A cost-effectiveness analysis of n-3 PUFA (Omacor) treatment in post-MI patients
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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
The study examined Omacor (900 mg n-3 polyunsaturated fatty acids per capsule) given to patients after myocardial infarction (MI) for the secondary prevention of cardiovascular disease.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of post-MI patients.

Setting
The setting was primary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness evidence and other clinical data were derived from studies published between 1996 and 2004. No dates for resource use were reported. The price year was 2004.

Source of effectiveness data
The effectiveness evidence came from a synthesis of published studies and authors’ opinions.

Modelling
A Markov model was developed to assess the costs and benefits of Omacor versus no supplements in the treatment of a hypothetical cohort of 1,000 post-MI patients. The model followed patients through yearly cycles until death or the age of 100 years. Patients transitioned through several health states, including post-MI, subsequent MI, post-subsequent MI, stroke, post-stroke, subsequent stroke, post-subsequent stroke and death. Survival during the first 4 years of the simulation was based on data derived directly from the GISSI-P trial, while lifetime survival was estimated using survival curves, which were extensively described. Transition probabilities between health states were age-specific. The three age groups considered were 64 to 74 years, 75 to 89 years, and 90 years or older.

Outcomes assessed in the review
The outcomes estimated from the literature were:

the efficacy of Omacor (in terms of reduced rates of death, nonfatal MI and nonfatal stroke),
expected survival,
transition probabilities, and
the utility weights associated with specific health states.

**Study designs and other criteria for inclusion in the review**
The authors stated that the GISSI-P trial was the most important clinical trial (large sample and adequate follow-up) that had estimated the clinical benefits of Omacor. A smaller trial conducted in Norway was excluded because it had insufficient power to detect a significant difference in clinical outcomes. Other inclusion criteria were not provided. Thus, all the clinical evidence relative to the first 4 years post-MI came from the GISSI-P clinical trial, which had enrolled 11,324 post-MI patients with a follow-up of 42 months. Long-term survival was obtained from a Canadian study adjusted to represent UK patients. The sources of the other clinical data were unclear. The utility values were derived from a health survey for England and from other studies.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
The data derived from the GISSI-P study were valid given the randomised design and the large sample of patients enrolled.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Nine primary studies provided the clinical data.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The rate of death, nonfatal MI and nonfatal stroke was 12.3% with Omacor and 14.6% with no treatment.

The rate of cardiovascular death, nonfatal MI and nonfatal stroke was 9.2% with Omacor and 11.4% with no treatment.

The starting age for the hypothetical patients entering in the model was 63 years.

The transition probabilities in the Omacor and control groups during the first 4 years of treatment were, respectively:

0.0028 and 0.0032 from post-MI to subsequent MI;

0.0083 and 0.0095 from post-MI to subsequent MI with percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting (CABG);
0.0041 and 0.0033 from post-MI to stroke; 
0.0083 and 0.0095 from stroke to subsequent MI with PTCA or CABG; 
0.0028 and 0.0032 from post-stroke to subsequent MI; 
0.0041 and 0.0033 from post-subsequent MI to stroke; and 
0.0245 and 0.0307 from any state to all-cause death.

Long-term annual transition rates for the three different age groups were reported in the appendix of the paper.

The utility weights for stroke and subsequent stroke were 0.11 (range: 0 to 0.35) for severe condition, 0.39 (range: 0.25 to 0.55) for moderate condition, and 0.76 (range: 0.55 to 0.95) for mild condition.

The health utility for MI was 0.87 (range: 0.80 to 0.95).

The health utility for post-MI was:
0.80 for men aged 55 to 64 years and 65 to 74 years, 
0.76 for men older than 75 years, 
0.78 for women aged 55 to 64 years, 
0.76 for women aged 65 to 74 years, and 
0.71 for women older than 75 years.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions regarding the extrapolation of 4-year results of the clinical trial to a long-term horizon.

**Estimates of effectiveness and key assumptions**
It was assumed that Omacor treatment would not be continued beyond the trial duration of 42 months. Thus, no further benefits from treatment were assumed to be incurred post-trial.

**Measure of benefits used in the economic analysis**
The three summary benefit measures used were the quality-adjusted life-years (QALYs), life-years (LYs) and number of deaths. The utility weights were obtained from three published studies, while age-specific survival associated with the different health state was obtained from a large Canadian study (adjusted for the UK). An annual discount rate of 3.5% was applied to all benefit measures.

**Direct costs**
The analysis of the costs was carried out from the perspective of the UK NHS. It included the costs associated with subsequent MIs, coronary heart disease-related death and all-cause death, nonfatal MI, fatal and nonfatal stroke, and drugs (e.g. aspirin, cholesterol-lowering treatments, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, nitrates, diuretics and Omacor). The authors stated that the model made a distinction between resource use in the year in which an event occurred and in the subsequent years when the patient was expected to be stable. The unit costs and the quantities of resources used were not presented separately. Data on resource consumption and costs related to health states were derived from the literature, although details of the sources used were not provided. The drug costs were derived from a published database. Discounting was relevant, as the long-term costs were calculated,
and an annual rate of 3.5% was applied. The price year was 2004. Where necessary, the costs were inflat ed to 2004 values using the recommended Hospital and Community Health Services inflation rate of 1.3%.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not relevant from the perspective of the study.

