OSTEOPOROSIS AND THE BENEFITS OF USING CALCIUM, VITAMIN D, AND MAGNESIUM

The total health care expenditure on managing and treating osteoporosis-attributed bone fractures among all U.S. women over the age of 55 with osteoporosis in the U.S. was over $14 billion per year in 2012.

Prevalence and Social Consequences

Osteoporosis is the most prevalent bone disease in the United States and is characterized by accelerated bone loss, which results in brittle and weak bones that are easily fractured. (PubMed Health, 2012) Normally, bones are continuously regenerated, with new bone replacing old bone. However, in older people this process is less efficient, and more bone is lost than is replaced. Patients with osteoporosis have an increased risk of fractures, particularly of the hip, spine, and wrist. (PubMed Health, 2012)

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. These fractures can lead to pain, severe disability, or loss of mobility.

Post-menopausal women are at the highest risk of having osteoporosis, and it is especially prevalent among white and Asian women. After menopause, estrogen hormone levels fall. The hormone is vital in maintaining bone density by retaining calcium in the bones. After menopause, the rate of bone degeneration outpaces bone formation, resulting in the thinning of bones and development of osteoporosis.

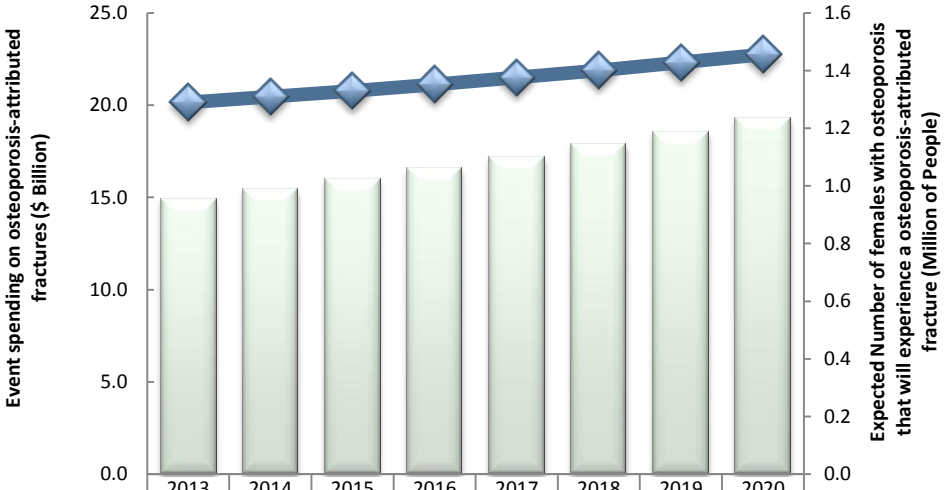
An estimated 8.2 million U.S. women over the age of 55 have developed osteoporosis. Among this target population, the number of fractures in the U.S. because of osteoporosis is as follows (Centers for Disease Control and Prevention, 2011; National Osteoporosis Foundation, 2013):

- More than 560,000 vertebral fractures
- More than 240,000 hip fractures
- More than 200,000 wrist fractures
- More than 240,000 other fractures

Thus, it is estimated that more than 1.2 million fracture events occurred in 2012 at an average treatment cost of $11,020 among women over the age of 55 with osteoporosis (Blume & Curtis, 2011, Agency for Healthcare Research and Quality, 2010, and Frost & Sullivan). This equates to more than $14.00 billion in annual direct health care costs just associated with treating the fracture; it excludes the added costs of lost productivity, mobility, and general quality of life.

The total cumulative direct health care costs related to osteoporosis-attributed bone fractures among all U.S. women over the age of 55 diagnosed with osteoporosis is expected to be nearly $136 billion from 2013 to 2020.

Figure 7.1—Total Expenditures Forecast for Osteoporosis-Attributed Fractures among Women over the Age of 55 diagnosed with Osteoporosis, 2013–2020



	2013	2014	2015	2016	2017	2018	2019	2020
Event Spending ($ B)	14.93	15.45	15.99	16.58	17.19	17.85	18.54	19.28
Events (M People)	1.29	1.31	1.33	1.35	1.38	1.40	1.43	1.46

Note: All figures are rounded. Source: Frost & Sullivan analysis.

Projecting these per-person expenditures forward at an average annual growth rate of 5% from 2013 to 2020 and assuming an average annual target population growth rate of 1.7% during the same period, it is expected that an average of 1.4 million women over the age of 55 and diagnosed with osteoporosis will experience a costly fracture and file a hospitalization claim. Hospitalization claims are defined as all inpatient hospitalizations and emergency room visits from 2013 to 2020, at an annual average per-person cost of $13,812 (Agency for Healthcare Research and Quality—MEPS). This implies that the total cumulative direct health care costs related to osteoporosis-attributed fractures among women over the age of 55 will be more than $135.81 billion over the forecast period—nearly $17.00 billion per year.

As osteoporosis becomes more prevalent in the U.S. due to the aging of America, new preventive options become more important as a means to control the financial burden of osteoporosis. Calcium, vitamin D, and magnesium are the key available dietary supplement options that have been shown to have a substantiated preventive effect on osteoporosis-attributed events. This will be explored in detail in this chapter.

