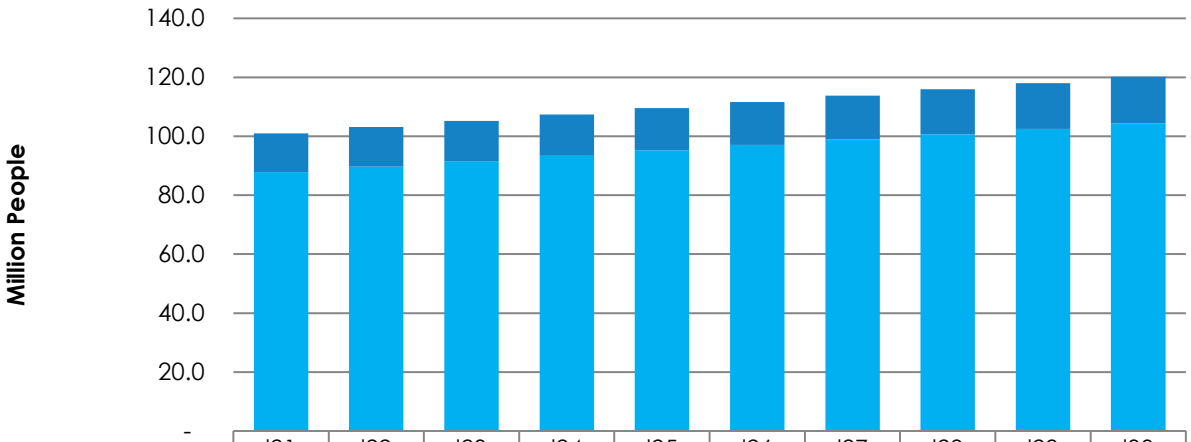
THE COST EFFECTIVENESS OF OMEGA-3, MAGNESIUM, SOLUBLE FIBER, AND VITAMIN K2 DIETARY SUPPLEMENTATION FOR MANAGING THE RISK OF CORONARY ARTERY DISEASE OUTCOMES

The Burden and Social Consequences

Coronary artery disease (CAD), also known as coronary heart disease (CHD) or ischemic heart disease (IHD), is caused by the buildup of plaque on arterial walls [6]. The plaque, being composed of cholesterol and other substances, causes the inside of arteries to narrow over time which in turn can cause blockages to occur and lead to heart attacks and heart failure.

CAD puts a heavy burden, both financially and in terms of reduced quality of life, on U.S. citizens, and Americans are increasingly struggling to cope with it, as well as the increasing costs of treating this disease condition. CAD continues to be the leading cause of death in the United States, ending 659,000 lives each year and accounting for 1 out of 4 deaths, according to the Centers for Disease Control and Prevention (CDC) [7]. According to the U.S. Department of Health & Human Services Agency for Healthcare Research and Quality, it is expected that 13.4 million U.S. adults aged 55 and older had experienced a CAD-attributed inpatient medical service or emergency room visit event in 2022, an event risk of 13.0% given a total population of 103.1 million Americans aged 55 and older [9].

Chart 1. Target Population Size of Coronary Artery Disease, United States, 2020-2030



	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
CAD Population	13.1	13.4	13.7	14.0	14.3	14.6	14.9	15.2	15.5	15.8
Heathy Adults	87.8	89.7	91.5	93.4	95.2	97.0	98.9	100.7	102.5	104.4
All Adults	101.0	103.1	105.2	107.4	109.5	111.7	113.8	115.9	118.1	120.2

Source: Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey (MEPS)., US Census, and Frost & Sullivan analysis

Table 1. Target Population Size of Coronary Artery Disease, United States, 2020-2030

