

1-Year outcomes of perioperative beta-blockade in patients undergoing noncardiac surgery

**Dr. PJ Devereaux on behalf of POISE Investigators
Population Health Research Institute, Hamilton, Canada**

Background

- 200 million adults globally undergo noncardiac surgery annually
 - >3 million will suffer MI
- We undertook PeriOperative ISchemic Evaluation (POISE) Trial, because beta-blockers attenuate effects of increased perioperative catecholamine levels
 - we hypothesized that perioperative beta-blockade would decrease risk of perioperative MI and its sequela

Background

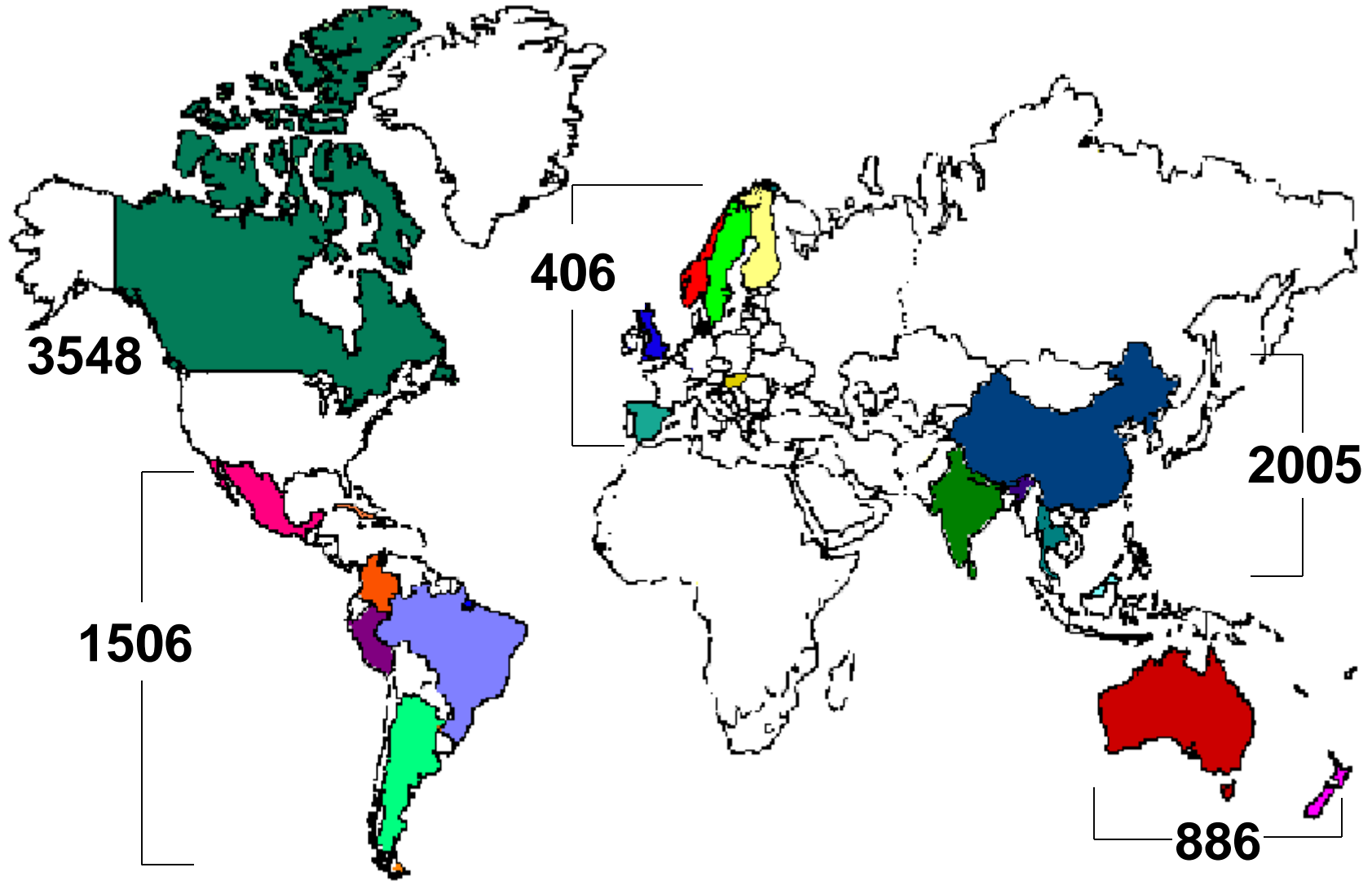
- POISE randomized patients undergoing noncardiac surgery to receive beta-blocker or placebo
- We previously reported 30-day results demonstrating that extended-release metoprolol
 - reduced risk of MI (HR, 0.73; 95% CI, 0.60-0.89) but
 - increased risk of stroke (HR, 2.17; 95% CI, 1.26-3.74) and mortality (HR, 1.33; 95% CI, 1.03-1.74)
 - risk of death due to sepsis/infection 36 vs 18 deaths P=0.016
- To facilitate insights into longer-term impact of perioperative beta-blockade, we designed POISE to evaluate secondary outcomes at 1 year after surgery