Figure 7.2—Osteoporosis Cost Summary for All U.S. Women Over the Age of 55, 2012–2020

Metric	Measure
Population of women over the age of 55 with osteoporosis (people at high risk of experiencing an event), 2012[31]	8.2 M
Number of women over the age of 55 with osteoporosis that claimed an osteoporosis-attributed fracture, 2012	1.3 M
Event rate—percent of the high risk population that will experience an osteoporosis-attributed fracture, 2012 (ER)	15.1%
Total claimed expenditures on osteoporosis-related inpatient procedures and emergency room visits among all U.S. women over the age of 55 with osteoporosis, 2012[32]	$14.02 B
Average expenditures on osteoporosis-related inpatient procedures and emergency room visits among all U.S. women over the age of 55 with osteoporosis, 2013–2020	$16.98 B
Cumulative hospital utilization expenditures osteoporosis-related inpatient procedures and emergency room visits among all U.S. women over the age of 55 with osteoporosis, 2013–2020	$135.81 B
Average claimed expenditures per osteoporosis-attributed fracture per person per year, 2012	$11,020
Expected average claimed expenditures per osteoporosis-attributed fracture per person per year, 2013–2020	$13,812

Source: Summary Health Statistics for U.S. Adults: National Health Interview Survey 2011—Centers for Disease Control and Prevention, Center for Financing, Access and Cost Trends—Agency for Healthcare Research and Quality; Medical Expenditure Panel Survey, 2010 and Frost & Sullivan

31 Includes all osteoporosis-attributed fracture treatments

32 An event is defined as any claimed treatment or disease management activity that requires expenditure to be paid out-of-pocket, by private insurance companies, or by Medicare or Medicaid and includes all hospital outpatient or office-based provider visits, hospital inpatient stays, and emergency room visits

Calcium is the major mineral comprising bone and a key determinant in bone density. Its absorption and metabolism depend importantly on vitamin D status.

Calcium and Vitamin D

Literature Review

Calcium is the major mineral comprising bone. Its absorption and metabolism depends, in part, on vitamin D, which is converted in the kidneys to the biologically active form calcitriol (Memorial Sloan-Kettering Cancer Center, 2013) (The American Society of Health-System Pharmacists, Inc and the U.S. National Library of Medicine, 2010). Calcitriol acts as a hormone in regulating many aspects of calcium function (The American Society of Health-System Pharmacists, Inc and the U.S. National Library of Medicine, 2010). Vitamin D is naturally synthesized by humans in the skin when it is exposed to ultraviolet light. Under conditions of low light exposure, dietary sources of vitamin D are needed to maintain adequate levels (Memorial Sloan-Kettering Cancer Center, 2013). Natural sources rich in vitamin D include fatty fish, eggs, and liver (Memorial Sloan-Kettering Cancer Center, 2013). Since the 1920s, milk in the United States has been fortified with vitamin D to prevent bone disease, especially in children. In the elderly, especially among women, calcium loss from bone can result in osteoporosis, and it is associated with reduced levels of circulating vitamin D. There has been much research on dietary supplementation of calcium and vitamin D in the elderly, with the goal of minimizing osteoporosis and its complications, such as increased risk of bone fractures (Memorial Sloan-Kettering Cancer Center, 2013).

In the United States, the Food and Nutrition Board (FNB) at the IOM has established Recommended Dietary Allowances (RDA) of 1200 mg of calcium and 600 IU of vitamin D per day for women 51-70 years of age. (Institute of Medicine, 2010). The UL for calcium for adults over 50 years of age is 2000 mg. The UL for calcium was established in 2010 on the basis of data from the Women's Health Initiative relating to potential formation of kidney stones. The IOM says this value "provides a reasonable degree of public health protection without overly restricting the intake of calcium (notably from calcium supplements) for both men and women" (Institute of Medicine, 2010).

For women over the age of 70, the RDA for calcium remains 1200 mg, but the RDA for vitamin D is increased to 800 IU/day. A UL for vitamin D of 4,000 IU per day was established for all U.S. adults (NIH MedlinePlus, 2011). The UL for vitamin D was established in 2010 on the basis of the potential risk of hypercalcemia (elevated blood levels of calcium).

In order to quantify the possible effects of calcium and vitamin D supplementation in the elderly on the risk of osteoporotic fractures, a rigorous search of the literature was conducted that focused on published studies quantifying the effect of supplementation on fracture risk. The objective was to identify a set of studies that represented the state of scientific literature on a these supplements. Studies that tested for a direct causal relation between intake of the dietary supplement and the relative risk of a disease event were preferred. The research team strove to include studies that were similar to each other in protocol in an attempt to control for observable variance. Studies were not selected on the basis of the magnitude, direction or statistical significance of the reported findings.

