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Healthcare Cost Savings of Omega 3 Food Supplements in the European Union

Economic Implication of Managing CVD through Targeted Enhanced Nutrition

food supplements europe

An Independent Economic Analysis Commissioned by Food Supplements Europe

Christopher Shanahan, M.S.

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Abstract

The objective of this report is to determine if cost savings could be realised, in the form of avoided healthcare-related expenditures from the use of an omega-3 EPA + DHA supplement. This report examines the body of clinical research that tests the hypothesis that the use of omega-3 EPA + DHA supplements can potentially reduce CVD-attributed hospital utilisation costs in the European Union among those at a high risk of experiencing a costly, CVD-attributed event. If the hypothesis is substantiated, then the targeted use of an omega-3 EPA + DHA supplement regimen can be recommended as a means to help control rising societal healthcare costs and as a means for high-risk individuals to minimise the chance of having to deal with potentially detrimental disease-attributed events.

Target Population—a total of 38.4 million CVD-attributed hospital events are expected over the next 5 years (2016 to 2020) among adults age 55 and older in the EU, or 24% of the target population will experience a CVD-attributed hospital event.1 The total cost of addressing CVD in the EU will be € 1,328 billion over the next 5 years, or € 34,637 per event over the same period.

Study Methods—a random-effects systematic review approach was used to infer the effect of using an omega-3 food supplement on the occurrence of a CVD-attributed medical event. A literature search was conducted and 18 randomised controlled trials (RCT) were identified that tested for the presence of a relationship between omega-3 EPA+DHA use and the occurrence of a CVD event. The study's findings were aggregated and the expected relative risk reduction was determined and then used as an input into a theoretical economic scenario model which determined the difference in benefits and costs EU health care policy makers can expect if everybody in a targeted population with high CVD risk adopted an omega-3 daily. Results of this theoretical economic analysis provides insight on potential health care cost savings per capita and per EU country that could be realised through the targeted use of omega-3 EPA+DHA food supplements.

Science-based Impact of Omega-3 Use—the relative risk of an individual in the target population experiencing a CVD-attributed adverse event is reduced by 4.9% given the daily use of 1,000 mg of omega-3 EPA + DHA food supplements. This corresponds to over 1.5 million avoided CVD-attributed hospital events throughout the EU over the next five years.

Economic Findings (Total EU)—It is expected that 20% of the target population in the EU today is already taking Omega-3 and realizing some of its potential health benefits. The below findings are the total potential economic benefits that could be realised if 100% of the EU target population used 1,000 mg omega-3 EPA+DHA food supplements daily

- Total Avoidable CVD-attributed Costs per year (S): € 12.9 billion
- Net Avoidable CVD-attributed Costs per year (B): € 7.3 billion
- Net Avoidable CVD-attributed Costs per person per year (B/Pop): € 188 per person
- Benefit/cost ratio (€ Avoided CVD-attributed Costs per € 1 spent on Omega-3): € 2.29

1 See page 2 for basis of this finding.

Study Implications—This analysis shows that significant healthcare cost savings can be realised through a concerted effort to identify high CVD-risk populations and motivate them to use omega-3 EPA + DHA supplements. Because a significant portion of benefits is in the form of saved consumer expenditures related to informal post-event CVD management costs such as home nurses, medical equipment for home use and lost productivity, a significant portion of economic benefits would be conferred to the final consumer of omega-3. However, avoided CVD-event costs also leads to derived benefits to other stakeholders, such as gained tax revenue from saved productivity, which is a benefit to the government, and from lower treatment costs incurred by both public and private healthcare payers such as private insurance companies. Overall, this health-to-wealth assessment can be used by all stakeholders including consumers, healthcare providers, employers, and policymakers as a means to better quantify the benefits of using omega-3 food supplements. Understanding this link will help key stakeholders—potential omega-3 supplement users, healthcare providers, governments, private insurance companies, and employers—make recommendations about the best course of action to help minimise current and future costs and maximise benefits.

The Burden of Cardiovascular Disease in the European Union

Cardiovascular disease (CVD) is a set of disorders of the heart and blood vessels supplying the heart and includes coronary heart disease and cerebrovascular disease [1]. In general, CVD encompasses certain conditions that result from the accumulation of atherosclerotic plaques in the coronary arteries, which restricts blood flow to the heart and brain. This restriction can lead to heart failure, angina pectoris, acute myocardial infarction, other ischemic heart diseases, and sudden death. Those individuals who have suffered a CVD event and survive face a life of ischemic heart failure, increased risk of stroke, and overall lower quality of life.[2]

Previous research has shown that CVD-attributed event risk is highly correlated to many variables such as age, gender, lifestyle choices and to risk-indicating biomarkers such as blood lipid levels and blood pressure baseline levels. Out of a total EU population of 157.6 million people age 55 and older in 2015, more than 40% of the population (63 million Europeans) had elevated blood pressure [2, 3]. Average baseline systolic blood pressure (SBP) and diastolic blood pressure (DBP) level across the European Union is 142.7 mm Hg/84.1 mm Hg, which is in the pre-hypertension level category with respect to SBP though still normal in the DBP range [4, 5]. Furthermore, 72 million people and 24 million people had with total cholesterol levels greater than or equal to 5.0 mmol/L and 6.2 mmol/L, respectively [6]. The typical baseline triglyceride (TG) level among all adults age 55 and older in the EU is 1.77 mmol/L, which according to the World health Organisation is borderline high [4, 7].

CVD-attributed event risk is highly correlated to many variables such as age, gender, lifestyle choices and to risk-indicating biomarkers such as blood lipid levels and blood pressure baseline levels.

2 For the purposes of this study, CHD is strictly defined as events associated with the following ICD /ISHMT codes: 0901 (Hypertensive diseases), 0902 (Angina pectoris), 0903 (Acute myocardial infarction), 0904 (Other ischaemic heart disease), 0907(Heart failure), 0908 (Cerebrovascular diseases), and 0909(Atherosclerosis).

The total expenditures of addressing CVD-attributed medical events will be €1,328 billion over the next 5 years.

Event risk is the total number of observed CVD-attributed outcomes requiring a set of hospital services observed in a given population relative to the total target population. A hospital event is defined as a person experiencing an event that requires professional medical attention and, consequently, hospital service utilisation such as outpatient or office-based provider visits, hospital inpatient stays, emergency room visits, prescribed medications, and home care such as home nursing and medical devices used at home [2]. For the purposes of this study, CVD is strictly defined as events associated with the following ICD/ISHMT codes: 0901 (hypertensive diseases), 0902 (angina pectoris), 0903 (acute myocardial infarction), 0904 (other ischaemic heart disease), 0907 (heart failure), 0908 (cerebrovascular diseases), and 0909 (atherosclerosis) [2]. The choice of ISHMT codes reflects the author's conservative judgment that these events are nearly always associated with CVD as the main underlying or direct cause.

According to hospital utilisation statistics provided by the World Health Organisation, Regional Office of Europe, over 38.0 million CVD-attributed hospital events occurred from 2011 to 2015 in the EU among adults age 55 and older as defined by the aforementioned ICD/ISHMT codes [2]. Thus, each individual adult age 55 and older in the EU has a one in four chance of experiencing a CVD-attributed event requiring formal and informal heath care services over the next five years[3]. These CVD-attributed events include both primary and secondary CVD cases. Given an average 0.8% growth in CVD-attributed events from 2016 to 2020, it is expected that a total of 38.4 million CVD-attributed hospital events are expected over the next 5 years (2016 to 2020) among adults age 55 and older in the EU, or 24% of the target population will experience a CVD-attributed hospital event. Growth trends in CVD-attributed events by EU country does vary by a number of reasons such as target market population growth, quality-of-care by EU country, and general health of the target population which was controlled for when projecting CVD-attributed events over the next five years. Table 1 shows the social burden of CVD on the EU population by nation.

Treating CVD is costly. The total expenditures of addressing medical events requiring a mix of hospital services for all EU adults age 55 and older is expected to be € 1,328 billion over the next 5 years, or approximately € 265.7 billion per year after controlling for purchasing power parity across each country within the EU [3, 6]. A significant portion of this cost is related to events that require expensive hospital care services, especially inpatient procedures and emergency room visits. This cost also includes treatment-specific pharmaceuticals, outpatient visits, and informal costs such as post-treatment home/nursing care services. Furthermore, there are significant indirect costs of CVD on society as a whole including less productivity income for the state due to CVD-attributed deaths. Table 2 shows the costs of CVD on the EU population by nation in terms of total hospital service utilisation and Chart 1 shows the average annual cost of a CVD-attributed hospital event by selected EU country.

3 World Health Organisation Regional Office for Europe. European Hospital Morbidity Database and Frost & Sullivan analysis

Table 1. Burden of Cardiovascular Disease: CVD-attributed Event Risk, 2011-2020[45]

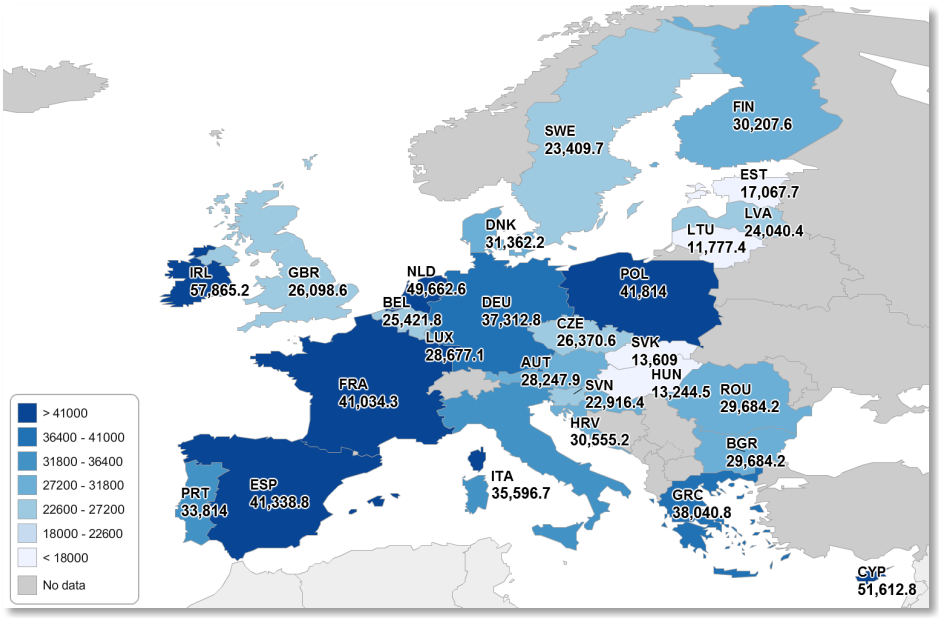
Country	Total Population, age 55 and older	Cumulative number of hospital events age 55 and over, 2011 - 2015	Cumulative number of hospital events age 55 and over, 2015 - 2020	Event rate (Risk) – Ratio of cumulative number of hospital events relative to total population age 55 and over, 2015 - 2020
Austria	2,574,872	942,292	984,797	38.2%
Belgium	3,378,041	716,025	740,876	21.9%
Bulgaria*	2,395,715	675,000	749,547	31.3%
Croatia*	1,366,757	290,000	321,820	23.5%
Cyprus	217,517	11,269	7,851	3.6%
Czech Republic	3,224,578	975,559	883,413	27.4%
Denmark	1,705,383	275,000	305,277	17.9%
Estonia*	408,180	100,000	110,814	27.1%
Finland	1,801,776	479,770	436,876	24.2%
France	20,023,397	3,611,817	3,722,127	18.6%
Germany	27,840,013	10,207,274	10,630,545	38.2%
Greece	3,544,810	658,000	730,662	20.6%
Hungary	3,107,068	1,190,036	985,327	31.7%
Ireland	1,051,651	202,666	277,842	26.4%
Italy	20,248,958	4,139,915	3,925,622	19.4%
Latvia	630,755	232,000	165,576	26.3%
Lithuania	900,267	564,173	582,852	64.7%
Luxembourg	139,939	32,740	38,016	27.2%
Malta	134,864	19,466	22,899	17.0%
Netherlands	5,078,117	816,770	842,161	16.6%
Portugal	3,233,995	668,000	741,686	22.9%
Poland	11,381,429	3,513,217	3,657,001	32.1%
Romania	5,966,193	2,154,991	1,836,771	30.8%
Slovakia	1,455,578	505,022	512,922	35.2%
Slovenia	647,904	133,468	145,398	22.4%
Spain	13,719,534	1,911,244	1,912,131	13.9%
Sweden	2,992,914	554,000	615,177	20.6%
United Kingdom	18,426,690	2,470,733	2,467,183	13.4%
Total EU	157,596,895	38,050,447	38,353,168	24.3%

It is expected that there will be a total of 38.4 million CVD-attributed hospital events over the next 5 years in the EU.

