

# Cost-effectiveness of 80 mg versus 10 mg atorvastatin in Canada based on results of the TNT study

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## Background

- The Treat to New Targets (TNT) study—a prospective, double-blind, randomized, controlled trial, carried out in 14 countries—compared treatment with 80 mg atorvastatin per day to 10 mg atorvastatin per day in 10,001 patients with clinically evident coronary heart disease (CHD) and low-density lipoprotein cholesterol of less than 3.4 mmol/L<sup>1</sup>
- Over a median follow-up of 4.9 years, patients randomized to atorvastatin 80 mg experienced a 22% relative risk reduction (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.69 to 0.89;  $P < .001$ ) in the rate of major cardiovascular (CV) events (death from CHD, nonfatal non-procedure-related myocardial infarction [MI], resuscitation after cardiac arrest, or fatal or nonfatal stroke)<sup>1</sup>
- It is unknown whether intensive lipid-lowering with a higher and more expensive atorvastatin dose is cost-effective in Canadian patients with stable CHD

## Objective

To assess the cost-effectiveness of intensive lipid-lowering with atorvastatin 80 mg/day versus atorvastatin 10 mg/day in patients with stable CHD from the perspective of the Canadian Ministries of Health based on results of the TNT study

## Methods

- A lifetime Markov model** with 1-year cycle length was developed to predict major and minor CV events, costs, survival, and quality-adjusted life years (QALYs) (Figure 1)
- Major CV Events:** first and second (if occurring within 1 year of the first event) MI, stroke, congestive heart failure (CHF), revascularization and resuscitated cardiac arrest (RCA)
- Minor CV Events:** peripheral artery disease, transient ischemic attack and documented angina
- Annual event probabilities and hazard ratios:** were based on TNT data. CV risks were treatment-specific for the first 10 years. Beyond year 10, risks were assumed to be equivalent for atorvastatin 10 and 80 mg and were based on TNT data pooled across the doses
- Mortality rates:** were based on the TNT data for the first 5 years. Beyond 5 years, general mortality rates were based on Canadian population data<sup>2</sup> and CHD mortality rates (age- and gender-specific) were based on Canadian published literature<sup>3-6</sup>
- Costs:** Only acute event costs were included and were based on Ontario Cost Case Initiative 2003-2004 acute inpatient cost data (including overhead).<sup>7</sup> Atorvastatin costs were derived from the current Quebec formulary<sup>8</sup>
- Health utility scores:** obtained from a published study<sup>9</sup>
- Benefits and costs were **discounted** at 5% annually
- One-way deterministic and probabilistic **sensitivity analyses** were performed

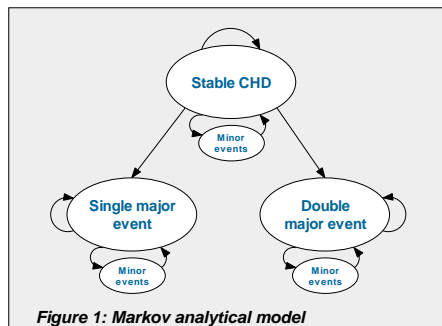


Figure 1: Markov analytical model

Table 1: Base-case input parameters

Major first events*			
1-yr probability in 10 mg atorvastatin arm	Year 1 to 10	Year 11 +	
MI	0.0123	0.0102	
Stroke	0.0055	0.0049	
CHF	0.0055	0.0046	
Revascularization	0.0350	0.0302	
Resuscitated cardiac arrest	0.0008	0.0009	
HR associated with 80 mg atorvastatin			
Year 1 to 10	Year 11 +		
MI	0.7850	1.000	
Stroke	0.7840	1.000	
CHF	0.6730	1.000	
Revascularization	0.7250	1.000	
Resuscitated cardiac arrest	1.0700	1.000	
Minor events*			
1-yr probability in 10 mg atorvastatin arm	Year 1 to 10	Year 11 +	
Peripheral artery disease	0.0108	0.0107	
Transient ischemic attack	0.0041	0.0037	
Documented angina	0.0264	0.0249	
HR associated with 80 mg atorvastatin			
Year 1 to 10	Year 11 +		
Peripheral artery disease	0.9770	1.000	
Transient ischemic attack	0.8130	1.000	
Documented angina	0.8850	1.000	
Costs			
2006 Can\$			
Daily atorvastatin drug costs <sup>8</sup>			
10 mg	1.60		
80 mg	2.15		
Acute event costs <sup>7</sup>			
MI	11,444		
Stroke	16,744		
CHF	10,320		
Revascularization			
CABG	21,603		
PTCA	8,856		
Resuscitated cardiac arrest	17,934		
Peripheral artery disease	12,343		
Transient ischemic attack	3,293		
Documented angina	4,499		
Utilities <sup>9</sup>			
Stable coronary heart disease	0.78		
MI	0.65		
Stroke	0.64		
CHF	0.63		
CABG	0.78		
PTCA	0.78		
Resuscitated cardiac arrest	0.68		
MI and stroke	0.61		
MI and revascularization	0.65		
Stroke and CHF	0.59		
Stroke and revascularization	0.59		
Minor event utility decrements			
Peripheral artery disease	-0.10		
Transient ischemic attack	-0.12		
Documented angina	-0.12		