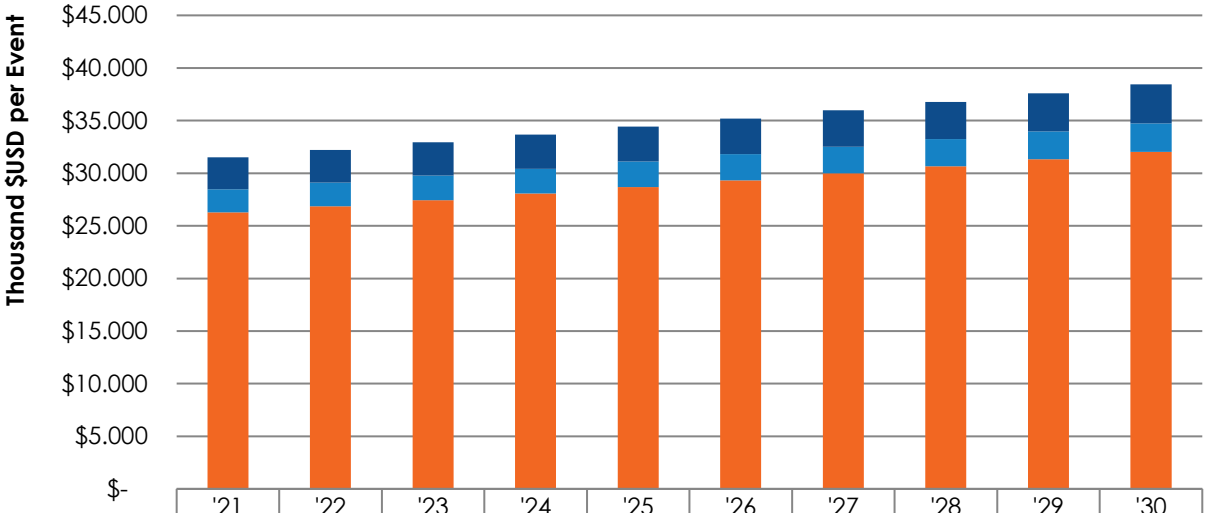
Year	Total Population, age 55 and older (million people)	Population of people experiencing CAD-attributed inpatient medical service or emergency room visits event, age 55 and older (million people)
2021	100.97	13.12
2022	103.11	13.43
2023	105.25	13.73
2024	107.38	14.03
2025	109.52	14.33
2026	111.66	14.63
2027	113.80	14.93
2028	115.93	15.23
2029	118.07	15.54
2030	120.21	15.84
Average ('22-'30)	111.66	14.63
CAGR	2.0%	2.0%

Source: Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey (MEPS)., US Census, and Frost & Sullivan analysis

Though the degree of effect varies, every CAD-attributed medical event entails financial burdens, including direct medical costs such as the costs of emergency room visits, hospitalization, surgery, medication, rehabilitation, and other costs tied to treating a medical event as well as indirect costs related to post-event disease management and the consequences of disability (e.g., lost wages and productivity losses). Based on a review of the Medical Expenditure Panel Survey (MEPS) database and Frost & Sullivan's analysis, the total expected direct medical expenditures on all CAD-attributed medical events for all U.S. adults aged 55 exceeded $413.6 billion in 2021 [9]. This is based on a mean per person expenditure on CAD-related inpatient procedures and emergency room visits plus the added monetary losses attributed to productivity which is expected to have equaled $31,517 in 2021. It should be noted that the financial burden per capita highly varies and depends on the severity of the event. Many CAD-attributed medical procedures cost more than the reported average and productivity losses can be much greater, especially for the younger individuals within the target population.

Given an expected compound annual population growth rate of 2.0% and an average inflation rate of 2.7% during the forecast period of 2022 to 2030, it is expected that the total expected direct medical expenditures on all CAD-related events for all U.S. adults aged 55 and older will exceed $608.9 billion by 2030. This equates to a mean per person expenditure on CAD-related inpatient procedures and emergency room visits of $38,455 in 2030, given an expected population of 120 million Americans aged 55 and older with CAD.

