FROST & SULLIVAN

Healthcare Cost Savings of Calcium and Vitamin D Food Supplements in the European Union

Exploring the Burden of Osteoporosis-attributed Bone Fractures in the European Union and the Benefits of Calcium + Vitamin D Food Supplements

food supplements europe

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Table of Contents

Abstract

The objective of this report is to evaluate whether healthcare cost savings can be realised through the use of a 1,000 mg calcium + 15 µg vitamin D supplement, which has a demonstrable and substantial effect on the risk of costly disease-attributed events in high-risk populations. This report examines aggregated indications demonstrating that the use of a 1,000 mg calcium + 15 µg vitamin D supplements can potentially reduce osteoporosis-attributed hospital utilisation costs in the European Union among those at a high risk of experiencing a costly, osteoporosis-attributed event. Thus, a targeted calcium + vitamin D supplement regimen is recommended as a means to help control rising societal healthcare costs and as a means for high-risk individuals to minimise the chance of having to deal with potentially detrimental disease-attributed events.

Target Population— Osteoporosis is a significant health burden faced by over 27.8 million people age 55 and older in the European Union, of which women account for approximately 80% of the prevalence of this condition (22.2 million women). The direct cost of osteoporosis-attributed bone fracture treatment in Europe is over € 26.4 billion per year and is expected to grow as Europe's population ages. This translates to an annual cost of an osteoporosis-attributed bone fracture in the EU of € 21,231 per event.

Event Risk—In terms of risk, prevalence of osteoporosis is especially higher in the European Union which varies from 15% to 21% of the total population of people age 55 and older depending on the country. In 2015, there was 1.2 million disease–attributed bone fractures among people age 55 and over with osteopenia or osteoporosis in the EU who are at risk of experiencing a costly disease-attributed bone fracture which is more than any other region of the world.

Science-based Impact of Calcium + Vitamin D Use— Weaver et al. 2015 show that the use of a calcium + vitamin D supplement resulted in a 15% reduced risk of total fractures (Relative Risk (RR) = 0.85; 95% CI: 0.73–0.98). Consequently, the deduced absolute risk reduction of an osteoporosis-attributed bone fracture of any type varies from as high as 1.3% of the total number of observed fractures to a low of 0.4% in the EU.

- Economic Implications (Total EU)
    - Total Avoidable Osteoporosis-attributed Costs per year (S): € 3.96 billion
    - Net Avoidable Osteoporosis-attributed Costs per person per year (B/Pop): € 2.82 billion
    - Benefit/cost ratio (€ Avoided Osteoporosis-attributed Costs per € 1 spent on calcium + vitamin D): €3.47

Osteoporosis and the Benefits of Using Calcium & Vitamin D

As osteoporosis becomes increasingly more prevalent, the importance of using regimen options known to decrease bone fracture risk becomes more apparent as a means to control the increasing financial burden of osteoporosis.

Background

Osteoporosis is a bone disease in which the density and quality of bone are reduced, leading to weakness of the skeleton [1, 2]. This condition significantly increases the risk of fracture from a fall, particularly at the hip, spine, and wrist. While osteoporosis alone usually does not directly cause deaths, osteoporotic fractures can lead to premature disability and death, especially among the elderly. 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.

Osteoporosis is a significant health burden faced by over 27.8 million people age 55 and older in the European Union, of which women account for approximately 80% of the prevalence of this condition (22.2 million women) [3, 4]. In terms of risk, prevalence of osteoporosis is especially higher in the European Union which varies from 15% to 21% of the total population of people age 55 and older depending on the country [3]. In 2015, 1.2 million osteoporosis–attributed bone fractures occurred among people age 55 and over with osteopenia or osteoporosis in the EU who were at risk of experiencing a costly disease-attributed bone fracture which was more than any other region of the world [3]. Furthermore, it is estimated that over 995,000 osteoporosis-attributed bone fractures occur each year among European women age 55 and older.

As shown on Table 1, the risk of an osteoporosis-attributed bone fracture varies by country. The risk of having an osteoporosis-attributed bone fracture is related to a wide range of risk factors including an individual's physical location (for example, north Europe versus south Europe) and physical altitude (for example, Alpine states versus Low Countries) which in turn impacts the amount of natural sunlight an individual is exposed to. Also, diet, lifestyle and quality of life impact the risk of developing osteoporosis and experiencing a related bone fracture. However, there are also likely other factors that can skew the observed risk such as type of house the individual lives in (for example a 2 story building versus a one story building) and other pre-existing medical conditions. Also, the medical professional diagnosing a given bone fracture might relate it to a different cause or not state the pre-conditions, which can result in under-reporting of the burden of osteoporosis for a given country. In other words, some medical professionals may be more likely to state a fracture as being linked to osteoporosis, whereas other medical professionals may not refer to this causal link, even if the person has osteoporosis. Despite all this, the health burden of the observed cases of osteoporosis is still immense. See Table 1 for a detailed description of the health burden of osteoporosis in the EU.

This health burden translates to a significant financial burden as well. According to a report developed by the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA) and a systematic review for the IOF Working Group on Epidemiology and Quality of Life, it is expected that the direct cost of osteoporosis-attributed bone fracture treatment in Europe is over € 26.4 billion per year, after adjusted for purchasing power parity, and is expected to grow as Europe's population ages [3, 4]. These costs only include hospital utilisation costs like ambulance services, in-patient stays, emergency department and outpatient services. The cost of long term care after an osteoporosis-attributed fracture, such as the cost of rehabilitation, home nurses, and community services is not included in this figure, but is expected to be at least an additional € 10 billion per year in the EU [3]. See Table 1 for a detailed description of the health burden of osteoporosis in the EU. Table 2 provides the financial implications of osteoporosis, including the cost of an osteoporosis-attributed bone fracture per EU country.

Table 1
The Burden of Osteoporosis: Population Descriptive Statistics and Event Risk, Annualised Average, 2016-2020

Country	Total Population, Adults age 55 and older[1]	Population with Osteoporosis, Adults age 55 and older[2]	Percent of Population with Osteoporosis	Total Osteoporosis-attributed Fractures per Year[3]	Risk of Fracture among Target Population
Austria	2,574,872	458,547	17.8%	31,975	7.0%
Belgium	3,378,041	597,570	17.7%	29,613	5.0%
Bulgaria	2,395,715	417,907	17.4%	18,919	4.5%
Croatia	1,366,757	257,044	18.8%	13,020	5.1%
Cyprus	217,517	40,295	18.5%	2,183	5.4%
Czech Republic	3,224,578	529,058	16.4%	30,567	5.8%
Denmark	1,705,383	283,368	16.6%	24,270	8.6%
Estonia	408,180	77,431	19.0%	4,281	5.5%
Finland	1,801,776	304,453	16.9%	13,267	4.4%
France	20,023,397	3,475,310	17.4%	132,128	3.8%
Germany	27,840,013	5,023,912	18.0%	212,845	4.2%
Greece	3,544,810	642,707	18.1%	27,128	4.2%
Hungary	3,107,068	547,107	17.6%	28,656	5.2%
Ireland	1,051,651	166,436	15.8%	13,337	8.0%
Italy	20,248,958	3,792,031	18.7%	149,889	4.0%
Latvia	630,755	130,446	20.7%	5,713	4.4%
Lithuania	900,267	175,511	19.5%	8,343	4.8%
Luxembourg	139,939	21,963	15.7%	1,302	5.9%
Malta	134,864	20,264	15.0%	1,120	5.5%
Netherlands	5,078,117	818,502	16.1%	30,967	3.8%
Portugal	3,233,995	593,620	17.6%	17,230	2.9%
Poland	11,381,429	1,848,528	16.6%	67,062	3.6%
Romania	5,966,193	1,033,950	17.3%	61,436	5.9%
Slovakia	1,455,578	231,637	15.9%	18,197	7.9%
Slovenia	647,904	110,032	17.0%	6,228	5.7%
Spain	13,719,534	2,449,355	17.9%	76,844	3.1%
Sweden	2,992,914	523,095	17.5%	37,725	7.2%
United Kingdom	18,426,690	3,206,755	17.4%	180,355	5.6%
Total EU	157,596,895	27,776,834	17.6%	1,244,600	4.5%

Note: All figures are rounded.