POISE Trial design

- Design – blinded RCT
- Eligibility – age ≥ 45 yrs, undergoing noncardiac surgery, and have or be risk of atherosclerotic disease
- Intervention – metoprolol CR or placebo
 - 100 mg given 2-4 hrs preop and at 6 hours after surgery
 - day after surgery for 30 days patients received 200 mg of study drug
 - dose decreased to 100 mg daily if patient became hypotensive or bradycardic

Final recruitment

8351 pts from 191 sites in 23 countries



Follow-up

- All centres actively contacted patients at 30 days after surgery
- Long-term follow-up occurred through
 - administrative databases in Canada (3,548 patients)
 - Statistics Canada (Stats Can) – mortality
 - Canadian Institute of Health Information (CIHI) – all other outcomes
 - unfortunately it took many years to obtain Canadian data
 - active follow-up in remaining 22 countries (4,803 patients)

Trial flow

- Among Canadian patients we were able to obtain
 - 1 year mortality data on 84% of metoprolol and 85% of placebo patients
 - 1 year data on all other outcomes was obtained on 88% of metoprolol and 88% of placebo patients
- Among non-Canadian patients we were able to obtain
 - 1 year follow-up data on 93% of metoprolol patients and 94% of placebo patients

Baseline characteristics

Characteristics	Metoprolol (N=4174)	Placebo (N=4177)
Age – (mean yrs)	69	69
Male	63%	64%
Preoperative heart rate - mean	78	78
blood pressure - mean	139/78	139/79
History of		
coronary artery disease	43%	43%
peripheral arterial disease	42%	40%
stroke	15%	15%