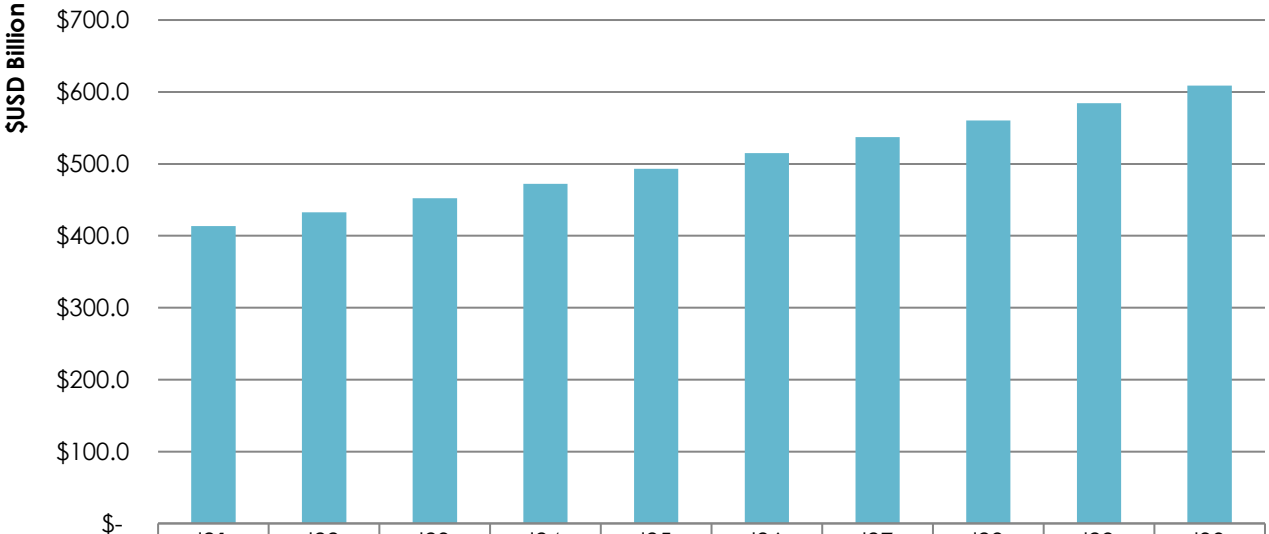
Chart 2. Average Health Care Losses and Productivity Losses per Coronary Artery Disease Event, Thousand $USD per Event, United States, 2020-2030



	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Productivity	$3.04	$3.11	$3.18	$3.25	$3.32	$3.39	$3.47	$3.55	$3.63	$3.71
Pharma	$2.21	$2.26	$2.31	$2.37	$2.42	$2.47	$2.53	$2.58	$2.64	$2.70
Medical	$26.26	$26.85	$27.45	$28.06	$28.69	$29.33	$29.98	$30.65	$31.34	$32.04
Total	$31.52	$32.22	$32.94	$33.68	$34.43	$35.20	$35.98	$36.78	$37.61	$38.45

Source: Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey (MEPS)., US Census, and Frost & Sullivan analysis

Chart 3. Total Population Health Care Losses and Productivity Losses Attributed to Coronary Artery Disease, $USD Billion, United States, 2020-2030



	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Total	$413.63	$432.58	$452.17	$472.41	$493.34	$514.96	$537.30	$560.38	$584.23	$608.86

Source: Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey (MEPS)., US Census, and Frost & Sullivan analysis

Table 2. Population Health Care Losses and Productivity Losses Attributed to Coronary Artery Disease, $USD Billion, United States, 2020-2030

Year	CAD, Cost of Medical ($ per Event Case)	CAD, Cost of Pharma ($ per Event Case)	CAD, Loss in Productivity ($ per Event Case)	CAD, Cost per Event Case ($ per Event Case)	CAD, Total Population Cost ($ billion)
2021	$26,265	$2,214	$3,038	$31,517	$413.63
2022	$26,851	$2,263	$3,106	$32,220	$432.58
2023	$27,450	$2,314	$3,176	$32,940	$452.17
2024	$28,063	$2,365	$3,246	$33,675	$472.41
2025	$28,690	$2,418	$3,319	$34,427	$493.34
2026	$29,330	$2,472	$3,393	$35,195	$514.96
2027	$29,985	$2,527	$3,469	$35,981	$537.30
2028	$30,654	$2,584	$3,546	$36,784	$560.38
2029	$31,339	$2,642	$3,625	$37,606	$584.23
2030	$32,038	$2,701	$3,706	$38,445	$608.86
Average ('22-'30)	$29,378	$2,476	$3,399	$35,253	$517.36
CAGR	2.2%	2.2%	2.2%	2.2%	4.0%
Cumulative ('22-'30)	--	--	--	--	$4,656.22

