13.5 ± 10.1
PCI for index MI - no. (%)	2192/2364 (92.7%)	2216/2375 (93.3%)
Aspirin - no. (%)	2334 (98.6%)	2352 (98.9%)
Other anti-platelet agent - no. (%)	2310 (97.6%)	2337 (98.2%)
Statin - no. (%)	2339 (98.9%)	2357 (99.1%)
Beta-blocker - no. (%)	2116 (89.4%)	2101 (88.3%)

Primary efficacy endpoint



No. at Risk							
Colchicine	2366	2284	1868	1230	628	153	0
Placebo	2379	2261	1854	1224	622	144	0

Primary efficacy endpoint

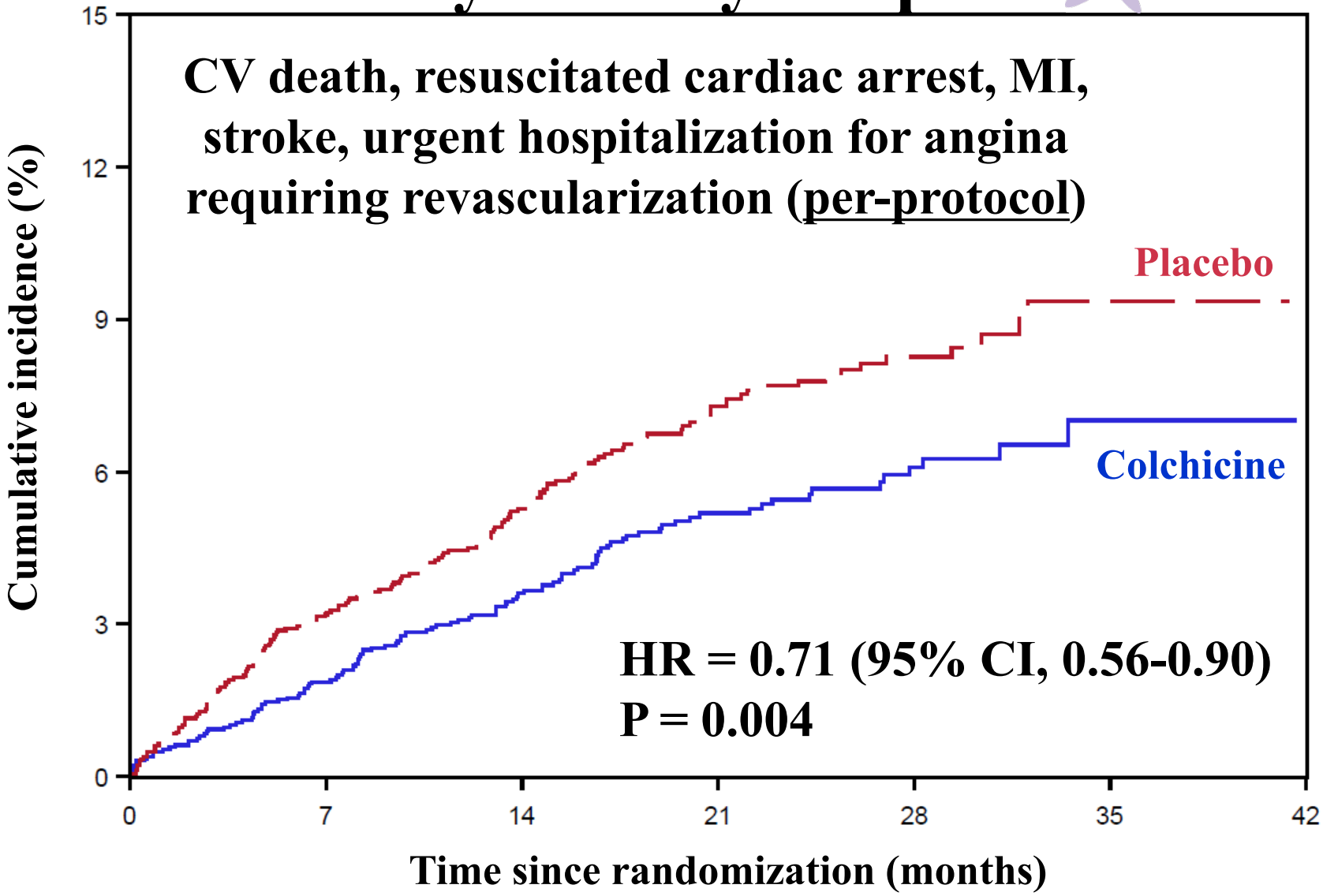


Major Clinical Outcomes

Clinical Outcome Intent-to-treat population	Colchicine N=2366	Placebo N=2379	Hazard Ratio (95% CI)	P Value
Primary composite endpoint - no. (%)	131 (5.5%)	170 (7.1%)	0.77 (0.61-0.96)	0.02
CV death - no. (%)	20 (0.8%)	24 (1.0%)	0.84 (0.46-1.52)	
Resuscitated cardiac arrest - no. (%)	5 (0.2%)	6 (0.3%)	0.83 (0.25-2.73)	
Myocardial infarction - no. (%)	89 (3.8%)	98 (4.1%)	0.91 (0.68-1.21)	
Stroke - no. (%)	5 (0.2%)	19 (0.8%)	0.26 (0.10-0.70)	
Urgent hospitalization for angina requiring revascularization - no. (%)	25 (1.1%)	50 (2.1%)	0.50 (0.31-0.81)	
Secondary composite endpoint - no. (%)	111 (4.7%)	130 (5.5%)	0.85 (0.66-1.10)	
Death - no. (%)	43 (1.8%)	44 (1.8%)	0.98 (0.64-1.49)	
DVT or pulmonary embolus - no. (%)	10 (0.4%)	7 (0.3%)	1.43 (0.54-3.75)	
Atrial fibrillation - no. (%)	36 (1.5%)	40 (1.7%)	0.93 (0.59-1.46)	

Primary efficacy endpoint

COLCOT



No. at Risk							
Colchicine	2260	2197	1791	1169	601	140	0
Placebo	2270	2169	1778	1173	596	135	0

Major Clinical Outcomes

Clinical Outcome Per-protocol population	Colchicine N=2260	Placebo N=2270	Hazard Ratio (95% CI)	P Value
Primary composite endpoint - no. (%)	115 (5.1%)	162 (7.1%)	0.71 (0.56-0.90)	0.004
CV death - no. (%)	19 (0.8%)	23 (1.0%)	0.83 (0.45-1.53)	
Resuscitated cardiac arrest - no. (%)	5 (0.2%)	5 (0.2%)	1.00 (0.29-3.46)	
Myocardial infarction - no. (%)	77 (3.4%)	92 (4.1%)	0.84 (0.62-1.14)	
Stroke - no. (%)	5 (0.2%)	19 (0.8%)	0.26 (0.10-0.71)	
