

# Access Economics Report: Fish Oils for prevention of further morbidity in those with CHD

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## 4 Fish oils for prevention of further morbidity and mortality in those with CHD

### 4.1 Background

Epidemiological studies have indicated links between the consumption of fatty fish (such as mackerel, herrings, sardines, salmon, tuna and other seafood) and lower incidence rates of Coronary Heart Disease (CHD), stroke and myocardial infarction (MI). However, studies that have used fish consumption as the main intervention have shown efficacy in the short term, although not in the long term. In addition, high levels of fish consumption may lead to poisoning with dioxin or methylmercury, although levels of these toxins in Australian fish stocks are very low.

Fish oil supplements offer a number of advantages through lower potential risk profiles as well as controllable concentrations of fish oil supplement per tablet. The World Health Organization (WHO), American Heart Association (Kris-Etherton et al, 2003), National Health and Medical Research Council (NHMRC), and the National Heart Foundation of Australia recommend fish oil as a complementary treatment in addition to standard treatments following a MI. These organisations mainly base their recommendations on the results of a large randomised clinical trial '*Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico*' –Prevenzione (GISSI-P) and later the Japan eicosapentaenoic acid (EPA) Lipid Intervention Study (JELIS) trial (Yokoyama et al, 2007). Since these recommendations were published, another seminal trial (the GISSI-HF trial) has been published (GISSI-HF Investigators, 2008).

### 4.2 Aim

To undertake a cost effectiveness analysis of fish oils as a complement to current preventive therapies for reduced death and morbidity among people with CHD (through reducing serum triglycerides), versus no fish oils.

### 4.3 Indication

In line with the recommendations of the organisations above, the indication is for secondary prevention of morbidity and mortality from CHD, evidenced through previous MI.

The target population was defined in line with the trial data evidence as people who have had a MI within three months and who are unable to eat sufficient amounts of oily fish (2-4 portions per week) to meet the recommended intake of approximately 3.5g eicosapentaenoic acid (EPA) and 2.5g docosahexaenoic acid (DHA) per week. Fish oil supplements are thus indicated.

Australian specific incidence rates for MI and stroke events were sourced from Begg et al (2007). Rates of revascularisation procedures were sourced and calculated from the AIHW hospital morbidity database (Table 4.1). Mortality rates from CVD were sourced using the AIHW General Record of Incidence of Mortality (GRIM) books.

**Table 4.1: Incidence and procedure rates in Australia, by age and gender**

	MI		Stroke		Revascularisation	
	Males	Females	Males	Females	Males	Females
0-1	0.00%	0.00%	0.01%	0.01%	0.02%	0.02%
1-4	0.00%	0.00%	0.01%	0.01%	0.01%	0.01%
5-9	0.00%	0.00%	0.01%	0.01%	0.00%	0.00%
10-14	0.00%	0.00%	0.01%	0.01%	0.00%	0.00%
15-19	0.00%	0.00%	0.01%	0.00%	0.01%	0.00%
20-24	0.00%	0.00%	0.01%	0.01%	0.01%	0.00%
25-29	0.01%	0.00%	0.01%	0.04%	0.02%	0.01%
30-34	0.02%	0.01%	0.01%	0.05%	0.06%	0.02%
35-39	0.06%	0.01%	0.02%	0.03%	0.13%	0.04%
40-44	0.12%	0.03%	0.04%	0.03%	0.30%	0.12%
45-49	0.24%	0.05%	0.06%	0.06%	0.58%	0.22%
50-54	0.36%	0.07%	0.09%	0.09%	0.97%	0.39%
55-59	0.47%	0.13%	0.11%	0.09%	1.48%	0.62%
60-64	0.63%	0.22%	0.15%	0.09%	2.00%	0.92%
65-69	0.79%	0.33%	0.23%	0.15%	2.58%	1.30%
70-74	1.06%	0.54%	0.35%	0.25%	2.94%	1.61%
75-79	1.36%	0.81%	0.53%	0.39%	3.15%	1.93%
80-84	1.67%	1.14%	0.82%	0.69%	2.93%	1.67%
85-89	2.09%	1.64%	1.29%	1.26%	1.39%	0.61%
90-94	2.34%	1.75%	1.85%	1.99%	-	-
95-99	1.48%	1.52%	2.42%	2.72%	-	-
100+	0.50%	0.47%	2.88%	3.29%	-	-

Source: Begg et al (2007).

