Cost-Effectiveness of Low-Dose Colchicine after Myocardial Infarction in the COLchicine Cardiovascular Outcomes Trial (COLCOT)

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Disclosures

- Nothing to disclose

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ORIGINAL ARTICLE

Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction

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[1]Tardif JC et al. *N Engl J Med.* 2019; 381:2497-2505.

Overview of COLCOT[1]

- Randomized, double-blind, placebo-controlled trial
- Patients who had a myocardial infarction ≤30 days were randomized 1:1 to low dose colchicine (0.5 mg per day) or placebo
- 4,745 randomized patients
  (Colchicine: N=2,366 and Placebo: N=2,379)
- Follow-up: 2 years
- Primary composite endpoint included:
  - Death from cardiovascular causes
  - Resuscitated cardiac arrest
  - Myocardial infarction
  - Stroke
  - Urgent hospitalization for angina leading to revascularization

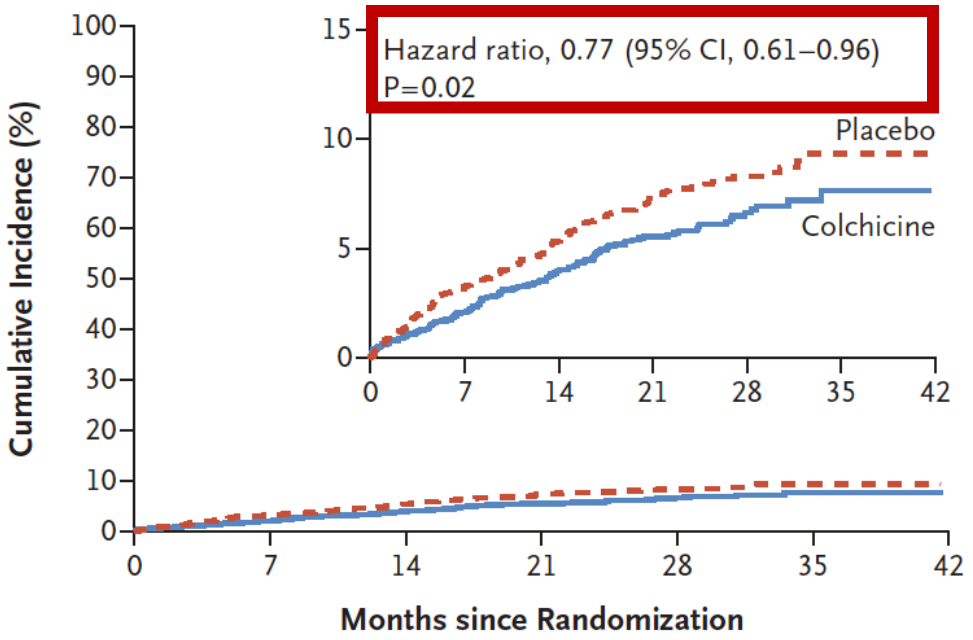


Figure 2. Cumulative Incidence of Cardiovascular Events (Intention-to-Treat Population).

Shown are the Kaplan–Meier event curves for the primary efficacy composite end point of death from cardiovascular causes, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina leading to coronary revascularization in the colchicine group and the placebo group in a time-to-event analysis. The inset shows the same data on an enlarged y axis.

[1]Tardif JC et al. *N Engl J Med.* 2019; 381:2497-2505.

Present Study

Objective

To assess the in-trial period and lifetime cost-effectiveness of low-dose colchicine compared to placebo in post-MI patients on standard-of-care therapy

Primary Methods

- Multi-state Markov model
- Based on the intent-to-treat results of COLCOT
- 1st and 2nd events included in base case model
- Deterministic approach was used to calculate the incremental cost-effectiveness ratio (ICER)
- In-trial (2-year) and lifetime (20 year) ICERs
- Canadian (primary) and United States perspectives

Health States in Markov Model

Table 2. Major Clinical End Points (Intention-to-Treat Population).*

End Point	Colchicine (N=2366)	Placebo (N=2379)	Hazard Ratio (95% CI)	P Value
	number (percent)			
Primary composite end point	131 (5.5)	170 (7.1)	0.77 (0.61–0.96)	0.02†
Components of primary end point				
Death from cardiovascular causes	20 (0.8)	24 (1.0)	0.84 (0.46–1.52)	
Resuscitated cardiac arrest	5 (0.2)	6 (0.3)	0.83 (0.25–2.73)	
Myocardial infarction	89 (3.8)	98 (4.1)	0.91 (0.68–1.21)	
Stroke	5 (0.2)	19 (0.8)	0.26 (0.10–0.70)	
Urgent hospitalization for angina leading to revascularization	25 (1.1)	50 (2.1)	0.50 (0.31–0.81)	
Secondary composite end point‡	111 (4.7)	130 (5.5)	0.85 (0.66–1.10)	
Death	43 (1.8)	44 (1.8)	0.98 (0.64–1.49)	
Deep venous thrombosis or pulmonary embolus	10 (0.4)	7 (0.3)	1.43 (0.54–3.75)	
Atrial fibrillation	36 (1.5)	40 (1.7)	0.93 (0.59–1.46)	

* Only the initial event was counted in the analyses of time to first event for the primary composite end point and for the secondary composite end point. In the component analysis, the different types of events were counted separately.
† The log-rank test and the multivariable Cox proportional-hazards model including age, history of diabetes, previous coronary revascularization, and previous heart failure yielded similar P values.
‡ The secondary composite end point included death from cardiovascular causes, resuscitated cardiac arrest, myocardial infarction, and stroke.