In a rigorous search conducted on PubMed, more than 49 studies were identified by matching a combination of terms such as "calcium" and/or "vitamin D"; "osteoporosis" and/or "fracture"; and "risk reduction." A search was conducted between February 1 and May 31, 2013. Of the various reported study methods, randomized controlled trials were preferred because they are designed to directly test for a cause-and-effect relationship between supplementation and outcome. Seven RCT studies were identified as being representative of the literature, and directly tested for the relationship between dietary supplement intake and the risk of an osteoporosis-attributed bone fracture. All seven studies were of people age 50 or older—most of them were over the age of 65. In four of the studies, the subjects were women only. The RCTs compared a treatment group that received daily calcium and vitamin D supplement with a group that received a placebo. The duration of supplementation ranged from 18 months to seven years. Reported study outcomes included the incidence of various clinical fractures; Frost & Sullivan selected the change in osteoporotic fracture risk as the input for modeling the health care utilization effects of calcium and vitamin D supplementation. Four of the seven key studies are referenced and discussed in the paragraphs below. The other three are referenced in the footnotes to Figure 7.3.

Figure 7.3—Calcium and Vitamin D Literature Review: Description of the Qualified Studies

Author	Year	Event definition
Jackson	2006	all fractures (hip, clinical vertebral, lower arm, or wrist)
Chapuy	1992	non-vertebral fractures
Dawson-Hughes[33]	1997	first non-vertebral fracture
Porthouse	2005	all clinical fractures
Grant	2005	new fractures (all subjects had previous fracture)
Larsen[34]	2004	Osteoporotic fractures leading to acute hospital admission
Chapuy[35]	2002	hip fractures

Note: All figures are rounded. Source: Frost & Sullivan

Among the studies included was that of Chapuy (1992), the subjects of which were 3,270 healthy women in France with a median age of 86 (Chapuy, et al., 2002). The treatment group received 1.2 g of calcium and 800 IU of vitamin D per day, while the remainder received a placebo. After 18 months, the incidence of all non-vertebral fractures was 32% lower in the treatment group compared with the placebo group.

33 Dawson-Hughes, Harris, Krall, & Dallal, 1997

34 Larsen, Mosekilde, & Foldspang, 2004

35 Chapuy, et al., 2002

Jackson et al., (2006) recruited 36,282 post-menopausal women in the U.S. aged 50 to 79 years for the Women's Health Initiative (Jackson RD et al., 2006). Half received 1 gram of calcium and 400 IU of vitamin D per day, while the other half received a placebo. After an average of seven years of follow-up, the hazard ratio for all fractures in the treatment group relative to placebo group was 0.97. The risk of kidney stones was significantly higher in the treatment group. The authors noted that, during the study, a fraction of the subjects ceased to adhere to the supplementation schedule, in part because of gastrointestinal symptoms. During the first three years, 60 to 63% adhered to medication by consuming at least 80% of their supplement. By the end of the study, 59% of the subjects were taking 80% or more of their supplement. Of these women, the hazard ratio for hip fracture was 0.71, compared with 0.88 for the entire study sample, suggesting that better adherence to supplementation resulted in a lower risk of fractures.

Porthouse et al., (2005) studied 3,314 women in the U.K. over 70 years of age with one or more risk factors for fracture (Porthouse, et al., 2005). The treatment group received 1 gram of calcium and 800 IU of vitamin D per day. After a median follow-up of 25 months, the rate of fractures in the treatment group was 4.8%, versus 5.0% in the placebo group.

Grant et al., (2005) studied men and women in the U.K. over the age of 70 (Grant, et al., 2005). The treatment group received 1 gram of calcium and 800 IU of vitamin D daily. They were followed for 24 to 62 months and compared with a placebo group. The rate of all new fractures in the treatment group was 14.1%, compared with 14.7% in the placebo group.

Dawson-Hughes et al., (1997) conducted a randomized placebo-controlled trial of 389 men and women in the U.S. over the age of 65. The treatment group received 500 mg of calcium and 700 IU of vitamin D daily; while the remainder received placebo. After three years the incidence of a first fracture was 5.9% in the treatment group and 12.9% in the placebo group.

Larsen et al., (2004) in Denmark studied men and women age 66 and over. The treatment group of 4,957 received 1 gram of calcium and 400 IU of vitamin D daily, while the control group of 2,116 received no intervention. After 42 months the relative risk of osteoporotic fractures was 0.81 for the treatment group compared to the group with no intervention.

Chapuy et al., (2002) conducted a placebo-controlled randomized study of 583 institutionalized women in France of average age 85 years. The treatment group received 1.2 grams of calcium and 800 IU of vitamin D daily. After 2 years the relative risk of hip fracture in the treatment group compared to the placebo group was 0.59.

Figure 7.4—Calcium and Vitamin D Literature Review: Description of the Qualified Studies

Author	Total sample (N)	Relative risk (RR)	Study weight based on within study and between study variance
Jackson	36,282	0.97	22.55%
Chapuy (1992)	3,270	0.75	16.62%
Dawson-Hughes	389	0.46	6.15%
Porthouse	3,314	0.96	19.89%
Grant	2,638	0.96	14.49%
Larsen	7,073	0.81	20.30%
Chapuy (2002)	583	0.59	23.40%

Note: All figures are rounded. Source: Frost & Sullivan

An average of 151,053 avoided osteoporosis-attributed bone fractures per year from 2013 to 2020 or 1.2 million accumulated avoided osteoporosis-attributed bone fractures over the same period is realizable if all U.S. women over the age of 55 diagnosed with osteoporosis were to use calcium and vitamin D dietary supplements to achieve daily protective intake levels.