## 4.4 Intervention

The intervention is fish oils as a dietary supplement to current secondary prevention of CHD. The economic review by Cooper et al (2007) (discussed later) considers two branded forms of fish oil – Omacor and Maxepa, with dosage of 510-540mg EPA/day and 345-360mg DHA/day.<sup>45</sup>

### 4.4.1 Literature search

An initial literature review was undertaken in June 2009 based on of the bibliography of Colquhoun et al (2008). Further to this, on 15 July 2009 a literature search was undertaken of NCBI and NIH Pubmed applying the following criteria: (1) in English; (2) published in 2006 to present (Colquhoun et al 2008 covered those prior to this); (3) studies in humans; and (4) studies on primary prevention discarded. Search terms were “Fish oil and cardiovascular” and “Fish oil and coronary heart disease”. A final search used the search term “Fish oils and heart disease” and involved additional search parameters of: (1) studies of adults; (2) studies on

<sup>45</sup> Note these are above the recommended levels of EPA and DHA assuming no dietary intake.

prevention in people with heart disease preferred; (3) studies on ventricular tachycardia and implantable cardioverter defibrillators discarded; and (4) studies on stroke discarded.

A summary of findings is in Table 4.2

**Table 4.2: Results from the literature search for fish oils and CHD**

<b>Study type</b>	<b>Study (within study type, from most recent to oldest)</b>
Review	Colquhoun et al (2008)
Meta-analysis	Leon et al (2008)
	Gapinski et al (1993)
Randomised controlled trials	Yokoyama et al (2007) (JELIS)
	Marchioli et al (2002) (GISSI-P)
	Johansen et al (1999)(CART)
	von Shacky et al (1998) (DART)
	Singh et al (1997)(IEIS)
	Cairns et al (1996)(EMPAR)
	Eritsland et al (1996)(Norwegian Council of Cardiovascular Diseases)
	Sacks et al (1995)(HARP)
Economic studies	Cooper et al (2007) (DART1 and GISSI-P)

Note: CART: Coronary Angioplasty Restenosis Trial

DART: Diet and Reinfarction Trial

EMPAR: Enoxaparin MaxEPA Prevention of Angioplasty Restenosis

GISSI-P: Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico – Prevenzione Trial

HARP: Harvard Atherosclerosis Reversibility Project

IEIS: Indian Experiment of Infarct Survival

Singh et al (1997), von Shacky et al (1998), Sacks et al (1995), Cairns et al (1996), and Johansen et al (1999) were subsequently removed on the advice of the Reference Group, since these trials studied the progression of coronary disease or restenosis and were thus irrelevant and distracting.

Detailed findings for the remaining studies are in Table 4.12 in the Appendix (Section 4.13).

## 4.5 Comparator

For the purpose of this study the comparator group is standard treatment without fish oil supplements.

## 4.6 Effectiveness

### 4.6.1 Previous cost effectiveness studies

Five cost effectiveness studies have been published previously on the use of fish oils for the prevention of further morbidity and mortality in patients with CHD. The majority of these studies are based on the clinical outcomes of treatment effectiveness from the GISSI-P trial. The standard length of duration for these studies is 3.5 years in line with the total study length of GISSI-P, although Quilici et al (2006) extrapolated the results to outcomes over a lifetime. Variations between study methodologies are mainly in the costing, including the perspective of the study as well as the country in which cost was determined (Table 4.3). Denominators in the incremental cost effectiveness ratios (ICERs) included life years gained (LYG) as well as deaths avoided, MIs avoided and QALYs gained.