Table 3. Adverse Events (Safety Population).*

Event	Colchicine (N=2330)	Placebo (N=2346)	P Value
	number of patients (percent)		
Any related adverse event†	372 (16.0)	371 (15.8)	0.89
Adverse events			
Gastrointestinal event	408 (17.5)	414 (17.6)	0.90
Diarrhea	225 (9.7)	208 (8.9)	0.35
Nausea	43 (1.8)	24 (1.0)	0.02
Flatulence	15 (0.6)	5 (0.2)	0.02
Gastrointestinal hemorrhage	7 (0.3)	5 (0.2)	0.56
Anemia	14 (0.6)	10 (0.4)	0.40
Leukopenia	2 (0.1)	3 (0.1)	0.66
Thrombocytopenia	3 (0.1)	7 (0.3)	0.21
Serious adverse events			
Any serious adverse event‡	383 (16.4)	404 (17.2)	0.47
Gastrointestinal event	46 (2.0)	36 (1.5)	0.25
Infection	51 (2.2)	38 (1.6)	0.15
Pneumonia	21 (0.9)	9 (0.4)	0.03
Septic shock	2 (0.1)	2 (0.1)	0.99
Hospitalization for heart failure	25 (1.1)	17 (0.7)	0.21
Cancer§	43 (1.8)	46 (2.0)	0.77

[1]Tardif JC et al. *N Engl J Med.* 2019; 381:2497-2505.

Cost Inputs (Canadian Perspective- single payer)

Event / Medication	Base value
Colchicine (per pill) [1]	$0.26
Acute event costs [2]	
Resuscitated cardiac arrest	$9,673
Myocardial infarction	$7,769
Stroke	$10,224
Coronary revascularization Coronary artery bypass graft surgery Percutaneous coronary intervention	 $24,283 $8,894
Pneumonia	$8,206
Long-term follow-up costs	
Resuscitated cardiac arrest [3]	$458
Myocardial infarction [4]	$766
Stroke [5]	$1,557
Coronary artery bypass graft surgery [3]	$1,276
Percutaneous coronary intervention [3]	$766

[1] Régie de l'assurance maladie du Québec. 2019.; [2] Ontario Case Costing Initiative. OCC Costing Analysis Tool. *Ontario Ministry of Health and Long Term Care*. 2018;; [3]Fernando SM et al. *Resusciation.* 2020;146:138-144.; [4] Trans DT et al. *Can J Cardiol*. 2018;34:1298-1305.

Utility Inputs

Utilities/Disutilities	Base value
Baseline utility[1]	0.682
Disutilities	
Resuscitated cardiac arrest[2]	0.101
Myocardial infarction[1]	0.147
Stroke [1]	0.178
Coronary revascularization[3]	
Coronary artery bypass graft surgery	0.090
Percutaneous coronary intervention	0.060
Pneumonia[4]	0.020

Mean age in trial= 60 years (Utility=0.829)

All patients had a prior MI (Disutility= 0.147)

[1]Nyman JA et al. *Med Care*. 2007;45:618-28.; [2]Marti J et al. *Resuscitation*. 2017;117:1-7.; [3] Ariyaratne TV et al. *Eur Heart J Qual Care Clin Outcomes*. 2016;2:261-270.; [4] Atwood M et al. *Can J Public Health*. 2018;109:756-768.

