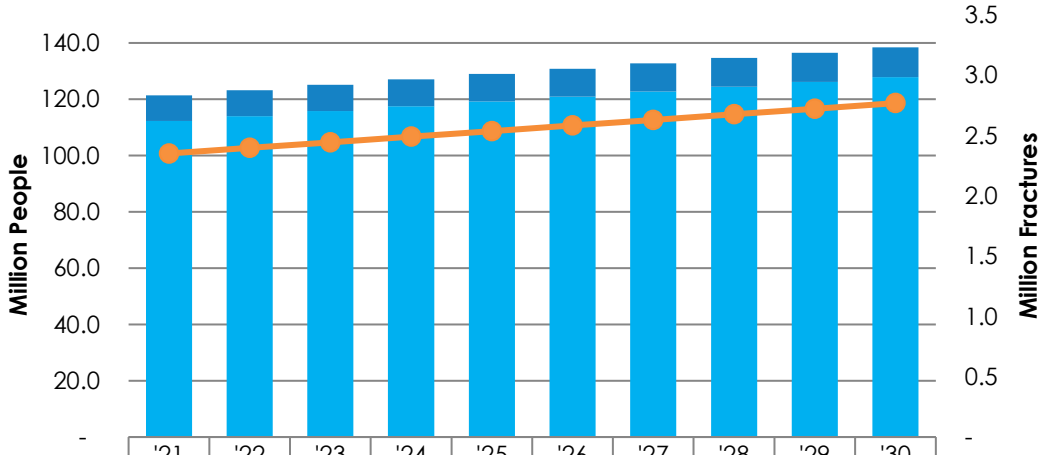
OSTEOPOROSIS AND THE BENEFITS OF USING CALCIUM & VITAMIN D TO REDUCE FRACTURE RISK

The Burden and Social Consequences

Osteoporosis, a metabolic bone disease that causes reduced mineral density and quality of bone, is a significant health and economic burden in the US [38, 39, 40]. During the osteoporotic process, the net rate of bone resorption exceeds that of bone formation and retention, resulting in a decrease in overall bone mass. When the bone mass available for skeletal support falls below the fracture threshold, it is easier to sustain a fracture with a simple fall or little to no trauma to the bone. At the onset of osteoporosis, outward symptoms are not visible. However, it can gradually result in fractures caused by relatively normal activities, such as exercising or lifting heavy objects [43]. These fractures can lead to pain, severe disability, or loss of mobility.

Women are at significantly greater risk of developing osteoporosis after menopause and thus bear a significantly heavier burden, both financially and in terms of reduced quality of life if osteoporosis is allowed to be developed uninhibited. 9.2 million people in the country suffer from osteoporosis with females accounting for over 87% of cases [41,42]. More than a quarter of the osteoporotic population (26.1%) will experience a bone fracture as a result of poor bone quality and reduced mineral density with a predicted 2.40 million fractures occurring among osteoporotic individuals aged 50 and older in 2022 [44].

Chart 13. Target Population Size and Prevalence of Osteoporosis, United States, 2020-2030



	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
All Adults	121.4	123.3	125.2	127.1	129.0	130.9	132.8	134.7	136.6	138.5
Osteoporotic Pop	9.0	9.2	9.4	9.5	9.7	9.9	10.0	10.2	10.4	10.6
Heathy Adults	112.3	114.1	115.8	117.5	119.3	121.0	122.7	124.4	126.2	127.9
Fractures (million)	2.4	2.4	2.4	2.5	2.5	2.6	2.6	2.7	2.7	2.8

Source: Kanis 2012, Wright et al. 2014, Weaver et al. 2019, US Census, and Frost & Sullivan analysis

Table 34. Target Population Size and Prevalence of Osteoporosis, United States, 2020-2030