**Table 4.3: GISSI-Prevenzione based CEA studies**

Perspective	Country	Endpoints	ICER
<b>Franzosi et al (2001)</b>			
Third party payer	Italy	MI Stroke Revascularisation rate Mortality	€24,603 / LYG 95% CI: 22,646 – 26,930
<b>Quilici et al (2006)</b>			
Health system (NHS)	United Kingdom	MI Stroke Revascularisation rate Mortality	£15,189 / QALY gained (4 years) £3,723 / QALY gained (lifetime) £12,011 / LYG (4 years) £2,812 / LYG (lifetime) £31,786 / death avoided (4 years)
<b>Lamotte et al (2006)</b>			
Healthcare payer	Australia Belgium Canada Germany Poland	MI Stroke Revascularisation rate Mortality	Varied between: €2,867 / LYG (Canada), and €5,154 / LYG (Belgium)
<b>Schmier et al (2006)</b>			
Health system <i>plus</i> productivity losses associated with CVD	United States	MI mortality CVD mortality	\$16,340 per MI avoided (one year) \$9,221 per MI avoided (3.5 years) Cost saving when productivity costs were included
<b>Cooper et al (2007)</b>			
Health system (NHS)	United Kingdom	MI Stroke Revascularisation rate CVD deaths Total mortality	£12,480 / QALY gained

Franzosi et al (2001) estimated that treatment with omega-3 acid ethyl esters resulted in a gain of 0.0332 life years compared to treatment without supplements. The ICER was

estimated to be €24,603 per life year gained, although this figure was sensitive to the cost of the supplements used.

Quilici et al (2006) was a cost effectiveness study conducted by Innovus Research on behalf of Solvay Pharmaceuticals and based on the perspective of the NHS. This study reported results for the short term (3.5 years) based on GISSI-P trial results as well as for the long term (life time) based on a survival curve extrapolated from the trial results. The intervention was cost effective as long as the NHS was willing to pay £15,189 per QALY in the short term or £3,717 per QALY over the lifetime. The NHS standard threshold to determine cost effectiveness is £20-30,000 per QALY. These results are comfortably below this threshold.

Lamotte et al (2006) conducted a cost effectiveness analysis based on five different countries (Australia, Belgium, Canada, Germany and Poland), using a decision model from the healthcare perspective. Costs of treatment were calculated for each specific country and converted back to a common currency (Euros). Country specific morbidity and mortality data were utilised as well in the estimation of treatment efficacy.

Differences in treatment outcomes ranged from gains of 0.261 (Poland) to 0.284 (Australia) in terms of life years gained. While, additional costs ranged between €787 (Canada) to €1,439 (Belgium). The resulting ICERs ranged between €2,788 (Canada) to €5,097 (Belgium) per LYG. Sensitivity analysis surrounding on effectiveness, costs of complications and discounting confirmed these results as robust. Results for each country were reported to be below specific societal willingness to pay thresholds<sup>46</sup>.

Schmier et al (2006) used a numbers of different studies to determine the effectiveness of treatment<sup>47</sup>, although the methodology used in this process was not outlined. Costs for this analysis were derived from hospitalization data as well as medication costs associated with prophylactic n-3 PUFA treatment. Lost earnings associated with CVD mortality were also included as a secondary analysis.

Both one year and 3.5 year results were reported, showing a cost per MI avoided of \$16,340 in one year and \$9,221 in 3.5 years (cost elements only included hospitalisations from MI and supplement costs). When lost earning was used in the calculations, supplementation became cost saving with a greater efficacy from a greater number of deaths avoided.

Cooper et al (2007) conducted cost effectiveness modelling as part of the NICE guidelines for post myocardial infarction secondary prevention review. Modelling was based on the meta-analysis of outcomes from GISSI-P and DART1 with sensitivity analysis including these results alone (Table 4.4). All of the studies in this area have analysed either the GISSI-P population or the DART1 population, hence the meta-analysis provided by Cooper et al (2007) is a comprehensive analysis of all available data.

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<sup>46</sup> The willingness to pay threshold is the maximum amount a person or society would be willing to pay, sacrifice or exchange for a good, or for a particular benefit. If outcomes are far below thresholds, as in this case, the intervention is cost effective by this benchmark.

<sup>47</sup> Marchioli et al (2002), Nilsen et al (2001), Singh et al (1997) and von Schacky et al (1999).