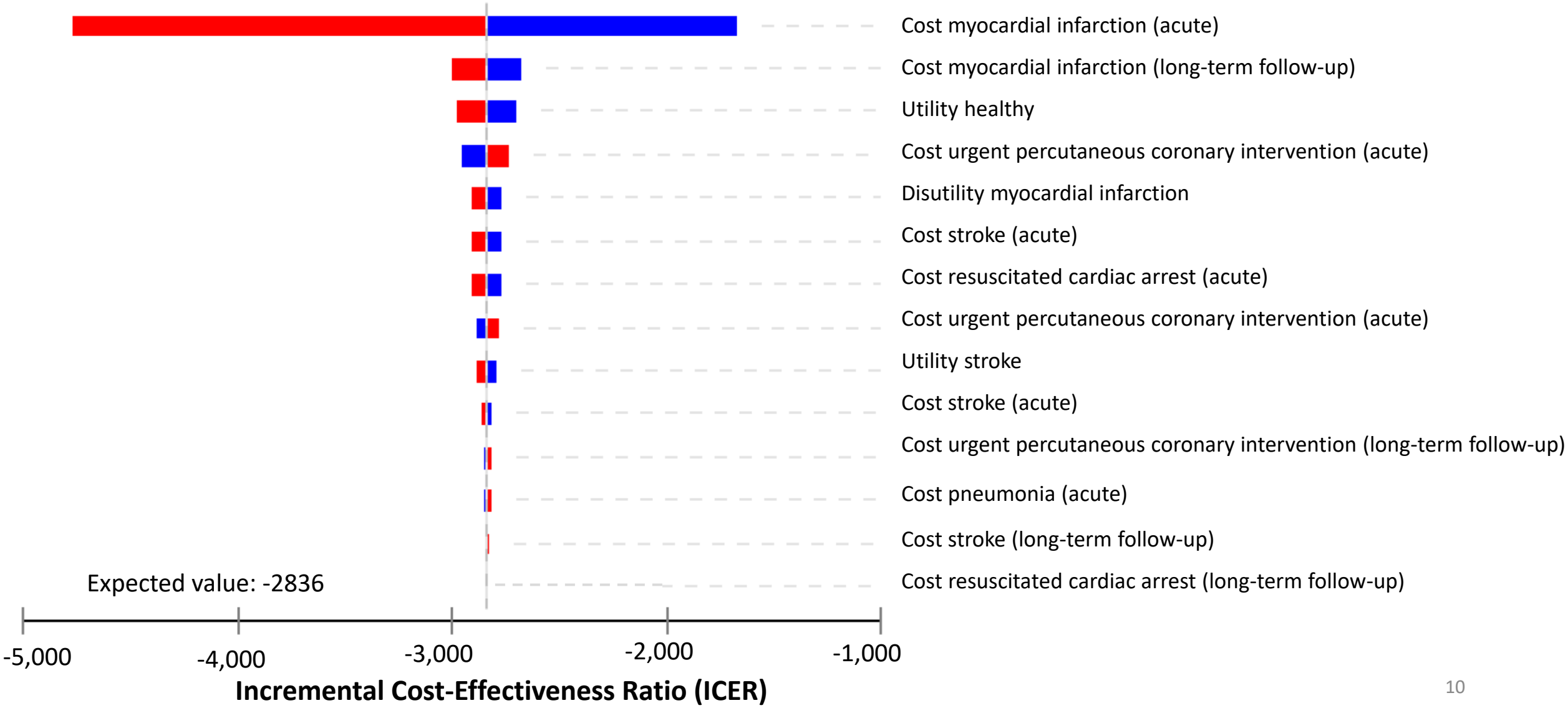
In-Trial (2-year) ICERs

Analysis	Average cost, CAD $			Average QALYs Gained			ICER†
	Colchicine	Placebo	Difference*	Colchicine	Placebo	Difference*	
Base case Primary endpoints, non-CV deaths, and pneumonia 1st and 2nd (recurrent) events	$265	$502	-$237 47%	1.34	1.30	0.04	**Dominant**
Sensitivity analyses							
Base case and inclusion of all recurrent events	$265	$494	-$222	1.34	1.30	0.04	**Dominant**
Base case and inclusion of tertiary endpoint: all coronary revascularizations	$745	$855	-$111	1.30	1.29	0.01	**Dominant**
Base case and inclusion of: all coronary revascularization and all recurrent events	$749	$858	-$98	1.30	1.29	0.01	**Dominant**

*Differences compare average costs and QALYs of colchicine to placebo.