17.6% of the adults age 55 and older are inflicted with osteoporosis in the European Union.

[1] Source: European Commission (Eurostat) (http://ec.europa.eu/eurostat/data/database),
[2] Source: Herlund et al. (2013)
[3] Source: Kanis et al. (2012)

The cost of osteoporosis-attributed fractures is a significant burden on society throughout the world in terms of direct hospital utilisation costs.

Table 2
The Burden of Osteoporosis: The Costs of Osteoporosis-attributed Bone Fracture Events, Annualised Average, 2016-2020[4]

Country	Total Cost of Osteoporosis-attributed Fractures, € Million[5]	Cost per Fracture
Austria	€ 551	€ 17,233
Belgium	€ 419	€ 14,149
Bulgaria	€ 66	€ 3,488
Croatia	€ 125	€ 9,848
Cyprus	€ 42	€ 19,039
Czech Republic	€ 302	€ 9,896
Denmark	€ 564	€ 23,244
Estonia	€ 35	€ 8,075
Finland	€ 247	€ 18,586
France	€ 3,497	€ 26,466
Germany	€ 7,279	€ 34,197
Greece	€ 671	€ 24,735
Hungary	€ 233	€ 8,125
Ireland	€ 125	€ 9,372
Italy	€ 4,696	€ 31,329
Latvia	€ 24	€ 4,479
Lithuania	€ 51	€ 6,484
Luxembourg	€ 14	€ 10,561
Malta	€ 15	€ 13,502
Netherlands	€ 360	€ 11,625
Portugal	€ 434	€ 25,182
Poland	€ 537	€ 8,010
Romania	€ 194	€ 3,151
Slovakia	€ 119	€ 6,563
Slovenia	€ 49	€ 7,948
Spain	€ 1,677	€ 21,822
Sweden	€ 784	€ 20,792
United Kingdom	€ 3,314	€ 18,376
Total EU	€ 26,424	€ 21,231

Note: All figures are rounded.

[4] Source: Kanis et al. (2012), Herlund et al. (2013), and author analysis.
[5] These costs only include hospital utilisation costs like ambulance services, in-patient stays, emergency department and outpatient services. The cost of long term care after an osteoporosis-attributed fracture, such as the cost of rehabilitation, home nurses, and community services is not included in this figure, but is expected to be at least an additional € 10 billion per year in the EU. Costs have been adjusted for purchasing power parity in order to ensure consistent comparability. All figures are rounded to the closest one million euro, which may cause some variance.

As osteoporosis becomes more prevalent in the EU, the option of using a calcium + vitamin D food supplement as a means to control the social financial burden of osteoporosis in the long run has never been greater. Specifically, calcium and vitamin D are a key combination food supplement that has been shown to contribute to osteoporosis-attributed health benefits. In the following case study, the potential healthcare cost savings in each country of the European Union that can be realised through the use of a calcium + vitamin D supplement are described. Specifically, the following case study on calcium + vitamin D considers the healthcare cost savings derived from avoided bone fracture hospital-based treatment and long term post treatment/disability costs for the population of adults age 55 and older diagnosed with osteoporosis.

Calcium and vitamin D food supplements has been shown to contribute to osteoporosis-attributed health benefits

Thus, the following case study provides a process whereby a decision maker can first examine the body of scientific literature that tests the link between the use of a calcium + vitamin D food supplement and the risk of an osteoporosis-attributed bone fracture, in order to determine an overarching expected level of risk reduction. These aggregated risk reduction metrics derived from the scientific literature can then be used to determine the potential healthcare cost savings that could be realised if the entire population of adults age 55 and older diagnosed with osteoporosis were to use a calcium + vitamin D. Substantially positive benefits per user will provide support for the decision maker, whether it's the payer of healthcare services or the individual, in arriving at an optimal health, and financial, choice.

Most Europeans are nowhere close to reaching tolerable intake levels of vitamin D.

The Benefits of Using Calcium and Vitamin D

Calcium is an essential mineral that is mainly stored in the bones of the human body [5, 6]. It is required for the normal development and maintenance of the skeleton and ensures the optimal operation of neuromuscular and cardiac functions [5, 6]. Required calcium intake is typically met through the consumption of calcium-rich foods such as dairy products, nuts, and fish, but the absorption and metabolisation of this mineral is dependent on vitamin D [5, 6]. Specifically, vitamin D improves the efficiency of the small intestine in absorbing calcium and phosphorus from a regular diet, which in turn helps to regulate the concentration of these minerals in the body within acceptable limits [5, 6]. Sufficient vitamin D intake is particularly important in low-sunlight conditions, as the body's ability to synthesise the compound cholecalciferol, or vitamin D3, is dependent on exposure to ultraviolet light. The other known vitamin D is vitamin D2, or ergocalciferol, which is found in a limited range of foods. Vitamin K has also been shown to be an important nutrient for bone health where vitamin K is involved in the activation of osteocalcin [7]. However, for the purposes of this case study, only the symbiotic relationship between vitamin D and calcium is considered for this analysis.

EFSA opines that "*at least 1200 mg of calcium from all sources or at least 1200 mg of calcium and 800 I.U. [20* µg/day*] of vitamin D from all sources to be consumed daily should be considered for the purpose of setting conditions of use for a risk reduction claim on the loss of BMD* [bone mineral density]*, which may contribute to a reduction in the risk of osteoporotic bone fracture. The target population is women 50 years and older* [8]." The tolerable upper intake level (UL) of calcium + vitamin D by all adults is 2500 mg/day of calcium and 100 µg/day of vitamin D [8]. Furthermore, the Population Reference Intake (PRI) for young adults was set at 1,000 mg/day for calcium and the EU Reference Intake (Nutrient Reference Value Requirement (NRV-R)) for vitamin D was set at 15 µg/day for adults by EFSA in 2015 [5, 9].

For the purposes of this case study, it is important to note that the adequate intake of calcium and 15 µg/day vitamin D in younger life stages (as young as childhood and adolescence) can help to lay the foundation of optimized prevention of osteoporotic fractures. Supplementation in later life stages can only counteract or slow down a decline of the status that has been built up in earlier ages. However, the age cohort threshold of 55 and older was adopted for this case study in order to provide a conservative assessment of the health and economic benefits to current and potential users.

