

The Cost-Effectiveness of Omega-3 Supplements For Prevention of Secondary Coronary Events

Dietary supplementation with omega-3 fatty acids in U.S. males is associated with fewer cardiovascular fatalities and lower costs

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ABSTRACT

Purpose: To project the clinical and economic benefits of omega-3 supplements for prevention of secondary (repeat) cardiovascular events in U.S. males.

Design: Decision-analytic model.

Methodology: Model clinical probabilities (rates of fatal myocardial infarction [MI] and cardiovascular death) were based on published trials. Costs were derived from standard U.S. sources. Outcomes include deaths delayed, cost per death delayed, fatal MIs avoided, and cost per fatal MI avoided. Costs, outcomes, and cost-effectiveness were determined for the initial year and over a 42-month model period. Sensitivity analyses were conducted to evaluate the robustness of key model assumptions.

Principal findings: According to the model, the use of omega-3 supplements results in fewer fatal MIs and fewer cardiovascular deaths in the short-term (1 year) and long-term (42-month) analyses. When including only direct medical treatment costs for fatal MIs, omega-3 supplementation is cost-effective compared to no supplementation. In terms of total costs (medical costs and decreased productivity), supplementation is cost-saving, providing better outcomes and lower/fewer costs. Supplementation remained cost-effective in all sensitivity analyses.

Conclusion: Under a variety of scenarios, omega-3 supplements are likely to improve health and lower total costs. Despite model limitations, omega-3 supplementation should be considered an important and cost-effective option for prevention of secondary cardiovascular events.

least one nonvitamin, nonmineral supplement, with echinacea and ginkgo biloba being the most common (Schaffer 2003). Supplement use was greatest in women, whites, and college graduates. Supplement-usage rates were even greater in women ages 65 and over (Gordon 2005).

Use of supplements also is common among patients with cardiovascular disease (CVD) (Satia-Abouta 2003). More than 20 percent of adults in the United States have CVD, which is responsible for an estimated 931,100 deaths annually (AHA 2004). The direct and indirect costs of CVD and stroke in the United States in 2004 are estimated at \$368.4 billion (AHA 2005). CVD also is common among managed care members, with the 2001 prevalence of coronary artery disease in this population reported as 59.9 per 1000 people (Zaher 2004). The prevalence of elevated cholesterol among managed care patients is even greater — 35.6 percent (Selby 2004).

Among dietary supplements, long chain polyunsaturated fatty acids (PUFAs), specifically omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are widely accepted as being effective in prevention and decreased progression of CVD (Din 2004). The American Heart Association (AHA) recommends the consumption of at least two servings of fish per week for all adults (Kris-Etherton 2003, Kraus 2000). Although there is not an ab-

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INTRODUCTION

Use of dietary supplements is common in the United States. In the 1999–2000 National Health and Nutrition Examination Survey, 52 percent of respondents indicated using a dietary supplement within the past month; most supplements were taken daily and for at least 2 years (Radimer 2004).

Supplement use is also common among managed care populations. A recent survey of HMO patients in northern California indicated that 32.7 percent of plan members used at

solute intake recommendation specific to EPA and DHA for patients with CVD, an amount between 0.5 to 1.8 grams/day is suggested, through dietary consumption or supplementation (Kris-Etherton 2003). The anti-inflammatory effects of EPA and DHA are believed to be capable of leading to a reduction in CVD and its clinical manifestations (Mori 2004).

There have not yet been any published analyses of the effect of increased omega-3 intake on U.S. costs associated with CVD. The objective of this study is to estimate the clinical and economic benefits of increased omega-3 intake as a preventive intervention among males in the United States who already have experienced a heart attack.

METHODS

We used standard cost-effectiveness modeling approaches to compare the costs and outcomes of omega-3 supplementation versus no supplementation for males with a history of heart attacks. Cost-effectiveness (C/E) is determined as the ratio of the difference in cost per difference in outcomes for patients with versus those without omega-3 supplementation. A C/E ratio that is below \$50,000 generally is considered

to be a positive result, but there are no absolute thresholds (Eichler 2004).

Model structure

Using data from published clinical trials, the model compares two identical cohorts, one receiving omega-3 supplements and the other not receiving supplements. During each year for which data were available (up to 42 months/3.5 years), members of the cohorts may die due to non-cardiovascular (CV) causes. Those who do not die from non-CV causes may experience adverse CV events, including repeat myocardial infarctions (MI), and may die as a result of CV causes. Cohort members with fatal CV events will experience increased utilization of medical care resources and associated additional costs. In addition to these mortality and medical care costs, the model incorporates costs for lost productivity due to morbidity and mortality from coronary heart disease (CHD). These lost productivity estimates are based on recently published data from the AHA (2005).

