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The cost-effectiveness of omega-3 polyunsaturated fatty acids – The Australian healthcare perspective

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ABSTRACT

Objectives: To examine the cost-effectiveness of a triglyceride lowering medication–icosapent ethyl added on to statin from Australian healthcare system perspective.
Methods: A Markov-model was developed using data from the pivotal trial of icosapent ethyl in a secondary prevention population. Probabilities of CVD events were derived and extrapolated from the published Kaplan-Meier curve using a valid algorithm. Management cost of CVD, health-related quality of life, and background non-CVD mortality were extracted from publicly available sources. Acquisition cost of icosapent ethyl from the United States was used in the current analysis. Australian patients with histories of CVD were modelled for a 25 year time horizon and costs and benefits were discounted. Sensitivity analyses (SA) were undertaken. Value of perfect information (VPI) was quantified.
Results: Treatment with icosapent ethyl was associated with both higher costs and benefits (i.e. quality-adjusted life year [QALY] and life year [LY]), resulting in an incremental cost-effectiveness ratio (ICER) of AUD59,036/QALY or AUD54,358/LY. Using the often quoted willingness-to-pay (WTP)/QALY of AUD50,000/QALY, icosapent ethyl was not considered cost-effective. SA showed that time horizon, drug cost, and discount rate were the key drivers of the ICER. Total monetary VPI for icosapent ethyl was over AUD15 million over 5 years.
Conclusions: Patients with established CVD in whom level of triglycerides is high would benefit from the treatment using icosapent ethyl, however, it is not a cost-effective from an Australian healthcare system perspective. The government may consider subsidising this medication given the clinical need but at a discounted acquisition cost.

1. Introduction

Cardiovascular disease (CVD) is among the leading causes of death worldwide even with the advances in the disease awareness, prevention and treatment [1]. It is the top cause of death in persons aged over 55 years in Australia [2]. In 2015–16, nearly 1 in 3 deaths (29% of deaths) and over 1.1 million hospitalisations (11% of all hospitalisations) were associated with CVD in Australia [3].

Patients with cardiovascular disease receiving treatment for secondary prevention still experience high rates of subsequent cardiovascular events. The residual cardiovascular risk for patients treated by statins (even for those who achieve optimal levels of lipids) is still considerable: the residual risk of an ischaemic event remained at 12.6% per annum at year 3 [4–6]. Among these patients, hyptertriglyceridemia (HTG) is an independent risk factor to predict increased risk of ischaemic events, as reported by epidemiologic and mendelian randomised studies this is primarily because elevated serum levels of triglycerides (TGs) are associated with atherosclerosis, and mounting evidence that associates HTG with CVD [7,8]. However, the emerging opinion is that TGs may be better suited as a biomarker of risk for CVD rather than an independent risk factor [9]. This was echoed by the United States Food and Drug Administration (US FDA) that indicated that it will no longer approve drugs that lower TGs (in the 5.63 mmol/L range) without evidence that such drugs actually reduce eventual CVD outcomes [10]. The current practice for patients with dyslipidaemia still details statin as the mainstay treatment for low density lipoprotein (LDL) [11]. If TGs level fail to respond to the optimal statin therapy, then adjunctive therapy can be initiated. The current guidelines to lower TGs recommend a combination of effort including weight loss, physical activity, smoking cessation, limiting alcohol intake, and

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treatment with statins, omega-3 polyunsaturated fatty acids (PUFAs), fibrates, or niacin [12–14]. Although non-prescription fish oil dietary supplements contain omega-3 PUFAs, their effectiveness in lowering TGs is controversial since they are not subject to the US FDA or Australian Therapeutic Goods Administration (TGA) regulations, as are prescription drugs [15,16].