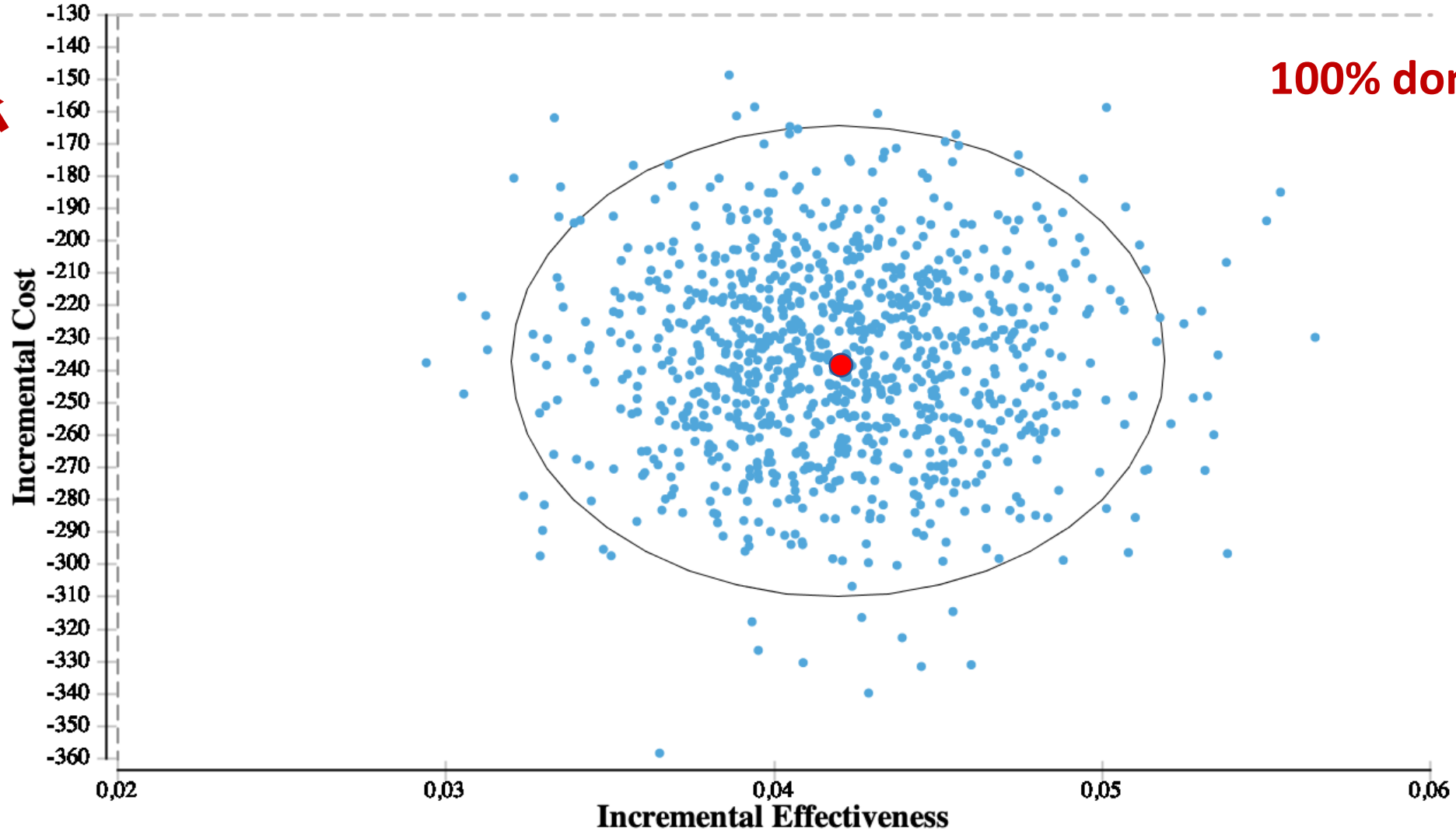
† Dominant ICERs are not presented and results from lower costs and higher QALYs for colchicine.

1-way Sensitivity Analysis: In-Trial



*The red bar shows the change in ICER with a high uncertainty value (+25%) and blue bar shows the change in ICER with a low uncertainty value (-25%).