Model clinical event probabilities

We conducted a literature search to identify double-blind, random-

ized controlled trials evaluating the effect of omega-3 supplements on CV outcomes. This literature search was updated through March 2005. We limited our review to studies that specified intervention with dietary supplements to avoid the problems associated with self-reporting and lack of standardized doses in dietary intervention studies (e.g., studies of different amounts of fish consumption). Table 1 lists these studies and the population and outcomes presented in each. All identified published trials with omega-3 supplement use and relevant outcomes measures were used to determine model parameters. As a majority of the subjects in all identified studies were male, the model results presented here are assumed to apply only to males.

Clinical events assessed from the identified studies are rates of fatal MI and CV death (of which fatal MI is a subset). The rates used in this model are aggregated across the included studies. Studies did not present data from the same time periods; curve fitting was used to interpolate outcome rates over time. Clinical parameters used in the model are included in Table 2. Based on these studies, at 12 months after omega-3

TABLE 1 Studies reviewed

Citation	Population	Interventions
Marchioli 2002	Italian patients (N=11,323) with recent (<3 months) MI, mean age 59, 85% male	1 g PUFA (n=2,836) Vitamin E (n=2,830) Both (n=2,830) Neither (n=2,828)
Nilsen 2001	Norwegian patients (N=300) with acute MI, mean age 64, 83% male	4 g PUFA (n=150), 4 g corn oil (n=150)
Singh 1997	Indian patients (N=360) with suspected MI, mean age 58-59, 94% male	1.08 g/d fish oil (n=122) Mustard oil (n=120) Placebo (n=118)
von Schacky 1999	German patients (N=223) with CAD, mean age 58-59, 80% male	Fish oil (6 g/d for 3 mos, 3 g/d for 21 mos, n=112) Placebo (n=111)

CAD=coronary artery disease, MI=myocardial infarction, PUFA=polyunsaturated fatty acids.

supplementation begins, there is expected to be a 20 percent reduction in the rate of CV deaths and a 24 percent reduction in fatal MI.

Model costs

The only medical care costs included in the model are for CV hospitalization; the model conservatively assumes that CV death will result in only a single additional hospitalization. These hospital costs were identified using CV diagnosis-related groups (DRGs) and were derived from Medicare Provider Analysis and Review (MEDPAR) data. The values used here are the most recent data available (from 2002) and have been inflated to 2004 values. Costs for omega-3 supplements are based on a review of “fish-oil pills” conducted by *Consumer Reports* in July 2003; the cost also is inflated to 2004. The median cost is used for the base case model, with the minimum and maximum costs included in sensitivity

TABLE 2 Clinical parameters

Parameter	Without supplements	With supplements
Cardiovascular death		
12 months	0.0332	0.0264
24 months	0.0470	0.0383
36 months	0.0599	0.0497
42 months	0.0653	0.0547
Myocardial infarction, fatal		
12 months	0.0239	0.0182
24 months	0.0363	0.0271
36 months	0.0501	0.0395
42 months	0.0501	0.0397

analyses. Table 3 presents the costs used in the model and their sources.

Model outcomes

Outcomes include incremental difference in number of deaths (i.e., deaths delayed), cost per death delayed, incremental difference in number of fatal MIs, and cost per fatal MI avoided. Costs, outcomes, and cost-

effectiveness are determined for the initial year and for the 42-month model period. Costs unrelated to CVD are not included in the model. Future costs and outcomes are discounted at 3 percent, per recommendations by the U.S. Public Health Service Panel on Cost-effectiveness in Health and Medicine (Gold 1996), reflecting a preference for health and

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TABLE 3 Cost parameters and sources

Resource	DRG	Cost at baseline	Source
Myocardial infarction, fatal	123	\$9,134	MEDPAR 2002
Omega-3 supplements	N/A	\$132	<i>Consumer Reports</i> 2003
Lost earnings	N/A	\$105,951	AHA 2005

DRGs=diagnosis-related groups.

money in the present rather than the future. As a secondary analysis, we included cost of lost productivity associated with CVD mortality (AHA 2005).

Analysis

The model determines the costs, outcomes, and cost-effectiveness of omega-3 supplements for U.S. males following MI. The primary analysis evaluated subsequent fatal MIs and their costs, along with supplement costs; secondary analyses included all fatal CV events and lost productivity costs. Sensitivity analyses assessed the effect of changing key model inputs and assumptions, including outcome probabilities and costs, on projected outcomes. Sensitivity analyses were conducted for cost of supplementation, cost of medical care, effectiveness of omega-3 supplements, and the discount rate.