**Currency**
UK pounds sterling (). 

**Sensitivity analysis**
A univariate sensitivity analysis was carried out to assess the robustness of the model results to variations in key inputs. Inputs varied included the discount rate, rehabilitation cost after stroke, follow-up cost after MI, and percentage of patients receiving post-MI treatment. A probabilistic sensitivity analysis was also performed by assigning probability distributions to the following model inputs: MI hospitalisation costs, PTCA and CABG costs, and health state utility values for both MI and stroke. Uniform distributions were used for all parameters in the absence of better data.

**Estimated benefits used in the economic analysis**
In a hypothetical cohort of 1,000 patients, the expected QALYs were 9,309 with Omacor and 9,102 with no treatment over lifetime (difference 207), and 2,839 (Omacor) and 2,797 (no treatment), respectively, over 4 years (difference 43).

The expected LYs were 12,037 with Omacor and 11,763 with no treatment over lifetime (difference 274), and 3,452 (Omacor) and 3,397 (no treatment), respectively, over 4 years (difference 54).

The expected deaths over 4 years were 85 with Omacor and 106 with no treatment (difference 20).

**Cost results**
In a hypothetical cohort of 1,000 patients, the expected costs were 6,471,024 with Omacor and 5,700,688 with no treatment over lifetime (difference 770,336), and 1,789,148 (Omacor) and 1,140,143 (no treatment), respectively, over 4 years (difference 649,005).

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios and cost-utility ratios were calculated in order to combine the costs and benefits of the alternative interventions.

The incremental cost per QALY gained with Omacor over no treatment was 3,723 over lifetime and 15,189 over 4 years.

The incremental cost per LY gained with Omacor over no treatment was 2,812 over lifetime and 12,011 over 4 years.

The incremental cost per death avoided with Omacor over no treatment was 31,768 over 4 years.

Both the deterministic and the probabilistic sensitivity analyses showed that the base-case results were robust to variations in key model inputs.
Authors' conclusions
Omacor added to conventional preventive therapy after myocardial infarction (MI) was a cost-effective treatment in the UK, both at 4 years and over a lifetime horizon. The cost-effectiveness of Omacor was comparable to that of other widely accepted preventive strategies.

CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparator was clear since the use of supplements was compared with the standard treatment for post-MI patients. The doses were reported. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The authors did not report the methods and conduct of a systematic review of the literature, thus the primary studies providing the clinical data might have been identified selectively. However, the authors stated that there was only one relevant trial that evaluated Omacor in post-MI patients. Hence, most of the evidence on the 4-year effectiveness of treatment and the rates of events were derived from this large clinical trial. This trial should have a high internal validity given its randomised design. Limited information on the other sources of data was provided. The authors made some key assumptions regarding the extrapolation of the clinical data to a long-term time horizon. However, all these assumptions were conservative for Omacor. The issue of uncertainty in the clinical estimates was not addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measures used in the analysis were appropriate for the study question. LYs and QALYs have the advantage of being comparable with the benefits of other health care interventions. In particular, QALYs are a recommended benefit measure because they capture the impact of the preventive strategy on both survival and quality of life, which are two relevant dimensions of health for post-MI patients. Few details on the sources of the utility weights used to calculate QALYs were reported, but the effect of these values on the results of the analysis was investigated in the sensitivity analysis. Discounting was applied to all benefit measures, which was appropriate given the long-term time horizon. The use of alternative discount rates (including no discounting) was tested in the sensitivity analysis.

Validity of estimate of costs
The analysis of the costs was consistent with the perspective chosen for the analysis. A detailed breakdown of the cost items was provided, but information on the unit costs and quantities of resources used was not presented, most costs being reported as macro-categories. This limits the possibility of replicating the cost analysis in other settings. Limited information on the source of the costs was provided and only a few estimates were varied in the sensitivity analysis. Probabilistic distributions were assigned to specific cost categories in the stochastic sensitivity analysis. The price year was reported, which will assist reflation exercises in other time periods. The authors stated that resource consumption did not reflect resource use in the trial, owing to the lack of patient-level data. However, resource use was closer to UK treatment patterns.

Other issues
The authors stated that their findings were similar to those achieved in another economic evaluation of the GISSI-P trial. With respect to the generalisability of the study results to other settings, the authors stated that the treatment of post-MI patients in the trial performed in Italy was comparable to that observed in the UK, thus the clinical results can be considered transferable to the UK setting. The authors stated that the results of the analysis should be seen as conservative since the assumptions did not favour the Omacor arm of the model. The study referred to the general population of post-MI patients and this was reflected in the authors' conclusions.

Implications of the study
The study results support the use of Omacor for the prevention of cardiovascular disease in post-MI patients.

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