The cost-effectiveness of omega-3 supplements for prevention of secondary coronary events

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Dietary supplementation with long chain polyunsaturated fatty acids (PUFAs), specifically the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid, was compared with no such supplementation. Pooled interventions included 1 g PUFAs, 4 g/day PUFAs, 1.08 g/day fish oil, or 3 to 6 g/day fish oil. The dose modelled for the cost of omega-3 supplementation in this study was that recommended by the American Heart Association, that is 1 g/day.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The target population comprised US males who had already experienced a previous heart attack, who were followed for 3.5 years.

Setting
The setting was primary and secondary care. The economic study was performed in the USA.

Dates to which data relate
The effectiveness evidence dated from 1997 to 2002. Resource use and cost data were from 2002 to 2005. The price year was 2004.

Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Modelling
A simple decision analytic model that compared two identical cohorts, one receiving omega-3 supplements and the other not receiving supplements, was constructed. During each year of follow-up (up to 3.5 years), patients could die due to non CV causes. If they survived these, they could experience adverse CV events such as repeat myocardial infarctions (MIs), and could die as a result of CV causes.

Outcomes assessed in the review
The parameters used in the model included probabilities of CV death and fatal MI in each follow-up period. Reductions in the rate of CV deaths and fatal MI were also included.
Study designs and other criteria for inclusion in the review
Double-blind, randomised controlled trials that evaluated the effects of omega-3 supplements on CV outcomes were included.

Sources searched to identify primary studies
Although the authors stated that they performed a literature search, updated through March 2005, the sources searched were not described.

Criteria used to ensure the validity of primary studies
To avoid the problems associated with self-reporting and lack of standardised doses in dietary intervention studies, the authors limited the review to studies that specified intervention with dietary supplements. No other criteria were reported.

Methods used to judge relevance and validity, and for extracting data
The validity of the primary studies does not appear to have been assessed.

Number of primary studies included
Four primary studies were included in the review.

Methods of combining primary studies
The method used to combine the primary studies was not explicitly reported. A narrative approach appears to have been used.

Investigation of differences between primary studies
The authors did not discuss differences between the studies. They did, however, report in detail the populations and the interventions evaluated in each study.

Results of the review
CV deaths without supplements were 0.0332 at 12 months, 0.0470 at 24 months, 0.0599, at 36 months and 0.0653 at 42 months.

CV deaths with supplements were 0.0264 at 12 months, 0.0383 at 24 months, 0.0497 at 36 months and 0.0547 at 42 months.

Fatal MI rates without supplements were 0.0239 at 12 months, 0.0363 at 24 months, and 0.0501 at 36 months and at 42 months.

Fatal MI rates with supplements were 0.0182 at 12 months, 0.0271 at 24 months, 0.0395 at 36 months and 0.0397 at 42 months.

A 20% reduction in the rate of CV deaths and a 24% reduction in fatal MI were used in the base-case scenario.

Measure of benefits used in the economic analysis
The measures of benefits used were fatal MIs and deaths avoided. The health benefits were discounted at an annual rate of 3%.
**Direct costs**
The only costs included in the primary analyses were those for CV hospitalisations and use of supplements. Hospital costs were identified using CV diagnosis-related groups and were derived from Medicare Provider Analysis and Review 2002 data. The model assumed that CV death would result in only a single additional hospitalisation. Median costs for omega-3 supplements were derived from a local 2003 review. The median cost used for the base-case estimation of quantities and costs was derived through modelling. Discounting was appropriately applied for future costs, at a rate of 3%. All costs were reflated to the year 2004, which was the price year for the study.

**Statistical analysis of costs**
The costs were treated deterministically and no statistical analysis was performed.

**Indirect Costs**
As a secondary analysis, the authors included the cost of lost productivity associated with CV disease mortality, using data from the American Heart Association 2005 as a source. Discounting was appropriately applied for future costs, at a rate of 3%. No deflation for these costs was reported, as the study price year was 2004.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were conducted around a number of parameters. Specifically, supplement cost, medical resources cost, discount ranges, and the effects of supplements on the MI and CV death rates. The authors did not justify the ranges they selected.

**Estimated benefits used in the economic analysis**
There were fewer fatal MIs or CV deaths in the supplement group, both in the short-term and long-term analyses. There were 52 fewer MIs per 100,000 individuals at 1 year, and 248 fewer MIs per 100,000 individuals at 42 months. There were 67 fewer CV deaths per 100,000 individuals at 1 year and 297 fewer CV deaths per 100,000 individuals at 42 months.