Icosapent ethyl, a FDA approved omega-3 PUFA, has been explored in its effect on ischaemic CVD events [17]. The Phase 3b randomised controlled trial (RCT) demonstrated that treatment with icosapent ethyl was able to significantly reduce the risk of ischaemic events including cardiovascular death, myocardial infarction, and stroke in patients with elevated TG levels despite the use of statins for primarily secondary prevention population [18,19]. A previous Japanese trial examined the efficacy of another omega-3 PUFA—eicosapentaenoic acid (EPA) added on statins in patients with hypercholesterolemia, and reported that the risk of major coronary events was lowered by 19% more in the EPA treatment group than in the statin only group [20].

Since the clinical efficacy and safety of icosapent ethyl have been demonstrated in RCTs, from the payer's perspective, it is equally important to ascertain the long-term cost-effectiveness of the drug in order to make more efficient use of limited healthcare resources. To the best of our knowledge, there has been no study assessing the lifetime cost-effectiveness of icosapent ethyl in patients with HTG as the secondary prevention treatment. We aimed to undertake a modelled economic evaluation of icosapent ethyl in the secondary prevention setting for patients with HTG from an Australian healthcare system perspective.

2. Methods

2.1. Model structure

A Markov-state transition model, consisting of four Markov states (no further event, post-CVD, CVD death, and non-CVD death) was developed to assess the long-term cost-effectiveness of icosapent ethyl in treating patients with established cardiovascular diseases as secondary prevention interventions. The economic model was constructed to maximise utilisation of the pivotal clinical trial [18]. Since the primary outcome of the trial was a composite of cardiovascular death, nonfatal myocardial infarction (including silent myocardial infarction), nonfatal stroke, coronary revascularisation, or unstable angina, and only the cumulative incidence of the primary outcome was graphically presented, the model was developed in accordance with the trial design. Patients undergoing any of the aforementioned CVD events were aggregated into a single health state (i.e. differentiated by fatal CVD or nonfatal CVD). Following a nonfatal CVD, patients could be alive or died due to background mortalities. The model was built using TreeAge Pro Healthcare software (TreeAge Pro 2018, R2. TreeAge Software, Williamstown, MA, USA). The Markov model is shown in Supplementary Fig. 1.

2.2. Population

A cohort of Australian patients aged 45 years and over with established CVD, a fasting triglyceride (TG) level of 1.69 to 5.63 mmol/L and a LDL cholesterol level of 1.06 to 2.59 mmol/L with at least 4 weeks treatment by any strength of statins were created based on the pivotal trial. Patients without diagnosis of CVD were not excluded. The median age of the patients was 64 years with 28.8% female, and the median LDL level was 1.94 mmol/L and TG level was 2.44 mmol/L [18].

2.3. Transition probabilities

All the patients commenced the modelling in the no further event state. The probabilities of experiencing non-fatal CVD and fatal CVD were derived from the published figure on the cumulative incidence of cardiovascular events (Fig. 1A of the pivotal trial [18]). Since the median follow-up of the study was approximately 5 years, the event probabilities of the first 5 years were directly read from the original figure for both icosapent ethyl and control groups. The treatment effect was assumed to last for 10 years only, and after that the rate of CVD events for the control group was applied to both groups, which was considered conservative. In order to model the long-term cost-effectiveness, the incidence of cardiovascular events was extrapolated using the parametric survival analysis model. Graphic digitiser (WebPlotDisitizer V3.9) was used to extract the graphic data. The extracted cumulative incidence of CVD (i.e. cumulative hazard function) was converted to a survival function (i.e. proportion of people with event-free survival) at various time-points [21]. The individual patient data (IPD) for the control group was reconstructed using the method proposed by Guyot [22]. Briefly, an algorithm was used to map from digitalised curves back to Kaplan-Meier (KM) data by finding solutions to the inverted KM equations, based on the published information about number of events and number at risk. Then parametric survival models (i.e. exponential, Weibull, log-normal, log-logistic, generalised gemma, Gompertz distribution) were fitted to the reconstructed IPD using the R 'flexsurv' package [23]. The best fit survival model was selected based on the criteria recommended by the National Institute for Health and Care Excellence [24,25] and Williams et al. [26] (visual inspection and Akaike Information Criterion, AIC, goodness-of-fit statistics). Based on the criteria set out, the log-logistic and log-normal distributions were selected for the placebo and intervention groups to extrapolate the long-term transition probability of CVD, respectively (Supplementary Table 1). The probability of CVD (both fatal and nonfatal) from year one to year ten was informed by the best survival analysis models corresponding to group membership. The probability of CVD events from year ten onwards was sourced from the control arm only and then applied to both treatment groups (the assumption of proportional effect was therefore not tested).

