

COST-EFFECTIVENESS OF INTENSIVE DOSE ATORVASTATIN IN ACUTE CORONARY SYNDROME PATIENTS IN THE UK

Thurston S¹, Thompson R², Ong S², Van Hout B¹
¹ Pharmerit Ltd, York, UK; ² Pfizer Ltd, Surrey, UK

OBJECTIVE

- To estimate the cost-effectiveness of 2 year treatment with intensive-dose atorvastatin (80mg) versus standard and high-dose simvastatin (40mg and 80mg respectively) in patients with acute coronary syndrome (ACS).
- ACS is defined according to the inclusion criteria of the three ACS statin trials which were used to inform the model.

METHODS

- A Bayesian meta-analysis is used to estimate and compare the relative efficacy of intensive (atorvastatin 80mg) versus high (simvastatin 80mg) and standard dose statin therapy (simvastatin 40mg).
- Prior information is combined with clinical trial data to obtain posterior distributions concerning the relative risk reductions in cardiovascular events due to a 1 mmol/L decrease in low density lipoprotein cholesterol (LDL-C).
- Priors are obtained from the Cholesterol Treatment Trialists Collaborator's (CTT) meta-analysis of statin therapy (Table 1)¹, and combined with data from the A to Z, PROVE-IT and MIRACL trials (Table 2) using a piece-wise exponential model that acknowledges the higher event rates during and directly after the acute period²⁻⁴.
- The resulting posterior estimates are multiplied by the average percentage relative reductions in LDL-C for specific statin doses as estimated in the Law et al meta-analysis (Table 3).
- The relative efficacies of the different statins in reducing lipid levels and thus improving cardiovascular outcomes are used in a Markov model which combines estimates of the occurrence of later events with UK cost and quality of life data.
- ACS patients who have recently suffered a non-fatal cardiac event enter the Markov model in a state of being 'free of subsequent events' (Figure 1).
- Patients may suffer any of a number of cardiac events over time, and may also suffer recurrent events through time.
- The Markov cycle length is six months. At the end of the cycle patients can move to another health state (new event or death) or remain in the current health state.
- The model distinguishes three sub-states within each health state

- Patients who enter the model may vary in risk and LDL-C level. The base line results represent patients whose risk is comparable to those in the CURE trial⁵.
- A baseline LDL-C level of 2.84 mmol/L, (the average baseline LDL-C level seen across the three ACS trials), was set for patients in the model.
- The event rates used in the model (estimated from CURE) were a 12.10% risk in the first half year and a 3.89% risk later (increasing with age). Rates for later events were obtained by calibration of epidemiologic data⁶.
- The analysis is carried out from an NHS payer perspective. Table 4 presents costs of treatment and events and estimates for the relative loss in utility following an MI or stroke⁷⁻¹³.

Table 1: Priors – Effect of 1 mmol reduction in LDL

		RR (95% CI)
Coronary Event	Year 1	0.86 (0.77 – 0.95)
	Year 2	0.78 (0.70 – 0.87)
Stroke	Year 1	0.96 (0.79 – 1.17)
	Year 2	0.75 (0.62 – 0.90)

Figure 1: Model Concept

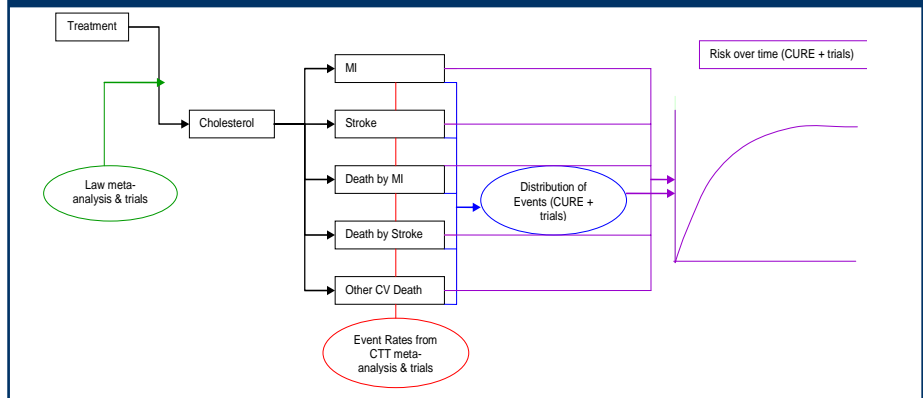


Table 2: Trial Data

	A to Z		Prove IT		Miracl	
	A	C	A	C	A	C
N	2265	2232	2099	2063	1538	1548
MI	161	165	139	153	102	113
Stroke	29	40	21	21	9	22
CV Death	93	121				
CHD Death			23	23		
Fatal Stroke					3	3
Fatal MI					11	12
Other Death	32	29	23	37	51	53
LDL-C BL	2.9	2.9	2.7	2.7	3.2	3.2

Table 3: Effect of treatment: Percentage reduction in LDL

	40 mg	80 mg
Atorvastatin		55%
Simvastatin	37%	42%

Table 4: Costs and Utilities

Cost of Simvastatin (per month)	£1.37 (40mg); £2.94 (80mg)
Cost of Atorvastatin (per month)	£28.21
NHS Cost of MI (1 st 6months)	£3300
NHS Cost of MI (2 nd 6months)	£1200
NHS Cost of MI (After 1 year)	£900
NHS Cost of Stroke (1 st 6months)	£5100
NHS Cost of Stroke (2 nd 6months)	£3500
NHS Cost of Stroke (After 1 year)	£2600
NHS Cost of Fatal MI	£1250
NHS Cost of Fatal Stroke	£3750
NHS Cost Other CV Death	£2500
NHS Cost Other Death	£250
Relative Utility Decrement MI	0.91
Relative Utility Decrement Stroke	0.66

Table 5: Results

	Δ Total Cost	Δ LYG	Δ QALY	ICER
Atorvastatin 80mg vs Simvastatin 40mg	£438	0.08	0.07	£6220
Atorvastatin 80mg vs Simvastatin 80mg	£434	0.06	0.05	£8433

RESULTS

- Base case results for a two year treatment period are shown in table 5.
- Compared with 40mg or 80mg of simvastatin, treatment with atorvastatin 80mg is more expensive but also produces greater health benefits.
- Intensive therapy with atorvastatin 80mg is associated with an incremental cost increase (drug and event) of £438 compared to simvastatin 40mg, but provides an additional gain of 0.07 quality adjusted life years, resulting in an incremental cost effectiveness ratio of £6220, and a number needed to treat (NNT) estimate of 59.
- When compared to higher dose simvastatin (80mg), atorvastatin 80mg remains within the usually acceptable boundaries of cost effectiveness (ICER=£8433, NNT=80).

CONCLUSIONS

- Our preliminary findings show that intensive-dose atorvastatin is estimated to be cost-effective in comparison to standard-dose and high-dose simvastatin in ACS patients over a 2 year period.
- Subsequent analyses to be conducted include probabilistic analyses to explore uncertainties around the cost and efficacy estimates for this time horizon and the development of another model to assess the cost-effectiveness of intensive atorvastatin over a longer time horizon.

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