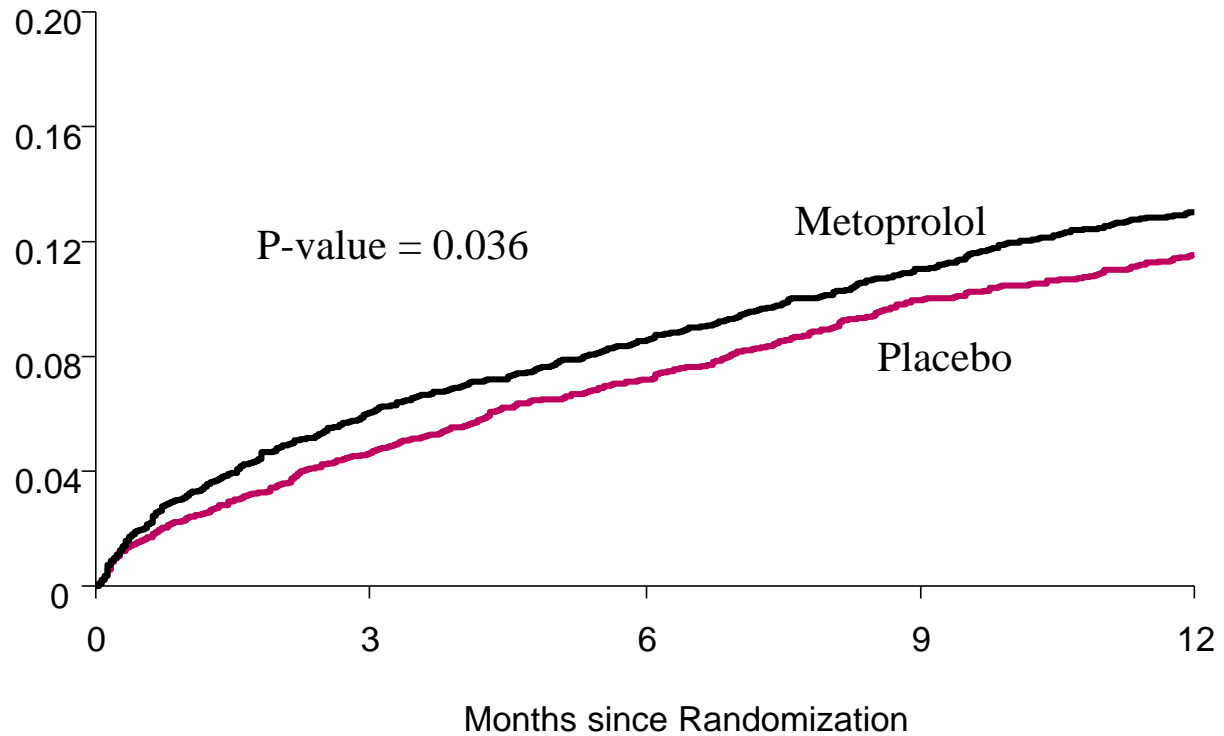
Type of surgery

	Metoprolol (N=4174)	Placebo (N=4177)
Surgery %		
vascular	42	41
intraperitoneal	21	22
orthopedic	21	21
other	16	16

1-year mortality outcomes

Outcome	metoprolol n=4174 no. (%)	Placebo n=4177 no. (%)	HR (95% CI)	P value
All cause mortality	410 (10)	356 (9)	1.16 (1.01-1.34)	0.036
CV mortality	182 (4)	167 (4)	1.10 (0.89-1.36)	0.37
Non-CV mortality	228 (6)	189 (5)	1.22 (1.01-1.48)	0.043