The probabilities of fatal and nonfatal CVD were estimated by weighting the proportion of fatal and nonfatal CVD observed in the pivotal trial. The probabilities of subsequent recurrent CVD was assumed to be the same as the first recurrent event over time (the model was targeted for secondary prevention population, the probabilities of subsequent recurrent CVD were not inflated to be conservative and considered not favouring the intervention).

The mortality due to non-CVD causes was sourced from the Australian Bureau of Statistics data on the causes of death by subtracting the CVD-related mortalities [27] (Supplementary Table 2) and adjusting by the relative risk of death among those with established CVD (Table 1).

2.4. Costs

The costs related to fatal and nonfatal CVD were weighted averages using the proportion of MI and stroke observed in the trial. The management cost of post-CVD health state was estimated from outpatient care utilised by patients post MI and/or stroke. The unit cost for base case analysis was sourced from the National Hospital Cost Data Collection (NHCDC) from Independent Hospital Pricing Authority, Australia (IHPA) and published literature. Alternative sources like the National Efficient Price (NEP) report was also used to derive the costs related to the hospitalisation care for CVD, and were tested in the sensitivity analysis. NEP reports the national price that the government will pay (prospectively) for admissions and procedures in public hospitals [28]. Acquisition cost of icosapent ethyl (2 g twice daily, USD 1.88/g, 1 USD = 1.38 AUD, 22 Nov 2018) [29] for a year was AUD3768 per patient. All the costs were half-cycle corrected to best reflect reality; for example, if patient died during a cycle, only half of the medication cost was assigned and half of the quality-adjusted life year (QALY) was accumulated. The cost of icosapent ethyl was only estimated for the first five years.