Empirical Results

Using the D-L approach (DerSimonian & Laird, 1986), the estimated relative risk reduction of a osteoporosis-related medical event (specifically osteoporosis-attributed fractures) given the use of calcium and vitamin D dietary supplements at preventive daily intake levels, was 18.6% after controlling for variance because of sample size, research methodologies and study protocols, and patient population differences within each study and among all studies. Using the D-L approach to calculate the NNT, it was determined that 58 people had to be treated with calcium and vitamin D supplements to avoid one osteoporosis-attributed fracture event.

Figure 7.5—Calcium and Vitamin D Literature Review: Summary Results—D-L Approach

Metric	Measure
Weighted relative risk (weighted for intra-study variance), (RR)	81.4%
Weighted relative risk reduction (weighted for intra-study variance), (RRR)	18.6%
Number of people needed to be treated to avoid one osteoporosis-attributed fracture (NNT), people	58
Average number of fractures avoided annually if everybody in the target population* used calcium and vitamin D supplements to achieve protective intake levels , 2013–2020, people	151,053
Cumulative number of fractures avoided if everybody in the target population* used calcium and vitamin D supplements to achieve protective intake levels, 2013–2020, people	1,208,422

*All women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

An average of $1.87 billion per year and a cumulative savings of $15.00 billion from 2013 to 2020 in avoidable hospital utilization costs is potentially realizable if all U.S. women over the age of 55 diagnosed with osteoporosis were to use calcium and vitamin D dietary supplements at preventive daily intake levels.

Given the estimated NNT of 58 people, the effect on avoided hospital utilization expenditures related to osteoporosis-attributed fractures among all U.S. women over the age of 55 would be an average annual total savings of $1.8 billion per year and cumulative savings of $15 billion from 2013 to 2020, assuming an average annual per person cost of an event at $11,020. This equates to an average of 151,053 avoided events per year over the next seven years or 1,208,422 accumulated avoided events over the same period.

A review of the retail calcium and vitamin D products on the market revealed that the cost of a daily dose of calcium and vitamin D ranges from $0.06 to $0.32. The median cost is $0.16 per day. Using this figure, the expected annual cost of supplementation for each woman over the age of 55 with diagnosed osteoporosis would be $43.22, for a total of more than $356 million per year for the entire subpopulation—more than $2.8 billion cumulatively from 2013 to 2020. The net cost savings, after accounting for the cost of calcium and vitamin D dietary supplementation, would average $1.5 million per year—$12.15 billion cumulatively from 2013 to 2020. See Figures 8.26 to 8.29 in the appendix for a detailed reporting of the empirical results.

Figure 7.6—Calcium and Vitamin D Cost Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population*, 2013–2020

Metric	Measure
Median cost of calcium and vitamin D supplementation at protective daily intake levels, 2013	$0.16
Expected annual median cost of calcium and vitamin D supplementation at protective daily intake levels, 2013	$43.22
Average annual cost of calcium and vitamin D dietary supplementation of the target population, 2013–2020	$355.8 M
Cumulative cost of calcium and vitamin D dietary supplementation of the target population, 2013–2020	$2.85 B

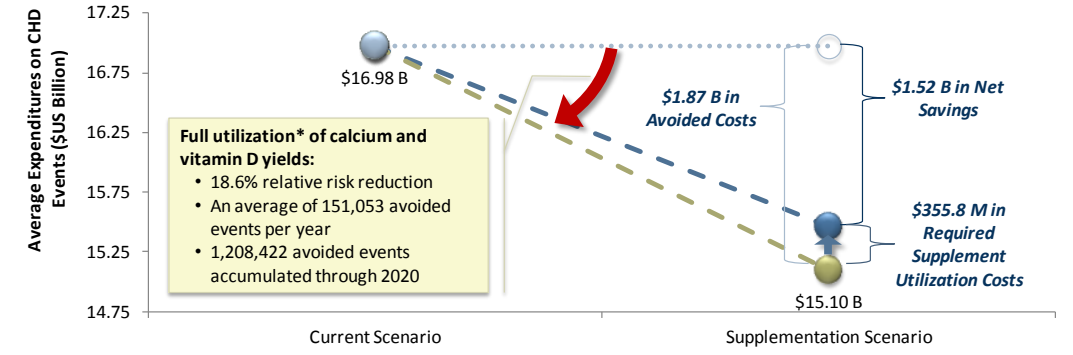
*Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

Figure 7.7—Calcium and Vitamin D Cost Analysis: Summary Results—Avoided Hospital Utilization Expenditures* due to Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average annual avoided hospital utilization expenditures related to osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of calcium and vitamin D supplements, 2013–2020	$1.87 B
Cumulative avoided hospital utilization expenditures related to osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of calcium and vitamin D supplements, 2013–2020	$15.00 B
Average annual hospital utilization expenditures osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of calcium and vitamin D supplements, 2013–2020	$15.10 B
Cumulative hospital utilization expenditures osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of calcium and vitamin D supplements, 2013–2020	$120.81 B

*Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

Figure 7.8—Calcium and Vitamin D Cost Analysis: Net Health Care Cost Savings* Summary Results, 2013–2020



* Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

Figure 7.9—Calcium and Vitamin D Cost Analysis: Summary Results—Net Cost Savings* due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average net potential direct savings per year from avoided osteoporosis-attributed fractures due to calcium and vitamin D dietary supplement intervention, 2013–2020	$1.52 B
Cumulative net potential direct savings from avoided osteoporosis-attributed fractures due to calcium and vitamin D dietary supplement intervention, 2013–2020	$12.15 B
Net benefit cost ratio, $ per one dollar spent on dietary supplement	$5.27

* Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

The prior cost-benefit analysis assumes that in the supplementation scenario all U.S. women over the age of 55 with osteoporosis use calcium and vitamin D dietary supplements at preventive daily intake levels from a base of zero usage among this population segment. In other words, the calculated net savings is actually the total potential net savings that are realizable. However, because a significant proportion of women over the age of 55 with osteoporosis are regular users of calcium and vitamin D dietary supplements, this segment of the target population already has a reduced risk of experiencing a costly osteoporosis-attributed fracture and is realizing the supplements' risk-reducing benefits.

Over $12 billion in cumulative net osteoporosis-attributed cost savings is potentially realizable if the entire target population were to use calcium and vitamin D dietary supplements at protective daily intake levels.

It is expected that there are significant potential cost savings yet to be realized valued at over $8.6 billion in cumulative net osteoporosis-attributed cost savings if all current non-regular users in the high-risk target population were to fully utilize calcium and vitamin D dietary supplements at protective intake levels from 2013 to 2020.

According to the 2012 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs and Frost & Sullivan estimates, 29% of women over the age of 55 in the United States are regular users of calcium and vitamin D dietary supplements (Ipsos Public Affairs, 2012).[36] This implies that 71% do not realize the benefits of regular usage. Because avoided expenditures and net cost savings are a direct function of the total number of people in the target population using calcium and 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.

Knowing this, it is expected that more than $440.0 million of the $1.52 billion in net potential direct savings per year from avoided osteoporosis-attributed fractures due to calcium and vitamin D dietary supplement intervention is already realized in the total expected costs. This equates to an average of 107,248 avoidable events per year yet to be realized because of underutilization of these supplements, which corresponds to an average of $1.08 billion per year in net savings yet to be realized—nearly $8.63 billion in cumulative net savings from 2013 to 2020. Thus, it is expected that there is significant cost savings yet be realized through the increased usage of calcium and vitamin D dietary supplements among the high-risk target population.

Figure 7.10—Calcium and Vitamin D Cost Analysis: Summary Results—Net Cost Savings* Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Percentage of women over the age of 55 who are regular users of calcium and vitamin D dietary supplements, 2012	29%
Average number of events avoided annually among the target population* yet to regularly use calcium and vitamin D supplements, 2013–2020	107,248
Cumulative number of events avoided among the target population* yet to regularly use calcium and vitamin D supplements, 2013–2020	857,980
Average net direct savings per year from avoided osteoporosis-attributed fractures due to calcium and vitamin D dietary supplement intervention yet to be realized, 2013–2020	$1.08 B
Cumulative net direct savings from avoided osteoporosis-attributed fractures due to calcium and vitamin D dietary supplement intervention yet to be realized, 2013–2020	$8.63 B

*Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Ipsos Public Affairs and Frost & Sullivan

36 It is not known what percentage of this target population also suffers from osteoporosis, but for the purposes of this analysis, Frost & Sullivan has made the assumption that approximately the same percentage—33% and 29%—of women over the age of 55 regularly takes calcium supplements and vitamin D supplements, respectively. Further, Frost & Sullivan took the lower of the two percentages—vitamin D at 29%—since it is necessary to realize a preventive effect. Finally, as the Ipsos survey did not ask dosage, Frost & Sullivan has made the assumption that regular users in this target population are highly likely to be consuming enough calcium and vitamin D to provide a protective effect. More research is required to test these assumptions.

Magnesium

Magnesium is a key structural constituent of bone.

Literature Review

About 60% of all magnesium in the body is found in bone, where it is a structural constituent, along with calcium phosphate; this magnesium makes up about 1% of the total bone mineral content (Memorial Sloan-Kettering Cancer Center, 2013). Major dietary sources of magnesium are leafy green vegetables, such as spinach; wheat bran and whole grains; nuts; and legumes, such as lentils and black-eyed peas (Memorial Sloan-Kettering Cancer Center, 2013).

The IOM recommends that women over the age of 31 consume 320 mg of magnesium per day (Memorial Sloan-Kettering Cancer Center, 2013). No UL has been established for magnesium consumed in foods because there are no reports of adverse effects from consuming magnesium through food; however, consumption of magnesium in a concentrated source, such as a tablet, can potentially have a laxative effect. Because of this, the IOM in 1997 established a UL of 350 mg for supplementary magnesium based on the potential for diarrhea from the use of supplemental or pharmacologic magnesium salts. A LOAEL of 360 mg for supplemental or pharmacologic magnesium sources was established, and an uncertainty factor close to 1 was applied to derive the UL of 350 mg. The low uncertainty factor was selected "due to the very mild, reversible nature of osmotic diarrhea caused by ingestion of magnesium salts" (Institute of Medicine, 1997).