4 Source: Eurostat. European Commission (http://ec.europa.eu/eurostat/data/database)
5 The World Health Organisation, Regional Office of Europe and Frost & Sullivan analysis

Physicians and scientists alike recognise that identifying physiological risk biomarkers and managing their respective levels through changes in behaviour and adopting proven risk-reduction regimens is one way to reduce an individual's risk of experiencing a costly CVD event in the future.

Chart 1.
Cost of CVD-attributed Events: Total Costs of Hospital Events and Post Treatment Informal Care Costs, Europe, Adjusted Annualised Average, 2016-2020



Source: [3] European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis and Frost & Sullivan

The average cost of a CVD-attributed hospital event in the EU will be € 34,637 per event[6]. The average cost of each CVD-attributed event is calculated by taking total expenditure over the next 5 years and dividing it by the cumulative number of events. This cost calculation approach was adopted because some CVD-attributed events and its residual post treatment disease management costs may stretch beyond one year for a given event. For example, the cost of inpatient care, which is the expenditure for care of patients who requires hospital admission at the beginning of the CVD-attributed event, and post-treatment informal costs such as home nurses, medical equipment for home use and lost productivity which is typically spent over several months or years after the initial event are nearly equal in share of cost burden at 32.9% each. The cost of medications for managing CVD makes up an additional 19.1% of the financial burden of CVD. The remaining services contributing to CVD-attributed healthcare costs make up a combined 15.1% of the cost burden include primary care (5.7%), outpatient care (8.3%) and ambulance and emergency (A&E) (1.1%). Chart 2 shows the average annual cost of a CVD-attributed hospital event by cost component for the total EU and Chart 3 shows the annual cost of a CVD-attributed hospital event by cost component by selected EU countries.

6 Source: European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis, Frost & Sullivan. The average cost of each CVD-attributed event is calculated by taking total expenditure over the next 5 years and dividing it by the cumulative number of events. This event cost was taken because some events and its residual post treatment disease management costs may stretch beyond one year for a given patient.

Table 2.
Total Burden of Cardiovascular Disease: CVD-attributed Event Costs, 2016-2020

Country	Average Annual Cost of CVD-attributed Hospital Event, € /event[7]	h: Adjusted Average Annual Cost of CVD-attributed Hospital Event, € /event[8]	5-year Cumulative Hospital Cost of CVD-attributed Events[6]	Average Annual Cost of CVD-attributed Hospital Events[6]
Austria	€ 27,683	€ 28,248	€ 27,818,445,704	€ 5,563,689,141
Belgium	€ 25,422	€ 25,422	€ 18,834,399,656	€ 3,766,879,931
Bulgaria	€ 13,493	€ 29,684	€ 22,249,720,094	€ 4,449,944,019
Croatia	€ 16,666	€ 30,555	€ 9,833,246,360	€ 1,966,649,272
Cyprus	€ 42,229	€ 51,613	€ 405,203,177	€ 81,040,635
Czech Republic	€ 14,384	€ 26,371	€ 23,296,141,569	€ 4,659,228,314
Denmark	€ 39,916	€ 31,362	€ 9,574,151,814	€ 1,914,830,363
Estonia	€ 10,861	€ 17,068	€ 1,891,345,354	€ 378,269,071
Finland	€ 32,954	€ 30,208	€ 13,196,985,463	€ 2,639,397,093
France	€ 37,304	€ 41,034	€ 152,734,696,698	€ 30,546,939,340
Germany	€ 33,921	€ 37,313	€ 396,655,829,240	€ 79,331,165,848
Greece	€ 27,666	€ 38,041	€ 27,794,959,991	€ 5,558,991,998
Hungary	€ 7,224	€ 13,244	€ 13,050,154,229	€ 2,610,030,846
Ireland	€ 57,865	€ 57,865	€ 16,077,351,031	€ 3,215,470,206
Italy	€ 32,361	€ 35,597	€ 139,739,088,150	€ 27,947,817,630
Latvia	€ 15,298	€ 24,040	€ 3,980,526,056	€ 796,105,211
Lithuania	€ 6,424	€ 11,777	€ 6,864,485,631	€ 1,372,897,126
Luxembourg	€ 31,284	€ 28,677	€ 1,090,187,145	€ 218,037,429
Malta	€ 27,954	€ 38,436	€ 880,153,528	€ 176,030,706
Netherlands	€ 49,663	€ 49,663	€ 41,823,904,485	€ 8,364,780,897
Portugal	€ 27,666	€ 33,814	€ 25,079,397,562	€ 5,015,879,512
Poland	€ 22,808	€ 41,814	€ 152,913,908,164	€ 30,582,781,633
Romania	€ 13,493	€ 29,684	€ 54,523,106,859	€ 10,904,621,372
Slovakia	€ 8,660	€ 13,609	€ 6,980,335,714	€ 1,396,067,143
Slovenia	€ 16,666	€ 22,916	€ 3,331,984,935	€ 666,396,987
Spain	€ 33,823	€ 41,339	€ 79,045,202,127	€ 15,809,040,425
Sweden	€ 27,666	€ 23,410	€ 14,401,121,863	€ 2,880,224,373
United Kingdom	€ 31,318	€ 26,099	€ 64,390,000,187	€ 12,878,000,037
Total EU	€ 29,118	€ 34,637	€ 1,328,456,032,787	€ 265,691,206,557

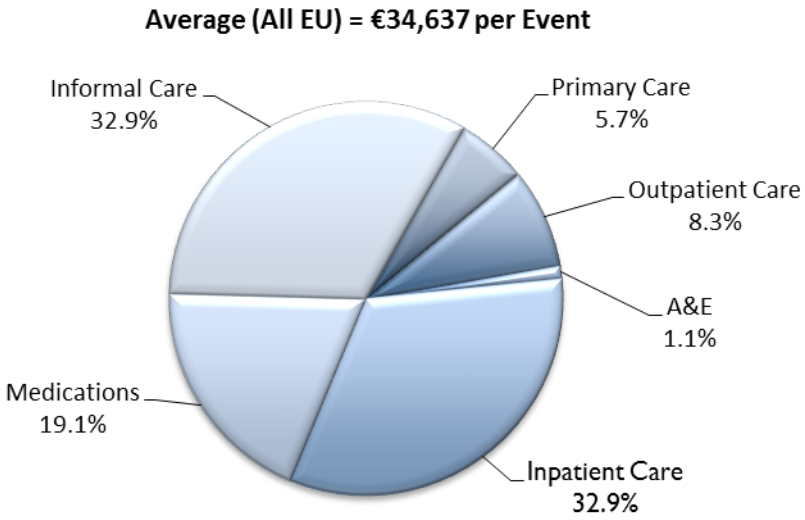
7 Source: European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis, Frost & Sullivan

8 Average annual cost of CVD-attributed hospital event, € /event adjusted for purchasing power parity (PPP) ratios provided by the World Bank. See Table 8 in this report or http://data.worldbank.org/indicator/PA.NUS.PPPC.RF for the PPP ratios

Informal care, or post-treatment disease management costs, is typically borne by the patient in the EU because a significant portion of this costs includes lost household wages and expenditure that increases the quality of life of the patient, but is not necessarily covered by government-backed coverage or private health insurance such as home nurses or ambulatory-enhanced home modifications.

On average, the cost of treating CVD per hospital event is the greatest in Ireland, where the per-event cost of CVD is nearly € 58,000. The cost of inpatient care in Ireland is the largest cost component in treating CVD in that country followed by the cost of medication. The lowest per-event cost of CVD is found in the Baltic state of Lithuania (€ 11,777) after controlling for purchasing power variance across the EU. The highest per-event cost countries are concentrated in Western Europe, where there is also higher quality-of-care options compared to Eastern Europe.

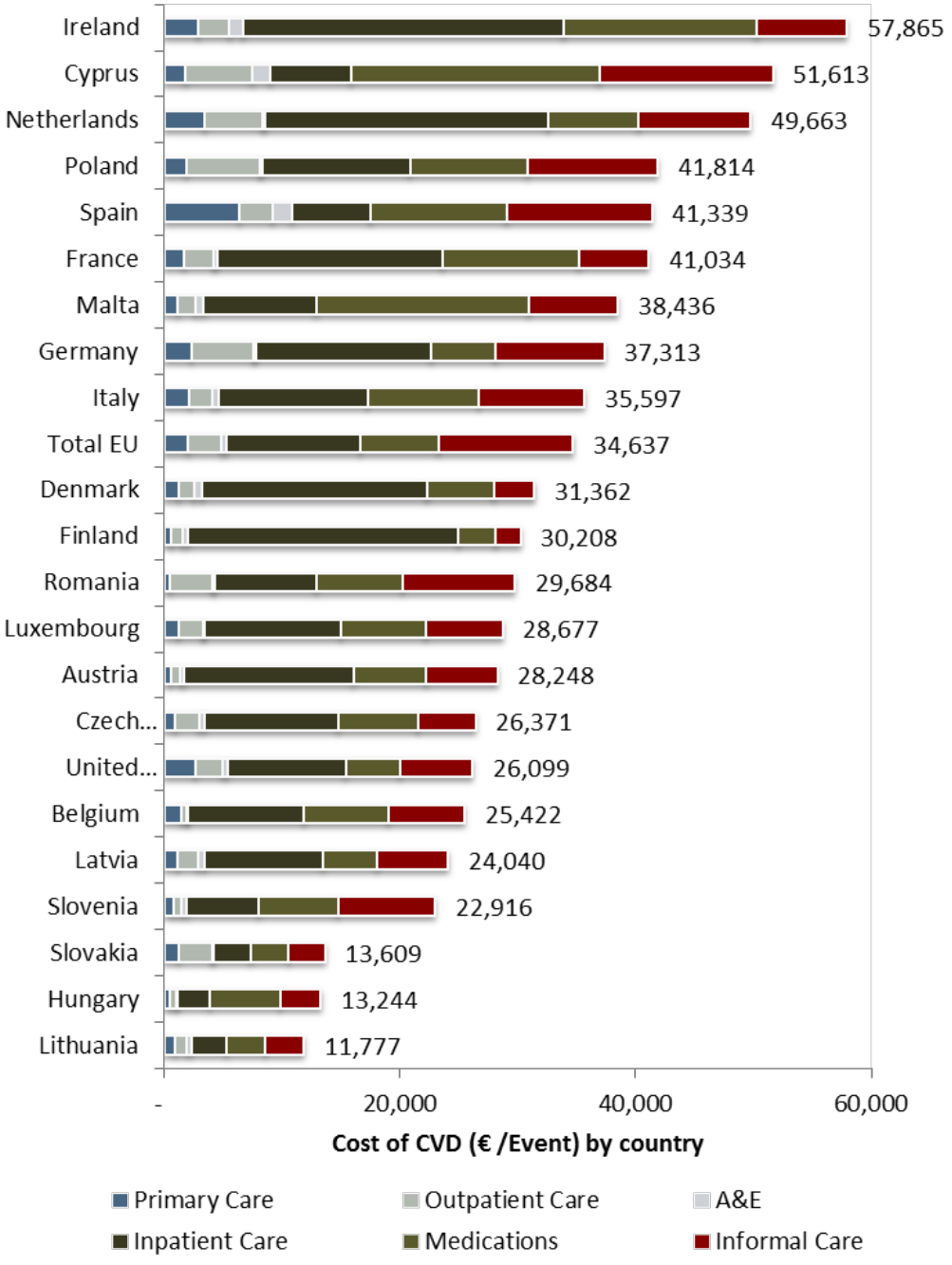
Chart 2
Total Burden of Cardiovascular Disease: CVD-attributed Event Costs by Service Type, European Union, 2015[9]



Note: A&E is ambulance and emergency services. Inpatient care is the expenditure for care of patients who requires hospital admission at the beginning of the CVD-attributed event. Informal Care includes post-treatment informal costs such as home nurses, medical equipment for home use and lost productivity which is typically spent over several months or years after the initial event. Outpatient care includes costs related to medical care provided on an outpatient basis, including diagnosis, observation, consultation, treatment, intervention, and rehabilitation services. Primary care is the day-to-day healthcare given by a health care provider. Source: European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis, Frost & Sullivan analysis

9 Adjusted for purchasing power parity (PPP). PPP ratios are provided by the World Bank and are reported in Table 8 of this report or http://data.worldbank.org/indicator/PA.NUS.PPPC.RF.