**Cost results**
The total intervention costs were not reported.

The incremental (direct) costs of supplementation were $85 at 1 year and $229 at 42 months.

The discount rate was 3%. Undiscounted results were not reported.

When including productivity costs of CV deaths, supplementation was cost-saving ($630 at 1 year and $2,548 at 42 months).

**Synthesis of costs and benefits**
The cost per fatal MI avoided by supplementation was $16,340 for the first year and $9,221 at 42 months. When estimating the cost per CV death avoided and including productivity costs, the supplementation group dominated the no supplementation group (i.e. more effective and less costly).

The most sensitive parameters for the cost per fatal MI avoided were supplementation costs (from being dominant at lower costs to costing $23,926 at 42 months at higher supplementation costs) and the effects of supplements on MI rates. For the total cost per CV death avoided, the sensitivity analyses were robust and supplementation was always
Authors' conclusions

The use of omega-3 supplements resulted in fewer fatal myocardial infarctions (MIs) and cardiovascular (CV) deaths, both in the short term and long term. When including only direct medical treatment costs for fatal MIs, omega-3 supplementation was cost-effective in comparison with no supplementation. When including decreased productivity, supplementation was cost-saving. The analysis was robust to the sensitivity analyses performed.

CRD COMMENTARY - Selection of comparators

The authors justified the choice of the comparators, both in terms of the evidence that PUFAs could be beneficial for secondary CV prevention and the frequent habit of the US population of taking dietary supplements. You should judge if the comparators are relevant in your own setting or whether other technologies could have been included.

Validity of estimate of measure of effectiveness

Though the authors stated that a literature search updated through March 2005 was performed, they do not appear to have performed a formal systematic review to identify and summarise all the relevant information. The sources searched were not explicitly stated. The sources included double-blind randomised trials, which are an adequate design for evaluating effectiveness, but it was unclear how the authors derived effectiveness data from the studies selected. They do not appear to have taken weights for differing sample sizes into account, nor did they consider the impact of differences between the primary studies when estimating effectiveness. Finally, it appears that the available data might have been used selectively. The estimates were investigated in sensitivity analyses, but the authors did not provide a justification for the ranges selected.

Validity of estimate of measure of benefit

The estimation of benefits was derived through modelling, by direct use of the effectiveness estimates (fatal MI and CV death). Though this could be useful when comparing study results with other CV interventions, it would be difficult to compare the results with other health care technologies.

Validity of estimate of costs

The cost perspective adopted by the authors was not stated and only a few cost categories (CV hospitalisations, supplements and productivity losses) were included. The predominant perspective in the base-case analysis appears to have been that of a hospital, whilst a societal perspective appears to have been used in a second analysis as the indirect costs were included. However, both analyses omitted some relevant costs, such as chronic ambulatory costs.

Nevertheless, their omission probably biases the results against supplementation. The unit costs were reported, whereas the quantities were modelled and were not reported separately, which will hinder the generalisability of the authors' results. The unit costs used were taken from published sources and a sensitivity analysis of the costs was conducted. The price date was adequately reported, which will aid any future inflation exercises.

Other issues

The authors made appropriate comparisons of their results with those from other studies. The generalisability of the results to other settings was not addressed. The authors' conclusions would appear to reflect the scope of their analysis though, as the authors acknowledged, the cost data were limited to available data. In addition, the methodology of the review of the literature review does not seem clear. The authors also reported other limitations. For example, the scarcity of longer term data, the different administration and/or formulations of omega-3 assessments used in the primary studies, the heterogeneity of study quality, and the inclusion of only limited CV benefits of omega-3.

Implications of the study

The results of this model, which should be viewed in comparison with other nutritional interventions, 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 have important implications for managed care organisations, which are increasingly considering covering or providing discounts for supplement use. Further, pending federal legislation would allow expenses for dietary supplements to be treated as medical expenses.

**Source of funding**
Supported by the Council for Responsible Nutrition.

**Bibliographic details**

**PubMedID**
16686171

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Coronary Artery Disease /prevention & control; Cost-Benefit Analysis; Dietary Supplements /economics; Fatty Acids, Omega-3 /administration & dosage; Humans; United States

**AccessionNumber**
22006006468

**Date bibliographic record published**
28/02/2007

**Date abstract record published**
28/02/2007