Most Europeans are nowhere close to reaching tolerable intake levels of vitamin D. According to Pérez-López et al. (2012), approximately 70% of the European population has sub-optimal levels of vitamin D, which means that they likely also have difficulty absorbing calcium from their diets [10]. Moreover, 35% of the total population has either deficient or severely deficient levels of vitamin D in their bodies. [11]. This suggests that a significant portion of the target population is not realising the potential benefits of regular intake of calcium + vitamin D from foods or food supplements and, thus, are at an increased risk of experiencing an osteoporosis-attributed bone fracture.

There has been a significant amount of research exploring the benefits of calcium + vitamin D utilisation among the elderly, where most of the research has focused on the correlation between calcium + vitamin D use and the risk of an osteoporosis bone fracture. In 2010, EFSA had evaluated the scientific evidence for vitamin D and calcium in osteoporotic fractures and concluded that a cause-effect-relationship had been found [12]. In 2014, Shanahan and de Lorimier conducted a search of the scientific literature that focused on published studies quantifying the effect of utilisation on fracture risk in Australia [13]. Forty nine studies from all parts of the world, including Europe, were identified in a search exercise conducted on PubMed using a combination of keywords including "calcium" and/or "vitamin D"; "osteoporosis" and/or "fracture"; and "risk reduction." RCTs were preferred because they are designed to directly test for a cause-and-effect relationship between utilisation and osteoporosis-attributed bone fracture and as a result 7 RCT studies were identified as being eligible of the literature. [13] 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 [13].

The use of a calcium + vitamin D food supplement can lead to a statistically significant 15% reduced risk of an osteoporosis-attributed bone fracture.

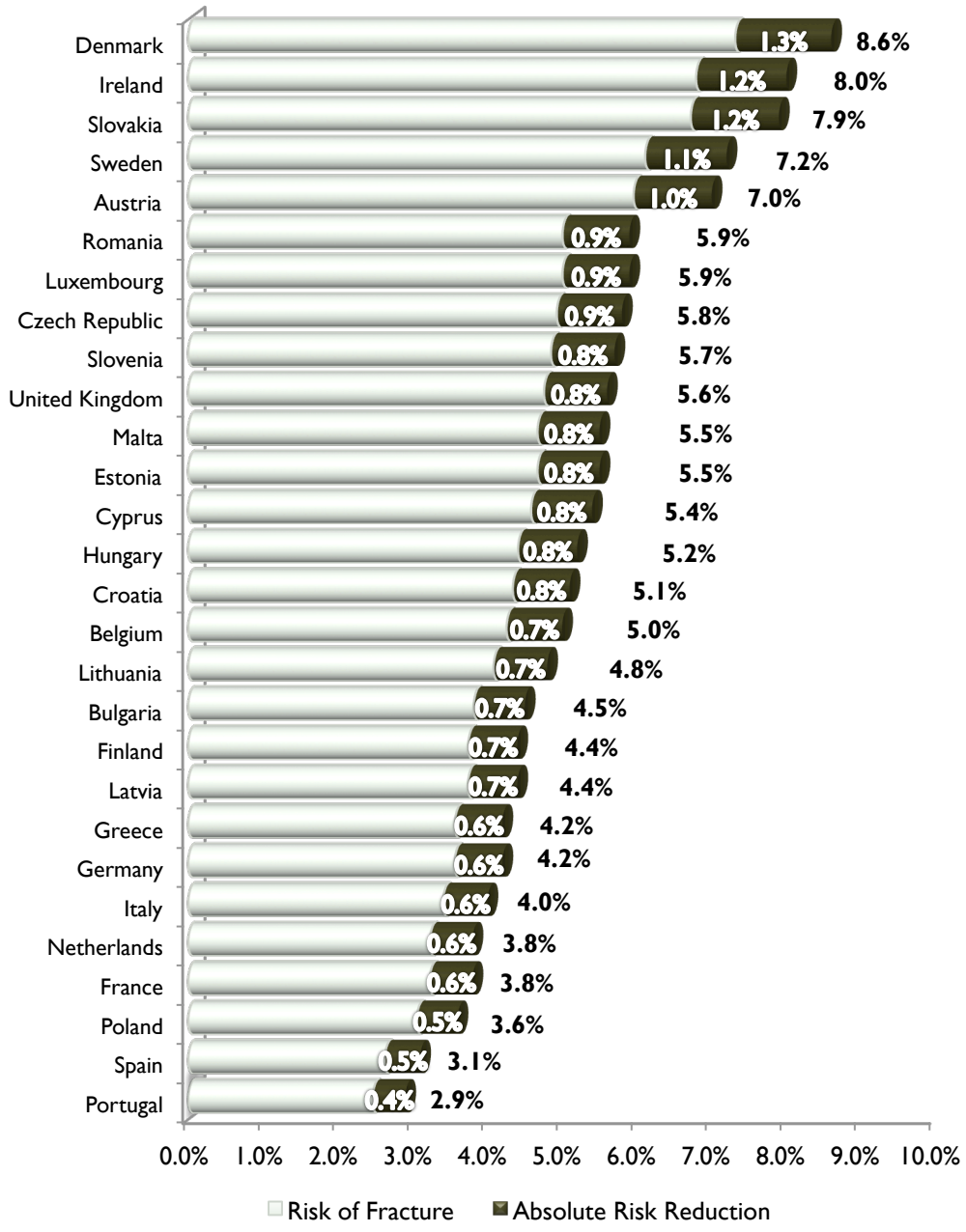
In 2015, researchers from the International Osteoporosis Foundation and National Osteoporosis Foundation [15] conducted the most up-to-date meta-analysis of the body of literature that tested the hypothesis between calcium + vitamin D supplement intake and the risk of a bone fracture [15]. The authors first conducted a PubMed literature search for all random control trials (RCTs) that reported a measured effect of calcium plus vitamin D supplementation on fracture incidence. In all, 8 studies including 30,970 subjects met their criteria for inclusion in their primary meta-analysis and included 2,231 total fractures [15]. The size of the food supplement regimen for calcium ranged from 1,000 to 1,200 mg/day in seven of the studies and in one study the regimen size was 500 mg/day. In six of the studies the regimen level for vitamin D was 800 IU [20 µg/day] and the remaining two studies were 10 µg/day and 17 µg/day. These use levels are in addition to normal dietary intake of calcium and vitamin D. The author's meta-analysis results show that the use of a calcium + vitamin D supplement resulted in a statistically significant 15% reduced risk of total fractures (Relative Risk (RR) = 0.85; 95% CI: 0.73–0.98) and a 30% relative risk reduction (RRR) of hip fractures (RR = 0.70; 95% CI: 0.56–0.87) [15].

By knowing the expected relative risk of an osteoporosis-attributed bone fracture between a user of a calcium + vitamin D supplement, the calculation of the absolute risk reduction for a given EU country's risk profile can be estimated using the following equation:

$$1.\quad N^{*} = Risk_{x}\,(1 - \mathrm{RR}_{x}) = 0.15 * Risk_{x}$$

where x is a given EU country's risk of an osteoporosis-attributed bone fracture and N* is the absolute risk reduction for a given EU country. For example, citizens of Denmark face an expected risk of experiencing an osteoporosis bone fracture is 8.6% as shown in Chart 1, but if an individual was to use a calcium and vitamin D supplement, they can lower their risk by 15%, or an absolute risk reduction of 1.3% basis points to a new, adjusted risk of 7.3%. Chart 1 and Table 3 shows the results of the application of Equation 1 for each EU country.