Chart 3
Total Burden of Cardiovascular Disease: CVD-attributed Event Costs by Service Type: Ranked by Total Hospital Event Costs, Selected EU Countries, 2015[10]



Source: European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis, Frost & Sullivan analysis

10 Adjusted for purchasing power parity (PPP). PPP ratios are provided by the World Bank and are reported in Table 8 of this report or http://data.worldbank.org/indicator/PA.NUS.PPPC.RF.

This report demonstrates that the use of omega-3 supplements among those Europeans that are at a high risk of experiencing a costly disease-related event can lead to positive healthcare cost savings.

Individual lifestyle choices directly impact the chance of experiencing adverse disease events. Choosing to exercise regularly, to have a nutritious and balanced diet, and avoiding the use of tobacco and alcohol are all activities at the decision maker's disposal that can reduce the risk of experiencing a CVD event, whether it is the first occurrence or secondary CVD events among the subset of people. In contrast, choosing a sedentary life coupled with an unbalanced diet and use of cigarettes and alcohol increases the risk of experiencing a CVD event. This is because all of these activities affect the individual's physical health, which is measured by known and quantifiable biomarkers such as blood lipid levels or blood pressure readings. Deviations of these biomarkers from healthy baseline levels determined by experts can provide a wide range of indications, including an individual's change in risk of experiencing a CVD event.

This analysis reviews clinical studies and other scientific research that test for a positive association between the use of an omega-3 EPA + DHA supplements and the reduction in the odds of experiencing a costly disease-related event. Furthermore, the omega-3 EPA + DHA supplement utilisation benefits that are deduced from the CVD-attributed event scientific literature are converted into estimated relative risk measures that can be used to calculate the number of avoided CVD-attributed healthcare expenditures by individual countries within the European Union. The overall aim is to deduce reasonable data regarding the relative risk of experiencing CVD-attributed events (both primary and secondary events) among Europeans age 55 and older using an omega-3 EPA + DHA supplement versus non-users within the same target population. These estimates are then fed into an economic benefit analysis that explores the possible monetary effects derived from using an omega-3 EPA + DHA regime as a tool to help manage an individual's risk of experiencing a CVD-attributed event.

It is expected that if there is significant relative disease risk reduction found for a given country's target population of all adults age 55 and older using omega-3 supplements, it is likely that there are also significant economic benefits to be realised. However, economic benefits are not only a function of reduced CVD risk, but are also a function of what each individual is currently expected to pay—on average—for treating a CVD-attributed event that requires hospital services and other informal post-treatment services. Countries with low average per CVD-attributed hospital event costs due to a lower quality of care or other external economic factors will likely have very small or negative net benefits after incorporating the cost of omega-3 EPA + DHA utilisation. However, these countries will still benefit from the decreased burden of CVD and the other non-monetary costs to society like reduced standards of living, lower individual quality of life, and overall country productivity and economic sustainability.

The Benefits of Omega-3 EPA + DHA Supplements

Omega-3 fatty acids are a class of polyunsaturated fatty acids found primarily in marine sources (such as fish and algae) and in certain plant sources [8]. Two types of omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are exemplary of a science- and research-driven category in the food supplements area. Specifically, omega-3 EPA + DHA are among the most extensively researched ingredients in food and beverages in terms of understanding the specific health benefits for users [9]. Marine-based omega-3 EPA+DHAs are the primary molecules studied in the context of their potential to reduce risk factors shown to directly affect CVD risk [10]. Moreover, there has been a significant amount of research in determining the underlying mechanism of action by which omega-3 might reduce CVD and it is likely that these compounds may have roles in regulating cell membrane properties or intracellular signal transduction [8].

The recommended daily intake of omega-3 food supplement is highly variable and depends on the individual user's health profile in terms of their cardiac function, blood pressure levels, blood triglyceride (TG) levels, and other health parameters. This has made it difficult for regulators, specifically the European Food Safety Authority's (EFSA) panel on Dietetic Products, Nutrition, and Allergies to set a standard intake level. However, there is a proposed adequate daily intake of 250 mg for EPA + DHA for all adults for normal health and wellness [11]. The typical amount level found in a single 1,000 mg non-concentrated omega-3 supplements capsule is 250 mg to 300 mg of EPA+DHA [11]. On the other hand, EFSA has investigated the quantity of EPA+DHA required for specific health benefits in the context of assessments of applications for health claims authorisations. These opinions indicate that on the basis of the research reviewed by EFSA, an intake of 2g of EPA/DHA is required for the maintenance of normal blood triglyceride levels and 3 g for the maintenance of normal blood pressure [12, 13].

The omega-3s EPA and DHA are the primary molecules studied in the context of their potential of reducing risk factors shown to directly affect the risk of a CVD-attributed event.

It is expected that if there is significant relative risk reduction found for a given country's target population of all adults aged 55 and older using omega-3 fish oil supplements, it is likely that there are also significant economic benefits to be realised.

The effect of omega 3 fatty acids is most likely the result of the cumulative effect of many cardiovascular-attributed aspects for which plausible biological mechanisms exist. A significant portion of the scientific literature suggests at least 1,000 mg of EPA + DHA per day is needed in order to realise observed health benefits of reduced risk of experiencing a costly CVD-attributed event and preferably from omega-3 EPA + DHA from fish oils.[11] The base of scientific research that explores the use of omega-3 and its impact on reducing the odds of experiencing a costly CVD-attributed event is significant and can be classified into two types – direct association and indirect association. The literature that is classified as testing for an indirect association is typically related to testing for relationships between omega-3 supplement intake and a change in a specified biomarker known to be associated to the risk of experiencing a CVD-attributed event. Examples of this type of literature related to omega-3 intake and the change in TG or BP levels.[12] These studies tend to be highly focused on specific target populations and/or conditions and effective levels of omega-3 supplements and have become much more common in the published literature in the last 5 years. The direct association literature includes studies that test for a direct association between omega-3 intake and the reduction of the risk of CVD-attributed event. Typically these types of studies are randomised controlled trials (RCTs) that literally count the number of CVD-attributed medical events that occur between a control population not using an omega-3 supplement and an experimental population that is using the omega-3 supplement. The direct association scientific literature tends to be easier to determine omega-3 use and the number of possible avoided events that can be realised because there is no need to determine the functional relationship between the omega-3 intake and a given mechanism of action of interest.

There have been various attempts at pooling the body of scientific literature using systematic review techniques to derive an overall level of expected efficacy, some of which resulted in mixed conclusions [14, 15, 16, 17, 18]. However, care should be taken to compare the results of one meta-analysis versus another because the greatest determinants to the variance in conclusions across these omega-3 studies are the study inclusion selection process adopted by the researcher, the researcher's definition of an event, and the researcher's interpretation of the results. An example of this debate is demonstrated in the work of Rizos et al. (2012), which reported that there was "no effect" on cardiovascular event rates when using an omega-3 food supplement [14]. This study aggregated the results of a set of 20 RCT studies representing an aggregated sample of 68,680 people that looked at all-purpose deaths, cardiac-attributed deaths, heart attacks, and/or strokes separately.

11 See Method section for a description of the studies used to deduce the effective quantity of intake for this case study.
12 Additional insights on the state of the indirect association scientific literature are provided in the Discussion section at the end of this study.

The authors concluded that there were no statistically-significant benefits derivable from the use of omega-3 on any of the event outcomes tested. However, the authors' interpretations of the results were strict due to the use of a p-value of 0.006 instead of the generally acceptable p-value of 0.05 and because the authors solely focusing on the null and negative results to infer their conclusions. The study does report statistically significant positive results in terms of reduced risk of a cardiac-attributed death and nearly statistically significant reductions in all-purpose and sudden cardiac death and heart attacks. Plus, the authors looked at each CVD event outcome independent of the other possible CVD-attributed event outcomes. This has the effect of reducing the sample size of each case study, and consequently, increasing the finding's statistical insignificance.

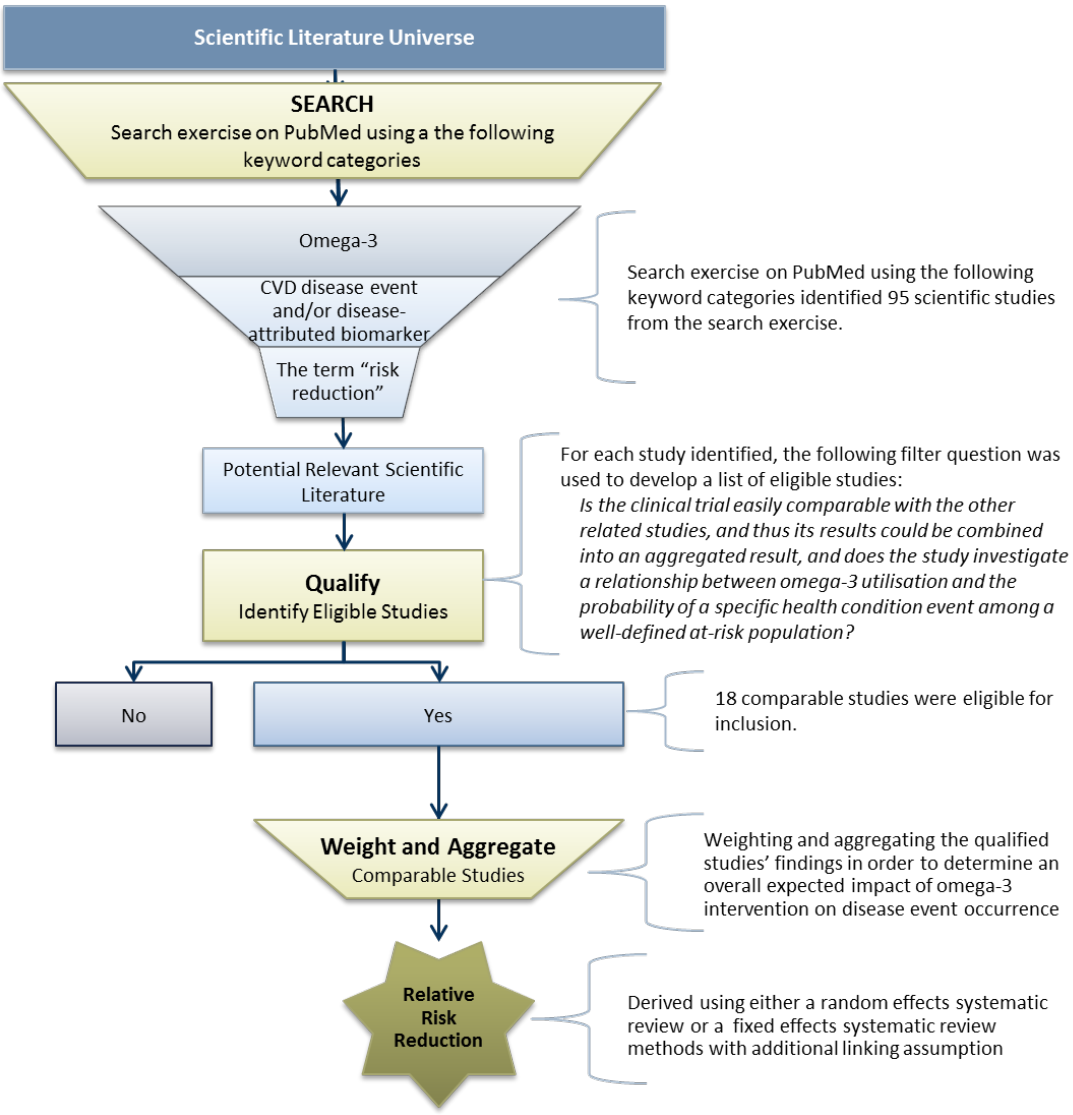
An example of an incomparable meta analysis due to variance in researcher's search criteria and definition of a CVD event is the work of Kotwal et al. (2012) [15]. These researchers conducted a meta analysis of studies that looked at Omega 3 food supplements, dietary (food) interventions, or both and cardiovascular outcomes. Twenty articles were included in this analysis representing 63,030 participants and the authors reported null results on a composite of cardiovascular events and cardiovascular deaths [15]. However, this meta analysis aggregated the results of both supplement regimens and food interventions which varies widely in EPA+DHA usage rates and the basis of the calculation of each qualified study's inclusion weight is not clear. Despite their methods, they did report statistically significant effects on CVD-attributed deaths [15]. Wen, Dai and Gao (2013) adopted a much stricter definition of the study participants, the definition of cardiovascular disease events included, and the study inclusion criteria [16]. Consequently, they too reported null results for omega-3's effect on overall cardiovascular events, but, like Rizos et al. (2012) and Kotwal et al. (2012) did find statistically significant results on CHD-attributed deaths.