**Table 4.4: Treatment effect of fish oils for post myocardial infarction secondary prevention**

Outcome	Meta-analysis			GISSI-P alone			DART1 alone		
	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL
MI	1.14	0.75	1.74	0.96	0.80	1.14	1.49	0.97	2.30
Stroke	1.22	0.91	1.64	1.19	0.88	1.61	2.51	0.49	12.89
Revascularisation	1.05	0.97	1.13	1.05	0.97	1.13	1.05	0.97	1.13
CVD death	0.79	0.67	0.93	0.84	0.72	0.97	0.70	0.53	0.91
Total mortality	0.81	0.68	0.96	0.86	0.77	0.97	0.71	0.55	0.92

Source: Cooper et al (2007). LCL – lower confidence level. UCL – upper confidence level.

Gastrointestinal side effects were included in the modelling based on Hooper et al (2004), with costs estimated from the perspective of the NHS. Results produced an ICER of £12,480 per QALY, with further analysis showing that cost effectiveness improved for older patients. These results are in line with the results presented in the other health economic analyses.

Assuming a YLG is of similar value to a DALY, all the studies reviewed showed cost effectiveness as defined by the WHO and Department of Finance and Deregulation thresholds in Section 1.4. Almost all were also cost effective by the more stringent DOHA standard.

## 4.6.2 Treatment effectiveness

Treatment efficacy with fish oil was modelled using the meta-analysis outputs presented in Cooper et al (2007) and shown in Table 4.4. Few side effects were reported resulting from the use of fish oil dietary supplementation. One cost effectiveness study (Cooper et al, 2007) incorporated gastro-intestinal side-effects (citing Hooper et al, 2004). However, data relating to these side effects could not be found from the reference documents. Side effects of fish oil supplementation have not been included in this evaluation.

## 4.7 Benefits

### 4.7.1 Burden of disease

Disease states were measured using the DALY method. This methodology differs from the studies reported in Section 4.6.1, which utilised measures of QALYs. The DALY measure differs from the QALY measure, as it includes both loss of life due to morbidity and mortality (both the YLD and YLL). The QALY measures the reduction in a person’s quality of life as a result of a disease or injury, but does not capture impacts of premature mortality. To compare the results presented in Section 4.10 to those from the literature in Section 4.6.1, additional analyses were completed using QALY (estimated as 1-YLD) values for disease states.

Disability weights for YLDs were sourced from AIHW reports on the burden of disease in Australia (Begg et al 2007 and Mathers et al 1999). These sources reported multiple disability weights depending on the disability present after the event, for example, disability weights for stroke were reported as follows.

- **No disability (0.00):** First ever stroke, no long term disability after 6 months.

- **Mild disability (0.36):** No mobility or self care problems, some problems with usual activities, pain, anxiety and depression.
- **Moderate/Severe disability (0.63):** Some mobility and self care problems, some problems with usual activities, pain, anxiety and depression.
- **Profound disability (0.92):** Some problems walking about, severe problems with self care, usual activities, pain, anxiety and depression.

Proportions of people with each disability (Table 4.5) reported by Mathers et al (1999) were used to estimate an overall disability weight for stroke events.

**Table 4.5: Disability weights and severity of stroke events by age and gender**

	No Disability	Mild	Moderate/ Severe	Profound	YLD weight
YLD	0.00	0.36	0.63	0.92	-
<b>Males</b>					
0-4	0.0%	84.6%	0.0%	15.4%	<b>0.45</b>
5-14	38.6%	51.9%	0.0%	9.5%	<b>0.27</b>
15-24	63.2%	31.1%	0.0%	5.7%	<b>0.16</b>
25-34	81.6%	15.6%	0.0%	2.8%	<b>0.08</b>
35-44	90.3%	8.2%	0.0%	1.5%	<b>0.04</b>
45-54	96.2%	3.2%	0.0%	0.6%	<b>0.02</b>
55-64	75.9%	1.7%	13.2%	9.2%	<b>0.17</b>
65-74	67.9%	11.5%	13.8%	6.8%	<b>0.19</b>
75+	58.0%	7.1%	6.7%	28.2%	<b>0.33</b>
<b>Females</b>					
0-4	0.0%	63.9%	29.4%	6.8%	<b>0.48</b>
5-14	0.0%	63.9%	29.4%	6.8%	<b>0.48</b>
15-24	17.1%	52.9%	24.4%	5.6%	<b>0.40</b>
25-34	68.9%	19.9%	9.1%	2.1%	<b>0.15</b>
35-44	86.2%	8.8%	4.1%	0.9%	<b>0.07</b>
45-54	93.3%	4.3%	2.0%	0.5%	<b>0.03</b>
55-64	87.3%	0.0%	0.0%	12.7%	<b>0.12</b>
65-74	48.3%	12.3%	8.8%	30.6%	<b>0.38</b>
75+	50.3%	2.7%	7.7%	39.3%	<b>0.42</b>