RESULTS

Base case

Results of the base case analysis are presented in Table 4. Both in the short-term (1 year) and long-term

(3.5 years) analyses, the use of omega-3 supplements results in fewer fatal MIs (52 fewer per 100,000 individuals at 1 year; 248 fewer per 100,000 at 42 months) and fewer CV deaths. Evaluating the change in direct medical costs per change in rate of fatal MI, omega-3 supplementation is cost-effective. Evaluating changes in total (medical plus productivity) costs per change in rate of CV deaths, supplementation is dominant, producing both better outcomes and lower/fewer costs. The cost-savings in this analysis reflects slightly higher direct medical costs but lower costs from lost productivity attributed to CVD mortality.

Sensitivity analyses

Sensitivity analyses were conducted around several key model input parameters for the long-term base case model (i.e., 3.5 years). Results for each analysis are presented in Table 5.

Supplement cost. The cost of the omega-3 supplements was varied to reflect the highest and lowest annual

costs from the *Consumer Reports* cost summary (\$240.23 and \$24.13, respectively). This does not change the rates of clinical events, only costs. When the cost of the supplement was lowered to \$24.13, the supplementation strategy also dominated over provision of no supplementation (provided better outcomes at lower costs) when considering direct medical costs only. When the cost of the supplement was increased to \$240.23, the medical care costs per fatal MI avoided increased to \$23,926, still within the limits of cost-effectiveness. For total costs per CV death avoided, the supplementation strategy dominates over provision of no supplementation even at the highest supplement cost.

Costs of medical care. The costs of medical care for fatal MI and CV death respectively were decreased and increased by 50 percent. Again, only the costs are changed; clinical events remain the same. When medical care costs are increased by 50 percent, the strategy of supplementation results in costs per event avoided of less than

TABLE 4 Results — base case, omega-3 supplement group vs. no-supplement group

Outcome measure and included costs	Year 1	Through year 3.5 (42 months)
Fatal MIs and related medical costs only		
Number avoided	-0.0052	-0.0248
Direct medical costs (MI, supplement)	\$85	\$ 229
Cost per MI avoided	\$16,340	\$9221
All cardiovascular deaths and total costs		
Number avoided	0.0067	0.0297
Total costs*	-\$630	-\$ 2548
Cost per death avoided	dominates	dominates

MI=myocardial infarction.
* Total costs=future earnings, MI costs, supplement cost.

TABLE 5 Results — sensitivity analyses (through year 3.5)

Sensitivity analysis	Medical cost per MI avoided	Total costs per CV death avoided
Base case	\$9221	dominates
Highest cost of supplement (\$240.23)	\$23,926	dominates
Lowest cost of supplement (\$24.13)	dominates	dominates
Cost of medical resources decreased by 50%	\$13,605	dominates
Cost of medical resources increased by 50%	\$4,836	dominates
Discount rate=0%	\$8,886	dominates
Discount rate=5%	\$9,439	dominates
Effect of supplements on MI rate is twice as large	\$44	dominates
Effect of supplements on MI rate is half as large	\$28,760	dominates
Effect of supplements on CV death rate is twice as large	\$9,813	dominates
Effect of supplements on CV death rate is half as large	\$8,939	dominates

CV=cardiovascular, MI=myocardial infarction.

\$20,000, remaining within the range of cost-effectiveness.

Rate of clinical events. The difference in rates of fatal MI between omega-3 and control groups was doubled and halved. For these analyses, the rate for the control group was left constant while the rate for the omega-3 group was modified to reflect doubling or halving of the effect of omega-3 supplementation. When the effect of supplements on MI rate is increased, there is a smaller medical care cost per MI avoided (\$44); when the effect is decreased, the medical care cost per MI avoided increases but remains under \$30,000. When the effect of supplements on the CV death rate is increased or decreased, omega-3 supplementation continues to dominate over provision of no supplementation (i.e., produce better outcomes at lower total costs).

Discount rate. Discount rates of 5 percent and 0 percent (no discounting) were used as alternatives to the base case 3 percent rate. Incremental medical costs per MI or total costs per death avoided were similar to

those in the base case.

The sensitivity analyses show that omega-3 supplementation remains generally cost-effective even when key model parameters are modified. Cost-effectiveness exceeds \$20,000 in a few cases but still remains acceptable (Eichler 2004).