For the purpose of modeling magnesium supplementation for health care, this analysis focused only on the risk of fractures attributed to osteoporosis. The objective was to identify a set of studies that represented the state of scientific literature on magnesium supplementation and its link to fracture risk. The only available studies that looked at this subject tested for a causal relationship between magnesium supplement intake and the level of bone density, which is correlated to the relative risk of fracture. The research team only included studies similar in protocol in an attempt to control for observable variance. Studies were not selected on the basis of the magnitude or statistical significance of the reported findings.

Through a rigorous search conducted on PubMed, 12 studies were identified as matching keyword combinations such as “magnesium”; “osteoporosis” and/or “fracture”; and “risk reduction.” The search was conducted between February 1 and May 31, 2013. Initially, the search focused on studies that directly linked magnesium supplementation to fracture risk in women because of their greater risk of fractures related to bone health; however, no such studies were identified. The search then expanded for studies relating magnesium dietary intake and its relation to bone mineral density (BMD). The research team’s search identified two representative epidemiological studies of dietary magnesium intake and BMD.

In a prospective study, Tucker et al., (1999) questioned 562 elderly U.S. women about dietary intake over one year (Tucker, Hannan, Chen, Cupples, Wilson, & Kiel, 1999). BMD was measured by dual photon absorptiometry (DPA) at three sites in the hip (femoral neck, trochanter, and Ward's area) and one site in the forearm (radius). The authors found that for every 100 mg increase in magnesium intake, BMD was significantly higher in the hip, by 0.02 g/cm2 in the trochanter and by 0.016 g/cm2 in Ward's area. The increase at the femoral neck was 0.012 g/cm2, but this was not statistically significant.

Ryder et al., (2005) prospectively studied black and white men and women in the U.S. between the ages of 70 and 79. Subjects were questioned on dietary variables, and BMD was measured by whole body dual energy X-ray absorptiometry (DXA) (Ryder, et al., 2005). In white women (n=534), magnesium intake was positively associated with increased BMD. The difference in BMD between the highest and lowest quintile of magnesium intake was 0.04 g/cm2. This relationship was not statistically significant in black women.

To estimate changes in fracture risk from changes in bone mineral density because of magnesium intake, the FRAX online tool (WHO Fracture Risk Assessment Tool) was employed (World Health Organization Collaborating Centre for Metabolic Bone Diseases, 2013). This tool takes inputs factors such as sex, age, height, weight, and BMD at the femoral neck. The FRAX outputs are 10-year probabilities for the following: (a) major osteoporotic fracture; and (b) hip fracture.

To model fracture risk with FRAX, Frost & Sullivan used the following input factors:

- Female
- 70 years of age, average
- 63 inches in height, average
- 140 pounds in weight, average
- Bone densitometry system: GE Lunar

The resulting calculated input value for BMD was 0.700 g/cm2, which is near the upper limit of the definition of osteoporosis (World Health Organization Collaborating Centre for Metabolic Bone Diseases, 2013). These inputs yielded a specific fracture risk from the FRAX tool. Frost & Sullivan then repeated the calculation to obtain a fracture risk using a BMD of 0.688 g/cm2. The difference between the two BMD values is 0.012 g/cm2. Tucker et al., (1999) found that a 100 mg/day increase in magnesium intake is correlated with an increase in BMD of 0.012 g/cm2 at the femoral neck. Frost & Sullivan chose to model a 100 mg/day increase in magnesium, noting that 100 mg/day is approximately one standard deviation of the mean magnesium intake in the study of Tucker et al., (Tucker, Hannan, Chen, Cupples, Wilson, & Kiel, 1999).

Having values of fracture risk for each of the two BMD values, Frost & Sullivan next calculated the relative risk at 0.700 g/cm2 compared with 0.688 g/cm2 and obtained a value of 0.93 relative risk. This process for calculating relative risk was repeated with inputs for a woman 80 years of age. In this case, the relative risk was 0.95. The average of these two (0.94) is the relative risk used as input for economic modeling, assuming a magnesium intake of 100 mg/day more than normal intake levels.

Empirical Results

The calculated relative risk reduction of an osteoporosis-related medical event, specifically osteoporosis-attributed fractures, given the use of magnesium dietary supplements at the preventive level of 100 mg per day, was 6% 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 1.3 million women over the age of 55 will experience an osteoporosis-related fracture out of the 8.2 million people who are classified as high-risk (15.1% of the total sub-population), using the CEBM approach, 129 people must use magnesium supplements at the preventive level of 100 mg per day to avoid one osteoporosis-attributed fracture.

An average of 68,536 avoided osteoporosis-attributed bone fractures per year from 2013 to 2020 or 548,284 accumulated avoided osteoporosis-attributed bone fractures over the same period is realizable if all U.S. women over the age of 55 diagnosed with osteoporosis were to use magnesium dietary supplements at the preventive intake level of 100 mg per day.