1-year all-cause mortality

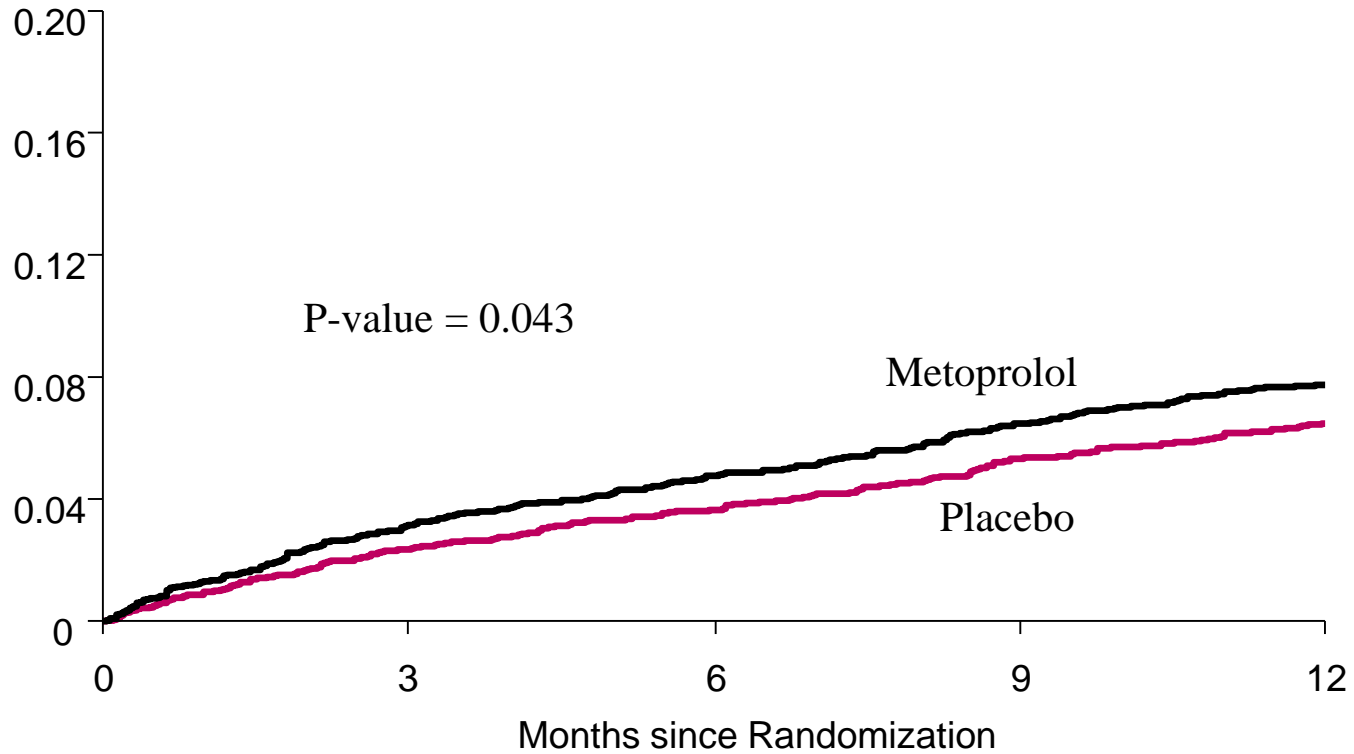


No. at Risk

Placebo 4177 2668 2559 2473 2408

Metoprolol 4174 2626 2522 2439 2347

1-year non-CV mortality



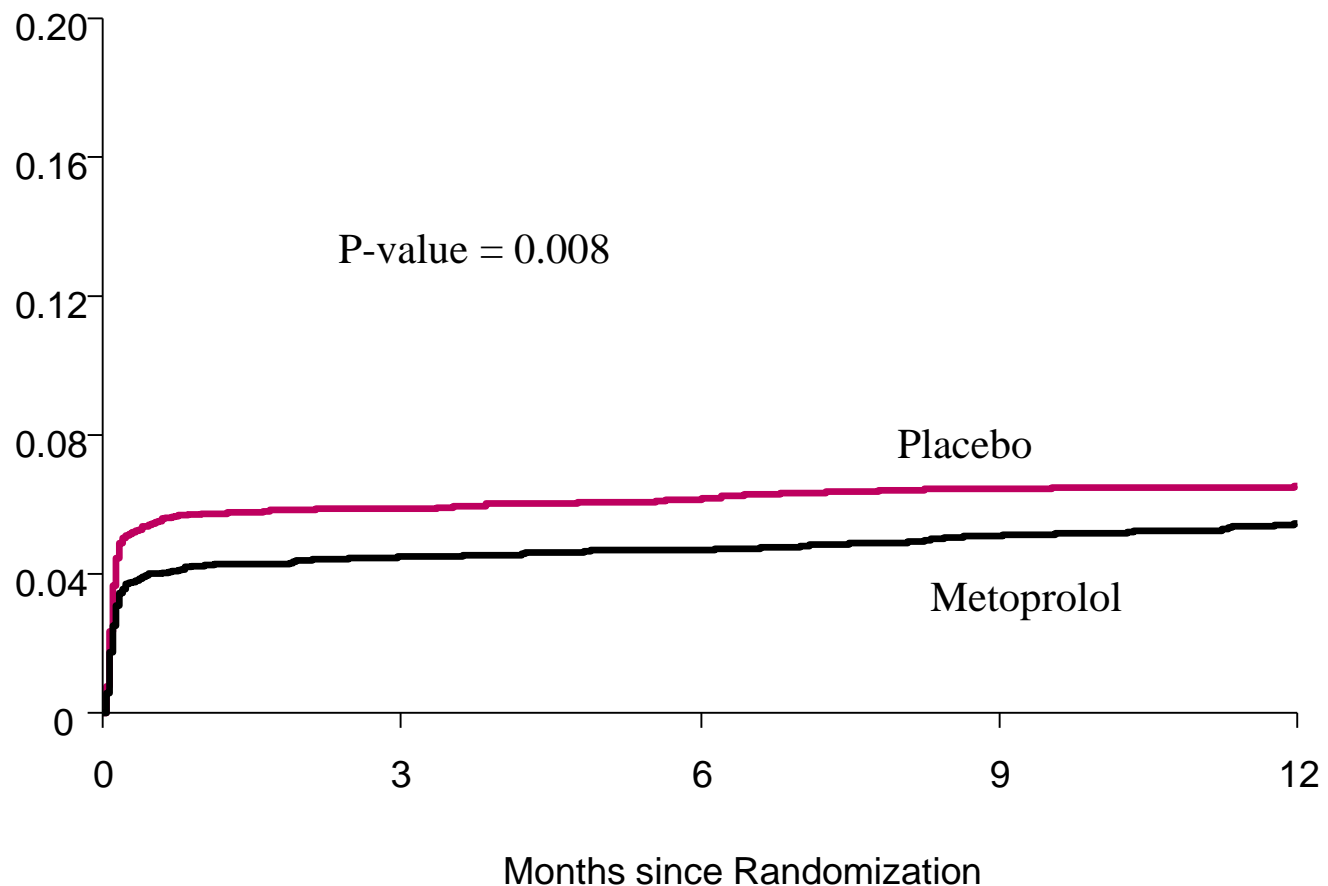
No. at Risk

Placebo	4177	2668	2559	2473	2408
Metoprolol	4174	2626	2522	2439	2347

1-year MI and revasc outcomes

Outcome	metoprolol n=4174 no. (%)	Placebo n=4177 no. (%)	HR (95% CI)	P value
Myocardial infarction	208 (5)	260 (6)	0.78 (0.65-0.94)	0.008
Cardiac revascularization	21 (1)	45 (1)	0.47 (0.28-0.78)	0.004