Another important observation on the state of the science related to omega-3 food supplement intervention has been made by Rice et al (2016) in their article reporting proceedings of a workshop held at a conference of the International Society for the Study of Fatty Acids and Lipids in 2014 [18]. The authors recognize that there has been a shift in expected reported relationship between intake of EPA+DHA omega-3 supplements and lower risk of CVD-attributed outcomes from mostly statistically significant to null over the last several decades [18]. The authors state that there has been significant changes to overall research protocols related to omega-3 clinical studies over time such as the greater use of other more aggressive CVD drug treatments that overshadow or offset the benefits of omega-3 among study participants, higher baseline serum levels among study participants without the associated change in dosage size due to higher omega-3 intake through dietary intervention outside of the study's requirements, intake of other lipids that can effect omega-3's efficacy such as omega-6 fatty acids, and an increasing lack of clarity of the mechanisms of action that is expected to be measured [18]. All of these changes makes it increasingly difficult to compare and aggregate the results of older studies versus newer findings and overall creates more uncertainty of omega-3's expected benefits and provide overarching recommendations.

Due to the increasing number of mixed results from recent meta analyses, a new random-effects systematic review of the omega-3 literature was conducted in order to deduce the expected effect on the occurrence of a CVD-attributed event from using an omega-3 food supplement [19, 20, 21]. This approach allow for an objective way to weighing each of the included study's findings and combining them to estimate an expected risk reduction factor that can be used to estimate the number of avoided CVD-attributed events if a given person were to use an omega-3 food supplement. The studies selected for this analysis tested for a direct causal relationship between the intake of an omega-3 food supplement and the risk of a CVD hospitalisation event or death. Randomised controlled trials (RCT) were preferred because they are designed to test for a direct relationship between omega-3 utilisation and event outcome. Studies were not selected on the basis of the magnitude, direction, or statistical significance of the reported findings. See the appendix for a detailed discussion on the calculation of the study weights used in this case study's literature review analysis.

A search exercise was conducted in March 2015 and 95 studies published up to December 2014 were identified in the National Center for Biotechnology Information (NCBI) PubMed database based on the keywords "omega-3" or "polyunsaturated fatty acids"; "coronary heart disease" or "cardiovascular disease"; and "risk reduction" as filtering keywords [22]. The term "risk reduction" and its variants were added in order to ensure that we were identifying studies that tested for explicit hypotheses related to change in risk of a CVD event. Eighteen RCT studies were identified as being eligible for analytical assessment and were used to infer efficacy. The treatment groups received omega-3 as a mixture including EPA and DHA—except in one study that administered EPA alone—with intakes ranging from 0.6 to 3.4 g of EPA and DHA per day in capsule form. The weighted average intake level of EPA and DHA was 1.14 g per day in capsule form. An intervention or placebo was given for various durations across the studies, ranging from 1 to 5 years. Chart 4 shows the process by which studies were selected for inclusion in the systematic review.

Chart 4
Omega-3 Food Supplement Literature Review Process[13]



18 studies were identified that tested for a change in relative risk for CVD events given omega-3 use compared with a placebo control group.

All 18 studies tested for a change in relative risk for CVD events given omega-3 use compared with a placebo control group. Reported primary outcomes usually included total deaths, as well as deaths due to cardiovascular reasons, myocardial infarctions (MI), angina pectoris, intervention by implanted cardioverter/defibrillator, and hospital admission due to cardiovascular reasons, stroke, and other specified events.

13 Source: Frost & Sullivan

The relative risk reduction of a CVD event requiring the utilisation of medical services, given the daily use of omega-3, is 4.9%.

For the purpose of this study, each of these outcomes was considered as a CVD event, as each uses healthcare services to some degree and would be recorded as a hospital event. Hence, the size of the effect of omega-3 supplement use on the occurrence of these outcomes can be directly inserted into the cost model.

Overall, it is expected that the relative risk reduction of a CVD event requiring the utilisation of medical services, given the effective daily use of omega-3, is 4.9% (95% CI: 3.3% to 6.4%) after controlling for variance due to sample size, research methodologies and study protocols, and patient population within and among all studies. The results of the literature review conducted for this case study is presented in Table 3.

Table 3
Omega-3 Literature Review: Expected Avoided Hospital Separation Results

Author	Year	Daily amount (grams of EPA+DHA)	Total sample (N)	TER[14]	CER[15]	Relative risk (RR)	Study weight
Leaf [23]	1994	0.59	551	0.00%	0.72%	0.00%	9.57%
Sacks et al. [24]	1995	4.8	80	17.07%	28.21%	60.53%	0.69%
Leng [25]	1998	0.27	120	28.33%	30.00%	94.44%	0.85%
Von Schacky [26]	1999	0.75	223	1.79%	6.31%	28.32%	4.81%
GISSI-prevenzione [27]	1999	0.85	11334	9.65%	10.73%	90.00%	9.48%
Nilsen [28]	2001	3.4	300	32.00%	26.67%	120.00%	1.89%
Burr [29]	2003	0.5	3114	11.46%	8.75%	130.96%	8.44%
Leaf [30]	2005	2.6	2501	6.46%	6.09%	106.15%	8.69%
Raitt [31]	2005	0.54	200	48.00%	49.00%	97.96%	1.14%
Brouwer [32]	2006	0.6	546	56.04%	57.14%	98.08%	2.63%
Svensson [33]	2006	1.7	206	60.19%	57.28%	105.08%	1.20%
Yokoyama [34]	2007	1.8	18645	4.61%	5.22%	88.41%	9.81%
GISSI-HF [35]	2008	0.85	6975	67.17%	70.44%	95.36%	8.36%
Galan [36]	2010	0.6	2501	6.46%	6.09%	106.15%	8.69%
Einvik [37]	2010	2.4	563	11.39%	12.77%	89.21%	4.59%
OMEGA Study Group [38]	2010	1.0	3453	10.39%	8.76%	118.59%	8.62%
Nodari [39]	2011	1.0	133	14.93%	39.39%	37.89%	1.04%
Risk and Prevention Study Collaborative Group [40]	2013	1.0	12,513	9.93%	11.88%	83.55%	9.50%

Metric	Measure
Weighted relative risk of a CVD-attributed hospital separation RR(x)	0.951 (95% CI: 0.936 to 0.982)
Weighted relative risk reduction of a CVD-attributed hospital separation RRR(x)	4.9% (95% CI: 6.4% to 3.3%)

14 TER: % of subjects in treatment group who experienced event relative to number in the treatment group
15 CER: % of subjects in control group who experienced event relative to number in the control group

Methods

This report explores the possible direct economic benefits derived from the daily use of a 1,000 mg omega-3 regimen by way of reducing the odds of experiencing a costly CVD-attributed medical event or a hospital discharge. Specifically, this report outlines a systematic approach to understanding and evaluating the scientific literature related to omega-3 use and CVD risk reduction, and shows how to translate these expected health benefits into economic net benefits in terms of avoided health care costs [41].

The direct economic benefits derived from the daily use of a 1,000 mg omega-3 regimen can be deduced by determining the difference in odds of experiencing a costly CVD-attributed medical event between use versus non-use.

To determine the number of CVD events that could be avoided from the use of an omega-3 regimen, two scenarios must be compared and modelled on the structure of a randomised clinical trial. In addition, the expected risk (***Risk***) of a specified target population experiencing a certain disease event must be known. The first theoretical scenario is a control scenario which will be representative of the case of non-use. This scenario is not the current state of affairs because there are already users of omega-3 food supplements in the EU. Specifically, it is expected that the EU as a whole reflects similar omega-3 consumption trends when compared to the U.S. or Australia, which is approximately 20% of the target population uses omega-3 in these two countries. The second scenario is the case of everybody who needs it, uses it. This second scenario, the experimental scenario, is also the maximum amount of benefit that is possible for the given target population. Once these two scenarios are developed in terms of determining how many people are in the specified target population, then a measure of total benefit in terms of avoided events can be calculated if the relative risk of omega-3 users versus non-users is known.

Relative risk (***RR***) is a measure of expected efficacy of a given regimen under study and this measure in turn can be used to determine the number of people who would need to follow a given regimen in order to prevent one disease-attributed event. In the case of omega-3, it can be shown that the number of people who would need to utilise a 1,000 mg omega-3 daily regimen in order to prevent one CVD-attributed event, defined as ***N*** is simply the inverse of the difference between observed risk of the control state (subscript i) and the observed risk of the treatment state (subscript j), or:

$$1.\ N = \frac{1}{Risk_i - Risk_j} = \frac{1}{Risk_i - Risk_i * RR_{j/i}}.$$

The number of possible avoided events (**A**) if everybody in a specified target population used omega-3 is simply the total target population (***Pop)*** divided by (***N)***, *or:*

$$2.\ A = \frac{Pop}{N} = Pop * (Risk_i - Risk_i * RR_{\frac{j}{i}}),$$

Table 4 provides a list of the key variables used to conduct this health-to-wealth theoretical economic analysis.

An average of one CVD-attributed hospital event is avoided for every 84 daily users of a 1,000 mg of 100% EPA + DHA equivalent supplement regimen among EU adults age 55 and older.

Table 4
List of Key Variables used in this Economic Analysis

A	Number of possible avoided events (A) if everybody in a specified target population used omega-3
B	total potential net economic benefits yet to be realised from use of a 1,000 mg omega-3 food supplement
B/Pop	Net Benefit per User
C	Total cost of an omega-3 regimen
d	The expected per person cost of omega-3 utilisation per year
h	The expected cost of a CVD-attributed medical event
N	Number needed to treat
Pop	Target Population
S	Total potential savings from reduced hospital service utilisation following CVD-attributed hospital events that are realizable if the entire target population were to sufficiently utilise a 1,000 mg omega-3 food supplement
S/C	Benefit Cost Ratio

Knowing that 4.9% relative risk reduction can be expected between the two scenarios of non-use versus 100% use of omega-3 (page 14), it is expected that an average of one CVD-attributed hospital event is avoided for every 84 daily users of a 1,000 mg of 100% EPA + DHA equivalent supplement regimen among EU adults age 55 and older. This corresponds to over 1.5 million avoided CVD-attributed hospital events throughout the European Union over the next five years (2016 to 2020). However, likely risk reduction benefits from using a 1,000 mg of 100% EPA + DHA equivalent supplement regimen per day varies by EU country based on the observed CVD-attributed event rates of each country. For example, one out of only 32 people who use a 1,000 mg of 100% EPA + DHA equivalent supplement regimen per day will avoid one CVD-attributed hospital event in Lithuania because of the nation's population's relatively high risk of experiencing a CVD-attributed event. On the other hand, only one person out of 569 people who use a 1,000 mg of 100% EPA + DHA equivalent supplement regimen per day will avoid a CVD-attributed hospital event in the relatively healthy country of Cyprus. The total number of avoided CVD-attributed events is presented in Chart 6 and Table 5.

Chart 5
Total Avoided CVD-attributed Events from use of Omega-3 Food Supplements, Europe, 2015

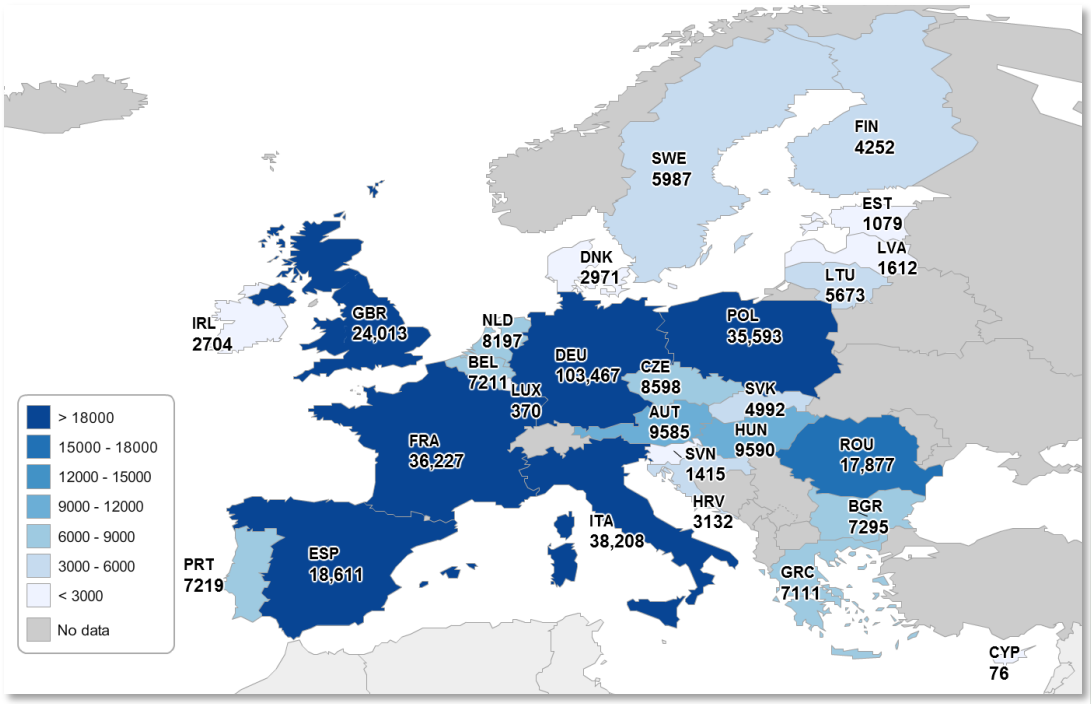
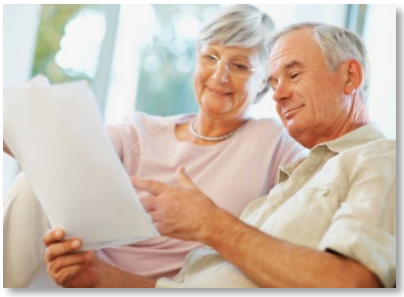