Probabilistic: In-Trial Incremental Cost-Effectiveness



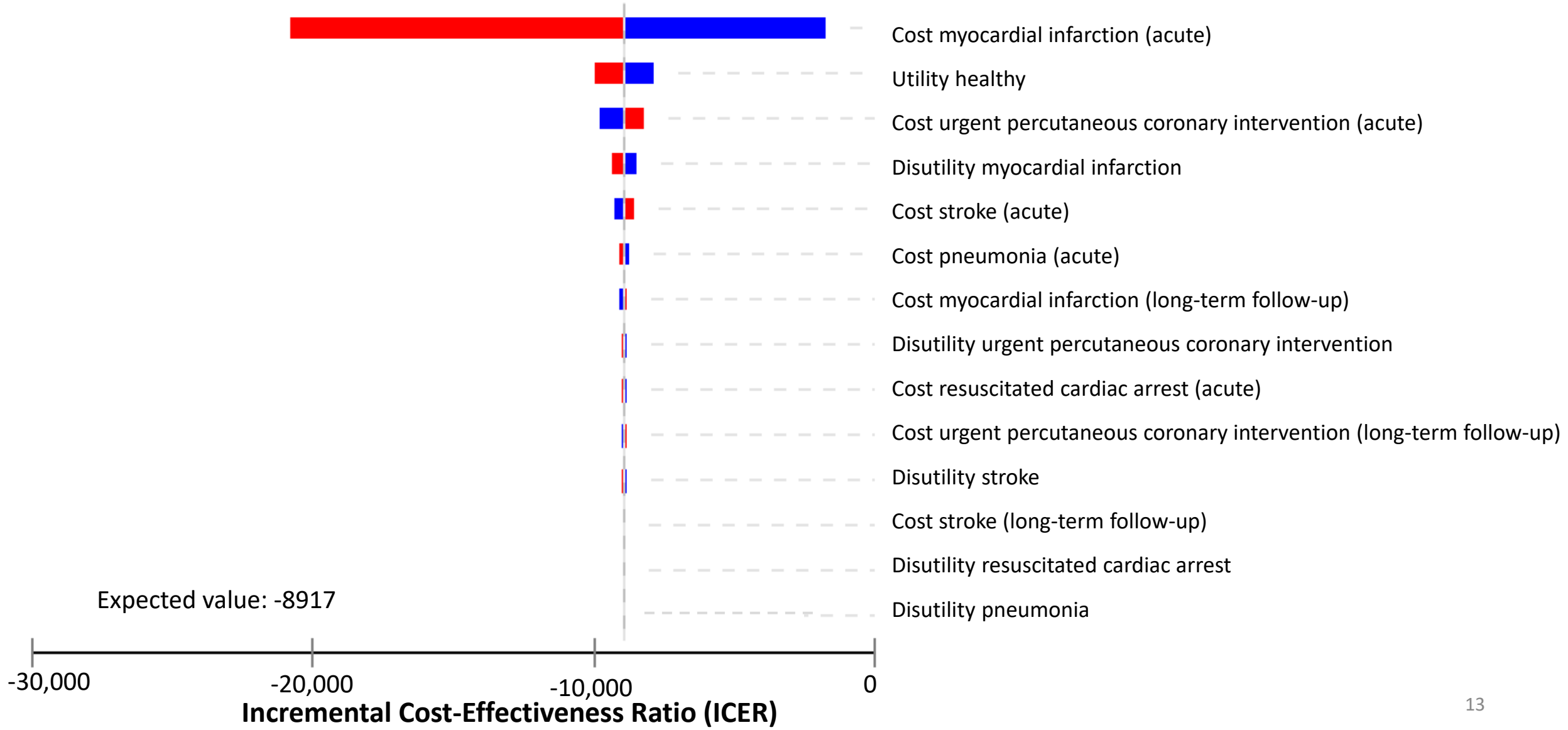
100% dominant

*Red dot marks deterministic ICER.

Lifetime (20-year) ICERs

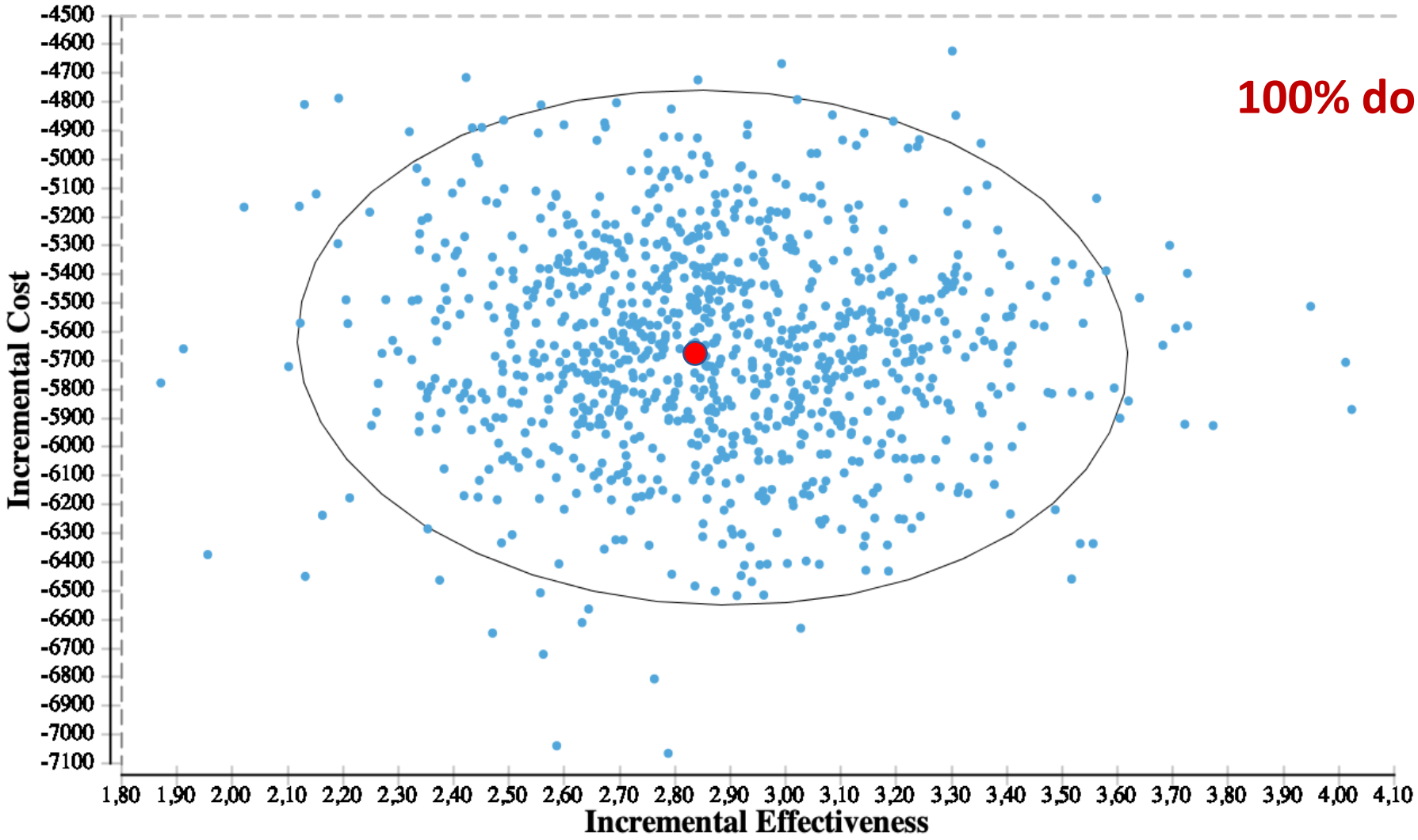
Analysis	Average cost, CAD $			Average QALYs Gained			ICER†
	Colchicine	Placebo	Difference*	Colchicine	Placebo	Difference*	
Base case Primary endpoints, non-CV deaths, pneumonia 1st and 2nd (recurrent) events	$2,590	$8,239	-$5,647 69%	11.68	8.82	2.86	**Dominant**
Sensitivity analyses							
Base case and inclusion of all recurrent events	$2,597	$8,172	-$5,539	11.69	8.73	2.96	**Dominant**
Base case and inclusion of tertiary endpoint: all coronary revascularizations	$13,737	$14,175	-$438	8.51	7.98	0.53	**Dominant**
Base case and inclusion of: all coronary revascularizations and all recurrent events	$13,825	$14,284	-$400	8.51	7.98	0.53	**Dominant**