Source: Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey (MEPS)., US Census, and Frost & Sullivan analysis

Preventive approaches are critical to the reduction in demand for disease management services. One way to control the burden of CAD costs is to minimize the number of serious events in a target at-risk population. A CAD event may be preventable at least in part, or its seriousness may be meaningfully reduced, by individual patient choices because the development of the disease is believed to be largely a result of lifestyle choices. There is scientific consensus that high blood pressure, high LDL cholesterol, and smoking are leading risk determinants for CAD. High blood pressure and high LDL cholesterol are influenced by lifestyle choices including poor diet, physical inactivity, and alcohol use [7]. On the other hand, choices that have been shown to help to minimize CAD-related events are also available to each patient. Beneficial changes in diet are an example of a step an at-risk individual could take to potentially reduce their chances of experiencing a costly event. Moreover, there is increasing amount of evidence that certain key dietary supplements may reduce a person's odds of experiencing a CAD event.

In the following sections, it will be shown that the use of specific nutritiously dense dietary supplement products have been reported to have positive effects on the cardiovascular health of their users. This may also result in economic benefits in avoided medical costs. Specifically, this chapter explores the possible health and economic effects that could be derived from using four different dietary supplement regimens including omega-3 fatty acids, magnesium, soluble fiber, and

vitamin K2. For each of the four supplements presented here, a description of the scientific literature assessing each supplement's efficacy will be provided as well as projected implications for US healthcare stakeholders in the number of events potentially avoidable with the use of each supplement and economic benefits that could accrue from use of each supplement by an at-risk individual.

Table 3. Coronary Artery Disease Cost Summary Statistics for All U.S. Adults Aged 55 and over, 2021–2030

Metric	'21	CAGR ('21 - '30)	Average ('22 - '30)	Cumulative ('22 - '30)
Total Population, million people	100.97 M	1.96%	111.66 M	--
Population with CAD (people at high risk of experiencing an event), million people	13.12 M	2.11%	14.63 M	--
Event rate—percent of the high-risk population diagnosed with CAD, %	13.0%	0.15%	13.1%	--
Direct cost of CAD, medical service utilization, $USD per Case	$26,265	2.23%	$29,378	--
Direct cost of CAD, pharmaceutical utilization, $USD per Case	$2,214	2.23%	$2,476	--
Indirect Cost of CAD, productivity losses, $USD per Case	$3,038	2.23%	$3,399	--
Total cost of CAD, $USD per Case	$31,517	2.23%	$35,253	--
Total target population cost of CAD, $USD billion	$413.63 B	4.39%	$517.36 B	$4,656.22 B
Price inflation rate, %	6.95%	--	2.23%	

Source: Centers for Disease Control and Prevention, Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey (MEPS)., US Census, and Frost & Sullivan analysis

Omega-3

Literature Review

Omega-3 fatty acids are one of the most well-researched dietary supplement ingredients available and one of those with the most evidence for the support of cardiovascular health. Omega-3 fatty acids are a class of polyunsaturated fatty acids primarily found in marine sources such as fish and algae as well as certain plants. The marine omega-3s eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the ones most studied in the context of many health conditions, including CAD. Past research has shown that omega-3 EPA improves the cardio-metabolic profiles of users [12]. The American Heart Association (AMA) recommends that patients with documented CAD consume about 1,000 mg per day of a combination of EPA and DHA, preferably from fish sources, and the AMA recommends that 2 to 4 grams of EPA and DHA per day be consumed by patients with high triglyceride levels [11]. The U.S Food & Drug Administration has permitted the use of qualified health claims for omega-3 EPA+DHA for coronary heart disease since 2004 and for hypertension since 2019 [204].