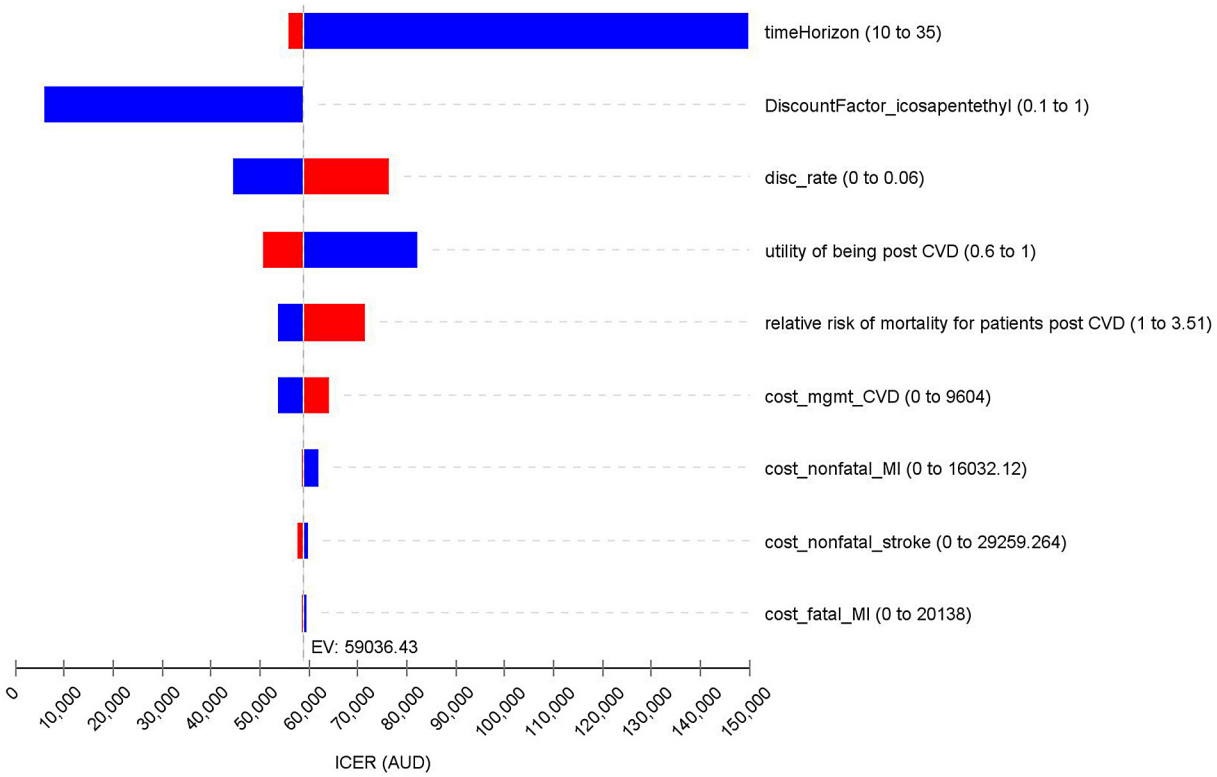

Fig. 1. Tornado diagram of one-way deterministic sensitivity analyses by varying the key model parameters.

2.5. Utilities

All individuals entered the model with a utility of 0.85 to reflect the population mean for persons with CVD. It was determined by the weighted average utility consistent with the proportion of the cohort who had a CHD or stroke [18] and the respective utility values of 0.88 and 0.76 [30]. To quantify the morbidity associated with a recurrent CVD event, the proportion of subsequent events due to nonfatal MI and nonfatal stroke in both arms were applied to the relevant utility decrement [30].

2.6. Cost-utility analysis

The cost-effectiveness analysis (CEA) was conducted from an Australian Healthcare system perspective with a time horizon of 25 years. All the costs and benefits were discounted at a rate of 3% per annum. The cycle length of the Markov model was set as one year. The incremental cost-effectiveness ratio (ICER)/incremental cost-utility ratio (ICUR) was estimated as the costs for the icosapent ethyl group minus the costs for the control group divided by the QALYs of the icosapent ethyl group minus the QALYs of the control group. The ICER was compared to a willingness-to-pay (WTP) threshold per QALY gained of AUD50,000, a commonly accepted value for health technology assessment in Australia [31].

2.7. Sensitivity analysis

A series of deterministic sensitivity analyses were undertaken to test model assumptions and determine key drivers of ICURs. The parameters varied included the following:

- Increase the duration of treatment effect of icosapent ethyl for the nonfatal and fatal CVD, i.e. the extrapolated survival curve for the icosapent ethyl group was used to inform the long-term probabilities of CVD events;
- Decrease the annual cost of icosapent ethyl ranging from AUD1000 to AUD3000 per person;
- Vary the relative risk of dying from background non-CVD causes for those with established CVD (i.e. 1 to 3.5);
- Vary the discount rate (i.e. 0% to 6%);
- Varying the overall time horizon (i.e. 10 to 35 years).

A tornado diagram was constructed to present all the one-way deterministic sensitivity analyses in the same graph with plausible ranges incorporated. The parameters examined in the one-way deterministic sensitivity analysis (DSA) are summarised in Supplementary Table 3.

In addition, probabilistic sensitivity analyses (PSA) by integrating uncertainty of key parameters (i.e. parameters defining the parametric survival models, utilities and costs related to the management and hospitalisation care) were performed to construct the 95% confidence interval (CI) for both costs and QALYs. A cost-effectiveness plane and acceptability curve were then produced to illustrate the PSA results of.

Lastly, the model was also run as a microsimulation with a hypothetical of 10,000 patients to estimate the number of total fatal and nonfatal CVD (including subsequent recurrent CVD) in each of the treatment arm over the entire time horizon.