Chart 1
Risk of an Osteoporosis-attributed Bone Fracture and the Absolute Risk Reduction Potential per Target User, EU, 2016



Source: Kanis et al. (2012), Herlund et al. (2013), and Frost & Sullivan analysis

It is expected that among adults age 55 and older with osteoporosis in the EU, 186,690 bone fractures per year can be avoided if the entire target population used a calcium + vitamin D supplement.

Table 3
Economic Benefits from Calcium + Vitamin D Food Supplement Use: Avoided Costs of Osteoporosis-attributed Bone Fractures Medical Services by EU Country, Annualised Average, 2016-2020

Country	N*: Absolute Risk Reduction per EU Country	A: Total Avoided Osteoporosis-attributed Bone Fractures from use of 1,000 mg/day of Calcium and 15 µg/day of Vitamin D Supplements
Austria	1.05%	4,796
Belgium	0.74%	4,442
Bulgaria	0.68%	2,838
Croatia	0.76%	1,953
Cyprus	0.81%	327
Czech Republic	0.87%	4,585
Denmark	1.28%	3,641
Estonia	0.83%	642
Finland	0.65%	1,990
France	0.57%	19,819
Germany	0.64%	31,927
Greece	0.63%	4,069
Hungary	0.79%	4,298
Ireland	1.20%	2,001
Italy	0.59%	22,483
Latvia	0.66%	857
Lithuania	0.71%	1,251
Luxembourg	0.89%	195
Malta	0.83%	168
Netherlands	0.57%	4,645
Portugal	0.43%	2,585
Poland	0.54%	10,059
Romania	0.89%	9,215
Slovakia	1.18%	2,730
Slovenia	0.85%	934
Spain	0.47%	11,527
Sweden	1.09%	5,659
United Kingdom	0.84%	27,053
Total EU	0.67%	186,690

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

Based on the calculations of absolute risk reduction per EU country, it was found that the expected absolute risk reduction of an osteoporosis-attributed bone fracture of any type that can be realised if all adults in the EU with osteoporosis or osteopenia were to use a 1,000 mg/day of calcium and 15 µg/day of vitamin D supplement varies from as high as 1.3% of the total number of observed fractures to a low of 0.4% in the EU. Denmark faces the greatest risk of an osteoporosis-attributed bone fracture of any type. It should be noted that these risk measurements do not include the potential reduction in bone loss among those adults age 55 and older yet to be diagnosed with either osteoporosis or osteopenia, which would likely add to the expected benefits of calcium and vitamin D use. For the purposes of this study, a conservative approach has been taken due to the difficulty in identifying a proper cut-off point for cost evaluation.

The potential benefits of using a calcium + vitamin D supplement could yield an absolute risk reduction at 1.3% of the total number of observed bone fractures.

Thus, the potential benefits of using a 1,000 mg/day of calcium and 15 µg/day of vitamin D supplement can yield an absolute risk reduction at 1.3% of the total number of observed bone fractures. Countries based in the south of Europe and with smaller proportions of their population being age 55 and older tend to have a lower risk of osteoporosis-attributed bone fractures. It is also consistent with expectations that Nordic countries, or countries in Northern Europe, would have relatively higher calculated N*s due to relatively lower exposure to sunlight on a yearly basis. Also consistent with expectations correlated to geographic considerations, the reported N*s for Spain and Portugal are the lowest calculated N*s in the set. Chart 1 and Table 4 shows the risk of an osteoporosis fracture event per EU country and provides the associated absolute risk reduction measures that can be expected from the use of a calcium + vitamin D supplement by the entire target population of adults age 55 and older given a relative risk of 0.85 from the more up-to-date and conservative findings of Weaver et al. [15].

Once the absolute risk reduction measures have been estimated, then the total number of possible avoidable osteoporosis-attributed bone fractures that could be realised if the entire target population of adults age 55 and older in the EU utilised a daily calcium + vitamin D regimen can be calculated. It is expected that among adults age 55 and older with osteoporosis in the EU, 186,690 bone fractures per year can be avoided if the entire target population used a 1,000 mg/day of calcium and 15 µg/day of vitamin D supplement. As shown in the above-mentioned term, the total number of avoided events is a function of both the size of the target population and the risk that population faces. Consequently, Germany can expect to avoid the greatest number of avoidable bone fractures if their target population used a calcium + vitamin D supplement, where it was estimated that a maximum of 25,530 osteoporosis-attributed bone fractures can be avoided if the entire target population used a daily calcium + vitamin D supplement. Table 4 shows the number of possible osteoporosis-attributed bone fractures that could be avoided per EU country.

The Economic Benefits of using Calcium and Vitamin D

In the case of calcium + vitamin D, this assessment considers the healthcare cost savings derived from avoided hospital-based bone fracture medical expenses for the population of Europeans aged 55 and older diagnosed with osteoporosis. Thus, the following equation is used to calculate total benefits:

$$2.\ S = h * A = h * Pop * N^*$$

where ***h*** is the expected per-person cost of an osteoporosis-attributed bone fracture for a member of the target population ***Pop*** [12, 13]. The combined term ***Pop x N**** is also the total number of avoided fractures that can be expected for a given target population. Of course, there is a cost of calcium + vitamin D utilisation that must be also considered. The net benefits that can be realised from avoided osteoporosis-attributed bone fractures are:

$$3.\ B = S - C = h * A - Pop * d$$

where ***S*** is the total potential savings from reduced hospital service utilisation following osteoporosis-attributed bone fracture events that are realisable if the entire target population was to sufficiently utilise a calcium + vitamin D food supplement daily and the cost of calcium + vitamin D utilisation is represented by the parameter ***C.***

The total cost of a 1,000 mg/day of calcium and 15 µg/day of vitamin D regimen, assuming 100% utilisation by the entire observed population can be represented by ***C=Pop*d*** where ***Pop*** is the total number of people in the target population at risk of experiencing a osteoporosis-attributed event outcome and ***d*** is the expected per person cost of calcium + vitamin D utilisation per year. Note that the entire target population must take the given regimen in order for the total number avoided events to be realised. The result of this calculation provides an economic indication of the net monetary benefits B that the use of calcium + vitamin D can yield for society through hospital cost reduction. Table 4 provides a list of the key variables used to conduct this health-to-wealth theoretical economic analysis.

This assessment considers the healthcare cost savings derived from avoided hospital-based bone fracture medical expenses for the population of Europeans aged 55 and older diagnosed with osteoporosis.

Table 4
List of Key Variables used in this Health Economic Analysis

A	Number of possible avoided events (A) if everybody in a specified target population used a calcium + vitamin D food supplement daily
B	Total potential net economic benefits yet to be realised from use of a calcium + vitamin D food supplement daily
C	Total cost of a calcium + vitamin D food supplement daily
d	The expected per person cost of a calcium + vitamin D food supplement utilisation per year
h	The expected cost of an osteoporosis-attributed bone fracture
N*	Absolute risk reduction that is realisable from the use of a calcium + vitamin D food supplement
Pop	Target Population
S	Total potential savings from reduced hospital service utilisation following osteoporosis-attributed bone fracture events that are realisable if the entire target population were to sufficiently utilise a calcium + vitamin D food supplement daily
S/C	Benefit Cost Ratio
S/Pop	Benefit per User

Source: Frost & Sullivan analysis

It should be noted that not all costs and benefits from using or not using a calcium + vitamin D supplement are incorporated into this equation. This equation is a generalised model that determines the net economic effect of using a given food supplement on the odds of a predefined set of event outcomes. Because of the additive nature of the model, one can easily add in additional expected health benefits that are related or not related to the disease condition of interest. However, for the purposes of this study, the cost and benefits mix is conservatively defined to be in line with the hypothesised relationship between calcium + vitamin D supplement use and a specified disease-attributed event—in this case osteoporosis-attributed bone fractures. Table 5 and Chart 2 show the total healthcare costs savings that are possible from avoided osteoporosis-attributed hospital events by EU country.