CABG: coronary artery bypass graft; CHF: congestive heart failure; HR: hazard ratio; MI: myocardial infarction; PTCA: percutaneous transluminal coronary angioplasty  
Sources: <sup>1</sup>TNT trial data; <sup>2</sup>Quebec formulary; <sup>3</sup>Ontario Case Costing Initiative; <sup>4</sup>Sullivan et al., 2005<sup>10</sup>

## Results

### 1 Base-case

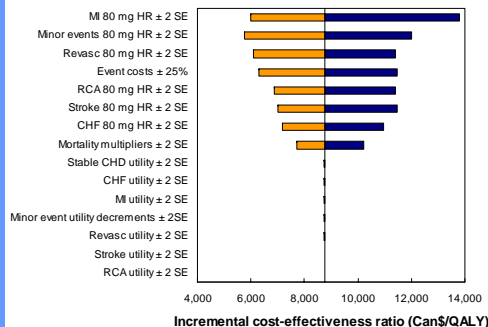
- Over a lifetime horizon, on average 0.072 fewer events occurred in patients treated with atorvastatin 80 mg than in those treated with atorvastatin 10 mg; the incremental cost per QALY gained was Can\$8,755 (95% CI 3,397 to 21,525) for atorvastatin 80 mg versus 10 mg
- The incremental cost-effectiveness ratio (ICER) decreased to Can\$539/QALY over a 10-year model horizon; atorvastatin 80 mg was dominant over a 5-year horizon

	80 mg atorvastatin	10 mg atorvastatin	Difference
Lifetime horizon			
<b>Benefits</b>			
Number of CHD events	0.699	0.771	-0.072
Life years	10.850	10.741	0.109
QALYs	8.260	8.143	0.116
<b>Costs (2006 Can\$)</b>			
Study drugs	8,520	6,277	2,243
Major events	7,139	8,254	-1,116
Minor events	2,698	2,810	-112
Total	18,357	17,341	1,016
Incremental cost per event averted (2006 Can\$)	14,066		
Incremental cost per life-year gained (2006 Can\$)	9,313		
Incremental cost per QALY (2006 Can\$) [95% CI]	8,755 [3,397 to 21,525]		
10-year horizon			
QALYs	5.835	5.780	0.054
Total costs (2006 Can\$)	12,980	12,951	29
Incremental cost per QALY (2006 Can\$) [95% CI]	539 [dominant to 14,563]		
5-year horizon			
QALYs	3.621	3.601	0.020
Total costs (2006 Can\$)	8,028	8,152	-125
Incremental cost per QALY (2006 Can\$) [95% CI]	Dominant		

CHD: coronary heart disease; CI: confidence interval; QALY: quality-adjusted life-year

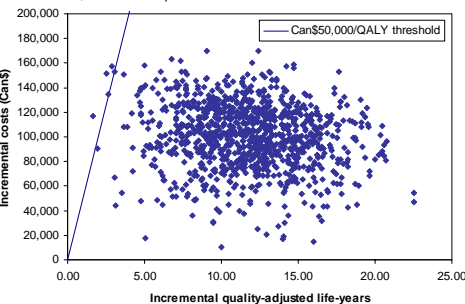
### 2 One-way sensitivity analysis – lifetime horizon

- The model was moderately sensitive to variations in the HRs for atorvastatin 80 mg versus 10 mg with respect to MI, minor events, revascularization, RCA, stroke, and CHF (maximum ICER: Can\$13,808/QALY; minimum: Can\$5,770/QALY)
- The model was also moderately sensitive to variations in event costs and not sensitive to variations in utility values



### 3 Probabilistic sensitivity analysis – lifetime horizon

- The likelihood that the ICER would be below Can\$50,000 per QALY was 99.5% (i.e., only 5 out of 1000 bootstrapping simulations resulted in ICERs above Can\$50,000/QALY)



## Conclusions

- Treatment of Canadian patients with CHD with atorvastatin 80 mg versus atorvastatin 10 mg resulted in an ICER of Can\$8,755 per QALY over a lifetime horizon
- The probability that the ICER would be below Can\$50,000 per QALY—a commonly cited cost-effectiveness threshold<sup>10</sup>—exceeded 99% in 1000 model simulations
- Results were robust with respect to effectiveness, cost and utility input parameters
- The ICER decreased to Can\$539/QALY over a 10-year horizon; atorvastatin 80 mg treatment was dominant over a 5-year horizon
- From the perspective of the Canadian Ministries of Health, intensive lipid-lowering therapy with atorvastatin 80 mg is cost-effective versus atorvastatin 10 mg in patients with stable CHD

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