Table 5
CVD Benefits from Omega-3 EPA + DHA Supplement Use: Average Expected Relative Risk Measurements by EU Country, 2016-2020

Country	N: Number of people using Omega-3 per Avoided CVD-attributed Event	A: Total Avoided CVD-attributed Events from use of Omega-3 Food Supplements, Annualised Average
Austria	54	9,585
Belgium	94	7,211
Bulgaria	66	7,295
Croatia	87	3,132
Cyprus	569	76
Czech Republic	75	8,598
Denmark	115	2,971
Estonia	76	1,079
Finland	85	4,252
France	111	36,227
Germany	54	103,467
Greece	100	7,111
Hungary	65	9,590
Ireland	78	2,704
Italy	106	38,208
Latvia	78	1,612
Lithuania	32	5,673
Luxembourg	76	370
Malta	121	223
Netherlands	124	8,197
Portugal	90	7,219
Poland	64	35,593
Romania	67	17,877
Slovakia	58	4,992
Slovenia	92	1,415
Spain	147	18,611
Sweden	100	5,987
United Kingdom	153	24,013
Total EU	84	373,290

Source: Frost & Sullivan analysis

Study Results



The economic analysis presented in this analysis is used to assess various cost scenarios and to identify the potential savings or loss that can be realised if one scenario of events occurred versus another.

The economic analysis presented here is used to assess the potential savings or loss that can be realised if one scenario of events occurred versus another [21]. The model compares the following two extreme scenarios in order to deduce the total savings potential: A) the hypothetical case of zero usage of omega-3 EPA + DHA supplements versus B) 100% utilisation of omega-3 among a specified target population. The difference between the two scenarios is the total potential savings (or loss) that is possible through 100% utilisation of omega-3 at protective intake levels and can also be interpreted as the total monetary value of all possible avoidable events if everyone used omega-3 at protective intake levels.

The model used to determine the total potential benefits of using omega-3 is simply $B = S - C$ where S is the avoided expenditures related to CVD-attributed hospital service utilisation and the cost of omega-3 utilisation at effective intake levels is represented by the parameter $\boldsymbol{C}$ The result of this calculation provides an economic indication of the net monetary benefits $\boldsymbol{B}$ that the use of omega-3 can yield for society through hospital cost reduction and increased productivity due to avoided bed rest and loss of life. As shown in equation 1, excluded from the net benefit calculations include all future residual quality of life gains from avoided CVD-attributed hospital events and CVD deaths and all other net benefits from using omega-3 daily not related to CVD-attributes events explored in this study. In the following section, a description of the calculation of each of the aforementioned parameters is provided.

The total potential savings from reduced hospital service utilisation following CVD-attributed hospital events that are realizable if the entire target population were to sufficiently utilise a 1,000 mg omega-3 food supplement can be expressed as:

$$3.\ S = h * A = \frac{h * Pop}{N}$$

The term $\boldsymbol{h}$ is the expected cost of a CVD-attributed medical event and $\boldsymbol{A}$ is the total number of people within the target population expected to avoid a costly CVD-attributed event (see page 17). It should be noted that a percentage of the target population already uses an omega-3 regimen and, therefore, these people should be accounted for if possible. An easy way to do this is to observe the population's purchasing behaviour from consumer research. The cumulative net savings achieved over consecutive years can also be calculated by summing the annual output over the indicated years while discounting future year's annual output to their present value using the term $(1 + r)^{-t}$ and cumulative cost can determined by dividing the cumulative net savings by the number of years *t*.

If net health care cost savings is positive, then the regimen in question should be considered an effective means to help reduce overall CVD-attributed healthcare costs.

The total cost of an omega-3 regimen, assuming 100% utilisation by the entire observed population can be represented by $C = Pop * d$ where *Pop* is the total number of people in the target population at risk of experiencing a CVD-attributed event outcome and d is the expected per person cost of omega-3 utilisation per year. Note that the entire target population must take the given regimen in order for the total number avoided events to be realised.

Regarding other research assumptions for this analysis, the compound annual growth rates were derived from a historic assessment of population growth rates, costs, and prices. Specifically, healthcare costs per person are likely to grow at an average annual growth rate of 4% from 2013 to 2020 [42]. Growth in the target EU population of all adults age 55 and older is likely to occur at a compound average annual growth rate of 3.6% during the forecast period, which is adjusted by individual country growth dynamics. Omega-3 retail prices are likely to grow at a compound annual growth rate of 2% per year. All future expenditures on healthcare costs and omega-3 were at a 3% discount rate, which is in line with health economic methods promoted by the World Health Organisation to reflect the present value of estimated future expenditures and net savings and control for inflationary effects [43].

Thus, combining the terms outlined in equations 2 and 3, the model used to estimate the total potential net economic benefits yet to be realised from use of a 1,000 mg omega-3 food supplement regimen in the EU is as follows:

$$4.\ B = S - C = h * A - Pop * d$$

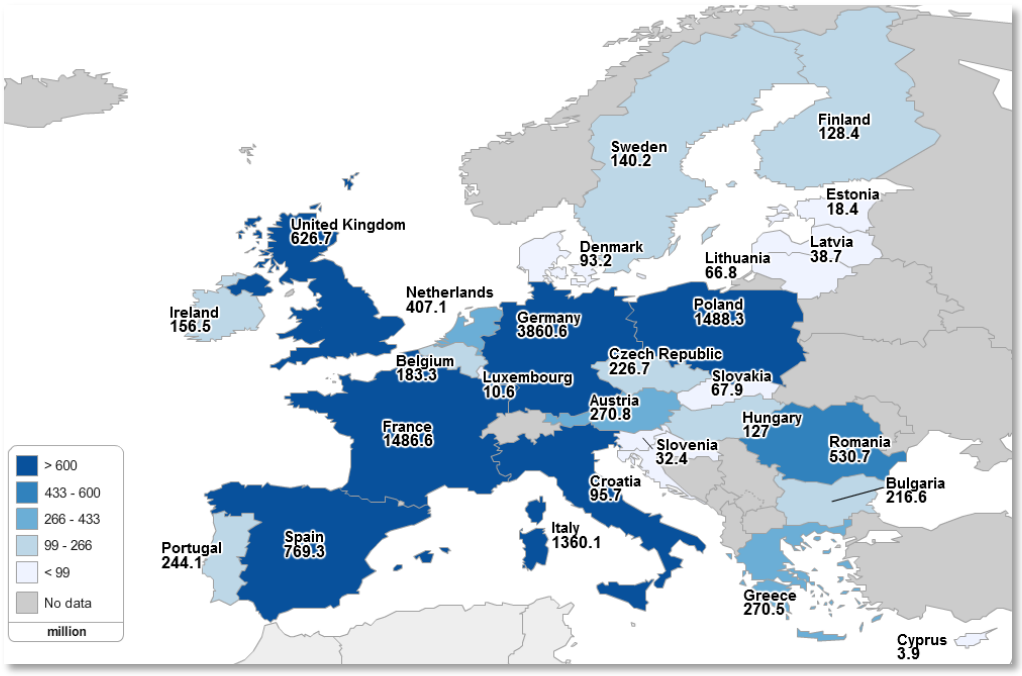
Overall, if the possible net health care cost savings is positive, then the regimen in question should be considered an effective means to help reduce overall CVD-attributed healthcare costs.

It should be noted that not all costs and benefits from using or not using an omega-3 supplement are incorporated into this equation. This equation is a generalised model that determines the net economic effect of using a given food supplement on the odds of a predefined set of event outcomes. Because of the additive nature of the model, one can easily add in additional expected health benefits that are related or not related to the disease condition of interest. However, for the purposes of this study, the cost and benefits mix is conservatively defined to be in line with the hypothesised relationship between omega-3 supplement use and a specified disease-attributed event. Table 6 and Chart 6 show the total healthcare costs savings that are possible from avoided CVD-attributed hospital events by EU country.

Given a mean per-event expenditure on a CVD-attributed hospital event of € 34,637, after controlling for purchasing power variance across EU countries, it is expected that the total annual average potential avoided expenditures related to CVD-attributed hospital service utilisation, S, for all represented EU adults age 55 and older would be as much as € 12.9 billion per year if the entire target population utilised a 1,000 mg of 100% EPA + DHA equivalent supplement daily (Table 5). Regarding the total annual average potential avoided expenditures related to CVD-attributed hospital service utilisation by EU country, Cyprus has the lowest potential savings (€ 3.9 million per year) and Germany had the highest potential savings (€ 3.8 billion per year) in avoided hospital event costs per year.

Total avoided expenditures related to CVD-attributed hospital service utilisation for all represented EU adults age 55 and older would be as much as € 12.9 billion per year if the entire target population utilised a 1,000 mg of 100% EPA + DHA supplement daily.

Chart 6
Total Avoided Cost of CVD-attributed Hospital Events from Omega-3 EPA + DHA Supplements Utilisation (S), € million, Europe, Annualised Average, 2016-2020



Source: Frost & Sullivan analysis

Table 6
Economic Benefits from Omega-3 EPA + DHA Supplements Use: Avoided Costs of Hospital Events by EU Country, 2015

Country	**S:** Expected 1 Year Total Avoided Cost of CVD-attributed Events	**C:** Total Cost of Omega-3 per year	**B:** Net Benefit
Austria	€ 270,755,588	€ 100,428,849	€ 170,326,739
Belgium	€ 183,314,302	€ 131,956,797	€ 51,357,505
Bulgaria	€ 216,555,450	€ 60,682,384	€ 155,873,067
Croatia	€ 95,706,512	€ 31,264,920	€ 64,441,591
Cyprus	€ 3,943,823	€ 1,144,068	€ 2,799,755
Czech Republic	€ 226,740,220	€ 85,824,011	€ 140,916,209
Denmark	€ 93,184,757	€ 69,201,440	€ 23,983,317
Estonia	€ 18,408,373	€ 12,559,957	€ 5,848,416
Finland	€ 128,445,622	€ 84,885,365	€ 43,560,257
France	€ 1,486,559,421	€ 602,677,245	€ 883,882,176
Germany	€ 3,860,632,015	€ 1,721,270,534	€ 2,139,361,481
Greece	€ 270,527,002	€ 94,645,561	€ 175,881,441
Hungary	€ 127,016,520	€ 95,724,996	€ 31,291,525
Ireland	€ 156,480,081	€ 49,486,148	€ 106,993,933
Italy	€ 1,360,073,791	€ 635,626,663	€ 724,447,128
Latvia	€ 38,742,268	€ 18,766,793	€ 19,975,474
Lithuania	€ 66,811,707	€ 56,624,300	€ 10,187,407
Luxembourg	€ 10,610,739	€ 7,386,523	€ 3,224,216
Malta	€ 8,566,492	€ 2,966,192	€ 5,600,300
Netherlands	€ 407,070,041	€ 149,996,577	€ 257,073,464
Portugal	€ 244,096,564	€ 108,082,739	€ 136,013,826
Poland	€ 1,488,303,677	€ 355,279,304	€ 1,133,024,373
Romania	€ 530,670,764	€ 148,702,639	€ 381,968,125
Slovakia	€ 67,939,270	€ 58,135,754	€ 9,803,516
Slovenia	€ 32,430,048	€ 18,833,928	€ 13,596,120
Spain	€ 769,343,132	€ 278,646,583	€ 490,696,549
Sweden	€ 140,165,423	€ 129,490,304	€ 10,675,119
United Kingdom	€ 626,704,760	€ 527,313,494	€ 99,391,266
Total EU	€ 12,929,798,360	€ 5,637,604,066	€ 7,292,194,294

Source: The World Bank, Innova Market Insights [44] and Frost & Sullivan analysis

In order to capture these potential cost savings from avoided CVD-attributed events, the purchase and utilisation of omega-3 food supplements is required. Thus, the expected total benefits can be adjusted to reflect this additional cost. However, the cost of omega-3 food supplements, like other healthcare costs, varies by country and distribution channel. Thus, the cost of omega-3 food supplements ought to vary to reflect these economic realities and one way to control for this variance is to adjust observed market prices by the purchasing power of each country's citizens. According to the World Bank, purchasing power parity (PPP) is a factor that adjusts a given country's domestic value of a Euro required to buy a given product to a baseline country's value of a Euro. For the purposes of this analysis, the purchasing power of a Euro in Belgium was assumed to be 100 versus the other European Union countries [43].[16] It should be noted that PPP merely reflects the relative value of a Euro across two and more countries and does not establish the baseline value of a Euro.