2.7.1. Value of perfect information

The incremental net monetary benefit (INMB), which is the incremental QALYs multiplied by the WTP minus the incremental costs of the intervention group compared to the standard management group was calculated for each treatment strategy. Further, the uncertainty in the results was explored using value of information techniques to estimate the expected value of perfect information (EVPI). EVPI represents a theoretical maximum value from future research that would eliminate all measured uncertainty included in the analysis. The EVPI per person was calculated using the difference between the NMB of each single iteration (i.e. one sample iteration) and the NMB over all iterations (in this case all sampled iterations from the PSA) of the proposed intervention. For example, if the iteration's NMB is the same

Table 1
Model parameters.

Model parameters	Base case	Sensitivity analyses	Reference
Cost	AUD	AUD	
Icosapent ethyl	$3768		Online resource
Hospitalisation			
Non-fatal MI	$16,032	$13,976	National Efficient
Fatal MI	$5764	$10,069	Price determination
Non-fatal stroke	$29,259	$12,035	2018–19 (21); Cobiac
Fatal stroke	$4222	$14,741	et al. 2012 [23]
Management			
Post MI	$5632		
Post stroke	$3972		
Utility weights			
Alive with CVD	0.85		Cobiac et al. 2012
Alive following MI	−0.12		[23]; Kumar et al.
Alive following stroke	−0.24		2017 [34]
Transition probabilities			
Non-CVD mortality	Age-dependent		ABS cause of death 2017 [2]
RR of dying from background mortality for people post CVD	1.755		Smolina 2012[b]; Hardie 2003[b]; Bhatt et al. 2018 [12]
CVD type			
Fatal	24.68%		Bhatt et al. 2018 [12]
Non-fatal	75.32%		
Parameters for long-term extrapolation[a]			
Icosapent ethyl	Log-normal	mu 3.579; sigma 2.107	Derived from survival analysis
Placebo	Log-logistic	a 16.849; b 1.028	

MI: myocardial infarction, CVD: cardiovascular disease; RR: relative risk.
Online resource: https://www.goodrx.com/icosapent-ethyl. Accessed on 15 Jan 2019.

[a] Using the parameters provided, the transition probabilities could be reproduced, thus they are not provided here;

[b] References: K. Smolina, F.L.Wright, M. Rayner,M.J. Goldacre, Long-term survival and recurrence after acute myocardial infarction in England, 2004 to 2010, Circ. Cardiovasc. Qual. Outcomes 5 (4) (2012) 532–540; K. Hardie, G.J. Hankey, K. Jamrozik, R.J. Broadhurst, C. Anderson, Ten-year survival after first-ever stroke in the Perth Community Stroke Study, Stroke 34 (8) (2003) 1842–1846.

as the overall NMB, its EVPI value is zero, however, when these two NMBs are not identical, there is some value to eliminating the uncertainties being simulated. The total EVPI was then estimated by multiplying the per person EVPI by the projected number of the population receiving the treatment [32,33] (i.e. assuming 50% of people with histories of CVD and high TG would be eligible for this treatment) and the likely length of patent of the medication (i.e. assuming 5 years) [34,35].

3. Results

3.1. Cost utility analysis

Treatment with icosapent ethyl was associated with both higher costs and benefits. The costs for hospitalisation, management and icosapent ethyl were AUD4,888 vs AUD6,264, AUD61,376 vs AUD59,892, and AUD16,804 vs AUD0, making up the total cost of AUD83,258 vs AUD66,453 for the two treatment groups, respectively. The cost of management comprised the single biggest cost component and people receiving icosapent ethyl incurred higher costs in this regard compared to the placebo because they collectively lived longer. Icosapent ethyl also contributed to greater gains in health benefits than the placebo (QALY: 10.57 vs 10.28, and LY: 12.78 vs 12.47). The corresponding ICER was AUD59,036/QALY or AUD54,358/LY from a healthcare system perspective. Given the current US acquisition cost for icosapent ethyl, this TG lowering agent is unlikely to be cost-effective from the Australian healthcare system perspective (Table 2).

Table 2
Results of cost-effectiveness analysis.