The total potential of avoided medical event expenditures, ***S***, can be as much as € 3.96 billion per year. This calculation is based on calculating each EU country's potential cost savings from avoided bone fractures among the target population of adult's age 55 and older and summing up the total value for the entire EU population. Luxembourg has the lowest potential savings (€2.1 million per year) followed by Malta (€2.3 million per year) and Germany had the highest potential savings of €1.09 billion in avoided hospital event costs related to osteoporosis-attributed bone fractures per year. Overall, the five largest EU countries (France, Germany, Italy, Spain, and the UK) combined can expect potential cost savings in excess of €200 million per country per year if the entire target population of adults age 55 and older used calcium and vitamin D on a daily basis. Table 5 describes the detailed results of the economic analysis by EU country.

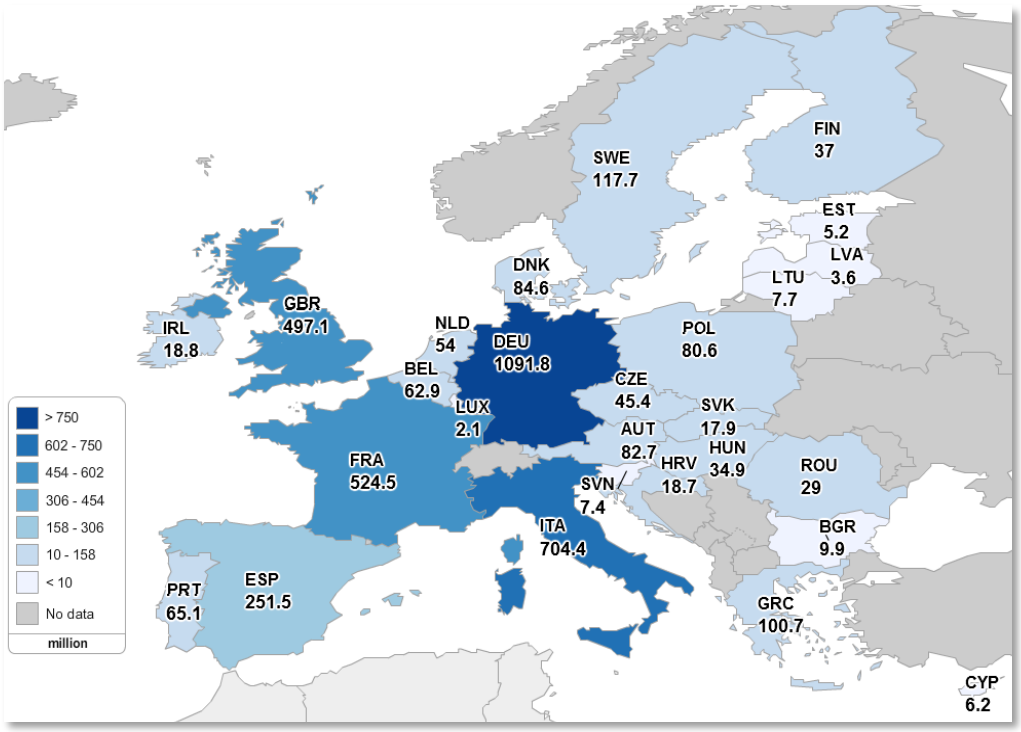
Table 5
Economic Benefits from Calcium + Vitamin D Food Supplement Use: Avoided Healthcare Costs by EU Country, 2016

Country	S: Expected 1 Year Total Avoided Cost of osteoporosis-attributed bone fractures	C: Total Cost of Calcium+Vitamin D per year	B: Net Benefit
Austria	€ 82,653,061	€ 20,631,010	€ 62,022,051
Belgium	€ 62,850,000	€ 27,429,103	€ 35,420,897
Bulgaria	€ 9,900,000	€ 7,632,027	€ 2,267,973
Croatia	€ 18,703,010	€ 6,488,704	€ 12,214,306
Cyprus	€ 6,233,333	€ 1,516,625	€ 4,716,708
Czech Republic	€ 45,375,000	€ 14,185,895	€ 31,189,105
Denmark	€ 84,621,429	€ 16,483,985	€ 68,137,443
Estonia	€ 5,185,714	€ 2,498,473	€ 2,687,241
Finland	€ 36,987,500	€ 15,635,081	€ 21,352,419
France	€ 524,535,000	€ 157,941,041	€ 366,593,959
Germany	€ 1,091,805,000	€ 214,620,560	€ 877,184,440
Greece	€ 100,650,000	€ 22,782,904	€ 77,867,096
Hungary	€ 34,925,000	€ 12,929,361	€ 21,995,639
Ireland	€ 18,750,000	€ 8,244,707	€ 10,505,293
Italy	€ 704,385,000	€ 161,994,840	€ 542,390,160
Latvia	€ 3,601,467	€ 2,382,270	€ 1,219,197
Lithuania	€ 7,680,205	€ 4,430,516	€ 3,249,689
Luxembourg	€ 2,062,500	€ 1,117,921	€ 944,579
Malta	€ 2,268,750	€ 678,977	€ 1,589,773
Netherlands	€ 54,000,000	€ 37,942,100	€ 16,057,900
Portugal	€ 65,083,333	€ 13,758,787	€ 51,324,546
Poland	€ 80,575,000	€ 61,326,805	€ 19,248,195
Romania	€ 29,040,000	€ 21,828,767	€ 7,211,233
Slovakia	€ 17,914,286	€ 6,632,083	€ 11,282,203
Slovenia	€ 7,425,000	€ 3,750,436	€ 3,674,564
Spain	€ 251,533,333	€ 93,504,491	€ 158,028,843
Sweden	€ 117,657,692	€ 25,912,452	€ 91,745,240
United Kingdom	€ 497,125,000	€ 176,340,715	€ 320,784,285
Total EU	€ 3,963,525,614	€ 1,140,620,637	€ 2,822,904,977

Note: All figures are rounded. Source: [16] The World Bank and Frost & Sullivan analysis

The total potential of avoided medical event expenditures can be as much as € 3.96 billion per year.

Chart 2
Calcium and Vitamin D Summary Economic Results, Total Benefit ((S) Potential Health Care Cost Savings), € million, Annualised Average, EU, 2016-2020
Total EU: €3.96 billion



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

As indicated above, the purchase and utilisation of 1,000 mg/day of calcium and 15 µg/day of vitamin D supplements is required to capture these potential cost savings from avoided osteoporosis-attributed bone fractures. Though, the cost of calcium + vitamin D food supplements, like other healthcare costs, varies by country and distribution channel. Thus, the cost of calcium + vitamin D food supplements ought to vary to reflect these economic realities. One way to control for this variance is to adjust observed market prices by the purchasing power of each country's citizens. According to the World Bank, purchasing power parity (PPP) is a factor that adjusts a given country's domestic value of a Euro required to buy a given product to a baseline country's value of a Euro. For the purposes of this analysis, the purchasing power of a Euro in Belgium was assumed to be 100 versus the other European Union countries [16]. It should be noted that PPP merely reflects the relative value of a Euro across two and more countries and does not establish the baseline value of a Euro.