A variety of clinical studies have explored the effects of EPA+DHA omega-3s on a variety of CAD outcomes, including mortality, myocardial infarction, and cardiovascular events in general. The strongest evidence may point toward reducing the number of CAD events and lowering triglyceride levels. In 2013, a meta-analysis of 10 qualified studies found that the relative risk reduction of a CHD event for daily users of Omega-3 EPA+DHA was 6.9% [4]. A meta-analysis published in 2020 identified 40 studies with a combined sample size of 135,267 participants that assessed the effects of Omega-3 EPA+DHA on cardiovascular outcomes including myocardial infarction (MI), coronary heart disease (CHD) including CAD events, CVD events, CHD mortality and fatal MI [12]. Of the 40 included studies, 28 studies representing 131,306 participants assessed the effects on the occurrence of CHD events specifically. The researchers found that supplement use was associated with a 10% reduced risk of experiencing a CHD event (RR, 0.90; 95% CI, 0.84 to 0.97) [12]. The average dose size across all of the included studies was 1,221 mg/day of Omega-3 EPA+DHA per day. Table 4 shows a summary of the key statistics derived from the meta-analyses used to derive the potential economic implications from using Omega-3 EPA+DHA dietary supplements to support coronary heart health.

Table 4. Expected Efficacy of Omega-3 EPA+DHA Supplement on CAD-attributed Event Occurrence

Metric	Measure
Relative risk (weighted for intra-study variance) (RR)	0.90 (95% CI: 0.84 to 0.97)
Relative risk reduction (weighted for intra-study variance) (RRR)	10.0% (95% CI: 3.0%-16.0%)
Absolute risk reduction (ARR)	1.3% (95% CI: 0.4%-2.1%)
Number of people needed to treat to avoid one CAD event (NNT), people	77 (95% CI: 48-256)
Estimated number of events that could have been avoided if the entire target population used Omega-3 EPA+DHA in 2022	174,811
Average number of events avoided annually if the entire target population used Omega-3 EPA+DHA, 2022-2030	191,727

Source: Bernasconi et al. 2021, Frost & Sullivan analysis

Economic Implications

After controlling for variability due to sample size, research methodologies and study protocols, and patient population differences among the studies, the calculated relative risk reduction of a CAD-attributed event with the use of Omega-3 EPA+DHA dietary supplements at preventive intake levels were 10.0%. Because it has been projected that 13.43 million people aged 55 and over will experienced a CAD-related event in 2022, or 13.0% of the target population, 77 people (95% CI: 48-256) could have used daily Omega-3 EPA+DHA supplements at preventive amounts to avoid one CAD-related event. This translates to 174,811 potentially avoidable CAD events in 2022 and could represent 191,727 avoided events per year from 2022 to 2030 given current population and disease risk growth expectations.

Consequently, the reduction in health care costs due to CAD-attributed events potentially avoided by patients consuming omega-3 EPA+DHA at protective levels was estimated at $5.63 billion in 2022, given an average CAD-event cost of $32,220 per case. The annual average cost savings from avoided CAD-attributed events could be $6.78 billion per year in total savings from 2022 to 2030 given current population growth, disease risk growth and price inflationary factors.

In order to account for the cost of daily supplement use, the cost of using Omega-3 EPA+DHA supplements were included in the cost savings assessment. Based on the review of the thirty best-selling retail products currently sold through online sales channels including Amazon and Vitamin Shoppe, the median cost of a daily dose of Omega-3 EPA+DHA is approximately $0.39 per day. Given this daily cost requirement, the median annual expected cost of Omega-3 EPA+DHA dietary

supplementation for all U.S. adults aged 55 and over is $144.01 per person per year or $2.31 billion per year for the total population over the period 2022 to 2030. Table 5 provides a summary of the cost of dietary supplementation with Omega-3 EPA+DHA of the entire target population.

Based the estimated cost of Omega-3 EPA+DHA supplementation, the net cost savings expected from reduced health care expenditures in 2022 resulting from avoided CAD-related events is projected to be $3.70 billion in 2022 or $4.47 billion per year in net savings during the period 2022 to 2030. Table 6 reports the economic implications of the systematic review finding of the beneficial use of Omega-3 EPA+DHA supplements to support cardiovascular health.