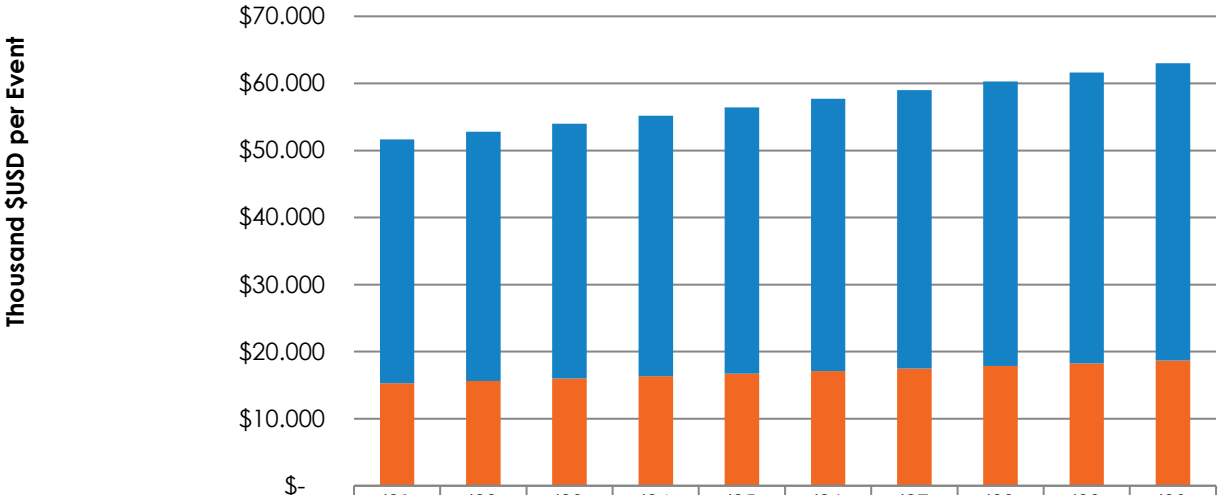
Year	Total Population, age 50 and older (million people)	Population, Diagnosed with Osteoporosis (million people)	Osteoporosis, Fractures (million fractures)
2021	121.35	9.03	2.35
2022	123.25	9.20	2.40
2023	125.16	9.37	2.44
2024	127.06	9.54	2.49
2025	128.96	9.71	2.54
2026	130.86	9.88	2.58
2027	132.76	10.05	2.63
2028	134.66	10.21	2.68
2029	136.56	10.38	2.72
2030	138.46	10.55	2.77
Average ('22-'30)	130.86	9.88	2.58
CAGR	1.5%	1.7%	1.8%

Source: Kanis 2012, Wright et al. 2014, Weaver et al. 2019, US Census, and Frost & Sullivan analysis

Every osteoporotic fracture result in a series of financial burdens that are a consequence of the event and includes expensive direct medical costs such as cost of hospitalization, cost of surgery, treatment pharmaceuticals, ambulatory services, emergency room visits and other hard costs tied to treating a medical event and indirect costs related to post-event disease management and the consequences of disability (e.g., productivity losses). A 2014 study of Medicare claims found that the direct and indirect economic impact per hip fracture on the US healthcare system was over $50,000 per case [45]. 70% of this cost was credited to costs tied to post-fracture disability [45].

Also, healthcare cost data related to preventing, treating, and managing the physical burden of osteoporosis for the entire US population was provided by Weaver et al 2019 [44]. This study reported that the direct cost of osteoporosis was over $28 billion per year given a per-person hospital-related cost of fracture of $12,197 in 2016 [44]. The direct cost per-person hospital-related cost of fracture included room and bed, medical supplies, operating room and laboratory expenditures, pharmaceuticals, and other hospital fees. An estimate for the direct cost of treating a given fracture in 2018 was determined by extrapolating to current 2018 dollars using a conservative inflationary rate of 1.5% per year.

Chart 14. Average Health Care Costs and Productivity Losses per Osteoporosis Event, Thousand $USD per Event, United States, 2020-2030



	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Indirect Medical, Pharma, and Productivity Losses	$36.36	$37.18	$38.01	$38.85	$39.72	$40.61	$41.52	$42.44	$43.39	$44.36
Direct Medical Costs	$15.30	$15.64	$15.99	$16.34	$16.71	$17.08	$17.46	$17.85	$18.25	$18.66
Total	$51.66	$52.81	$53.99	$55.20	$56.43	$57.69	$58.98	$60.29	$61.64	$63.02

