

Cost Effectiveness of Prescription Strength Omega-3 in Individuals with Severe Hypertriglyceridemia

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Abstract:

Background: Clinical trials in individuals with severe (≥500 mg/dl) hypertriglyceridemia (SHTG) have demonstrated that 4 g/day of prescription-strength omega-3 (P-OM3) can reduce TG levels by 45%. Individuals with elevated triglyceride (TG) levels are at higher risk for coronary heart disease (CHD). However, a study is lacking to support the potential cost effectiveness (CE) of P-OM3 in individuals with SHTG.

Objective: The objective of this research was to estimate the long-term CE of P-OM3 in SHTG individuals using the Archimedes Model.

Methods: The Archimedes Model is a physiologically based mathematical model that is clinically and administratively detailed and has been rigorously validated using clinical trial data. To simulate the CE of P-OM3, a model of omega-3s was constructed and calibrated to match cardiovascular outcomes based on numerous publications and then incorporated into the Archimedes Model. SHTG individuals from NHANES 1999-2006 with age > 45 years were randomly selected and then used to create a population of 5000 simulated individuals. The CE analysis compared costs and clinical outcomes for P-OM3 as monotherapy versus placebo over a 20-year period.

Results: The average age at baseline was 54.6 years, with 64% males, 42% diabetics, mean BMI of 30.6 kg/m², blood pressure of 132/79 mmHg, total cholesterol (TC) of 267 mg/dl, HDL of 37 mg/dl, LDL of 85 mg/dl, TG of 891 mg/dl, FPG of 140 mg/dl, and HbA1c of 6.6%. P-OM3 administration was associated with an average decrease in TG level of 41%, a 12% decrease in TC, a 2% decrease in systolic blood pressure, a 4% increase in HDL, and a 24% increase in LDL. Compared to placebo, administration of P-OM3 resulted in a reduction of 32% (p<0.05) for myocardial infarctions, a 19% (p<0.05) reduction in stroke, a 29% (p<0.05) reduction in CHD death, a 24% (p<0.05) reduction in cardiovascular death, and a 24% (p<0.05) reduction in composite major adverse cardiovascular events (MACE). The cost-effectiveness ratio for P-OM3 versus placebo was \$47,000/QALY.

Conclusion: The findings from this simulation demonstrate that the use of P-OM3 results in significant reductions in long-term cardiovascular events in SHTG. P-OM3 is a cost-effective treatment for individuals with SHTG using a threshold of \$50,000/QALY.

Introduction

- Hypertriglyceridemia is commonly prevalent in the US with 33.1% of adults of age 20 years and above with elevated triglycerides (TG) levels above 150 mg/dL. The prevalence of severe hypertriglyceridemia (SHTG), as characterized by TG ≥500 mg/dL, is about 1.7% in the US¹.
- Published studies indicate an increased risk of coronary heart disease (CHD) in individuals with elevated TG levels^{2, 3}.
- In individuals with SHTG, the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP III) guidelines recommend first lowering TG levels⁴.
- One of the treatment options which has been shown to reduce TG levels in individuals with SHTG is prescription strength omega-3 (P-OM3). Findings from clinical trials demonstrate that in individuals with SHTG, 4 g/day of P-OM3 can reduce TG levels by 45%^{5, 6}. However, there is no published evidence to demonstrate the cost-effectiveness (CE) of P-OM3 in the treatment of SHTG.

Objectives

- The objective of this research was to estimate the long-term CE of P-OM3 in SHTG individuals using the Archimedes Model.

Methods

- The Archimedes Model is a physiologically based mathematical model that is clinically and administratively detailed and has been rigorously validated using clinical trial data⁷⁻⁹. This model uses ordinary and differential equations to represent normal physiology, and incorporates a wide range of diseases and disorders related to cardiovascular disease. In addition, the model also represents the use of tests, treatments, care processes, health outcomes, visits and hospital admissions, procedures, and related costs.
- To help simulate outcomes in SHTG individuals, the lipid component of the Archimedes Model was made more robust using data from individuals with TG≥500mg/dL from a managed care plan. The lipid model was validated in this region by reproducing the correct changes in TG, HDL and total cholesterol for 34 intervention scenarios drawn from 20 publications.