Table 5. Omega-3 EPA+DHA Cost Savings Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population, 2022-2030

Metric	Measure
Median daily cost per person of Omega-3 EPA+DHA supplementation at protective daily intake levels, 2022	$0.39
Expected daily median cost per person of Omega-3 EPA+DHA supplementation at protective daily intake levels, 2022-2030	$0.44
Median annual cost per person of Omega-3 EPA+DHA supplementation at protective daily intake levels, 2022	$144.01
Expected annual median cost per person of Omega-3 EPA+DHA supplementation at protective daily intake levels, 2022-2030	$157.65
Total target population cost of Omega-3 EPA+DHA supplementation at protective daily intake levels, 2022	$1.93 B
Total target population cost of Omega-3 EPA+DHA supplementation at protective daily intake levels, 2022-2030	$2.31 B

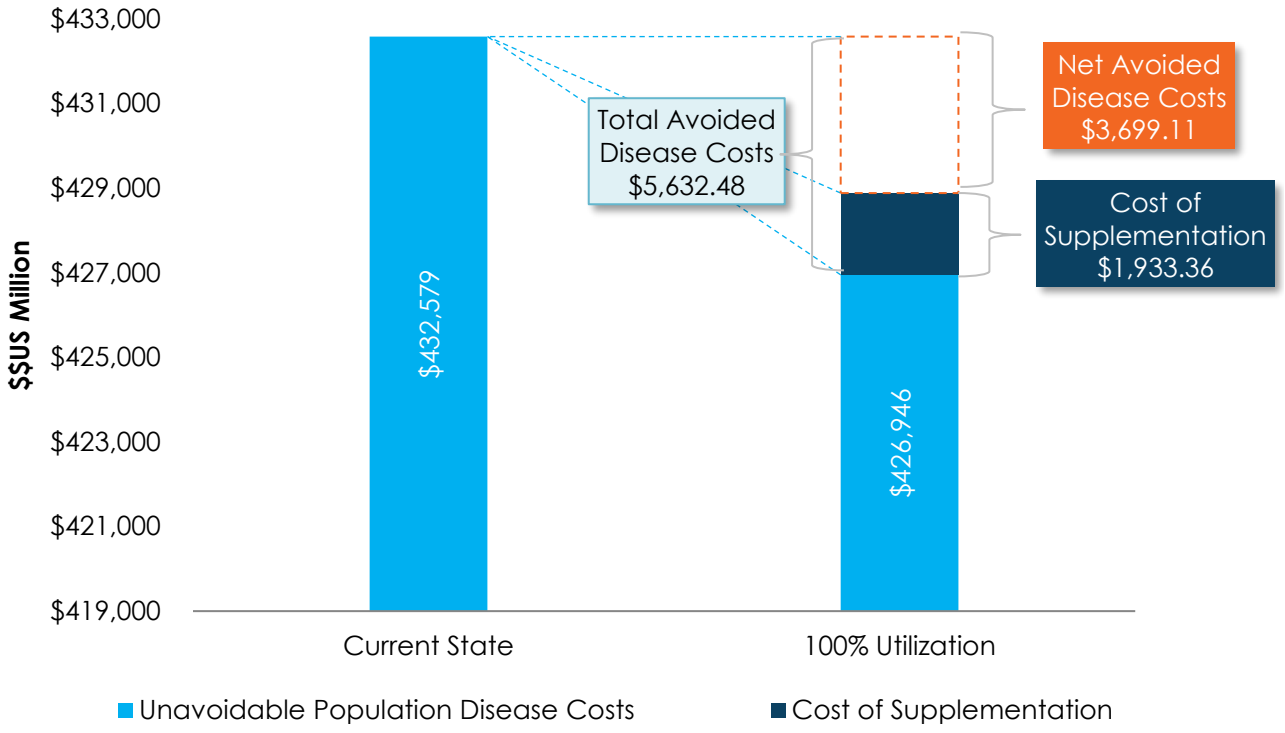
Note: B indicates billion. Source: Frost & Sullivan analysis

Table 6. Omega-3 EPA+DHA Cost Savings Analysis: Summary Results—Avoided Hospital Utilization Expenditures due to Dietary Supplement Intervention, 2022-2030

Metric	Measure
Avoided CAD-attributed hospital utilization expenditures given Omega-3 EPA+DHA supplement intervention per year, 2022	$5.63 B
Average avoided CAD-attributed hospital utilization expenditures given Omega-3 EPA+DHA supplement intervention per year, 2022-2030	$6.78 B
Net avoided CAD-attributed hospital utilization expenditures given Omega-3 EPA+DHA supplement intervention per year, 2022 (includes cost of supplementation)	$3.70 B
Net average avoided CAD-attributed hospital utilization expenditures given Omega-3 EPA+DHA supplement intervention per year, 2022-2030 (includes cost of supplementation)	$4.47 B
Net benefit cost ratio, $ Savings per one dollar spent on dietary supplement	$2.91
Cumulative net target avoided costs, 2022-2030 (NET BENEFITS) ($ billion)	$40.20 B