Source: Weaver et al. 2019 and Frost & Sullivan analysis

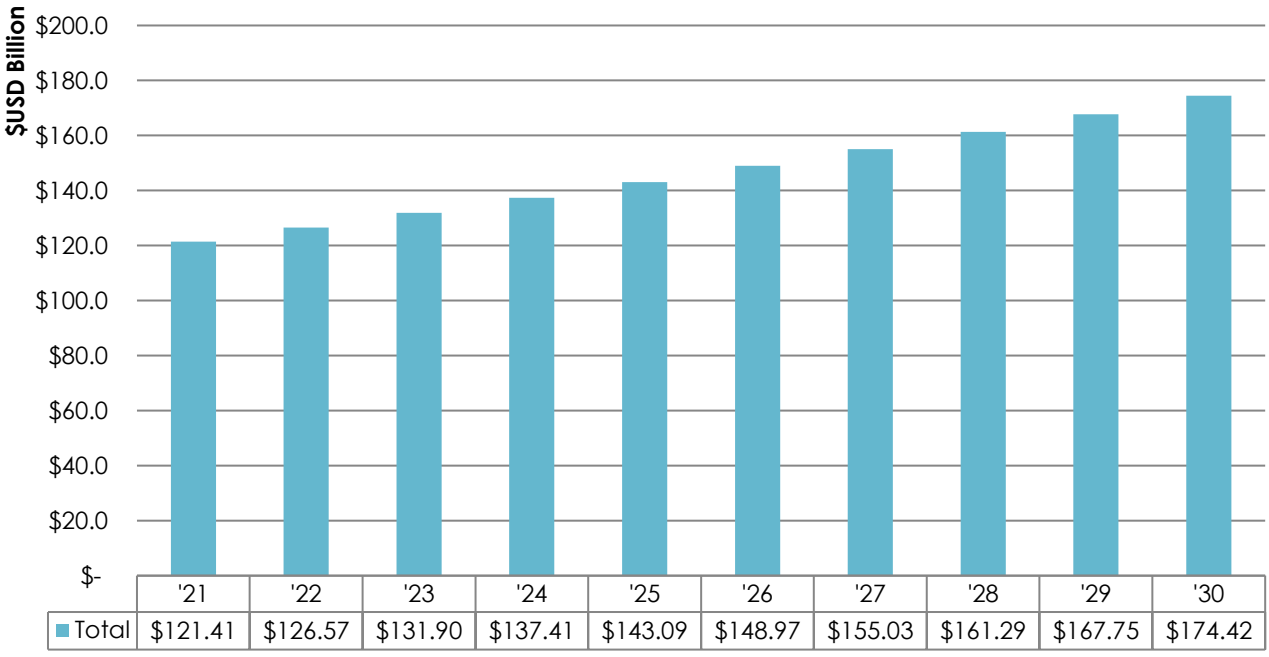
Table 35. Average Health Care Costs and Productivity Losses per Osteoporosis Event, Thousand $USD per Event, United States, 2020-2030

Year	Osteoporosis, Direct Medical Costs ($ per Event Case)	Osteoporosis, Indirect Medical, Pharma, and Productivity Losses ($ per Event Case)	Osteoporosis, Cost per Event Case ($ per Event Case)	Osteoporosis, Total Cost ($ billion)
2021	$15,296	$36,364	$51,660	$121.41
2022	$15,637	$37,176	$52,813	$126.57
2023	$15,986	$38,006	$53,992	$131.90
2024	$16,343	$38,855	$55,198	$137.41
2025	$16,708	$39,722	$56,430	$143.09
2026	$17,081	$40,609	$57,690	$148.97
2027	$17,462	$41,516	$58,978	$155.03
2028	$17,852	$42,442	$60,294	$161.29
2029	$18,250	$43,390	$61,640	$167.75
2030	$18,658	$44,358	$63,016	$174.42
Average ('22-'30)	$17,109	$40,675	$57,784	$149.60
CAGR	2.2%	2.2%	2.2%	4.1%
Cumulative ('22-'30)				$1,346.43

Source: Weaver et al. 2019, US Census, and Frost & Sullivan analysis

After application of this method, it was found that the expected total direct hospital costs of treating a spinal fracture was $15,296 [44,45,46]. Expected indirect costs of post-fracture disability and lost productivity amounted to an additional $36,364 per year [44,45,46]. This equates to a mean per person expenditure of $51,660 in 2021 of which over 30% is attributed to direct medical costs and nearly 70% attributed to indirect medical costs. Therefore, it is expected that the total expected medical expenditures on all osteoporotic fractures for all U.S. adults aged 50 will exceed $174.4 billion by 2030 given an expected compound annual population growth rate of 2.0% and an average rate of inflation rate of 2.7% during the forecast period of 2022 to 2030.