Based on an author review of calcium + vitamin D food supplements sold throughout both brisk & mortar and online retailers in the EU, it is expected that the daily consumer cost of a 1,000 mg/day of calcium and 15 µg/day of vitamin D food supplement ranges from as low as € 0.05 per day to more than € 0.16 per day based on a review of 28 calcium + vitamin D products sold in France, Germany, Italy, Spain, and the United Kingdom. The average cost of using 1,000 mg/day of calcium and 15 µg/day of vitamin D regimen daily is approximately € 0.14 per day, or approximately € 51.29 per year. This average price was then weighted by each country's PPP ratio in order to best represent the expected variance in calcium + vitamin D food supplement prices observed in the market. Furthermore, these PPP-adjusted daily regimen prices was then scaled up to reflect expected annual prices and then multiplied further by the total number of people age 55 and older at risk of experiencing a osteoporosis-attributed bone fracture per country in order to reflect expected total social costs of 100% utilisation of calcium + vitamin D food supplements. Accordingly, the cost of calcium + vitamin D utilisation required to realise the expected benefits by the total target population of all EU adults age 55 and older at risk of experiencing a osteoporosis-attributed bone fracture per year, ***C***, is expected to be € 1,140 million per year. Table 6 shows the expected daily and annual costs of using calcium + vitamin D daily in the EU after ensuring purchasing power parity across all EU countries and the total potential cost of calcium + vitamin D food supplements per country.

The median cost of using calcium + vitamin D daily is approximately €0.14 per day, or approximately €53 per year.

Table 6
Economic Benefits from Calcium + Vitamin D Food Supplement Use: Expected Consumer Price per Calcium + Vitamin D Supplements per Day per EU Country, adjusted for Purchasing Power Parity, 2016

Country	d/day: Average Daily Cost of 1,000 mg/day of Calcium and 15 µg/day of Vitamin D Food Supplement, € /day	d: Average Annual Cost of 1,000 mg/day of Calcium and 15 µg/day of Vitamin D Food Supplement, € /year	PPP: Purchasing Power Parity Weights, 2014/2015 (Belgium € = 100)
Austria	€ 0.12	€ 44.99	98
Belgium	€ 0.13	€ 45.90	100
Bulgaria	€ 0.05	€ 18.26	45
Croatia	€ 0.07	€ 25.24	55
Cyprus	€ 0.10	€ 37.64	82
Czech Republic	€ 0.07	€ 26.81	55
Denmark	€ 0.16	€ 58.17	127
Estonia	€ 0.09	€ 32.27	64
Finland	€ 0.14	€ 51.35	109
France	€ 0.12	€ 45.45	91
Germany	€ 0.12	€ 42.72	91
Greece	€ 0.10	€ 35.45	73
Hungary	€ 0.06	€ 23.63	55
Ireland	€ 0.14	€ 49.54	100
Italy	€ 0.12	€ 42.72	91
Latvia	€ 0.05	€ 18.26	64
Lithuania	€ 0.07	€ 25.24	55
Luxembourg	€ 0.14	€ 50.90	109
Malta	€ 0.09	€ 33.51	73
Netherlands	€ 0.13	€ 46.36	100
Portugal	€ 0.06	€ 23.18	82
Poland	€ 0.09	€ 33.18	55
Romania	€ 0.06	€ 21.11	45
Slovakia	€ 0.08	€ 28.63	64
Slovenia	€ 0.09	€ 34.08	73
Spain	€ 0.10	€ 38.18	82
Sweden	€ 0.14	€ 49.54	118
United Kingdom	€ 0.15	€ 54.99	120
Total EU	€ 0.14	€ 51.29	--

Note: All figures are rounded. Source: [16]The World Bank and Frost & Sullivan analysis

Table 7
Economic Benefits from Calcium + Vitamin D Food Supplement Use: Net Benefit per User (Adjusted Avoided Osteoporosis-attributed Healthcare Costs per person per EU country), € 1/person, Europe, Annualised Average, 2016-2020

Country	S/C: Benefit Cost Ratio (€ Avoided Costs and Gains per € 1 spent on Calcium + Vitamin D Food Supplements)	B/Pop: Net Benefit per User (Adjusted Avoided Osteoporosis-attributed Healthcare Costs per person per EU country), € /person, Europe, Annualised Average, 2016-2020
Austria	4.01	€ 135.26
Belgium	2.29	€ 59.27
Bulgaria	1.30	€ 5.43
Croatia	2.88	€ 47.52
Cyprus	4.11	€ 117.05
Czech Republic	3.20	€ 58.95
Denmark	5.13	€ 240.46
Estonia	2.08	€ 34.70
Finland	2.37	€ 70.13
France	3.32	€ 105.49
Germany	5.09	€ 174.60
Greece	4.42	€ 121.15
Hungary	2.70	€ 40.20
Ireland	2.27	€ 63.12
Italy	4.35	€ 143.03
Latvia	1.51	€ 9.35
Lithuania	1.73	€ 18.52
Luxembourg	1.84	€ 43.01
Malta	3.34	€ 78.45
Netherlands	1.42	€ 19.62
Portugal	4.73	€ 86.46
Poland	1.31	€ 10.41
Romania	1.33	€ 6.97
Slovakia	2.70	€ 48.71
Slovenia	1.98	€ 33.40
Spain	2.69	€ 64.52
Sweden	4.54	€ 175.39
United Kingdom	2.82	€ 100.03
Total EU	3.47	€ 101.63

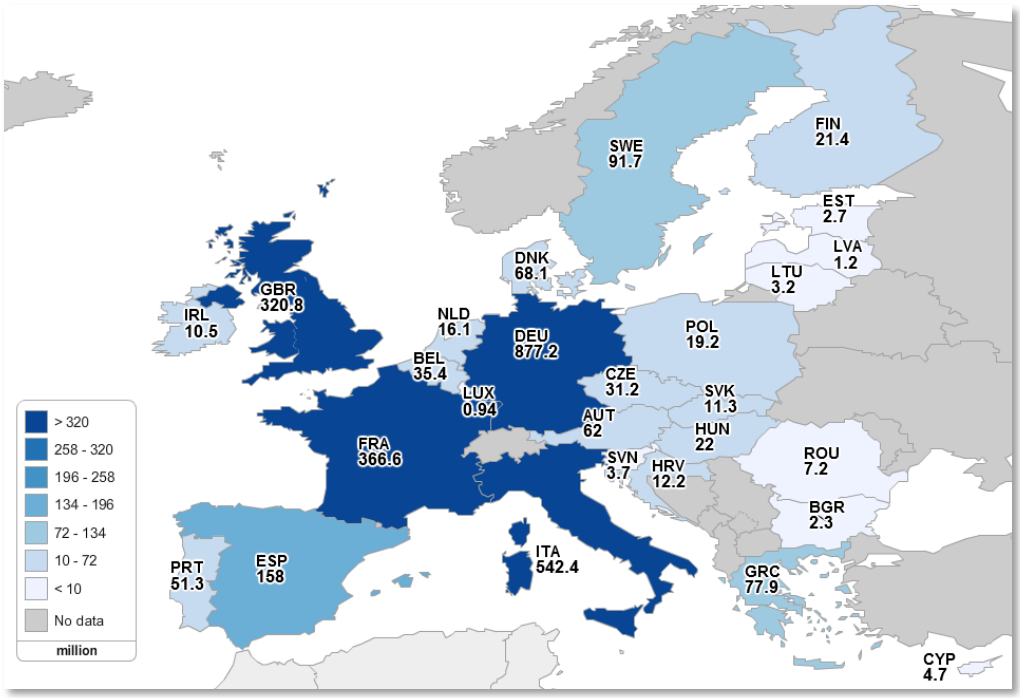
Note: All figures are rounded. Source: Frost & Sullivan analysis

For every € 1.00 spent on a calcium + vitamin D food supplement, there would be a certainty equivalent return of €3.47 to users and society as a whole in the form of avoided healthcare expenditures attributed to osteoporosis.