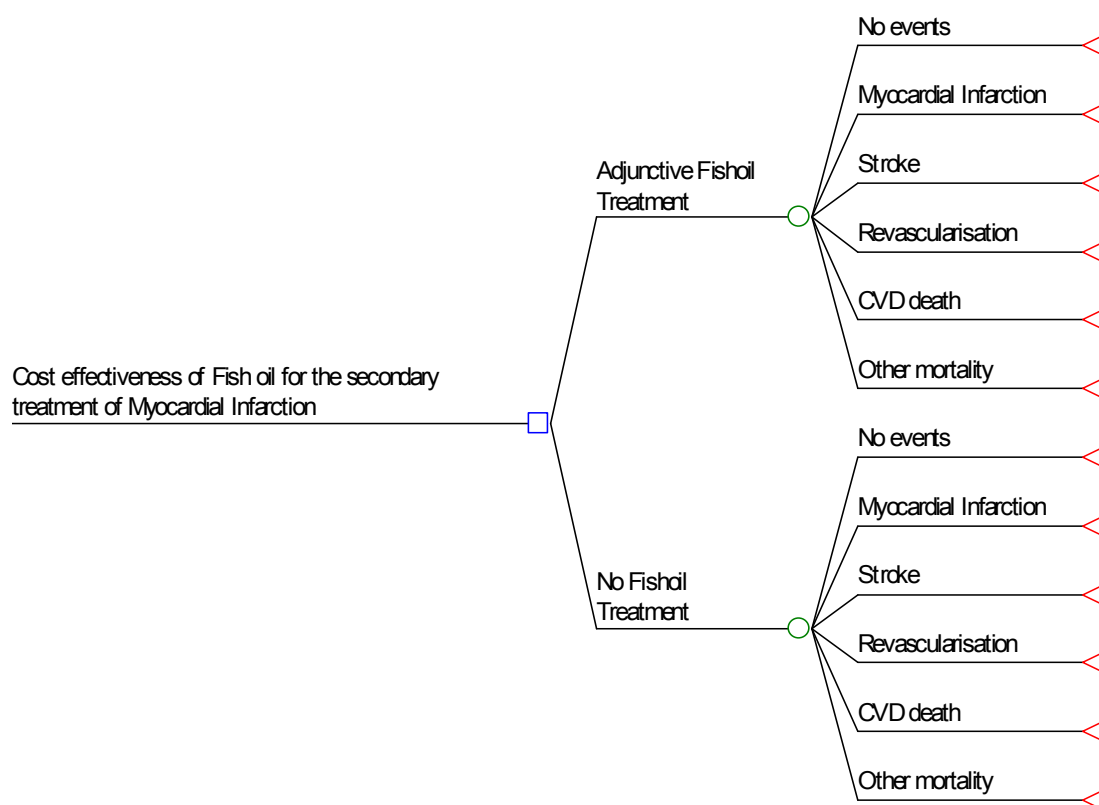
Source: Mathers et al (1999)

Disability weights for an acute MI were taken from Mathers et al (1999) at 0.395, while it was assumed that the disability weight for a revascularisation would be zero (with no associated long term disabilities).

## 4.8 Model

To estimate the cost effectiveness of fish oils in the treatment protocol for secondary prevention of MI, a two-arm decision model was constructed in TreeAge with a modelled time period of one year (Figure 4.1). Six health outcomes were modelled based on the evidence from clinical trials as well as the Australian age and gender specific incidence rate.