Chart 15. Total Population Health Care Losses and Productivity Losses Attributed to Osteoporosis, $USD Billion, United States, 2020-2030



	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Total	$121.41	$126.57	$131.90	$137.41	$143.09	$148.97	$155.03	$161.29	$167.75	$174.42

Source: Weaver et al. 2019, US Census, and Frost & Sullivan analysis

One way to control the burden of growing costs of osteoporosis is to minimize the number of costly osteoporotic fractures that are possible in a target at-risk population. Accordingly, adopting new regimens or routines that have been shown to help to minimize osteoporotic fractures that a person might experience and pay for ought to be considered. The daily use of calcium & vitamin D supplements is one tool that people with osteoporosis can employ to help to gain and realize these obtainable benefits. Specifically, the objective of this case study is to demonstrate that the use of calcium & vitamin D dietary supplement products which have been shown to have positive effects on reducing the risk of fracture will in turn result in positive economic benefits in terms of avoided medical costs.

Table 36. Osteoporosis Cost Summary Statistics for All U.S. Adults aged 50 and over, 2021–2030

Metric	'21	CAGR ('21 - '30)	Average ('22 - '30)
Total population, million people	121.35 M	1.48%	130.86 M
Population with Osteoporosis (people at high risk of experiencing an event), million people	9.03 M	1.75%	9.88 M
Number of Osteoporotic fracture cases, million cases	2.35	1.83%	2.58
Event rate—percent of fracture cases among osteoporotic population, %	26.0%	0.08%	26.1%
Direct cost of Osteoporosis, medical service utilization, $USD per Case	$15,296	2.23%	$17,109
Direct cost of Osteoporosis, pharmaceutical utilization, $USD per Case	$36,364	2.23%	$40,675
Total cost of Osteoporosis, $USD per Case	$51,660	2.23%	$57,784
Total target population cost of Osteoporosis, $USD billion	$121.35 B	1.48%	$130.86 B
Price inflation rate, %	6.95%	--	2.23%

Source: Kanis 2012, Wright et al. 2014, Weaver et al. 2019, US Census, and Frost & Sullivan analysis

Calcium and Vitamin D

Literature Review

Calcium is an essential mineral that plays a vital role in human physiology. Calcium can be obtained naturally through the diet by eating dairy products, such as milk, yoghurt, ice cream and cheese [10]. It is also found in seafood and many plant-based products. Lower amounts of calcium are found in leafy greens, legumes, and nuts [10]. Vitamin D is a fat-soluble vitamin that aids in the absorption of calcium, helps to build overall bone mass, and supports muscles, nerves, and the immune system [10]. The body can produce vitamin D endogenously with exposure to the sun's ultraviolet (UVB) rays. However, most Americans do not naturally produce enough vitamin D through sun exposure to maintain sufficient blood levels of vitamin D [47]. Dietary sources of vitamin D include egg yolks, and fish as well as fortified foods such as milk and cereals [10].

Calcium is an essential mineral for human body to build and maintain bone structure as well as teeth. Calcium is the key to maintain structure and hardness of these body parts. Its absorption and metabolism depend, in part, on vitamin D, and is converted in the kidneys to the biologically active form calcitriol. If an individual is not getting sufficient amounts of calcium and vitamin D, then a decrease in overall bone mass can occur and thus the bones become more brittle and easier to break. There has been a significant amount of research exploring the benefits of calcium and vitamin D utilization among the elderly, where most of the research has focused on the correlation between calcium and vitamin D use and the risk of an osteoporotic bone fracture. Under the regulation of 21 CFR 101.72, the U.S Food & Drug Administration has permitted the use of qualified health claims for calcium & vitamin D for reduced risk of osteoporosis since 2008 [205]. In order to quantify the possible effects of calcium and vitamin D supplementation in the elderly on the risk of osteoporotic fractures, a search for recent meta-analytical studies on this topic was conducted. In 2010, EFSA evaluated the scientific evidence for vitamin D and calcium in osteoporotic fractures and concluded that a cause-effect-relationship had been found [49]. In 2014, Shanahan and de Lorimier conducted a search of the scientific literature that focused on published studies quantifying the effect of utilization on fracture risk in Australia [50]. Forty nine studies from all parts of the world and 7 RCT studies were identified as being eligible of the literature and it was found that the relative risk reduction of an osteoporosis-attributed fracture event given the use of 1,000 mg/day of calcium and 20 µg/day of vitamin D was a statistically significant 19.7% (95% CI: 21.1% to 18.3%) after controlling for variance because of sample size, research methodologies and study protocols, and patient population differences within each study and among all studies [50].