The total net benefit, B, for the entire EU target population of calcium + vitamin D daily users is €2.82 billion per year.

The total net benefit, ***B***, for the entire EU target population of calcium + vitamin D daily users is € 2.82 billion per year. This means that for every € 1.00 spent on a calcium + vitamin D daily regimen, there would be a certainty equivalent return of € 3.47 to society in the form of avoided healthcare expenditures attributed to osteoporosis. In other words, there would be a significant portion of cost savings to the primary payers of healthcare costs, which include governments and insurance companies. In fact, all 28 EU countries have benefit cost ratios greater than € 1.00 which is an indication of cost effectiveness as shown in Table 7 and Charts 4 and 5. The greatest net benefits are found in Germany, where an expected annualised net benefit from avoided osteoporosis-attributed healthcare costs is € 877.2 million per year. Germany is followed by Italy and France with € 542.4 million and € 366.6 million in per year in total net benefits, respectively. Chart 3 shows the net benefits from avoided osteoporosis-attributed events through the use of calcium + vitamin D supplements.

Chart 3
Calcium and Vitamin D Summary Economic Results, Total Net Benefit (Potential Health Care Cost Savings excluding the Expected Cost of Supplement),
€ million, Annualised Average, EU, 2016-2020
Total EU: €2.82 billion



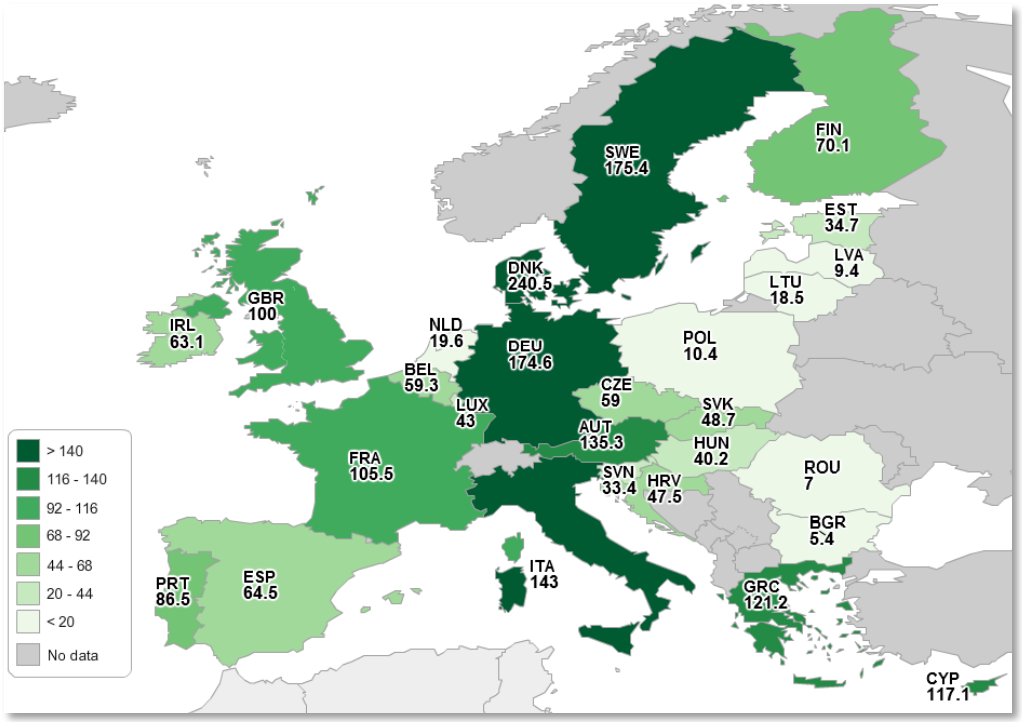
Note: All figures are rounded. Source: Frost & Sullivan analysis

In order to gauge the potential cost-effectiveness of calcium + vitamin D, a measure of benefits per user can also be determined which can be derived by taking the total potential avoided costs, S, and dividing this amount across all supplement users in the target population. Overall, the average total potential benefits per calcium + vitamin D user with diagnosed osteoporosis is €101.63 per person per year. These total benefits per calcium + vitamin D supplement user from the target population of adults age 55 and older at risk of experiencing an osteoporosis-attributed bone fracture is highly variable and is dependent on relative healthcare costs in each country and the risk of that given individual experiencing an event. Specifically, the benefits per person in Denmark (€240 per person) are the greatest due to the country's high cost of healthcare and its high osteoporosis-attributed bone fracture risk rate. On the other hand, the net benefits per person in the eastern European Union countries of Bulgaria, Latvia, and Romania are relatively lower (less than €10 per person) due to lower healthcare cost burden these countries have in general. This does not mean that these countries' target users would not significantly benefit from using a calcium + vitamin D supplement daily because these countries are still avoiding a significant number of events that are directly attributed to lower productivity, higher healthcare costs, and a lower quality of life. Also, these metrics can be used as a guide to determine cost-effectiveness. Specifically, any regimen that cost less than the reported amounts would mean that the given regimen would be cost effective.

The average total potential benefits per calcium + vitamin D user with diagnosed osteoporosis is €101.63 per person per year.

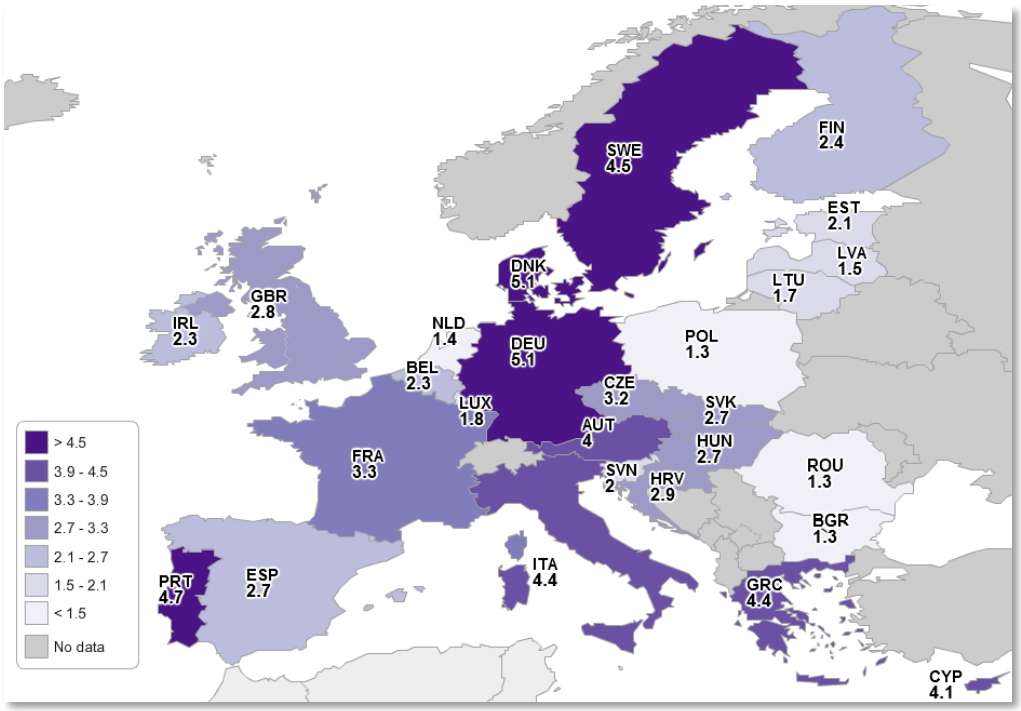
Chart 4
Calcium and Vitamin D Summary Economic Results, Total Potential Health Care Cost Savings per Capita, €/Target User, Annualised Average, EU, 2016-2020