	Icosapent ethyl	Placebo	ICER
Base case			
Total cost	$83,258	$66,453	
Cost of icosapent ethyl	$16,804	$0	
Cost of hospitalisation	$4888	$6264	
Cost of management	$61,376	$59,892	
Benefits			
QALY	10.57	10.28	$59,036
LY	12.78	12.47	$54,358
Probabilistic sensitivity analysis			
Total cost	$84,537 (75,623-94,582)	$66,497 (58,579-75,800)	
QALY	10.58 (8.14–12.19)	10.31 (7.94–11.88)	$67,212
LY	12.77 (12.19–13.32)	12.48 (11.91–13.00)	$61,893

Note: all the costs are the average across the entire hypothetical population while not all patients incurred the cost due to hospitalisation. ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year; LY: life year.

3.2. Sensitivity analyses

The DSA showed that the base case ICER was sensitive to the variation in time horizon, discount rate, and the RR of mortality for CVD vs general population. The cost of management for post-ACS and post-stroke states and acquisition cost for icosapent ethyl also contributed to the variation in the base case ICER to a lesser extent. Using the unit cost for hospitalisation from NEP yielded a slightly lower ICER of AUD57,929/QALY. The PSA also generated similar results to the base case scenario (Table 2), with an ICER of AUD67,212/QALY or AUD 61,893/LY. The Tornado diagram is presented in Fig. 1 and the cost-effectiveness plane is shown Fig. 2. In addition, threshold analysis was undertaken to determine the cost-effective acquisition cost for icosapent ethyl. It showed that if the drug cost could be reduced by 15.3%, it would become cost-effective from an Australian healthcare system perspective. The cost-effectiveness acceptability curve is shown in Supplementary Fig. 2.

The total number of fatal-CVD and non-fatal CVD events were lower in the cohort treated with icosapent ethyl than that in the placebo group (fatal-CVD: 1231 vs 1546, non-fatal CVD: 3752 vs 4588 per 10,000 patients) over a 25 year time horizon.

3.2.1. Value of perfect information

The uncertainty of the results was valued in monetary terms using value of perfect information techniques. With an estimated total number of 76,477 persons (assuming 50% of the 152,953 prevalent cases of elevated level of TG in 2017 based on National Health Survey statistics [36] would be eligible to receive icosapent ethyl treatment) eligible for the treatment in 2017, the total value of perfect information for icosapent ethyl was estimated as AUD 15 million over five years of its likely patent life.

4. Discussion

This is the first study to evaluate the long-term cost-effectiveness of icosapent ethyl in treating HTG. The value of lowering TG is under debate due to insufficient evidence showing the long-term health benefits. This modelled economic evaluation was based on the efficacy observed in the most recent clinical trial that demonstrated health benefits in terms of lowering TG in secondary prevention and high CVD risk population. The results showed that the icosapent ethyl is not a cost-effective treatment modality for CVD secondary prevention in