In 2015 and 2016, researchers from the International Osteoporosis Foundation and National Osteoporosis Foundation [51,52] conducted a more recent meta-analysis of the body of literature that tested the hypothesis between calcium and vitamin D supplement intake and the risk of a bone

fracture [51,52]. The authors first conducted a search for all randomized controlled trials (RCTs) that reported a measured effect of calcium plus vitamin D supplementation on fracture incidence. In all, 8 studies including 26,000 subjects met their criteria for inclusion in their primary meta-analysis and included over 1,700 total fractures [51,52]. The final analysis reported a summary relative risk estimate of 0.86 (95% CI: 0.75–0.98), indicating that supplementation would reduce the overall population risk of osteoporotic fracture by 14%. Thus, this current analysis utilized a relative risk reduction (RRR) for total fracture of 0.14 with calcium and vitamin D supplementation. Table 37 shows the descriptive statistics used to derive the economic implications of using calcium & vitamin D dietary supplements to support bone health.

Table 37. Expected Efficacy of Calcium & Vitamin D Supplement on CAD-attributed Event Occurrence

Metric	Measure
Relative risk (weighted for intra-study variance) (RR)	0.86 (95% CI: 0.75-0.98)
Relative risk reduction (weighted for intra-study variance) (RRR)	14.0% (95% CI: 2.0%-25.0%)
Absolute risk reduction (ARR)	3.6% (95% CI: 0.5%-6.5%)
Number of people needed to treat to avoid one osteoporotic fracture (NNT), people	27 (95% CI: 15-192)
Estimated number of events that could have been avoided if the entire target population used calcium & vitamin D in 2022	335,518
Average number of events avoided annually if the entire target population used calcium & vitamin D, 2022-2030	361,507

Source: Weaver et al. 2016, Weaver et al. 2015 and Frost & Sullivan analysis

Economic Implications

The calculated relative risk reduction of an osteoporotic fracture given the use of calcium & vitamin D dietary supplements at the preventive intake levels was 14.0% after controlling for variance due to sample size, research methodologies and study protocols, and patient population differences within each study and among all studies. Given that 9.20 million people aged 50 and over would have experienced an osteoporotic fracture in 2022, or 26.1% of the population diagnosed with osteoporosis, 27 people (95% CI: 15-192) would have needed to use calcium & vitamin D supplements at the daily preventive levels to avoid one osteoporotic fracture. This translates to 335,518 potentially avoidable osteoporotic fractures that could have been saved in 2022 and an average of 361,507 avoided events per year from 2022 to 2030 given current population and disease risk growth expectations.

Subsequently, the expected reduction in expenditures in 2022 attributed to avoided osteoporotic fractures would have been $17.7 billion in 2022 given an estimated average osteoporotic fracture cost of $52,813 per case. Given current population growth, disease risk growth and price inflationary factors, the expected cost savings derived from avoided osteoporotic fractures caused by the use of calcium & vitamin D at daily protective intake levels is $20.9 billion per year in total savings from 2022 to 2030.

The cost of daily supplement use also needs to be accounted for in order to ensure all cost factors are considered. Based on the review of the thirty best-selling retail products currently sold through online sales channels, the median cost of a daily dose of calcium & vitamin D is approximately $0.26 per day. Given this daily cost requirement, the median annual expected cost of calcium & vitamin D dietary supplementation for all U.S. adults aged 50 and over would be $94.13 per person per year or $1.02 billion per year for the total population over the period 2022 to 2030. Table 38 provides a summary of the cost of dietary supplementation with calcium & vitamin D of the entire target population.