Methods (Cont'd)

- The simulations randomly selected adults of ages 45-75 years from NHANES 1999-2006 with TG ≥ 500mg/dL (and TG ≤ 2000 mg/dL). These individuals were used as a basis for generating a cohort of individuals (N=5000) with SHTG, thereby capturing the distributions and correlations of risk factors seen in the real SHTG population.
- For the purposes of estimating the impact of P-OM3 as monotherapy, outcomes and costs were first estimated for these individuals without any treatment for SHTG and then after treatment with P-OM3 as monotherapy. The difference in outcomes and cost over the period of the simulation was used to compute cost-effectiveness of P-OM3 in reducing TG in individuals with SHTG. The use of any other TG-lowering medication for SHTG was not considered for this purpose (i.e., no statins, fibrates or niacin use was considered).
- The simulations were run over a period of 20 years or until death, with outcomes reported annually. Baseline, 10-year and 20-year results are displayed here. Outcomes assessed included the risk of myocardial infarction (MI), stroke, CHD death, cardiovascular disease (CVD) death, and composite major adverse cardiovascular event (MACE). Costs and QALYs were discounted using a discount rate of 3%.
- A number of assumptions were made for this simulation:
 - The effects on CVD outcomes for P-OM3 can be determined from low-dose studies (dose extrapolation).
 - The effects on CVD outcomes for a TG ≥ 500 mg/dL population can be determined from studies involving individuals with "normal" TG levels (TG extrapolation).
 - The benefits of OM-3's as determined from reductions in myocardial infarctions (MIs) and MI death extend to all heart-related outcomes including angina and heart failure.
 - The effects of OM-3's on secondary prevention are the same as on primary prevention.
 - National statistics for OM-3 consumption for the general US population apply to the SHTG population. These statistics are that approximately 25% of Americans eat three or more fish meals per week and/or take a fish oil supplement and that 8% of Americans eat more than one but fewer than three fish meals per week and do not take fish oil supplements. In the simulation it was assumed that such OM-3 consuming individuals would benefit less from P-OM3.

Results

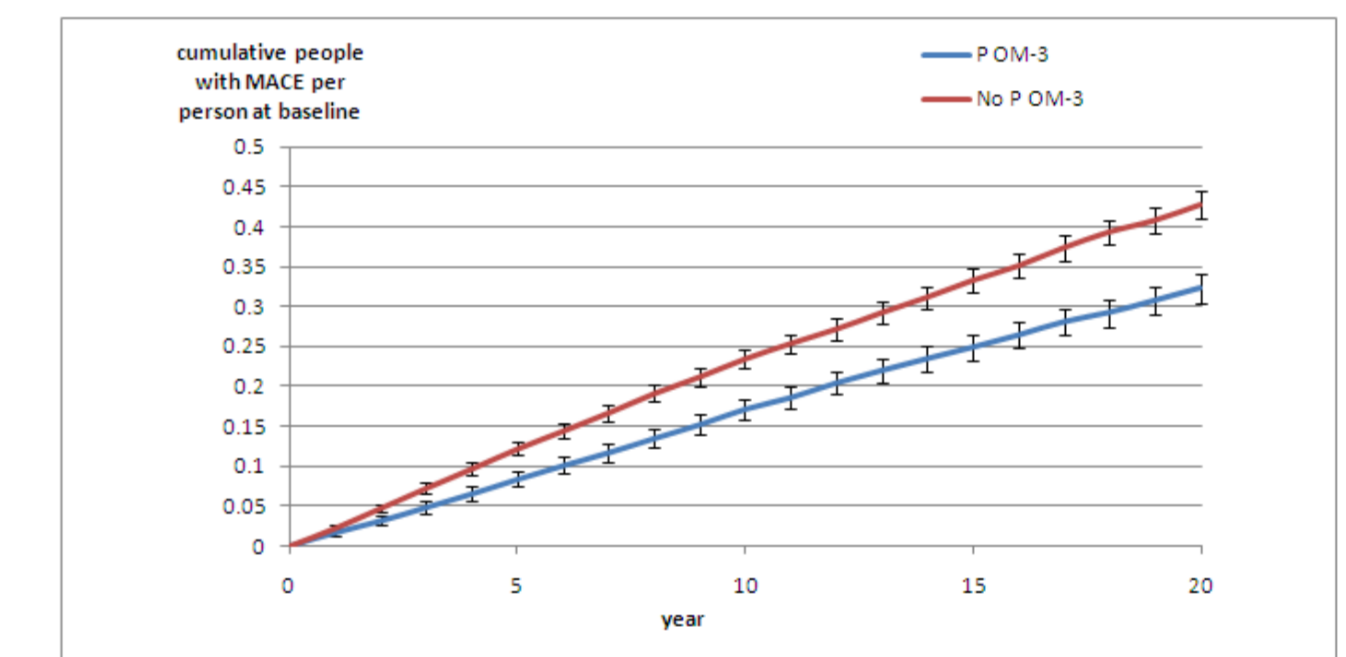
- The average age at baseline was 54.6 years, with 64% males, 42% diabetics, mean BMI of 30.6 kg/m², blood pressure of 132/79 mmHg, total cholesterol (TC) of 267 mg/dl, HDL of 37 mg/dl, LDL of 85 mg/dl, TG of 891 mg/dl, FPG of 140 mg/dl, and HbA1c of 6.6%.
- The risk of CV events in individuals with SHTG as simulated using the Archimedes Model is presented in Table 1.
- P-OM3 administration was associated with an average decrease in TG level of 41%, a 12% decrease in TC, a 2% decrease in systolic blood pressure, a 4% increase in HDL, and a 24% increase in LDL.
- Compared to placebo, administration of P-OM3 resulted in a reduction of 32% for myocardial infarctions, a 19% reduction in stroke, a 29% reduction in CHD death, a 24% reduction in cardiovascular death, and a 24% reduction in composite major adverse cardiovascular events (MACE) at 20 years. The p-values associated with these reductions in CV events were all less than 0.05.
- The cost-effectiveness ratio of P-OM3 in treating elevated TG in SHTG individuals was observed to be \$47,000/QALY over the 20 year period.