1-year myocardial infarction



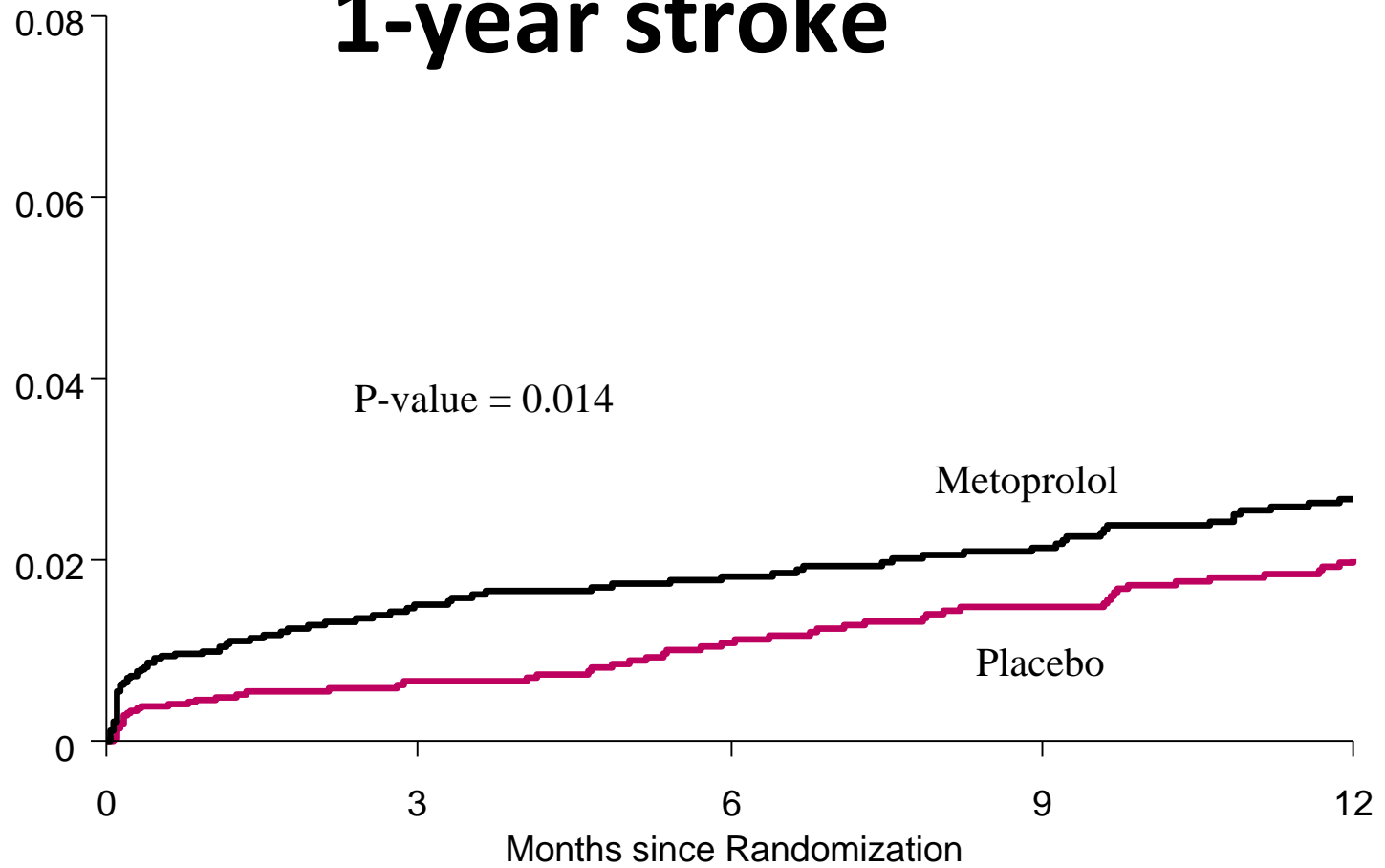
No. at Risk

	0	3	6	9	12
Placebo	4177	2548	2450	2370	2308
Metoprolol	4174	2542	2445	2357	2264

1-year outcomes

Outcome	metoprolol n=4174 no. (%)	Placebo n=4177 no. (%)	HR (95% CI)	P value
Stroke	85 (2)	59 (1)	1.52 (1.09-2.12)	0.014
Cardiac arrest	24 (1)	26 (1)	0.93 (0.53-1.62)	0.79
Pulmonary embolism	15 (<1)	11 (<1)	1.36 (0.63-2.97)	0.43

1-year stroke



No. at Risk

Placebo	4177	2654	2539	2449	2379
Metoprolol	4174	2596	2492	2407	2315

Independent predictors of 1-year mortality

	Frequency of complication no. (%)	OR (95% CI)
Myocardial infarction	468 (6)	3.07 (2.39-3.94)
Coronary revascularization	66 (1)	0.31 (0.13-0.76)
Stroke	144 (2)	5.94 (4.16-8.48)
Cardiac arrest	50 (1)	11.80 (6.51-21.3)
Pulmonary embolism	26 (<1)	11.6 (5.32-25.20)

Implications and conclusions

- POISE results suggest at 1 year, for every 1000 patients having noncardiac surgery, metoprolol CR would
 - prevent 12 patients from experiencing an MI and 6 from undergoing cardiac revascularization but
 - result in excess of 13 deaths and 6 strokes
- Research is needed to establish way to derive benefit of perioperative beta-blockade while mitigating risk