Table 38. Calcium & Vitamin D Cost Savings Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population, 2022-2030

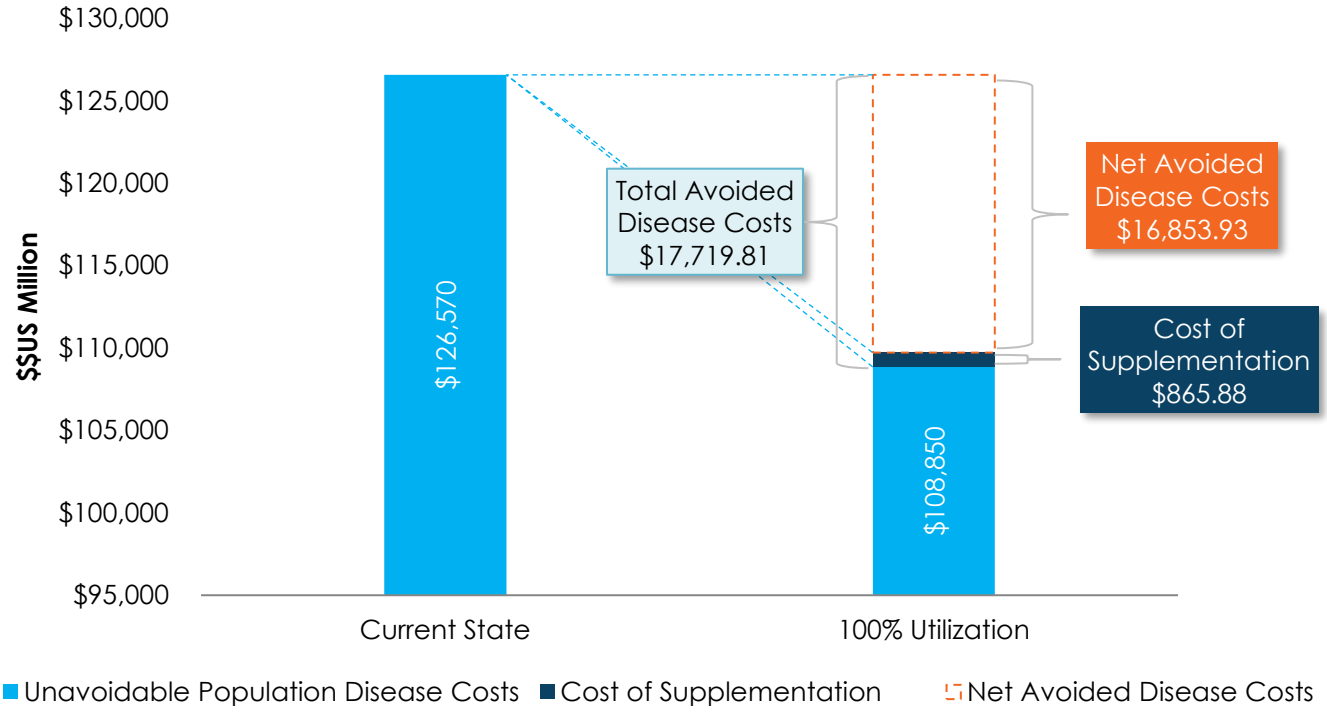
Metric	Measure
Median daily cost per person of Calcium & Vitamin D supplementation at protective daily intake levels, 2022	$0.26
Expected daily median cost per person of Calcium & Vitamin D supplementation at protective daily intake levels, 2022-2030	$0.28
Median annual cost per person of Calcium & Vitamin D supplementation at protective daily intake levels, 2022	$94.13
Expected annual median cost per person of Calcium & Vitamin D supplementation at protective daily intake levels, 2022-2030	$103.05
Total target population cost of Calcium & Vitamin D supplementation at protective daily intake levels, 2022	$0.87 B
Total target population cost of Calcium & Vitamin D supplementation at protective daily intake levels, 2022-2030	$1.02 B

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

After consideration of the cost of calcium & vitamin D dietary supplementation, the net cost savings expected from reduced expenditures in 2022 derived from avoided osteoporotic fractures would have been $16.85 billion in 2022 or $19.92 billion per year in net savings, or $179.32 billion cumulatively, during the period 2022 to 2030.