1-way Sensitivity analysis: Lifetime



*The red bar shows the change in ICER with a high uncertainty value (+25%) and blue bar shows the change in ICER with a low uncertainty value (-25%).

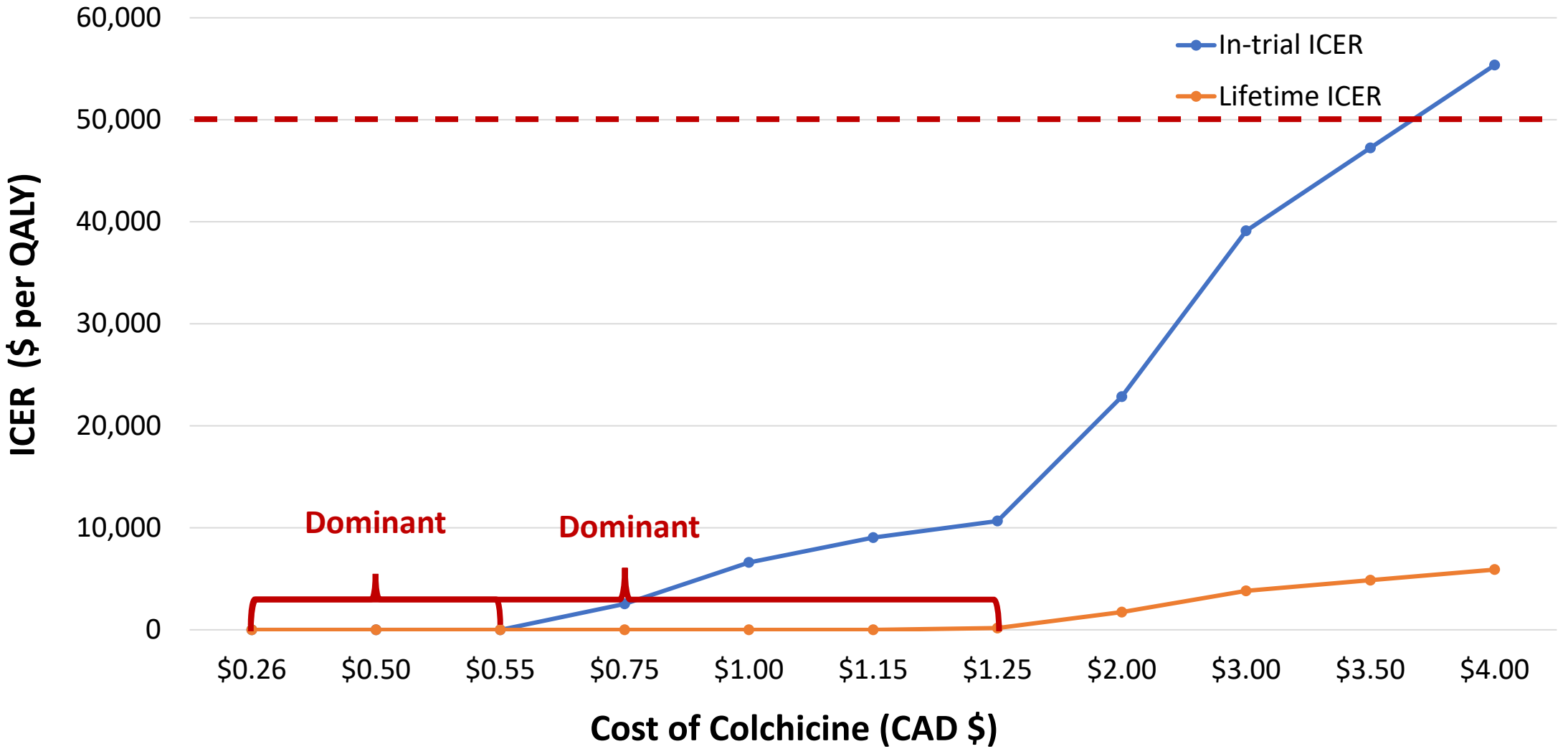
Probabilistic: Lifetime Incremental Cost-Effectiveness



100% dominant

*Red dot marks deterministic ICER.