Note: B indicates billion. Source: Frost & Sullivan analysis

Chart 4. Omega-3 EPA+DHA Cost Savings Analysis: Health Care Cost Savings from the Use of Health Supplement, 2022 Scenario Analysis



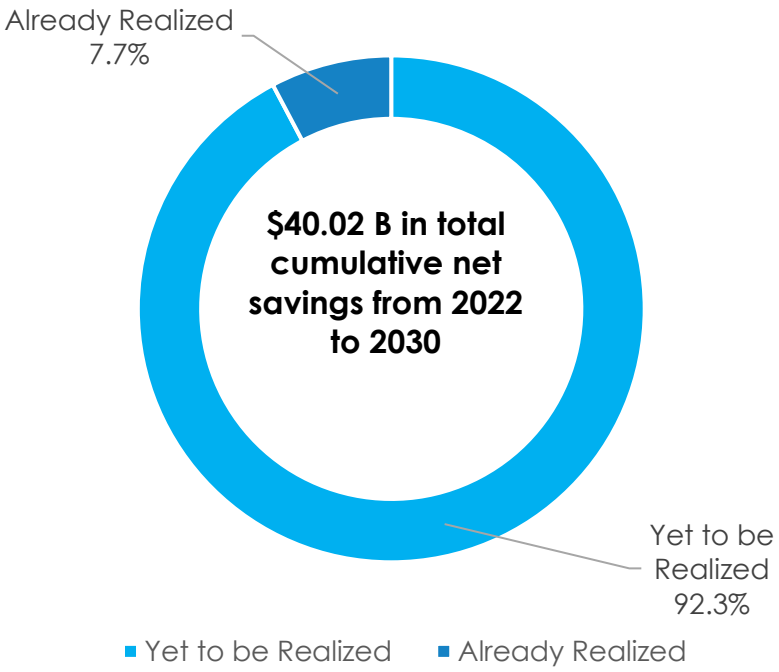
Note: B indicates billion. Source: Frost & Sullivan analysis

The above cost savings results are the maximum savings potential that is obtainable if everyone in the target population (all adults aged fifty-five and older) had not used this product prior to the base year of analysis (e.g., 2022) and then 100% of the population adopted the Omega-3 EPA+DHA regimen in the same year and gained all potential benefits. This assumption was made in order to calculate per capita net benefits which in turn can be used to calculate the net avoided cost savings for the subset of the population yet to use Omega-3 EPA+DHA.

According to the 2021 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs, over 40% of US adults aged 55 and older are regular users of dietary supplements and 18**%** of supplement users aged fifty-five and over are regular users of Omega-3 EPA+DHA dietary supplements [152]. This suggests that approximately 7.7% of the total population of US adults aged 55 and older are regular users of Omega-3 EPA+DHA dietary supplements and the remaining 92.3% of the target population 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 EPA+DHA dietary supplements, the calculation of avoided health care expenditures and net cost savings yet to be realized is simply a proportional adjustment of the total potential avoided expenditures and net cost savings.

Thus, it is expected that approximately $3.41 billion of the $3.70 billion in net potential direct savings from avoided CAD hospitalization events because of Omega-3 EPA+DHA dietary supplement intervention is already realized in total expected CAD costs. If utilization rates go unchanged, an average cost savings opportunity of $4.12 billion per year, or $37.09 billion from 2022 to 2030 in cumulative savings, could be lost because of underutilization of Omega-3 EPA+DHA dietary supplements. Hence, it is clear that significant cost savings can be realized from the use of Omega-3 EPA+DHA dietary supplements by the target high-risk population.