**Figure 4.1: Model structure – fish oil for secondary prevention of MI**



## 4.9 Costs

### 4.9.1 Health system costs

Health system costs for the five health states were included in the model. Costs associated with disease states were based on AIHW health expenditure by disease and injury estimates which were inflated to 2009 prices (Table 4.6). Cost estimates were converted into a cost per case using Australia incidence rate data.

**Table 4.6: Cost in Australia per case of MI and stroke, 2009 (\$)**

Age group	MI		Stroke	
	Male	Female	Male	Female
0-4	83.3	27.3	0.0	891.6
5-14	32.0	0.7	0.0	448.4
15-24	132.2	115.1	0.0	1,111.1

25-34	1,647.8	523.5	3,587.8	1,513.0
35-44	3,054.5	3,515.1	2,271.5	1,146.4
45-54	4,487.8	2,652.1	2,088.4	3,459.0
55-64	3,704.3	2,442.5	2,236.8	3,225.3
65-74	3,179.4	2,915.8	5,264.7	4,246.2
75-84	3,993.9	2,912.4	7,940.0	6,875.2
85+	4,037.5	3,818.8	12,688.8	15,699.6

Source: AIHW (special data request), Access Economics.

Costs of revascularisation procedures and CVD death were estimated from published hospitalisation data. Private inpatient cost data for 2006-07 were obtained from the Department of Health and Ageing National Hospital Cost Data Collection and projected to 2009 values using an average health care cost inflation rate of 3.1% (AIHW, 2008).

However, as the National Hospital Cost Data Collection does not record expenditure on specialist fees within private hospitals, cost data was supplemented by schedule fee data derived from the Medicare Benefits Schedule (MBS). Adjustments to the schedule fees were made for additional out-of-pocket expenses.

In summary, cost components included in the model relate to:

- salaries, including ward medical, ward nursing, and non clinical;
- pathology and diagnostic imaging;
- allied health;
- in-hospital pharmacy;
- critical care;
- operating rooms;
- emergency department;
- supplies;
- special procedural suites;
- stents;
- specialist fees;
- on-costs;
- hospital bed (hotel); and
- depreciation.

These data showed that on average the cost of a revascularisation procedure was approximately \$16,570, while the hospitalisation cost associated with a CVD related death was approximately \$4,367.

### 4.9.2 Cost of fish oil supplements

Fish oil supplements are an over-the-counter medication with cost variations between brands.<sup>48</sup> Retail prices of fish oil supplements were sourced from Pharmacy Online. Supplements that included additional products such as Gingko were excluded. Supplements that had a EPA:DHA ratio of approximately 1.5:1 were included (in line with dosages used in the clinical trials). Table 4.7 shows the brands, volumes and retail prices sourced.

**Table 4.7: Fish oil treatment costs**

Brand	Capsules per bottle	mg per capsule	mg (EPA) per capsule	mg (DHA) per capsule	Retail Price (\$)	Cost per capsule (\$)	Cost per diem (\$)	Cost per annum (\$)
Blackmores	200	1,000	180	120	19.95	0.0998	0.2993	109.23
Blackmores	400	1,000	180	120	37.50	0.0938	0.2813	102.66
Bio-Organics	220	1,000	180	120	29.95	0.1361	0.4084	149.07
Bioglan	200	1,000	180	120	19.95	0.0998	0.2993	109.23
Bioglan	400	1,000	180	120	33.75	0.0844	0.2531	92.39
clear Fish Oil	400	1,000	180	120	18.95	0.0474	0.1421	51.88
Natures Own	100	1,000	180	120	12.45	0.1245	0.3735	136.33
Natures Own	200	1,000	180	120	18.95	0.0948	0.2843	103.75
Natures Own	400	1,000	180	120	35.95	0.0899	0.2696	98.41
Natures Own - MaxEPA	100	1,000	171	114	18.95	0.1895	0.5685	207.50
Natures Way	100	1,000	180	120	9.96	0.0996	0.2988	109.06
Natures Way	200	1,000	180	120	17.95	0.0898	0.2693	98.28
Natures Way	400	1,000	180	120	32.95	0.0824	0.2471	90.20

Source: Pharmacy online, accessed on 10<sup>th</sup> September 2009

Note: Cost per diem is estimated on three capsules per day (as per the average trial dosages). Cost per annum uses 365 days per year.