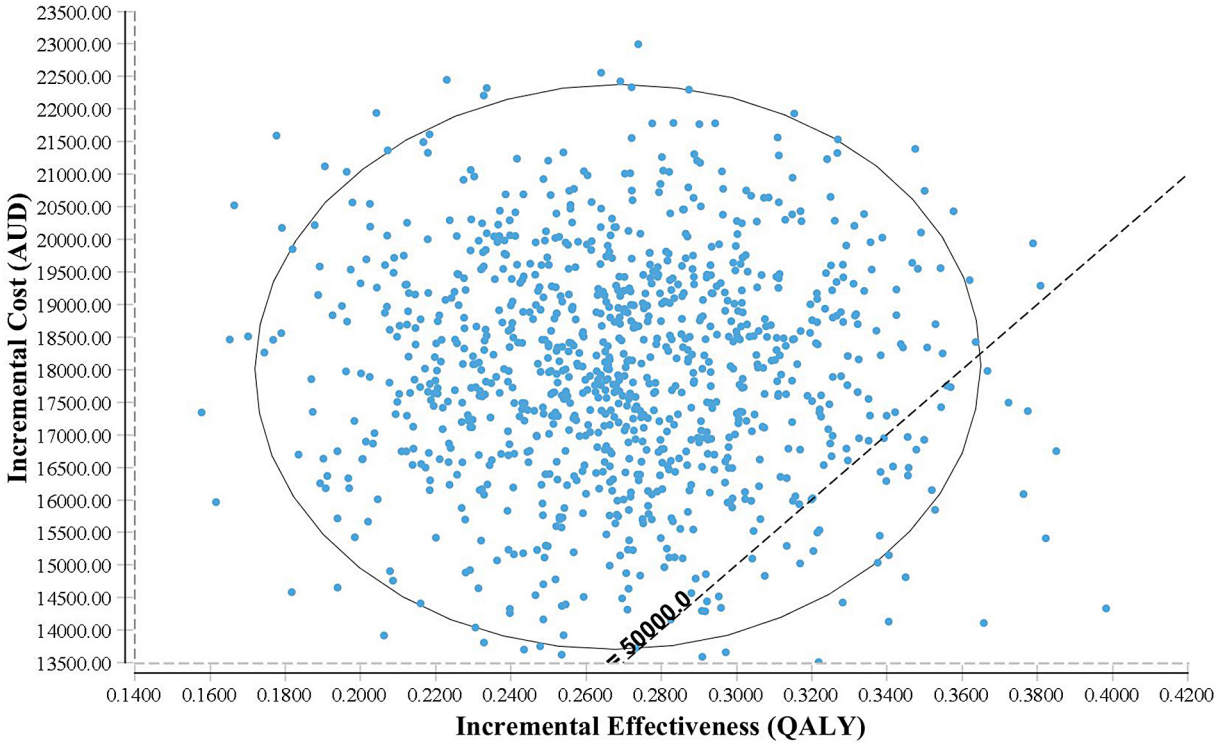

Fig. 2. Incremental cost-effectiveness plane.

patients with HTG from a healthcare system perspective. The base case results are robust in a way that the efficacy was assumed to be maintained for the first five years only and the CVD event probabilities were set the same for the icosapent ethyl and the control arm. Treatment with icosapent ethyl would avoid 315 cases of fatal CVD and 836 number of nonfatal CVD over 25 years per 10,000 patient population.

Other economic evaluations around the lipid-lowering medications predominantly focus on the drug's effectiveness in reducing the level of LDL, given its established effect in the primary and secondary prevention of CVD. Comparing to results from another CEA of LDL-lowering medications in Europe [37], the incremental benefits (intervention vs control) were similar between icosapent ethyl (0.29 QALY) and statin (from 0.22 to 0.30 across eight European countries). However, due to the significantly higher drug acquisition cost of icosapent ethyl, the incremental cost from our study was substantially greater than those reported [37], thus rendering it unlikely to be cost-effective. A recent systematic review identified 15 modelled cost-effectiveness analyses for lipid lowering drugs, with most studies adopting a Markov cohort model to evaluate the long-term economic credentials of the corresponding treatment [38]. The health states incorporated were similar to our study, normally involving death due to non-CVD cause, death due to CVD cause, and post-CVD event state, half of the studies adopted the assumption of lifetime or 10 years of treatment effect and 11 out 15 studies projected cost-effectiveness over a lifetime horizon. Therefore, our assumption around the duration of treatment effect and time horizon are considered conservative. The majority of studies applied the relative risk reduction/risk difference observed in the trial to represent the treatment effect and only two studies derived the event rate per treatment arm from the trial (based on individual patient level data) [39]. Our study is the first to demonstrate the cost-effectiveness of icosapent ethyl in secondary prevention and a high CVD risk population. Whilst there have been substantial advances in the treatment of CVD over the past decade, the occurrence/recurrence of CVD still poses significant burden to society and individuals. The residual CVD risk borne by high levels of triglyceride can be the next target to avert recurrent CVD events. Independent of the reduction in the level of LDL, decrease in triglyceride was associated with avoidance in the cardiovascular events that translated into increased quality adjusted survival (the QALY is higher in the icosapent ethyl than the placebo group).