Table 1: Risk of CV Events in SHTG Individuals with and without P-OM3 – Archimedes Simulation

Outcomes	10 Years					20 Years						
	No Treatment (%)	2 SE	P-OM3 (%)	2 SE	Relative Reduction	2 SE	No Treatment (%)	2 SE	P-OM3 (%)	2 SE	Relative Reduction	2 SE
People with MI's per person alive	11.2	1	7.5	0.8	33	7.4	23.6	1.6	16	1.4	32.1	5.8
First MI (Kaplan Meier event rate)	15.9	1.1	10.4	1	34.7	6	32.6	1.7	22.3	1.5	31.5	4.7
Total MI's per person at baseline	20.7	1.8	12.6	1.4	39.1	6.7	41.8	2.8	26.8	2.3	35.7	5.4
People with stroke per person alive	3.5	0.6	3	0.5	14.2	15.3	6.5	0.9	5.2	0.8	19	12.7
First stroke (Kaplan Meier event rate)	6.2	0.8	5.3	0.7	15.6	11.2	14.9	1.3	12.1	1.2	18.6	8.1
Total strokes per person at baseline	6.1	1	5.1	0.9	16.9	14.8	14.3	2	11.6	1.8	19.1	12.7
CHD Death per person at baseline	8.1	0.9	5.5	0.7	32.4	8.8	15.9	1.4	11.2	1.2	29.3	7.4
Stroke Death per person at baseline	3.2	0.5	2.7	0.5	13.8	16.1	7.3	1	6.4	0.9	13.4	12.3
CVD death per person at baseline	11.3	1	8.2	0.9	27.2	7.6	23.2	1.6	17.6	1.4	24.2	6.1
Cumulative people with MACE	23.4	1.3	17.1	1.2	26.9	5	42.7	1.8	32.3	1.7	24.4	4.1
Any death per person at baseline	21.5	1.3	18.5	1.2	13.7	5.7	46.3	1.8	41.7	1.8	9.9	3.9

Note: Relative reduction was calculated based on difference in % risk between the two groups.

Figure 1: SHTG Individuals with MACE with and without P-OM3 – Archimedes Simulation



Conclusions

- The findings from this simulation demonstrate that the use of P-OM3 results in significant reductions in long-term cardiovascular events associated with SHTG.
- P-OM3 is a cost-effective treatment for individuals >45 years of age with SHTG using a threshold of \$50,000/QALY.
- There is a lack of long-term trials to determine the risk of CV events in individuals with SHTG and to demonstrate the impact of P-OM3 on CV events in individuals with SHTG. In the absence of clinical trial data, the Archimedes Model provides estimates for the potential benefit of treatment with P-OM3 in individuals with SHTG.

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