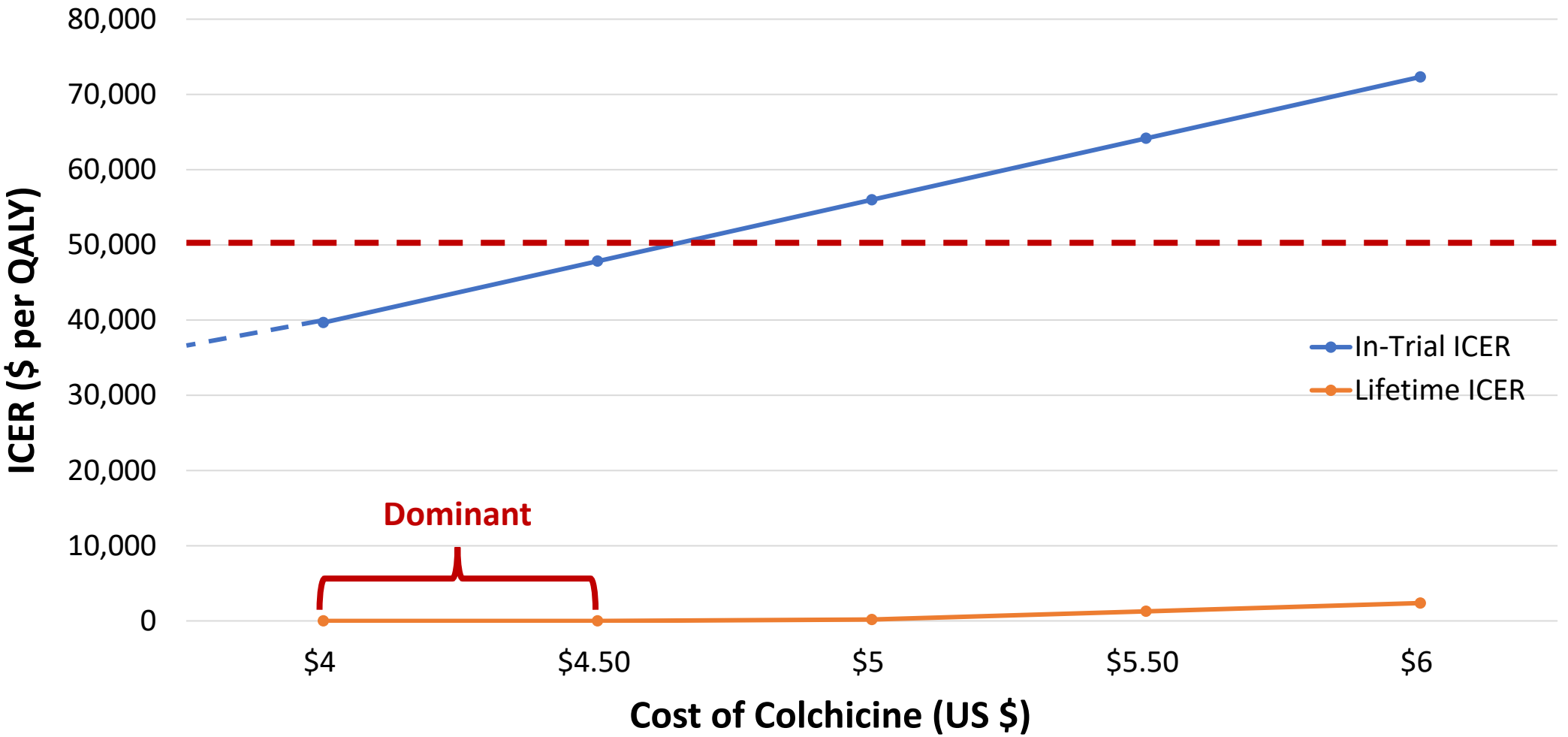
Varying the Cost of Colchicine (Canada)



*Base case includes all primary outcomes, non-cardiovascular mortality, and pneumonia (1st and 2nd event)

**The price points of maximum dominance and maximum cost effectiveness were the same when all recurrent events were included

US Cost-Effectiveness: Medicare



*Base case includes all primary outcomes, non-cardiovascular mortality, and pneumonia (1st and 2nd event)