It is not surprising to observe that if the extrapolated transition probabilities (i.e. from year ten onwards) from the icosapent ethyl arm were applied, the cost-effectiveness would become more favourable. It could be argued that the extrapolated event probabilities from the icosapent ethyl arm should be applied, since the lowered TG for the first five years (i.e. the assumption around the treatment effect duration) would carry on some of the residual benefits (i.e. delay the formation of atherosclerosis [7,40] or reduced inflammation in the key vessels [41]) and it is not uncommon for patients to stay on the preventive medications for their lifetime (i.e. aspirin, statin, anticoagulants for patients with atrial fibrillation). Taking these factors into consideration, the current ICER might be overestimated to a certain extent.

A recent published cost-effectiveness of PCSK9 inhibitors in lowering lipids in Australia adopted a similar model structure [42]. Their Markov cohort model had a cycle length of 5 years with no consideration of the long-term recurrent CVD events, and the treatment effect was assumed to remain for the modelled duration (i.e. 25 years). Due to the high acquisition cost of evolocumab, the cost-effectiveness credentials were not favourable in the Australia setting. Therefore, the authors concluded that the acquisition costs of PCSK9i in Australia would need to be reduced for them to be considered cost-effective. For the current cost-effectiveness analysis, the drug acquisition cost was derived from the United States, where healthcare expenditures are generally higher than the other developed countries. It is very likely that the pricing of icosapent ethyl would be more complex than just a currency conversion as applied in this modelled economic evaluation, that leading to the possible overestimation of its true cost-effectiveness in the Australian healthcare setting.

Besides assessing the uncertainty around model parameters via PSA, the value of perfect information was also explored by measuring the monetary value of perfect information, given the 95%CI presented in the PSA does not supply information about the magnitude of the uncertainty. Due to the uncertainty in terms of treatment effect,

management and drug cost, and utility weights of health state, the total value of perfect information was estimated as AUD15M for five years. New evidence has substantial value to reduce the financial losses from decisions made with this uncertainty. Policy maker could potentially use this information to weigh between making a decision now (to accept the uncertainty that may mean subsidising suboptimal treatment) and deferring a decision until future research (i.e. large Australian study with longer term follow up) is undertaken to eliminate the uncertainty (thus reducing the chance of making suboptimal decision) at a cost of delaying market access [43]. Incorporating the value of perfect information into the formal decision-making process will optimise the funding decision [35,44].

The current study utilised the published Kaplan-Meier curve from the landmark trial to derive the transition probabilities. The time-dependent treatment effect for the duration of trial follow up was informed by the trial directly, which is a key strength of the study. In addition, the subsequent CVD events following the first recurrent CVD were also accounted for in the model to best reflect the clinical reality. The ICER is considered conservative given the assumption of a five-year treatment effect. However, the study is not without limitations. We did not inflate the transition probabilities for the subsequent recurrent CVD following the first recurrent CVD. To test this in the sensitivity analysis, the long-term transition probabilities for CVD were extrapolated based on the parametric survival analysis; the modelled population (mean age of 64 years) is not necessarily the Australian population that will receive the treatment. Moreover, the PUFAs are reported to be effective in terms of preventing arrhythmias, reducing the age-related cognitive decline [45], and attenuating inflammation in rheumatological disorder [46], etc. [47], which could potentially contribute to improved ICER for icosapent ethyl given the high rate of comorbidities in the CVD population. Another important limitation of the study is the severity of MI and stroke was not considered in the economic modelling, thus the costs and disutilities associated with different severities were not captured.

5. Conclusions

Patients with established CVD and a high level of TG with statin therapy would benefit from treatment with HTG using icosapent ethyl, however, it is not a cost-effective treatment modality in this population from an Australian healthcare system perspective. The government should consider subsidising this medication given the clinical need (i.e. the residual CVD risk of patients under statin therapy, CVD patients with end stage renal failure comorbid with hypertricyceridaemia in the absence of treatment option) but at a discounted acquisition cost.

Declaration of Competing Interest

All the authors affirm that they have nothing to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejim.2019.07.001.

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