Urgent hospitalization for angina requiring revascularization - no. (%)	22 (1.0%)	47 (2.1%)	0.47 (0.28-0.78)	

Total (First + Recurrent) Primary Endpoint Events (ITT)

Endpoint / Model		Colchicine N=2366	Placebo N=2379	Hazard / Rate Ratio (95% CI)
Total number of primary endpoint events		154	223	
Rate of primary endpoint events per 100 patient-months		0.29	0.42	
Negative binomial model				0.66 (0.51; 0.86)
Andersen-Gill model				0.69 (0.54; 0.88)
Wei-Lin-Wessfeld model	1st event			0.77 (0.61; 0.96)
Wei-Lin-Wessfeld model	2nd event			0.73 (0.48; 1.11)
Wei-Lin-Wessfeld model	3rd event			0.64 (0.37; 1.10)
Wei-Lin-Wessfeld model	Average			0.77 (0.61; 0.96)

Adverse events

Safety population	Colchicine (N=2330)	Placebo (N=2346)	P Value
Any related AE - no. (%)	372 (16.0%)	371 (15.8%)	0.89
Any SAE - no. (%)	383 (16.4%)	404 (17.2%)	0.47
Gastro-intestinal AE - no. (%)	408 (17.5%)	414 (17.6%)	0.90
Gastro-intestinal SAE – no. (%)	46 (2.0%)	36 (1.5%)	0.25
Diarrhea AE - no. (%)	225 (9.7%)	208 (8.9%)	0.35
Nausea AE - no. (%)	43 (1.8%)	24 (1.0%)	0.02
Flatulence AE - no. (%)	15 (0.6%)	5 (0.2%)	0.02
GI haemorrhage AE - no. (%)	7 (0.3%)	5 (0.2%)	0.56
Infection SAE - no. (%)	51 (2.2%)	38 (1.6%)	0.15
Pneumonia SAE - no. (%)	21 (0.9%)	9 (0.4%)	0.03
Septic shock SAE - no. (%)	2 (0.1%)	2 (0.1%)	0.99
HF hospitalization - no. (%)	25 (1.1%)	17 (0.7%)	0.21
Cancer - no. (%)	43 (1.8%)	46 (2.0%)	0.77
Anemia - no. (%)	14 (0.6%)	10 (0.4%)	0.40
Leukopenia - no. (%)	2 (0.1%)	3 (0.1%)	0.66
Thrombocytopenia - no. (%)	3 (0.1%)	7 (0.3%)	0.21

Limitations

- **The duration of follow-up was relatively short at approximately 23 months. The risks and benefits of longer-term treatment with colchicine were not evaluated.**

- **Although the inclusion of 4745 patients was sufficient to demonstrate a significant benefit on the primary composite efficacy endpoint, a larger trial could have allowed a better assessment of individual endpoints and subgroups and the risks associated with colchicine.**