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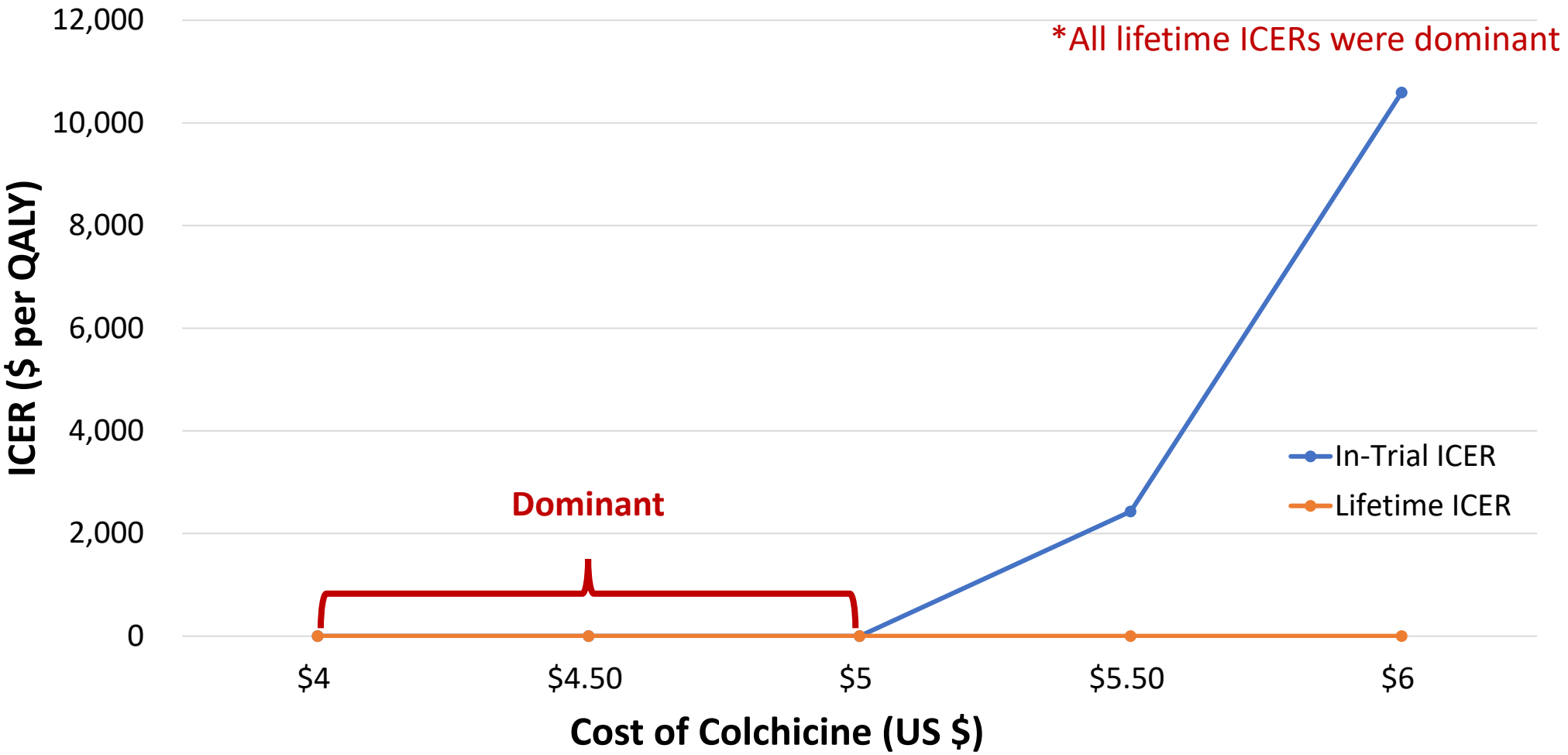
[1] Analytics TH. Red Book Online. https://truvenhealth.come/Portals/0/Assets/Brochures/InternationalINTL_12543_0413)RedbookPS_WEB1.pdf. [2]Healthcare cost and utilization project. https://hcupnet.ahrq.gov. [3]Centers for Medicare and Medicaid Services. http://www.cms.gov/app/physician-fee-schedule/overview.

US Cost-Effectiveness: Private Insurance



*Base case includes all primary outcomes, non-cardiovascular mortality, and pneumonia (1st and 2nd event)

**The price points of maximum dominance and maximum cost effectiveness were the same when all recurrent events were included

[1] Analytics TH. Red Book Online. https://truvenhealth.come/Portals/0/Assets/Brochures/InternationalINTL_12543_0413_RedbookPS_WEB1.pdf. [2]Wallace PJ et al. *Health Aff (Millwood).* 2014;33(7):1187-1194.

Limitations

- Utility and disutility measures were obtained from published literature on populations that closely resembled the COLCOT study population
- The magnitude of disutility for recurrent events were assumed same as the disutility for the 1st event (few published studies measure utilities and disutilities for recurrent events)- underestimates cost-effectiveness
- Effect estimates based on COLCOT (2-year study) and assumed hazards were constant over 20-year lifetime perspective

Conclusions

- From the Canadian healthcare system perspective, the addition of low-dose colchicine (0.5 mg daily) to standard of care therapy after MI is **economically dominant**
  - Mean overall per patient costs **reduced** by **47%** for the in-trial period and **69%** for the lifetime period
  - Quality adjusted life years (QALYs) **increased**

- From the US Medicare system perspective, low-dose colchicine therapy post- MI was cost-effective (<$50,000 per QALY) for the in-trial period and economically dominant at a price of <$5 per pill

- From the US private insurance system perspective, low-dose colchicine post-MI was economically dominant at ≤$5 per pill for the in-trial period and $4-6 per pill for the lifetime period

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Thank You

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