The median cost of using a single 1,000 mg of EPA + DHA across the five countries is approximately €0.44 per day, or approximately €150 per person per year.

It is expected that the consumer cost of a 1,000 mg of 100% EPA+DHA omega-3 ranges from as low as € 0.25 per 1,000 mg to more than € 0.90 per 1,000 mg based on a review of 55 omega-3 products sold in France, Germany, Italy, Spain, and the United Kingdom from the Innova Database[17] [44]. The median cost of using a single 1,000 mg of EPA+DHA across the five countries is approximately € 0.44 per day, or approximately € 150 per year. This median price was then weighted by each country's PPP ratio in order to best represent the expected variance in omega-3 food supplement prices observed in the market. Furthermore, these PPP-adjusted daily regimen prices was then scaled up to reflect expected annual prices and then multiplied further by the total number of people age 55 and older at risk of experiencing a CVD event per country in order to reflect expected total social costs of 100% utilisation of omega-3 food supplements.

This median price was then weighted by each country's PPP ratio in order to best represent the expected variance in omega-3 food supplement prices observed in the market. Furthermore, these PPP-adjusted daily regimen prices was then scaled up to reflect expected annual prices and then multiplied further by the total number of people age 55 and older at risk of experiencing a CVD event per country in order to reflect expected total social costs of 100% utilisation of omega-3 food supplements. Thus, the cost of omega-3 EPA + DHA daily utilisation required to realise CVD benefit by the total target population of all EU adults age 55 and older at risk of experiencing a CVD event per year, *C*, is expected to be € 5.6 billion per year.

Note that the maximum potential cost of omega-3 food supplement utilisation is significantly less than the total annual average potential avoided expenditures related to CVD-attributed hospital service utilisation, S, for all represented EU adults age 55 and older (€ 12.9 billion per year). This suggests that even if the cost of omega-3 food supplement are taken into account, there is still significant cost savings to be realised. Table 7 shows the expected daily and annual costs of using 1,000 mg of omega-3 daily in the EU after ensuring purchasing power parity across all EU countries and the total potential cost of omega-3 food supplements per country.

Table 7

16 The World Bank. http://data.worldbank.org/indicator/PA.NUS.PPPC.RF
17 Innova Market Insights. http://www.innovadatabase.com/login/index

Omega-3 EPA + DHA Supplements: Expected Consumer Price per 1,000 mg of EPA/DHA omega-3 per EU Country, adjusted for Purchasing Power Parity, 2015/2016

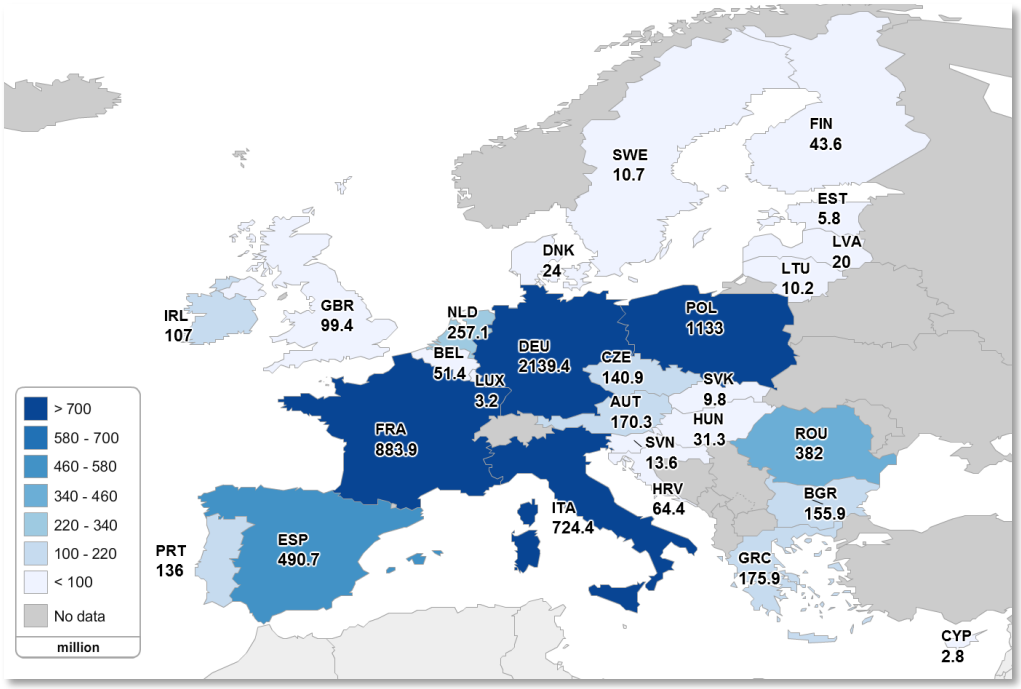
Country	d/day: Average Daily Cost of 100% EPA/DHA Omega-3, € /1,000 mg	d: Average Annual Cost of 100% EPA/DHA Omega-3, € /year	PPP: Purchasing Power Parity Weights, 2014/2015 (Belgium € = 100)
Austria	€ 0.48	€ 174.55	98
Belgium	€ 0.49	€ 178.11	100
Bulgaria	€ 0.22	€ 80.96	45
Croatia	€ 0.27	€ 97.15	55
Cyprus	€ 0.40	€ 145.73	82
Czech Republic	€ 0.27	€ 97.15	55
Denmark	€ 0.62	€ 226.68	127
Estonia	€ 0.31	€ 113.34	64
Finland	€ 0.53	€ 194.30	109
France	€ 0.44	€ 161.92	91
Germany	€ 0.44	€ 161.92	91
Greece	€ 0.35	€ 129.53	73
Hungary	€ 0.27	€ 97.15	55
Ireland	€ 0.49	€ 178.11	100
Italy	€ 0.44	€ 161.92	91
Latvia	€ 0.31	€ 113.34	64
Lithuania	€ 0.27	€ 97.15	55
Luxembourg	€ 0.53	€ 194.30	109
Malta	€ 0.35	€ 129.53	73
Netherlands	€ 0.49	€ 178.11	100
Portugal	€ 0.40	€ 145.73	82
Poland	€ 0.27	€ 97.15	55
Romania	€ 0.22	€ 80.96	45
Slovakia	€ 0.31	€ 113.34	64
Slovenia	€ 0.35	€ 129.53	73
Spain	€ 0.40	€ 145.73	82
Sweden	€ 0.58	€ 210.49	118
United Kingdom	€ 0.59	€ 213.73	120
Total EU	€ 0.44	€ 144.56	98

Source: The World Bank, Innova Market Insights and Frost & Sullivan analysis

Overall, the total net benefit for the entire EU target population of 1,000 mg of omega-3 EPA + DHA daily users, *B*, is € 7.3 billion per year. This means that for every € 1.00 spent on a 1,000 mg of omega-3 EPA + DHA daily regimen, there would be a certainty equivalent return of € 2.29 to society in the form of avoided healthcare expenditures attributed to CVD. In other words, there would be a significant portion of cost savings to the primary payers of healthcare costs, which include governments and insurance companies. In fact, all 28 EU countries have benefit cost ratios greater than € 1.00 which is an indication of cost effectiveness as shown in Table 8 and Chart 9. The greatest net benefits are found in Germany, where an expected annualised net benefit from avoided CVD-attributed healthcare costs is € 2.1 billion per year from 2016 to 2020. Germany is followed by Poland and France with € 1.1 billion and € 884 million in per year in total net benefits, respectively. Chart 7 shows the net benefits from avoided CVD-attributed events through the use of omega-3 EPA + DHA supplements at effective intake levels. Tables 6 and 8 describes the detailed results of the economic analysis by EU country.

The total net benefit for the entire EU target population of 1,000 mg of omega-3 EPA+DHA daily users, B, is €7.3 billion per year. This also means that for every € 1.00 spent on a 1,000 mg of omega-3 EPA+DHA daily regimen, the user can expect a certainty equivalent return of € 2.29.

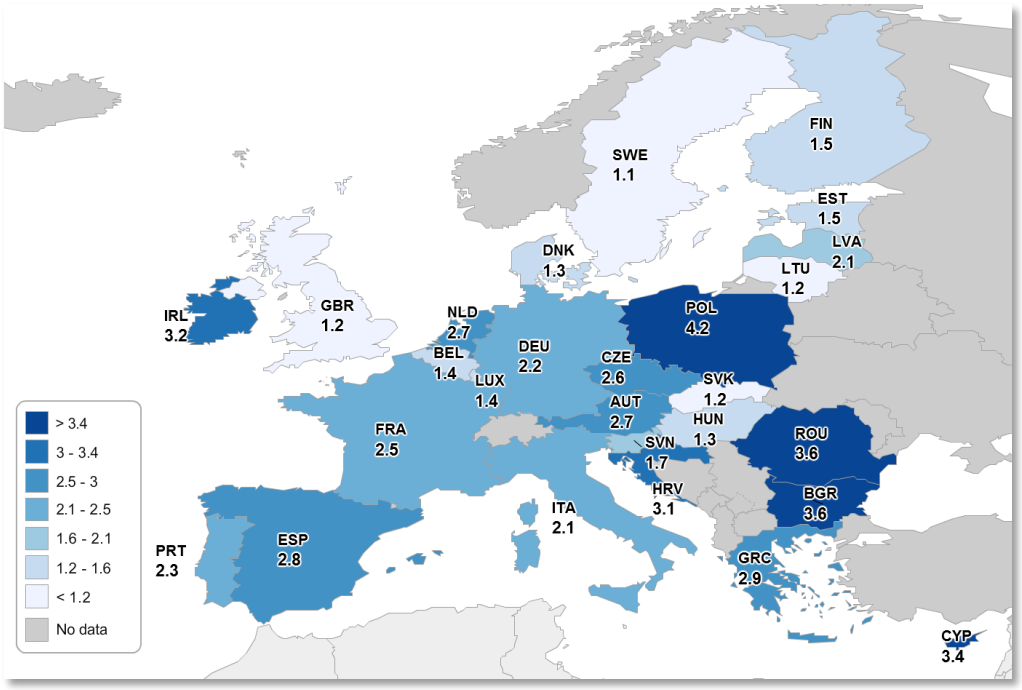
Chart 7
Annualised Expected Net Economic Benefit from Avoided Cost of CVD-attributed Hospital Events from Omega-3 EPA + DHA Supplements Utilisation, € Million, Europe, 2016 to 2020



Source: Frost & Sullivan analysis

All 28 EU countries have benefit cost ratios greater than € 1.00 which is an indication of omega-3 food supplement's cost effectiveness.