DISCUSSION

This model provides projections of the effect of omega-3 supplementation on CV outcomes and net costs. Model results indicate that use of omega-3 supplements results in decreased rates of fatal MIs and is cost-effective when considering medical care costs only. In addition, omega-3 supplementation results in fewer overall CV deaths and decreased total net costs. The sensitivity analysis showed that varying key model assumptions, including the price of omega-3 supplements and the effect of supplements on MI rates, did not result in substantially different conclusions. Thus, under a variety of scenarios, omega-3 supplements may improve health and lower total costs.

These results have important im-

plications for managed care organizations. As recently discussed by Baker (2005), MCOs increasingly are considering covering or providing discounts for supplement use by their members. Further, federal pending legislation would allow expenses for dietary supplements to be treated as medical expenses (H.R. 1545, H.R. 2486). The results presented in this model suggest that covering omega-3 supplements would lead to better health outcomes and would either be cost-saving or cost-effective using standard economic thresholds.

These results also should be viewed in comparison to other nutritional intervention studies. For example, linking the intermediate outcomes of decreased homocysteine levels to projected reductions in CHD, one study found that grain fortification with folic acid and folic acid supplementation would lead to both lower costs and improved CHD outcomes (Tice 2001). This model included all medical costs associated with CHD, while the present omega-3 study was limited by available data to events and costs associated with hospital admis-

sion for fatal MI and related lost productivity costs; thus, the studies are not directly comparable. Nonetheless, it is likely that both grain fortification and omega-3 supplementation could have important roles in reducing costs associated with CVD. In a different clinical area, daily calcium supplementation for hip-fracture prevention was found to result in both better outcomes (fewer hip fractures) and lower cost than did additional calcium intake (Bendich 1999).

There are a number of limitations to this model. First, there are few randomized, controlled intervention trials that have examined the long-term outcomes of increased omega-3 intake in a manner useful for C/E modeling. Existing publications differ as to the administration and/or formulations of omega-3 assessments — e.g., supplement use versus food-frequency diaries versus blood-concentration measurements. Even the supplement studies include a variety of dosages and ingredients. Although at least one meta-analysis assessed the effect of omega-3 intake on CV outcomes, the criteria for study selection were not consistent with our methodology, i.e., only dietary intervention studies were included (Bucher 2002).

Given concerns regarding the quality of dietary self-reporting and the lack of dosage standardization, we limited our review to studies with specified dietary supplement interventions. Meta-analyses exploring outcomes with fish oils also have found important differences in study design, reporting, and general study quality (Gapinski 1993, Morris 1993).

Although there is general consensus that omega-3 contributes to improved CV health (AHA 2005), there is as yet no agreement on the recommended dosage. In assigning a cost for omega-3 supplementation, this analysis used the dosage that appears most frequently in the literature and that which the AHA recommends for adults with CVD, 1 g/day. This dosage

recommendation may change over time, however.

We identified one published study that reported on the cost-effectiveness of PUFAs for prevention of secondary CV events after an MI (Franzosi 2001). This study was limited to the data from the GISSI study in Italy. Although we also included data from this study in our analysis (Marchioli 2002), we used clinical outcomes from a range of studies, included U.S. costs, and applied a discount rate that is more widely accepted in the health economic literature in our base case (Gold 1996). In addition, we included lost earnings for a broader evaluation of the costs and cost-effectiveness of omega-3 supplementation.

This model only includes limited CV benefits of omega-3, particularly rates of fatal MI and overall CV death. Omega-3 intake may have beneficial effects on other cardiovascular conditions, such as nonfatal MI and stroke, but the lack of sufficient data on the rates of these other relevant clinical events in a usable form precluded their inclusion in this model. Further, reductions in CV death rates may allow patients to live longer and thereby to potentially experience additional medical conditions (and costs) they would have averted with an earlier death. Nevertheless, economic analyses generally do not include these potential additional costs, which would penalize the value of life-saving interventions.

Numerous recent studies suggest that increased omega-3 intake also may have a positive effect on other conditions, including asthma; bipolar disorder, cognitive function, and the development of Alzheimer's disease, depression, and other mental health conditions; rheumatoid arthritis; schizophrenia; and neonatal development. * Although more research is necessary, omega-3 supplementation

* Cleland 2003, Cooper 2003, Cunnane 2004, Endevelt 2004, MacLean 2005, Noaghui 2003, Oh 2005, Post 2003, Schachter 2004.

may show greater cost-savings or cost-effectiveness than reported here by simultaneously improving outcomes in multiple clinical areas.

Assessing the effects of omega-3 fatty acids in these other areas is beyond the scope of the present model, but it will be important to evaluate the additional benefits, in terms of health and costs, as new data become available. This, in turn, will allow MCOs to quantify the cost of providing or subsidizing supplement use relative to the saving and improved health outcomes that potentially result from supplementation.

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