PCV47: DOES THE COST-EFFECTIVENESS OF ICOSAPENT ETHYL IN COMBINATION WITH STATIN THERAPY COMPARED TO STATIN ALONE DIFFER BETWEEN PRIMARY AND SECONDARY PREVENTION?

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1 Background

Given the high rates of cardiovascular events among people undergoing treatment for primary and secondary prevention of cardiovascular disease (CVD), there is increasing interest in additive therapies that have potential to minimize this residual risk. The results of Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial (REDUCE-IT) have generated interest for a broader use of icosapent ethyl, although its cost-effectiveness has not been established.

Aim

To assess the cost-effectiveness, from the perspective of the Australian public healthcare system, of icosapent ethyl in combination with statin therapy compared to statin alone for the prevention of CVD in people with established CVD or at high risk, and with hypertriglyceridemia.

2 Methods

A cohort state-transition Markov model was constructed to simulate the progress of the target population of icosapent ethyl in combination with statin therapy compared to statin alone. The health states comprised 'Alive without CVD', 'Alive with CVD' and 'Dead' (Figure 1). Primary prevention subjects began the simulation in the 'Alive without CVD' health state, and with each annual cycle were at risk of experiencing a non-fatal CVD (myocardial infarction (MI) and/or stroke) event, a fatal CVD event or dying from non-CVD causes.

Secondary prevention subjects began the simulation in the 'Alive with CVD' health state and were at risk of a recurrent non-CVD events after which they remained in the 'Alive with CVD' health state, or cardiovascular or non-cardiovascular death, which channeled them into the 'Dead' health state. In any cycle, living subjects were also at risk of coronary revascularisation, hospitalisation for atrial fibrillation or flutter, and bleeding, but these latter events did not alter the health states to which subjects were assigned in the following cycle. The analyses were performed from an Australian public healthcare system approach over a 20-year time horizon (equivalent to lifetime) and all outcomes were discounted by 5% per annum beyond the first year, in line with Australian recommendations. Key input parameters used to build the model are displayed in Table 1.

Participants

The model population was profiled on participants in REDUCE-IT. The key inclusion criteria were patients aged ≥45 years with established CVD or aged ≥50 years with diabetes and at least one additional risk factor. All eligible patients had elevated triglycerides despite statin therapy.

The main outcome of interest was incremental cost-effectiveness ratios (ICERs) in terms of cost per quality adjusted life year (QALY) gained and per year of life saved (YoLS).

3 Results

Use of icosapent ethyl in combination with statin therapy exclusively in the primary prevention setting, resulted in an ICER of AUD 96,136 per QALY gained. Whereas, use of icosapent ethyl in combination with statin therapy in existing CVD patients only (secondary prevention) produced an ICER of AUD 35,935 per QALY gained (Table 2).