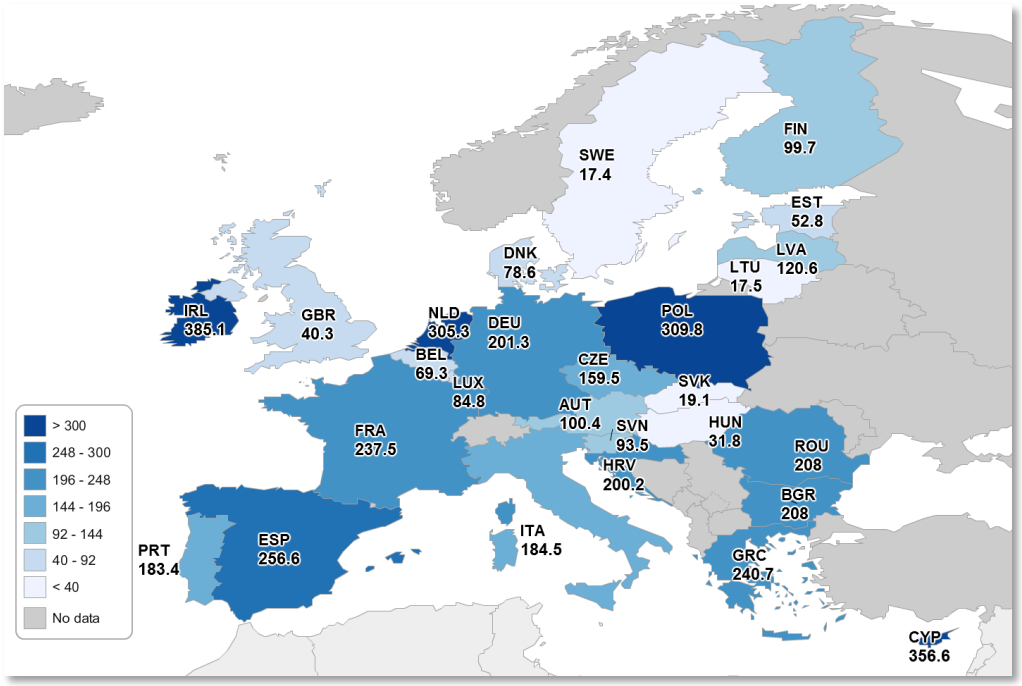
Chart 8
Benefit Cost Ratio (Avoided Costs and Gains per € 1 Spent on Omega-3), Europe, Annualised Average 2015



Source: Frost & Sullivan analysis

As shown in Chart 9 and Table 8, the average net benefits per omega-3 food supplement user from the target population of adults age 55 and older at risk of experiencing a CVD-attributed event in the EU was € 188 per person. However, net avoidable CVD-attributed costs per person per year highly varies and is dependent on relative healthcare costs in each country and the risk of that given individual experiencing a CVD-attributed event. Specifically, the net benefits per person in Ireland (€ 385 per person) are the greatest due to Ireland's high cost of healthcare and its moderately high CVD event risk rate. On the other hand, the net benefits per person in the eastern European Union countries of Slovakia, Hungary, Lithuania, and Estonia are relatively lower (less than € 50 per person) due to lower healthcare cost burden these countries have even after adjusting for purchasing power parity. Overall, there is a strong negative correlation between CVD event risk and the average PPP-adjusted cost of a CVD-attributed hospital event across EU countries. This does not mean that individuals in these countries would not significantly benefit from using omega-3 supplements daily, because these individuals in these countries are still avoiding a significant number of costly CVD-attributed events that can lead to lower productivity and a lower quality of life.

Chart 9
Net Benefit per User (Adjusted Avoided CVD-attributed Healthcare Costs per person per EU country), € /person, Europe, Annualised Average, 2016-2020



Source: Frost & Sullivan analysis

Table 8
Net Benefit per User (Adjusted Avoided CVD-attributed Healthcare Costs per person per EU country), € 1/person, Europe, Annualised Average, 2016-2020

Country	S/C: Benefit Cost Ratio (€ Avoided Costs and Gains per € 1 spent on Omega-3)	**B/Pop:** Net Benefit per User (Adjusted Avoided CVD-attributed Healthcare Costs per person per EU country), € /person, Europe, Annualised Average, 2016-2020
Austria	€ 2.70	€ 100
Belgium	€ 1.39	€ 69
Bulgaria	€ 3.57	€ 208
Croatia	€ 3.06	€ 200
Cyprus	€ 3.45	€ 357
Czech Republic	€ 2.64	€ 160
Denmark	€ 1.35	€ 79
Estonia	€ 1.47	€ 53
Finland	€ 1.51	€ 100
France	€ 2.47	€ 237
Germany	€ 2.24	€ 201
Greece	€ 2.86	€ 241
Hungary	€ 1.33	€ 32
Ireland	€ 3.16	€ 385
Italy	€ 2.14	€ 185
Latvia	€ 2.06	€ 121
Lithuania	€ 1.18	€ 17
Luxembourg	€ 1.44	€ 85
Malta	€ 2.89	€ 245
Netherlands	€ 2.71	€ 305
Portugal	€ 2.26	€ 183
Poland	€ 4.19	€ 310
Romania	€ 3.57	€ 208
Slovakia	€ 1.17	€ 19
Slovenia	€ 1.72	€ 94
Spain	€ 2.76	€ 257
Sweden	€ 1.08	€ 17
United Kingdom	€ 1.19	€ 40
Total EU	€ 2.29	€ 188

Source: Frost & Sullivan analysis

Discussion

Omega-3 EPA + DHA Supplements have the potential to confer significant cost savings for all EU adults age 55 and old, especially for those at greatest risk of experiencing an adverse CVD event as indicated by their individual risk biomarker levels. As shown in this analysis, a significant amount of scientific research has already been conducted involving the use of 1,000 mg of EPA+DHA omega-3 and the lower risk of experiencing a CVD-attributed event. Also, there is an indication that omega-3 reduces the risk of experiencing a CVD event through a mechanism of action correlated with specific risk biomarkers such as TG and BP.

Omega-3 EPA+DHA fish oils have the potential to confer significant cost savings for all EU adults aged 55 and older, especially for those at greatest risk of experiencing an adverse CVD event.

Thus, physicians and scientists alike recommend identifying physiological risk biomarkers and managing their respective levels through changes in behaviour and adopting proven risk-reduction regimens. Furthermore, food supplements with omega-3 EPA + DHA, have a substantial and growing body of scientific research that tests the relationship between food supplement intake among a target population and changes in either observed CVD events or changes in biomarker levels that are known to indicate changes in the risk of a CVD event occurrence. Specifically in the case of omega-3 EPA + DHA, recent clinical research has focused on the benefits to TG and BP biomarker levels when using omega-3 EPA + DHA at specified levels.

For example, a significant portion of the omega-3 scientific research is focused on TG level management from the use of omega-3. High TG levels are a product of lifestyle and diet choices. Specifically, low physical activity, being overweight or obese, eating too much food at one time, and smoking are all leading predictors of having high TG levels [45]. TGs are an important component of the body's energy storage and utilisation system and it is critical to have an optimal level in the blood for normal health and wellness. However, it can be a problem if an individual's baseline TGs are too high. Baseline TGs have been shown to be positively associated with increased risk of experiencing a cardiovascular disease event, including CVD-attributed hospital events like a heart attack, metabolic syndrome (a combination condition composed of having high blood pressure, high blood sugar, obesity, and a blood lipid level imbalance), and even diabetes. However, there is still debate on the degree of association. According to Hokanson JE and Austin MA (1996), the risk of experiencing a CVD event was found to be 1.12 for men and 1.37 for women per one mmol/L of TGs, which some consider to be minor [46].

The use of omega-3 EPA+DHA fish oils has been shown to significantly reduce triglyceride baseline levels.

More recent research has shown a significant positive association between the odds of experiencing a CVD event and TG baseline levels. Sarwar et al. 2007 conducted a detailed meta-analysis of 29 studies that tested the positive association hypothesis between TG baseline levels and risk of a CVD event among 262,525 participants [47]. The study included a report of the Reykjavik (2002) and the EPIC-Norfolk (1999) clinical studies, which stated that the odds of an individual in the upper tertile of TG levels (or relatively elevated TG levels) versus an individual in the lower tertile (or normal TG levels), experiencing either a fatal or non-fatal CVD event was 1.76 (95% CI, 1.39-2.21) and 1.57 (95% CI, 1.10-2.24), respectively [48, 49]. The authors included 27 additional studies and derived an updated adjusted odds ratio of an individual in the upper tertile of TG levels versus an individual in the lower tertile experiencing either a fatal or non-fatal CVD event of 1.72 (95% CI, 1.56-1.90). In other words, the odds of an individual experiencing either a fatal or non-fatal CVD event was 72% greater for those individuals in the upper tertile of the population versus those individuals in the lower tertile.

Nordestgaard BG et al. (2007) is a prospective cohort study consisting of 13,981 participants from Copenhagen that followed participants from the late 1970s to 2004 that aimed to test the hypothesis that elevated TG levels can be used as a predictor of a myocardial infarction event (MI), an ischemic heart disease (IHD) event, and CHD-attributed death [50]. Results were reported by gender and adjusted for other risk factors including age and HDL-cholesterol levels. Among women subjects, the adjusted risk of an individual with a 1 mmol/L increase in baseline TG level experiencing an fatal MI event, an IHD event, or an CVD-attributed death was 1.41 (95% CI, 1.26-1.57), 1.25 (95% CI, 1.14-1.37), and 1.18 (95% CI, 1.11-1.26), respectively. Furthermore, the adjusted risk of a male individual with a 1 mmol/L increase in baseline TG level experiencing a fatal MI event, an IHD event, or a CVD-attributed death was 1.16 (95% CI, 1.10-1.22), 1.12 (95% CI, 1.07-1.18), and 1.18 (95% CI, 1.06-1.15), respectively.

Another example of a disease-indicating biomarker that has been shown to be influence by the intake of omega-3 food supplements is blood pressure (BP) and hypertension. Hypertension is in many ways a silent killer because it does not show many specific symptoms [51]. However, if left untreated, a number of serious complications can develop. Specifically, hypertension can cause the heart to deteriorate over time and lead to a higher risk of experiencing a heart disease event, a heart attack, and heart failure. Thus, it is generally accepted that the higher the level of hypertension an individual has, the higher the chance that individual will experience an adverse CVD-attributed event.

This acceptance of the positive association between blood pressure levels and the risk of a CVD-event was substantiated in the pinnacle work of Blood Pressure Lowering Treatment Trialists' Collaboration meta-analysis, which was published in 2014 [52]. In this study, 67,475 participants from 11 clinical trials and 26 randomised groups were included in the calculation of the risk of experiencing a CVD event. The subjects were stratified by 5-year cardiovascular disease-risk quartiles and the estimated average baseline levels of 5-year cardiovascular risk for each of the four risk groups were 6.0%, 12.1%, 17.7%, 26.8% [53] The authors discovered that at each higher risk group, the use of any BP-lowering regimen relative to a placebo reduced the odds of experiencing a cardiovascular events by 18% (95% CI, 7%-27%), 15% (95% CI, 4%-25%), 13% (95% CI, 2%-22%), and 15% (95% CI, 5%-24%), respectively.

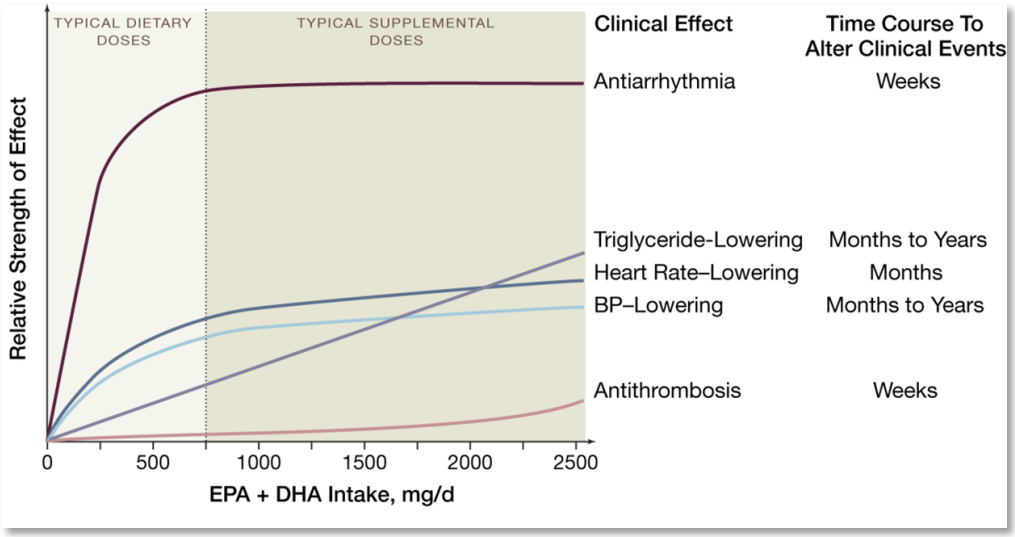
Also, a recent meta-analysis published in the American Journal of Hypertension that explored RCT studies tested for an association between the use of omega-3 EPA + DHA and changes in baseline BP levels found that the use of an omega-3 EPA + DHA supplement was associated with a reduction in SBP of -1.75 mm Hg (95% CI, -2.55 to -0.94) and a reduction in DBP of -1.11 mm Hg (95% CI, -1.75 to -0.50) [10]. The average experiment duration of the studies that the authors reviewed was 69 days or just over 2 months and the studies analysed that had the strongest effects was those where the average daily intake amount was 2 or more grams per day [10].