The above cost saving results are the maximum savings potential that is obtainable if everyone in the target population (all adults aged 50 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 calcium & vitamin D 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 calcium & vitamin D.

Chart 16. Calcium & Vitamin D Cost Savings Analysis: Health Care Cost Savings from the Use of Health Supplement, 2022 Scenario Analysis



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

Table 39. Calcium & Vitamin D Cost Savings Analysis: Summary Results—Avoided Hospital Utilization Expenditures due to Dietary Supplement Intervention, 2022-2030

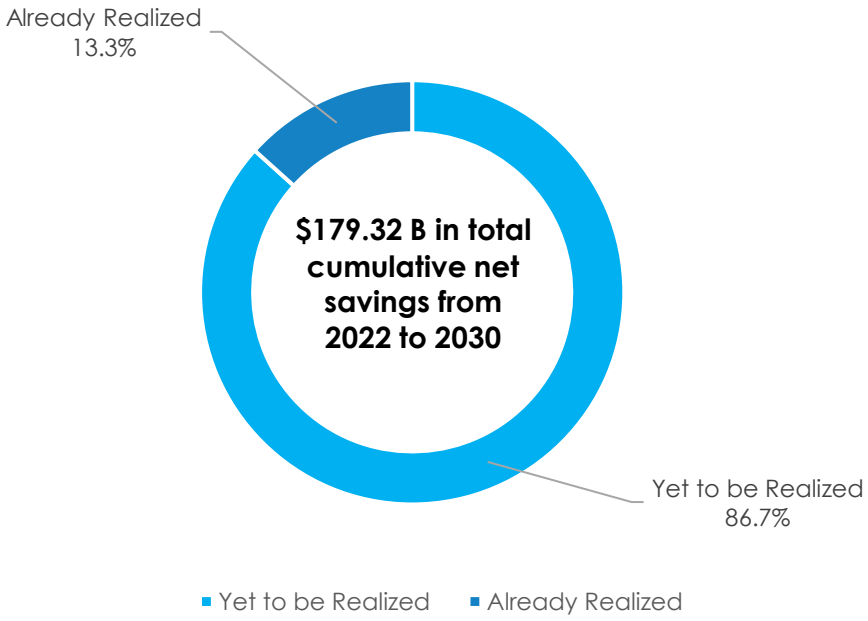
Metric	Measure
Avoided fracture-attributed hospital utilization expenditures given Calcium & Vitamin D supplement intervention per year, 2022	$17.72 B
Average avoided fracture-attributed hospital utilization expenditures given Calcium & Vitamin D supplement intervention per year, 2022-2030	$20.94 B
Net avoided fracture-attributed hospital utilization expenditures given Calcium & Vitamin D supplement intervention per year, 2022 (includes cost of supplementation)	$16.85 B
Net average avoided fracture-attributed hospital utilization expenditures given Calcium & Vitamin D supplement intervention per year, 2022-2030 (includes cost of supplementation)	$19.92 B
Net benefit cost ratio, $ Savings per one dollar spent on dietary supplement	$20.46
Cumulative net target avoided costs, 2022-2030 (NET BENEFITS) ($ billion)	$179.32 B

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

According to the 2021 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs, 43% of US adults aged 55 and older are regular users of dietary supplements and approximately 31% of supplement users aged 55 and over are regular users of calcium dietary supplements [152]. It is expected that the calcium products used by these sample of users likely include preventive levels of vitamin D based on formulation standardization across the major manufacturers in the US marketplace. This implies that approximately 13.3% of the total population of US adults aged 55 and older are regular users of calcium & vitamin D dietary supplements and the remaining 86.7% 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 calcium & vitamin D 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. It should be noted that the target population of this case study includes individuals younger than 55, so the use of these consumer research findings for deducing the proportion of the population yet to realize the benefits from using this supplement is likely underestimated since use of dietary supplements generally increases with age.