Chart 5. Omega-3 EPA+DHA Cost Savings Analysis: Summary Results—Cumulative Net Cost Savings Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2022-2030



Source: Council for Responsible Nutrition

Table 7. Omega-3 EPA+DHA Cost Savings Analysis: Summary Results—Net Cost Savings Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2022-2030

Metric	Measure
Net avoided CAD-attributed hospital utilization expenditures given Omega-3 EPA+DHA supplement intervention yet to be realized per year, 2022	$3.41 B
Net average avoided CAD-attributed hospital utilization expenditures given Omega-3 EPA+DHA supplement intervention yet to be realized per year, 2022-2030	$4.12 B
Cumulative net target avoided costs yet realized, 2022-2030 (NET BENEFITS) ($ billion)	$37.09 B

Note: B indicates billion. Source: Frost & Sullivan analysis

Detailed Results

Table 8. Omega-3 EPA+DHA Cost Savings Analysis: Detailed Results—Cost of Dietary Supplementation of the Target Population, 2022-2030

Year	Omega-3 EPA+DHA, Per Capita Daily Cost of Supplementation ($ per day)	Omega-3 EPA+DHA, Per Capita Annual Cost of Supplementation ($ per year)	Omega-3 EPA+DHA, Population Cost of Supplementation ($ billion)
2021	$0.386	$140.79	$1.848
2022	$0.395	$144.01	$1.933
2023	$0.403	$147.22	$2.021
2024	$0.412	$150.92	$2.117
2025	$0.422	$153.87	$2.205
2026	$0.431	$157.30	$2.302
2027	$0.441	$160.81	$2.401
2028	$0.450	$164.85	$2.511
2029	$0.460	$168.07	$2.611
2030	$0.471	$171.83	$2.721
Average ('22-'30)	$0.432	$157.65	$2.314
CAGR	2.24%	2.24%	4.40%
Cumulative ('22-'30)	--	--	$20.823

Source: Frost & Sullivan.

Table 9. Omega-3 EPA+DHA Cost Savings Analysis: Detailed Results—Avoided Hospital Utilization Expenditures due to Dietary Supplement Intervention, 2022-2030

Year	Omega-3 EPA+DHA & CAD, Number of Avoided Events if 100% Utilization by Target User Base (# of Avoided Event Cases)	Omega-3 EPA+DHA & CAD, Total Target Avoided Costs (BENEFITS) ($ billion)	Omega-3 EPA+DHA & CAD, Net Target Avoided Costs (NET BENEFITS) ($ billion)	Omega-3 EPA+DHA, Benefit/Cost Ratio: $Value of Reduced Risk per $1 spent on Supplement ($/$1 supplement spend)
2021	170,585	$5.376	$3.529	$2.91
2022	174,811	$5.632	$3.699	$2.91
2023	179,038	$5.897	$3.877	$2.92
2024	183,266	$6.171	$4.054	$2.91
2025	187,495	$6.455	$4.250	$2.93
2026	191,724	$6.748	$4.446	$2.93
2027	195,955	$7.051	$4.649	$2.94
2028	200,187	$7.364	$4.852	$2.93
2029	204,419	$7.687	$5.076	$2.94
2030	208,652	$8.022	$5.300	$2.95
Average ('22-'30)	191,727	$6.781	$4.467	$2.93
CAGR	2.26%	4.55%	4.62%	0.14%
Cumulative ('22-'30)	1,725,545	$61.028	$40.204	--

Source: Frost & Sullivan.

Table 10. Omega-3 EPA+DHA Cost Savings Analysis: Detailed Results—Net Cost Savings Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2022-2030

Year	Omega-3 EPA+DHA & CAD, Total Target Avoided Costs Yet Realized (BENEFITS) ($ billion)	Omega-3 EPA+DHA & CAD, Net Target Avoided Costs Yet Realized (NET BENEFITS) ($ billion)
2021	$4.96	$3.26
2022	$5.20	$3.41
2023	$5.44	$3.58
2024	$5.69	$3.74
2025	$5.96	$3.92
2026	$6.23	$4.10
2027	$6.50	$4.29
2028	$6.79	$4.48
2029	$7.09	$4.68
2030	$7.40	$4.89
Average ('22-'30)	$6.26	$4.12
CAGR	4.55%	4.62%
Cumulative ('22-'30)	$56.30	$37.09

Source: Frost & Sullivan.