It should be noted that a significant portion of the scientific literature that explores the link between TG and BP levels and omega-3 use tests this association using high intake levels (> 2 grams per day) which is significantly greater than the 250 mg per day recommendation for general health and wellness by EFSA or the average 1,000 mg per day deduced from the scientific literature that tests for the association between omega-3 intake and risk of experiencing a CVD-attributed medical event [12, 13]. This suggests that it is likely that the mechanisms of action, and therefore the benefits, of using omega-3 is multifaceted and likely realizable at smaller intake levels. Specifically, Rice et al (2016) noted in a recent article that references the work of Mozaffarian D and Rimm EB (2006) that the relative protective effects of omega-3 food supplement use typically increases at a decreasing rate for a wide range of CVD-related biomarkers as shown in Chart 10 [18, 54].

It is likely that the mechanisms of action, and therefore the benefits, of using omega-3 is multifaceted and likely realizable at smaller intake levels.

Chart 10

Relative protective efficacy for a selected number of cardiovascular biomarkers by daily EPA+DHA daily use size



Source: Mozaffarian D and Rimm EB (2006)

The potential healthcare cost saving calculations in this case study only include the direct and indirect expenditures most likely to be associated with the use of omega-3. These estimates do not include a number of additional benefits that can be gained from the use of omega-3, including additional monetary benefits related to avoiding other CVD related events. It also does not include productivity gains that can be derived from helping otherwise healthy people avoid CVD events, which directly impacts additional benefits to the state in the form of tax revenue. However, the economic model utilised for this

The savings calculations in this analysis are direct medical expenditures most likely to be associated with the use of omega-3 and its heart health benefits. These estimates do not include a number of additional benefits that can be gained from the use of omega-3.

analysis is a generalised model that determines the economic effect of using omega-3 on the chance a set of CVD event outcomes can be avoided, which is directly relevant to healthcare. Although the choice of codes[18] is an imprecise exercise for the assessment of the true causality and role of specific risk biomarkers and CVD in the disease outcome process, the utilised codes are probably underestimating the far more pervasive influence of CVD in health outcomes.

Due to the additive nature of the model, one can easily add in additional expected health benefits that are less directly related or potentially related to the disease condition of interest. However, for the purposes of this study, the cost and benefit mix is deliberately defined to be conservative and directly in line with the hypothesised relationship between omega-3 use and the risk of a given type of CVD event for a given time period. The total net financial benefits from using omega-3 reviewed in this study are likely to be higher than these directly measured estimates.

The prior cost-benefit analysis also makes the conjecture that in the supplementation scenario all adults over the age of 55 with CVD use omega-3 food supplements from a base of zero usage among this population segment. In other words, the calculated net savings is actually the total potential net savings. However, because a percentage of adults over the age of 55 are known regular users of omega-3, this target population segment already has a reduced risk of experiencing a costly CVD event and is already realizing omega-3's risk-reducing benefits.

According to the 2012 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs, 28% of U.S. adults over the age of 55 are regular users of omega-3/fish oil dietary supplements which implies that the remaining 72% of target population has not yet realised the potential CVD-attributed health benefits of using omega-3 [55]. Furthermore, 17% of Australians age 55 and older are regular users of omega-3 supplements implying that 83% has yet to realize the potential benefits of the supplements' regular use. Because avoided expenditures and net cost savings are a direct function of the total number of people in the target population using omega-3 food supplements, the calculation of avoided health care expenditures and net cost savings yet to be realised is simply a proportional adjustment of the total potential avoided expenditures and net cost savings. It is expected that the EU as a whole reflects similar omega-3 consumption trends when compared to the U.S. or Australia, but consumption patterns highly varies by each EU country. Thus, this is the key reason why benefits per user were calculated so that once consumption trends per EU country are known, then calculation of total potential benefits yet to be realised per country can be easily determined.

It should be noted that the reported findings from this report represent the total potential savings that could be realised if everyone in the at-risk target population used omega-3. However, it is generally agreeable that to fully realise this potential benefit that it may not be feasible to obtain given the current circumstances related to patient access and

18 For the purposes of this study, CHD is strictly defined as events associated with the following ICD /ISHMT codes: 0901 (Hypertensive diseases), 0902 (Angina pectoris), 0903 (Acute myocardial infarction), 0904 (Other ischaemic heart disease), 0907(Heart failure), 0908 (Cerebrovascular diseases), and 0909(Atherosclerosis).

availability to omega-3 food supplements, and patient and doctor level of awareness of omega-3's potential benefits. Specifically, it is expected that only a portion of these potential benefits will actually be realised. Thus, it may be best to actually focus on per capita benefits of using omega-3 or the cost benefit ratio as a means to deduce the certainty equivalent value of a CVD attributed event per person and the overall cost-effectiveness of omega-3 food supplements as a useful tool for managing the costs of CVD.

Due to data availability limitations, the current model does not follow individual people over time. This economic model currently treats all of the people in the target population per EU country as a homogeneous set of people, including the expected risk of experiencing a CVD-attributed disease-attributed event. Thus, total social benefits are measured. Actual benefits realised per individual user will be a function of the specific CVD risk they face as indicated by their risk biomarker levels. Also, the current model looks at each observed time period as a separate independent scenario analysis and thus, only average benefits are calculated on a 5-year basis. This is then adjusted by the time period and cost/price inflation. The ideal situation would be to track an individual's risk over time and also understand how individual risk factors—such as their age, gender, and specific biomarkers—vary during the same time period, and then calculate each individual's potential costs and benefits to arrive at the total target population figures. Finally, this study currently does not consider the total economic benefits that are realisable at lower intake levels; the reason being that the scientific literature is not mature enough to deduce what these health benefits are and how they tie to the utilisation of costly medical services. Future clinical research testing for a possible health and wealth benefit is required in order to fully understand these effects.

In summary, this analysis demonstrates that significant healthcare cost savings can be realised through a concerted effort to identify high CVD-risk populations and motivate them to use omega-3 EPA + DHA supplements. In this theoretical statistical and economic analysis, the total potential benefits in avoided costly CVD-related hospital events and CVD death due to the use of omega-3 EPA + DHA supplements at 1,000 mg per day would average more than € 64.6 billion over the next 5 years for the entire EU population age 55 and older. Because a significant portion of benefits is in the form of saved consumer expenditures from informal post-treatment costs, the majority of this benefit would be conferred to the final consumer of omega-3 (see page 4 for an explanation of the healthcare cost structure used for this study). In addition, the use of omega-3 fatty acids by a target population at risk of experiencing a costly CVD event also leads to derived benefits to other stakeholders, such as gained tax revenue from saved productivity, which is a benefit to the government, and from lower treatment costs incurred by both public and private healthcare payers such as private insurance companies. Overall, this health-to-wealth assessment can be used by all stakeholders including consumers, healthcare providers, employers, and policymakers as a means to better quantify the benefits of using omega-3 food supplements. Understanding this link will help key stakeholders—potential omega-3 supplement users, healthcare providers, governments, private insurance companies, and employers—make recommendations about the best course of action to help minimise current and future costs and maximise benefits.

The potential economic benefits from omega-3 use can be realised by identifying those people at the greatest risk of experiencing a costly CVD-attributed event and helping these people consider that an omega-3 regimen can be an important tool for protecting against costly CVD-attributed events.

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Appendix

Literature Review Methodology

DerSimonian and Laird (D-L) Random-effects Literature Review Methodology

For this study, a random-effects literature review model was adopted for use in cases where the dietary supplement in question had a significant number of scientific/clinical studies that explored the specific question this study aims to address: What is the impact on the odds of a disease event occurring, given the use of the dietary supplement in question? This question is in the same mold of many questions that pharmacoeconomic/clinical studies aim to address, which is the determination of an overall treatment effect on a given event outcome when a treatment regimen is applied to one group versus a control group. From these type of analyses, risk—and, subsequently, risk reduction—of an event can be calculated and applied into a cost-effectiveness model, which helps key decision makers (including physicians, patients, governments, insurance companies, and employers) determine whether it is worth the increased cost of treatment for the potential savings derived from avoided events.

However, the key problem is how one properly assesses the results of a set of studies, which we define as ***K***, that address the same research question, when each study (element of set ***K*** = study ***i***) varies significantly in terms of sample size, study protocol, the research team, and a host of other study qualities. Researchers, specifically DerSimonian and Laird (DerSimonian & Laird, 1986, DerSimonian & Kacker, 2007), have addressed this critical issue over the last several decades, and the research consensus has determined that the random-effects model is one of the best approaches available to researchers when key quality variables are unknown.

The random-effects model assumes that the observed effect of a treatment in a given study ***i***, $\boldsymbol{Y_i}$ is a function of two components, the overall effect of treatment, $\boldsymbol{Y_i}^*$, and a sampling error in study ***i***, $\boldsymbol{\varepsilon_i}$. It is assumed that the functional relationship is linear, or

$$5. \quad Y_i = Y_i^* + \varepsilon_i.$$

Sampling error can be caused by many factors internal to the given study, such as inadvertently selecting a biased sample from the population, but it mostly due to the relative size of the study sample, $\boldsymbol{N_i}$. The sampling error also provides insight into the precision of the findings—the larger the error, the more likely the findings are less precise and, consequently, the lower the confidence one should have in the results when compared with another study's results, if that study has a smaller sampling error.

Sampling error is not the only variance that must be considered when assessing a set of studies. The true effect of treatment, Y_i^*, can also vary based on many factors, such as the dosage size of treatment, the demographics of the population receiving the treatment, the study's methodology, and/or protocol that impacts the treatment's effect. All of these true treatment effects vary by study and must be accounted for in order to understand the true treatment effect on the total population. Thus, equation (1) must be transformed to account for intra-study variance, thus

$$6.\quad Y_i = \mu^* + \delta_i + \varepsilon_i$$

Where $\mu*$ is the true treatment's effect on a given population independent of the studies and $\delta\iota$ is the difference in study ***i***'s observed effect from the true treatment's effect on a given population, or intra-study error.

Thus, the goal is to provide an estimate of $\mu*$, by controlling for δ_i and ε_i, which is done through a weighting process where the weights are functions of the variance in inter-study error (ε_i), defined as s_i^2, and the variance in intra-study error (δ_i), defined as τ^2. In other words, each study's observed treatment effect is adjusted using the following equation:

$$7.\quad X = (\Sigma_i w_i * Y_i) / \Sigma_i w_i$$

$$8.\quad w_i = (s_i^2 + \tau^2)^{1/2}$$

Where X is the deduced treatment effect that is used in the cost-saving calculations and w_i is the variance weight applied to each study to control for inter-study and intra-study variance in the observed treatment effect of each study **i**.

Various approaches to calculating s_i^2 and τ^2 which are sufficiently outlined by many prior studies, including the work of DerSimonian and Kacker (2007); however, for the purposes of this study, the two-step DerSimonian and Laird was adopted to calculate s_i^2, τ^2, and X.

List of Abbreviations

A	Number of possible avoided events (A) if everybody in a specified target population used omega-3
A&E	Ambulance and emergency services
B	total potential net economic benefits yet to be realised from use of a 1,000 mg omega-3 food supplement
B/Pop	Net Benefit per User
BP	Blood Pressure
C	Total cost of an omega-3 regimen
CBA	Cost-benefit analysis
CI	Confidence interval
CVD	Cardiovascular disease
d	The expected per person cost of omega-3 utilisation per year
DBP	Diastolic blood pressure
DHA	Docosahexaenoic acid
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic acid
EU	European Union
g	gram
h	The expected cost of a CVD-attributed medical event
HDL	High-density lipoprotein
ICD	International Classification of Diseases
IHD	Ischemic heart disease
ISHMT	International Shortlist for Hospital Morbidity Tabulation
LDL	Low-density lipoprotein
mg	milligram
MI	myocardial infarction
mmol/L	millimole per liter
N	Number needed to treat
NCBI	National Center for Biotechnology Information
Pop	Target Population
PPP	Purchasing Power parity
PUFA	Polyunsaturated fatty acids
RCT	Randomised controlled trials
RRR	Relative risk reduction
S	Total potential savings from reduced hospital service utilisation following CVD-attributed hospital events that are realizable if the entire target population were to sufficiently utilise a 1,000 mg omega-3 food supplement
S/C	Benefit Cost Ratio
SBP	Systolic blood pressure
TG	Triglycerides
U.S.	United States of America
UL	Tolerable Upper Intake Level
WHO	World Health Organisation

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- Food Supplements Foundation was founded in June 2013 with the aims of:
- Stimulating scientific and technical research about food supplements and functional ingredients
- Providing a forum for discussion of all issues affecting the legal and regulatory framework for food supplements in Europe
- Implementing appropriate standards of quality and good manufacturing practice, e.g. through the provision of information and training.

Food Supplements Foundation is a private foundation including among its Council of affiliates leading companies of food supplements and ingredients and national associations in Europe.

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Frost & Sullivan
331 E. Evelyn Ave. Suite 100
Mountain View, CA 94041
myfrost@frost.com

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