Figure 7.11—Magnesium Literature Review: Overall Results—CEBM Approach

Metric	Measure
Weighted relative risk (weighted for intra-study variance)	94.0%
Weighted relative risk reduction (weighted for intra-study variance)	6.0%
Number of people needed to be treated to avoid one osteoporosis-attributed fracture event (NNT), people	129
Average number of fractures avoided annually if everybody in the target population* used magnesium supplements at the preventive intake level of 100 mg per day, 2013–2020, people	68,536
Cumulative number of fractures avoided if everybody in the target population used magnesium supplements at the preventive intake level of 100 mg per day, 2013–2020, people	548,284

Note: All figures are rounded. Source: Frost & Sullivan

Given the NNT of 129 people, which is achievable if every individual high-risk in the target population—all U.S. women over the age of 55 with osteoporosis—were to take magnesium supplements at the preventive intake level of 100 mg per day, the effect on avoided expenditures related to osteoporosis-attributed fractures would be an average annual total savings of up to $851 million per year and cumulative savings of $6.8 billion from 2013 to 2020. This equates to an annual average of 68,536 avoided events over the next seven years and 548,284 accumulated avoided events over the same period.

An average of $850.6 million per year and a cumulative savings of $6.80 billion from 2013 to 2020 in avoidable hospital utilization costs is potentially realizable if all U.S. women over the age of 55 diagnosed with osteoporosis were to use magnesium dietary supplements at the preventive intake level of 100 mg per day.

Based on the review of best-selling magnesium supplement products in leading brick-and-mortar, online, and mail-order retail establishments, the cost of a daily dose of magnesium is between $0.03 and $0.34. The median daily price is $0.085—$31.01 per year. Given this median price, the total expected average annual cost of supplementation for 8.2 million people would be $255.3 million per year and $2.04 billion in cumulative expenditures from 2013 to 2020.

Figure 7.12—Magnesium Cost Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population*, 2013–2020

Metric	Measure
Median cost of magnesium supplementation at protective levels, 2013	$0.09
Expected annual median cost of magnesium supplementation at protective levels, 2013	$31.01
Average annual cost of magnesium dietary supplementation of the target population* , 2013–2020	$255.3 M
Cumulative cost of magnesium dietary supplementation of the target population* , 2013–2020	$2.04 B

*All women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

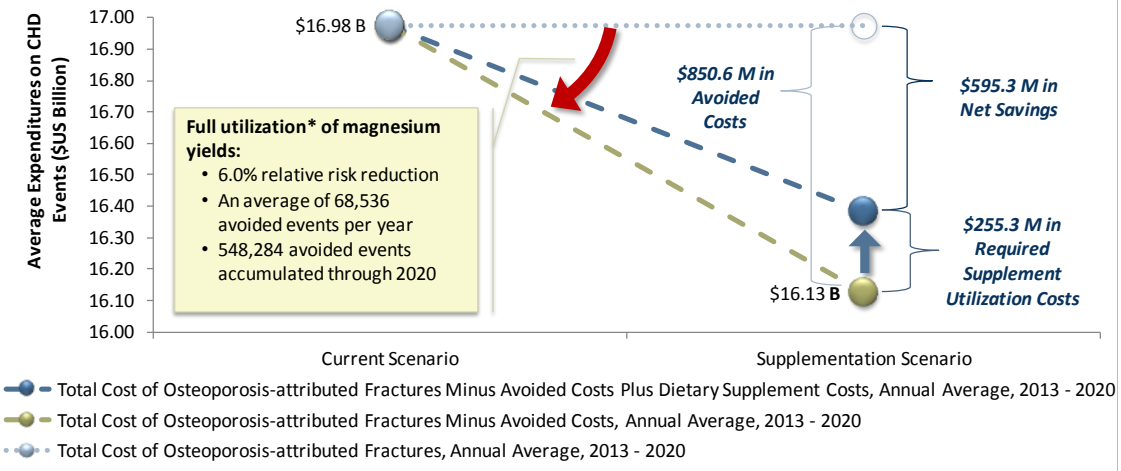
Figure 7.13—Magnesium Cost Analysis: Summary Results—Avoided Hospital Utilization Expenditures* due to Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average annual avoided hospital utilization expenditures related to osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of magnesium supplements, 2013–2020	$850.6 M
Cumulative avoided hospital utilization expenditures related to osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of magnesium supplements, 2013–2020	$6.80 B
Average annual hospital utilization expenditures osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of magnesium supplements, 2013–2020	$16.13 B
Cumulative hospital utilization expenditures osteoporosis-attributed fractures among the target population* if incidence is reduced through the use of magnesium supplements, 2013–2020	$129.00 B

*Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

Thus, the total hospital utilization cost savings derived from avoided osteoporosis events for the same population was, on average, $851 million per year and nearly $6.8 billion in cumulative savings during the forecast period. The net savings, after accounting for the cost of magnesium dietary supplementation, would average $595.3 million per year and total $4.76 billion from 2013 to 2020. See Figures 8.30 to 8.33 in the appendix for a detailed reporting of the empirical results.