A mean annual price of fish oil treatment (\$112.15) was used in the cost effectiveness analysis.

### 4.9.3 Parameter summary

A summary of the parameters used in the analysis is in Table 4.8.

**Table 4.8: Summary of model parameters**

Parameter	Source and Methods	Estimate	Sensitivity
Efficacy of fish oil treatment	Cooper et al (2007)	Table 4.4	Upper and lower bound for the meta-analysis 95% confidence interval.  Mean results for GISSI and DART1.

<sup>48</sup> For example, many patients use super strength or liquid formulations for convenience, e.g. Blackmore’s Omega, Bioglan superstrength etc.

Incidence, mortality and procedure rates	Begg et al (2007) as well as AIHW hospital morbidity dataset	Table 4.1	N/A
Quality of life	Mathers et al (1999)	Disability weights for an MI event were taken as 0.395, while revascularisation rates were assumed to have a disability weight of 0. Disability weights associated with stroke used an age gender weighted average based on data describing post disability severities Table 4.5.	N/A
Costs – Fish oil	Pharmacy Online	\$112.15	N/A
Costs – Revascularisation	National Hospital Cost Data Collection	\$16,570	N/A
Costs – MI and Stroke	AIHW (special data request)	Table 4.6	N/A
Costs – CVD mortality	Department of Health and Ageing National Hospital Cost Data Collection	Approximately \$4,367	N/A

## 4.10 Results

A second order Monte Carlo simulation was undertaken (with 1 million trials) on the decision model shown in Figure 4.1. Age and gender distributions were sampled in the model so that the overall results represented the same profile as those reported to have had a MI from Begg et al (2007).

Incremental effects are greater under the DALY approach compared to the QALY approach. The difference results from the inclusion of years of life lost due to premature mortality (YLLs) which is not included in the QALY approach. Meta-analysis of trial data in Table 4.4 shows that the main significant effect of fish oil treatment is the reduction of mortality from CVD or other causes. The DALY approach thus generates a lower ICER (\$2,041 per DALY averted) compared to the QALY approach (\$15,980 per QALY gained), as detailed in Table 4.9. Both the DALY and QALY approaches show that **fish oils are cost effective in the secondary prevention of CHD relative to all benchmarks in Section 1.4.**

The incremental cost per person is \$128 per annum and the incremental effectiveness 0.06 DALYs. Incremental costs per person include the additional costs of fish oil supplementation as well as the expected costs per person of the health outcomes (myocardial infarction, stroke, revascularisation and CVD death).

**Table 4.9: Cost effectiveness of fish oils for the secondary prevention of CHD (\$ per annum)**

Strategy	Cost	Incremental cost	Effectiveness	Incremental effectiveness	C/E	ICER
<b>DALY approach</b>						
No fish oil	450		0.33		1,360	
Adjunctive fish oil	579	128	0.27	0.06	2,159	2,041
<b>QALY (1-YLD) approach</b>						
No fish oil	450		0.95		475	
Adjunctive fish oil	580	130	0.96	0.008	607	15,980

Note: Incremental effectiveness refers to the average number of DALYs avoided or the average number of QALYs gained. C/E – cost effectiveness ratio. ICER – incremental cost effectiveness ratio. Cost difference is not exactly 128 due to rounding.

The ICER results in Table 4.9 are similar to those from previous cost effectiveness studies, reported in Section 4.6.1. A large difference in the ICER values can be observed between the QALY and DALY approaches, since the DALY approach places greater weight on mortality.

Sensitivity analysis was undertaken to determine the influence of the trial results used in the modelling on the cost-effectiveness result. The treatment effect variables presented in Table 4.4. Results were most greatly affected by the upper bound of the ‘other mortality’ and ‘myocardial infarction’ variables (Table 4.10). Both the GISSI-P and DART1 variables increase the cost per DALY avoided and cost per QALY gained estimates.