Thus, it is expected that approximately $14.61 billion of the $16.85 billion in net potential direct savings from hospital utilization events related to avoided osteoporotic fractures has yet to be realized. If utilization rates go unchanged, an average cost savings opportunity of $17.27 billion per year, or $155.41 billion from 2022 to 2030 in cumulative savings, could be lost because of underutilization of calcium & vitamin D dietary supplements. Hence it is expected that there are still significant cost savings yet be realized through the increased usage of calcium & vitamin D dietary supplements among the high-risk target population.

Chart 17. Calcium & Vitamin D 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 40. Calcium & Vitamin D 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 fracture-attributed hospital utilization expenditures given Calcium & Vitamin D supplement intervention yet to be realized per year, 2022	$14.61 B
Net average avoided fracture-attributed hospital utilization expenditures given Calcium & Vitamin D supplement intervention yet to be realized per year, 2022-2030	$17.27 B
Cumulative net target avoided costs yet realized, 2022-2030 (NET BENEFITS) ($ billion)	$155.41 B

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

Detailed Results

Table 41. Calcium & Vitamin D Cost Savings Analysis: Detailed Results—Cost of Dietary Supplementation of the Target Population, 2022-2030

Year	Calcium & Vitamin D, Daily Cost of Supplementation ($ per day)	Calcium & Vitamin D, Annual Cost of Supplementation ($ per year)	Calcium & Vitamin D, Population Cost of Supplementation ($ billion)
2021	$0.25	$91.09	$0.822
2022	$0.26	$94.13	$0.866
2023	$0.26	$96.23	$0.902
2024	$0.27	$98.65	$0.941
2025	$0.28	$100.58	$0.976
2026	$0.28	$102.82	$1.015
2027	$0.29	$105.12	$1.056
2028	$0.29	$107.76	$1.101
2029	$0.30	$109.86	$1.141
2030	$0.31	$112.32	$1.185
Average ('22-'30)	$0.28	$103.05	$1.020
CAGR	2.4%	2.4%	4.1%
Cumulative ('22-'30)			$23.240

Source: Frost & Sullivan.

Table 42. Calcium & Vitamin D Cost Savings Analysis: Detailed Results—Avoided Hospital Utilization Expenditures due to Dietary Supplement Intervention, 2022-2030

Year	Calcium & Vitamin D & Osteoporosis, Number of Avoided Events if 100% Utilization by Target User Base (# of Avoided Event Cases)	Calcium & Vitamin D & Osteoporosis, Total Target Avoided Costs (BENEFITS) ($ billion)	Calcium & Vitamin D & Osteoporosis, Net Target Avoided Costs (NET BENEFITS) ($ billion)	Calcium & Vitamin D, Benefit/Cost Ratio: $Value of Reduced Risk per $1 spent on Supplement ($/$1 supplement spend)
2021	329,021	$17.00	$16.17	$20.67
2022	335,518	$17.72	$16.85	$20.46
2023	342,015	$18.47	$17.56	$20.48
2024	348,513	$19.24	$18.30	$20.45
2025	355,010	$20.03	$19.06	$20.52
2026	361,507	$20.86	$19.84	$20.54
2027	368,005	$21.70	$20.65	$20.55
2028	374,502	$22.58	$21.48	$20.51
2029	381,000	$23.48	$22.34	$20.59
2030	387,497	$24.42	$23.23	$20.60
Average ('22-'30)	361,507	$20.94	$19.92	$20.52
CAGR	1.83%	4.11%	4.11%	-0.04%
Cumulative ('22-'30)	3,253,567	$188.500	$179.317	

Source: Frost & Sullivan.

Table 43. Calcium & Vitamin D 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	Calcium & Vitamin D & Osteoporosis, Total Target Avoided Costs Yet to be Realized (BENEFITS) ($ billion)	Calcium & Vitamin D & Osteoporosis, Net Target Avoided Costs Yet to be Realized (NET BENEFITS) ($ billion)
2021	$14.73	$14.02
2022	$15.36	$14.61
2023	$16.00	$15.22
2024	$16.67	$15.86
2025	$17.36	$16.52
2026	$18.08	$17.20
2027	$18.81	$17.90
2028	$19.57	$18.62
2029	$20.35	$19.37
2030	$21.16	$20.14
Average ('22-'30)	$18.15	$17.27
CAGR	4.11%	4.11%
Cumulative ('22-'30)	$163.37	$155.41

Source: Frost & Sullivan.