3 Results (continued)

Figure 1: Markov model, depicted in state transition format

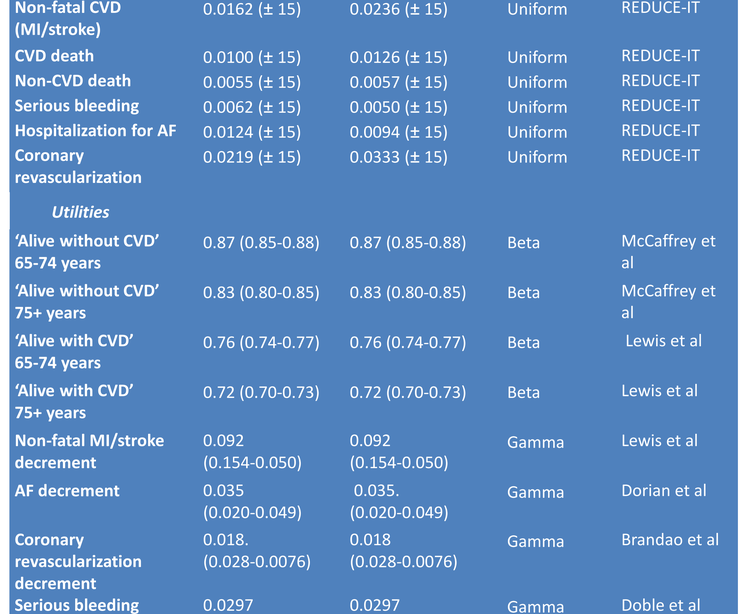


Table 1. Description of input parameters

Parameters	Icosapent ethyl and statin	Statin alone	Distribution	Reference
Annual transition probabilities				
'Alive without CVD' (primary prevention)				
Non-fatal CVD. (MI/stroke)	0.0103 (± 15)	0.013 (± 15)	Uniform	REDUCE-IT
CVD death	0.0063 (± 15)	0.007 (± 15)	Uniform	REDUCE-IT
Non-CVD death	0.0035 (± 15)	0.003 (± 15)	Uniform	REDUCE-IT
Serious bleeding	0.0039 (± 15)	0.0026 (± 15)	Uniform	REDUCE-IT
Hospitalization for AF	0.0078 (± 15)	0.0050 (± 15)	Uniform	REDUCE-IT
Coronary revascularization	0.0138 (± 15)	0.0177 (± 15)	Uniform	REDUCE-IT
'Alive with CVD' (secondary prevention)				
Non-fatal CVD (MI/stroke)	0.0162 (± 15)	0.0236 (± 15)	Uniform	REDUCE-IT
CVD death	0.0100 (± 15)	0.0126 (± 15)	Uniform	REDUCE-IT
Non-CVD death	0.0055 (± 15)	0.0057 (± 15)	Uniform	REDUCE-IT
Serious bleeding	0.0062 (± 15)	0.0050 (± 15)	Uniform	REDUCE-IT
Hospitalization for AF	0.0124 (± 15)	0.0094 (± 15)	Uniform	REDUCE-IT
Coronary revascularization	0.0219 (± 15)	0.0333 (± 15)	Uniform	REDUCE-IT
Utilities				
'Alive without CVD' 65-74 years	0.87 (0.85-0.88)	0.87 (0.85-0.88)	Beta	McCaffrey et al
'Alive without CVD' 75+ years	0.83 (0.80-0.85)	0.83 (0.80-0.85)	Beta	McCaffrey et al
'Alive with CVD' 65-74 years	0.76 (0.74-0.77)	0.76 (0.74-0.77)	Beta	Lewis et al
'Alive with CVD' 75+ years	0.72 (0.70-0.73)	0.72 (0.70-0.73)	Beta	Lewis et al
Non-fatal MI/stroke decrement	0.092 (0.154-0.050)	0.092 (0.154-0.050)	Gamma	Lewis et al
AF decrement	0.035 (0.020-0.049)	0.035. (0.020-0.049)	Gamma	Dorian et al
Coronary revascularization decrement	0.018. (0.028-0.0076)	0.018 (0.028-0.0076)	Gamma	Brandao et al
Serious bleeding decrement	0.0297 (0.0093-0.050)	0.0297 (0.0093-0.050)	Gamma	Doble et al
Annual disease costs				
'Alive without CVD'*	$5,866 (± 25)	$5,866 (± 25)	Uniform	Colagiuri et el.
'Alive with CVD'	$5,229 (± 25)	$5,226 (± 25)	Uniform	Cobiac et al
Acute disease costs				
Non-fatal CVD (MI/stroke)	$10,593 (± 25)	$10,595 (± 25)	Uniform	AR-DRG
CVD death	$2,592 (± 25)	$2,592 (± 25)	Uniform	AR-DRG
Non-CVD death	$2,592 (± 25)	$2,592 (± 25)	Uniform	AR-DRG
Serious bleeding	$4,528 (± 25)	$4,528 (± 25)	Uniform	AR-DRG
Atrial fibrillation hospitalizations	$3,904 (± 25)	$3,904 (± 25)	Uniform	Reinhold et al
Coronary revascularization	$19,894 (± 25)	$19,894 (± 25)	Uniform	
Annual treatment costs				
Icosapent ethyl plus statin	$1,637 (± 25)	$173 (± 25)	Fixed	Khera et al
Statin alone		$173 (± 25)		PBS
Discounting	5%			

The results were sensitive to time horizon, age-related trends and the price of icosapent ethyl. The probabilistic sensitivity analysis, using 10,000 Monte Carlo simulations, demonstrated icosapent ethyl in combination with statin therapy had a 64.4% probability of being cost-effective compared to statin alone, at a willingness-to-pay threshold of AUD 50,000 per QALY gained (Figure 2).

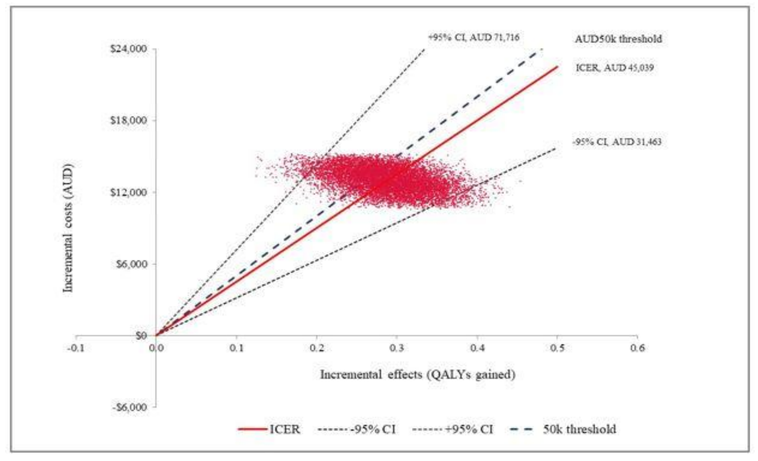
Table 2. Base case results in our model population of 1000 individuals over a 20-year time horizon.

Effectiveness (discounted)	Icosapent ethyl and statin	Statin alone	Difference
Total life years	10,119	9,780	338
Total QALYs	7,825	7,536	289
Costs (discounted)			
Treatment costs	$18,315,224	$1,690,150	$16,625,074
Disease costs	$71,018,097	$74,620,865	$3,602,768
Total costs	$89,333,322	$76,311,015	$13,022,306
Incremental cost-effectiveness ratios		AUD	USD
Cost per QALY gained (Overall)		$45,039	$79,971
Cost per QALY gained (Primary prevention)		$96,136	$169,697
Cost per QALY gained (Secondary prevention)		$35,935	$63,990
Cost per YoLS (Overall)		$38,480	$68,330
Cost per YoLS (Primary prevention)		$113,916	$201,083
Cost per YoLS (Secondary prevention)		$29,250	$52,087

4 Limitations

Firstly, the benefits of icosapent ethyl plus statin therapy was derived from a trial with a short timeframe (median 4.9 years). Secondly, hospitalisation for AF or flutter was considered to be an acute event because REDUCE-IT did not specify if AF was transient or permanent. Lastly, our analysis adopted an Australian healthcare perspective, in which there is a publicly-funded healthcare system with subsidised medication access.

Figure 2: Cost-effectiveness plane demonstrating the probability of cost-effectiveness with 10,000 iterations



5 Conclusions

Compared to statin alone, icosapent ethyl in combination with statin therapy would be cost-effective for the prevention of CVD at a willingness-to-pay threshold of AUD 50,000 per QALY gained, especially if targeted to people with existing CVD.