Figure 7.14—Magnesium Cost Analysis: Net Health Care Cost Savings* Summary Results, 2013–2020



* Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

$4.76 billion in cumulative net osteoporosis-attributed cost savings is potentially realizable if the entire target population were to use magnesium dietary supplements to increase intake by 100 mg per day.

Figure 7.15—Magnesium Cost Analysis: Summary Results—Net Cost Savings* due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average net potential direct savings per year from avoided osteoporosis-attributed fractures among the target population* due to magnesium dietary supplement intervention, 2013–2020	$595.3 M
Cumulative net potential direct savings from avoided osteoporosis-attributed fractures among the target population* due to magnesium dietary supplement intervention, 2013–2020	$4.76 B
Net benefit cost ratio, $ per one dollar spent on dietary supplement	$3.33

* Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Frost & Sullivan

This cost-benefit analysis assumes that in the supplementation scenario all U.S. women over the age of 55 with osteoporosis use magnesium dietary supplements from a base of zero use among this population segment. In other words, the calculated net savings is actually the total potential net savings that are realizable. However, because some women over the age of 55 with osteoporosis are already regular users of magnesium dietary supplements, this segment of the target population has a reduced risk of experiencing a costly osteoporosis-attributed fracture and is realizing the supplement's risk-reducing benefits.

It is expected that there are significant potential cost savings yet to be realized valued at nearly $4.24 billion in cumulative net osteoporosis-attributed cost savings if all current non-regular users in the high-risk target population were to utilize magnesium dietary supplements at the preventive intake level of 100 mg per day.

According to the 2012 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs and Frost & Sullivan estimates, 11% of U.S. women over the age of 55 are regular users of magnesium dietary supplements (Ipsos Public Affairs, 2012).[37] This implies that 89% do not realize the benefits of regular magnesium supplement usage. Because avoided expenditures and net cost savings are a direct function of the total number of people in the target population using magnesium 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 is estimated that more than $65.5 million of the $595.3 million in net potential direct savings per year from avoided osteoporosis-attributed fractures because of magnesium dietary supplementation is already realized. This equates to an average of 60,997 avoidable events per year yet to be realized due to underutilization of magnesium supplements, which corresponds to an annual average of $529.8 M per year in net savings yet to be realized due to underutilization of magnesium dietary supplements or nearly $4.24 B in cumulative net savings from 2013 to 2020. Thus, it is expected that there is significant cost savings yet to be realized through the increased usage of magnesium dietary supplements among the high-risk target population.

37 It is not known what percentage of this target population also suffers from osteoporosis, but for the purposes of this analysis, Frost & Sullivan has made the assumption that approximately the same percentage—11%—of women over the age of 55 regularly takes magnesium supplements. Also for the purposes of this analysis, as the Ipsos survey did not ask dosage, Frost & Sullivan has made the assumption that regular users in this target population are highly likely to be consuming enough magnesium supplements to provide a protective effect. More research is required to test these assumptions.

Figure 7.16—Magnesium Cost Analysis: Summary Results—Net Cost Savings* Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Percentage of women over the age of 55 who are regular users of magnesium dietary supplements, 2012	11%
Average number of events avoided annually among the target population* yet to regularly use magnesium supplements ,2013–2020	60,997
Cumulative number of events avoided among the target population* yet to regularly use magnesium supplements, 2013–2020	487,973
Average net direct savings per year from avoided osteoporosis-attributed fractures among the target population* due to magnesium dietary supplement intervention yet to be realized, 2013–2020	$529.8 M
Cumulative net direct savings from avoided osteoporosis-attributed fractures among the target population* due to magnesium dietary supplement intervention yet to be realized, 2013–2020	$4.24 B

* Among all U.S. women over the age of 55 with osteoporosis
Note: All figures are rounded. Source: Ipsos Public Affairs and Frost & Sullivan

Conclusion

Osteoporosis is the most prevalent bone disease in the United States, with more than $14.00 billion in annual direct health care costs for treatment of osteoporosis fractures. This cost does not include post-procedure care, loss of mobility and independence, and a general reduction in a patient's quality of life. Given the full usage of calcium and vitamin D at preventive daily intake levels among all U.S. women over the age of 55 diagnosed with osteoporosis, upwards of $1.5 billion per year and more than $12.20 billion from 2013 to 2020 can be saved because of avoided osteoporosis-attributed fractures. This equates to $5.27 in savings per $1 spent on calcium and vitamin D supplements. For magnesium dietary supplementation, the total net cost savings from avoided osteoporosis events among the same high-risk population would average $595.3 million per year and over $4.8 billion in cumulative health care cost savings over the next seven years could be realized from 2013 to 2010, or $3.33 per $1 spent on magnesium supplements. As fractures attributed to osteoporosis become more prevalent in the U.S. due to the general aging of America, the importance of leveraging the substantiated benefits of calcium, vitamin D, and magnesium to help prevent costly events is an obvious means to help control the increasing financial burden of this disease.

As fractures attributed to osteoporosis become more prevalent in the U.S. due to the general aging of America, the importance of leveraging the substantiated benefits of calcium, vitamin D, and magnesium as a means to help prevent these costly events is an obvious means to help control the increasing financial burden of this disease.