**Table 4.10: One way sensitivity analysis, fish oils for CHD**

Results	\$ per DALYs avoided	\$ per QALYs gained
Results	<b>2,041</b>	<b>15,980</b>
Meta-analysis, upper bound		
MI	2,446	25,382
Stroke	2,390	20,211
Revascularisation	2,422	18,904
CVD mortality	2,811	21,888
Other mortality	4,782	35,528
Meta-analysis, lower bound		
MI	1,789	12,183
Stroke	1,782	13,762
Revascularisation	1,656	12,994
CVD mortality	1,606	11,700
Other mortality	1,435	10,165
GISSI-P	2,620	18,319
DART1	2,163	20,557

The results presented in Table 4.9 and Table 4.10 lie below all the cost effectiveness thresholds in Section 1.4. Fish oils for the secondary prevention of CHD are thus considered cost effective under all of the scenario analyses.

Applying the unit cost difference (using the DALY approach) of \$128/person/annum to overall CHD prevalence – estimated as 309,726 people (Begg et al, 2007:282) - provides an overall higher cost of the fish oil intervention of \$39.6 million per year. Naturally there is unlikely to be 100% treatment so this represents an upper cost bound. Given the ICER of \$2,041/DALY, the estimated maximum wellbeing gain is thus 19,424 DALYs averted per annum.

**Table 4.11: Population wide applications**

1. Prevalence of CHD (Begg et al, 2007)	309,726
2. Unit cost difference (from model)	\$128 pa
3. Total cost (\$m) (1.*2.)	\$39.6m pa
4. ICER (\$/DALY) (from model)	\$2,041/DALY
5. DALYs averted (3./4.*1,000,000)	19,424

## 4.11 Conclusions

Dietary interventions are commonly suggested by GPs following a MI. Evidence of the effectiveness of these interventions has been developed from the first epidemiological studies on different populations and their dietary intakes.

Where dietary changes cannot be made (or sustained) there is a clear role for the use of dietary supplements to provide the necessary dietary intake of EPA and DHA. Evidence for the benefit of these interventions is broadly based on two large clinical trials (GISSI-P and DART1). Both of these studies showed that the primary benefit of fish oils is in the reduction of CVD death as well as the overall mortality within the populations.

Cooper et al (2007) conducted a cost effectiveness analysis based on a meta-analysis of these two clinical trials. Our study has used the same treatment effects to model the cost effectiveness of fish oil intervention within the Australian setting. Results from our analysis are comparable to previous cost effectiveness studies and are within the bounds of broadly accepted cost effectiveness thresholds.

The use of fish oil supplements is a cost effective intervention to prevent future cardiovascular mortality and morbidity in Australia.

Despite evidence of effectiveness and cost-effectiveness of fish oils, these supplements are not currently subsidised under the PBS, and indeed, are currently subject to the GST levy. As the evidence of improved health outcomes and cost effectiveness of complementary medicine interventions build it would be strategic for governments to review these arrangements.

## 4.12 References

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### 4.13 Appendix: Detailed summary of literature studies relating to fish oils and CHD

The findings of the literature review are summarised in Table 4.12.

**Table 4.12: Literature on effectiveness of fish oils for CHD**

Source	Aim of study	Method	Comparator	Outcome measure	Findings
<b>REVIEWS</b>					
Colquhoun et al (2008)	Determine whether a daily intake of low amounts of a number of nutrients would exert beneficial effects on risk factors and clinical variables in patients that suffered from MI and were following a cardiac rehabilitation program	RCT with 40 male MI patients. Supervised exercise training, lifestyle and dietary recommendation and instructed to consume products in addition to their regular diet. Blood extractions and clinical examinations were performed after 0, 3, 6, 9 and 12 months.	<u>Active group</u> 500 mL/day of a fortified dairy product containing EPA, DHA, oleic acid, folic acid and vitamins A, B-6, D and E. <u>Control group</u> 500 mL/day of semi-skimmed milk with added vitamins A and D.	Clinical outcome measures – through blood extractions and clinical examinations	Increased plasma concentrations of EPA, DHA oleic acid, folic acid, vitamin B-6 and vitamin E after supplementation (P < 0.05). Total plasma and LDL-cholesterol, apolipoprotein B and high-sensitivity C-reactive protein concentrations decrease in the supplemented group (P < 0.05). No changes in heart rate, blood pressure, or cardiac electrocardiographic parameters in either group.