Conclusion

- **Colchicine 0.5 mg/day significantly reduces the risk of first and total ischemic cardiovascular events by 23% and 34% respectively compared to placebo in patients with a recent myocardial infarction.**

- **Rates of adverse effects were low, including a small increase in pneumonias (0.9 vs. 0.4%) but no significant increase in diarrhea with colchicine, on background therapy with aspirin, a 2nd antiplatelet agent and a statin in 99, 98 and 99% of patients.**

- **The COLCOT results apply to patients who have recently suffered a myocardial infarction. Further research is needed to assess the benefits of colchicine in other high-risk patients.**

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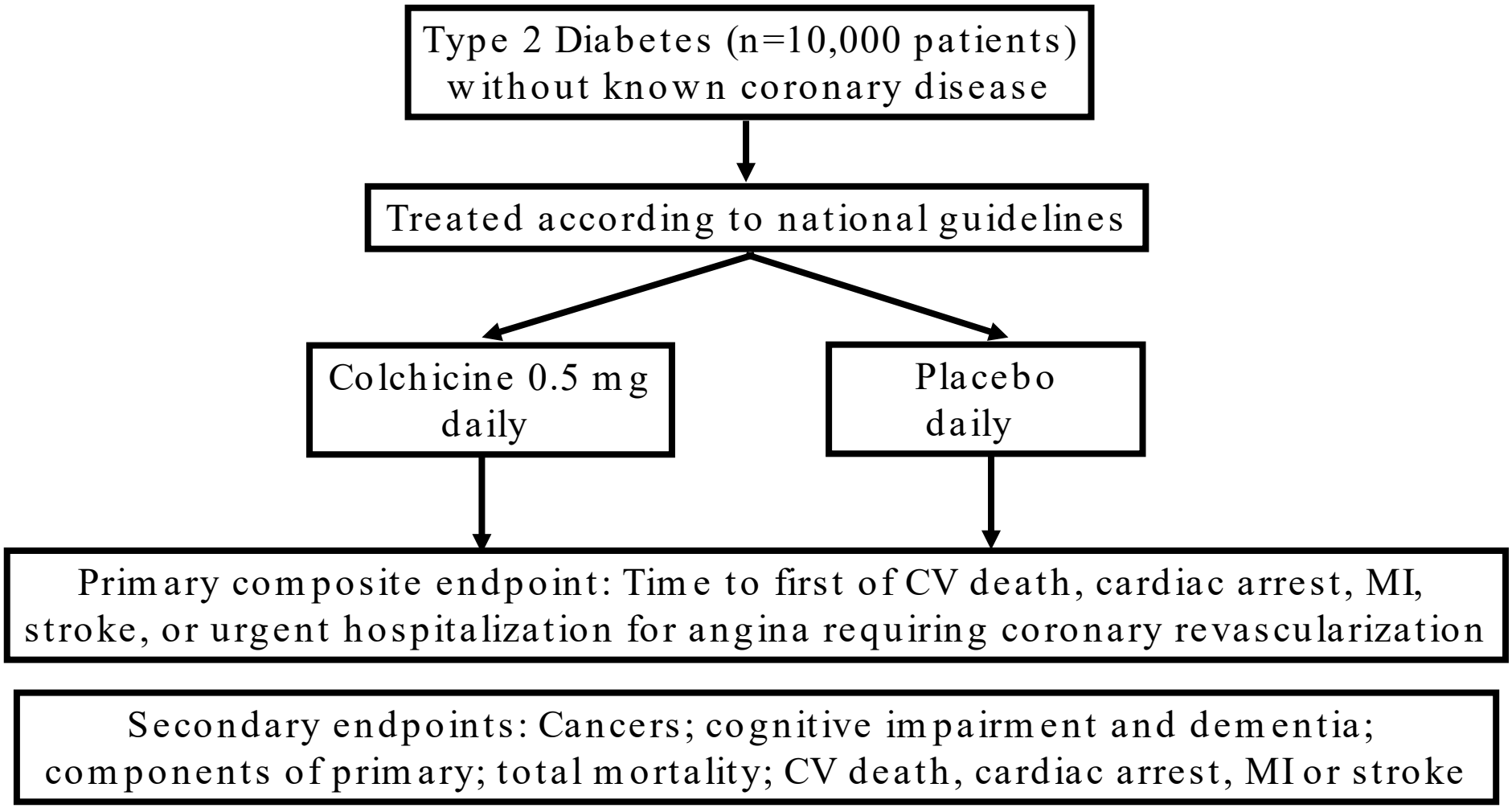
COLCOT-T2D – Study design



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The NEW ENGLAND JOURNAL of MEDICINE

COLCOT

ORIGINAL ARTICLE

Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction

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