Total EU: €101.63/Target User



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

Chart 5
Calcium and Vitamin D Summary Economic Results, Expected Cost Effectiveness of Supplement Use, € Gains in Health Care Cost Savings per € Spent on Supplement, EU, 2016-2020
Total EU: €3.47/ €1 Spent on Calcium and Vitamin D Supplement



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

Discussion

As demonstrated in this case study, a significant amount of clinical research has already been conducted over the last several decades globally showing that the use of a daily calcium + vitamin D regimen is highly correlated to a lower risk of experiencing an osteoporosis-attributed bone fracture. Thus, physicians and scientists alike recommend identifying physiological risk biomarkers such as bone mineral density (BMD) or serum-level vitamin D levels and managing these respective levels through changes in behaviour and adopting proven risk-reduction regimens as a means to lower the health and economic burden of osteoporosis. These potential health economic benefits can be realised by proactively identifying the population at greatest risk of experiencing a costly osteoporosis-attributed bone fracture and helping these high risk populations consider a calcium + vitamin D regimen as an important tool for protecting against costly osteoporosis-attributed events. This is an approach that can be used by consumers, healthcare providers, employers, and policymakers as a means to reduce personal and societal healthcare costs. Understanding this link will help key stakeholders—potential calcium + vitamin D supplement users, healthcare providers, governments, private insurance companies, and employers—make recommendations about the best course of action to help minimise current and future costs and maximise benefits.

In terms of potential shortcomings from this field of research, the potential healthcare cost saving calculations in this case study only include the direct expenditures associated with the use of calcium + vitamin D. These estimates do not include a number of additional benefits that can be gained from the use of calcium + vitamin D, including additional benefits related to avoiding other osteoporosis-attributed bone fractures such as reduced stress and worry experienced by patients and the families of patients. It also does not include productivity gains that can be derived from helping otherwise healthy people avoid osteoporosis-attributed bone fractures, which directly impacts additional benefits to the state in the form of tax revenue. However, the economic model utilised for this analysis is a generalised model that determines the economic effect of using a calcium and vitamin D regimen on the odds of an osteoporosis-attributed bone fracture outcome, which in turn is directly relevant to the social cost of healthcare.

As stated earlier in this case study, one can easily add in additional expected health benefits that are less directly related or potentially related to the disease condition of interest. However, for the purposes of this study, the cost and benefit mix is deliberately defined to be conservative and directly in line with the hypothesised relationship between calcium and vitamin D use and the risk of a given type of osteoporosis-attributed bone fracture. The total net financial benefits from using calcium + vitamin D reviewed in this study are likely to be higher than these directly measured estimates.

The health economic approach presented in this case study can be used by consumers, healthcare providers, employers, and policymakers as a means to make more effective health decisions.

The prior cost-benefit analysis also makes the conjecture that in the supplementation scenario all adults over the age of 55 with osteoporosis-attributed bone fractures use calcium + vitamin D food supplements from a base of zero usage among this population segment. In other words, the calculated net savings is actually the total potential net savings. However, because a percentage of adults over the age of 55 are known regular users of calcium + vitamin D, especially those who have been diagnosed with osteoporosis or osteopenia this target population segment already has a reduced risk of experiencing a costly osteoporosis-attributed bone fracture and is already realising calcium + vitamin D's risk-reducing benefits.

According to the 2012 Council for Responsible Nutrition Consumer Survey on Dietary Supplements, 29% of U.S. adults over the age of 55 are regular users of calcium + vitamin D supplements which implies that the remaining portion of the of target population has not yet realised the potential osteoporosis-attributed health benefits of using calcium + vitamin D [13]. Moreover, nearly 34% of Australians age 55 and older are regular users of calcium + vitamin D supplements implying that the rest of the target population has yet to realise the potential benefits of the supplements' regular use [14]. 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 food supplements, the calculation of avoided health care expenditures and net cost savings yet to be realised is simply a proportional adjustment of the total potential avoided expenditures and net cost savings. It is expected that the EU as a whole reflects similar calcium + vitamin D consumption trends when compared to the U.S. or Australia, but more research is required to verify this point. Also, it is likely that consumption patterns highly vary by EU country. Thus, this is the key reason why benefits per user was calculated so that once consumption trends per EU country are known, then calculation of total potential benefits yet to be realised per country can be easily estimated.

Due to data availability limitations, the current model does not follow individual people over time. This economic model currently treats all of the people in the target population per EU country as a homogeneous set of people, including the expected risk of experiencing an osteoporosis-attributed disease-attributed event. Thus, total social benefits are measured. Actual benefits realised per individual user will be a function of the specific osteoporosis-attributed bone fracture risk they face. The ideal situation would be to track an individual's risk over time and also understand how individual risk factors—such as their age, gender, and specific biomarkers—vary during the same time period, and then calculate each individual's potential costs and benefits to arrive at the total target population figures. Finally, this study currently does not consider the total economic benefits that are realisable at lower intake levels; the reason being that the scientific literature is not mature enough to deduce what these health benefits are and how they tie to the utilisation of costly healthcare services. Future clinical research testing for a

possible health and wealth benefit is required in order to fully understand these effects.

In summary, osteoporosis is the most prevalent bone disease in the European Union, with more than € 24 billion being spent on the treatment of osteoporosis-attributed fractures alone, plus an additional € 10 billion in long-term care costs related to osteoporosis-attributed disability. These costs do not include informal costs related to the loss of mobility and independence, and a general reduction in a patient's quality of life. Given the full usage of 1,000 mg calcium + 15 µg vitamin D among all adults over the age of 55 diagnosed with osteoporosis in the EU, upwards of € 2.8 billion per year can be saved because of avoided osteoporosis-attributed fractures. This equates to nearly € 101.63 per target user in healthcare cost savings typically payable by government or private insurance companies. As fractures attributed to osteoporosis become more prevalent in the European Union due to the aging of its population, the importance of the substantiated benefits of calcium + vitamin D supports its use as a tool that can be leveraged to help minimise the financial burden of this disease in the future.

Given the full usage of calcium + vitamin D among all adults over the age of 55 diagnosed with osteoporosis in the EU, € 2.8 billion per year can be saved because of avoided osteoporosis-attributed fractures.

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Appendix

List of Abbreviations

A	Number of possible avoided events (A) if everybody in a specified target population used calcium + vitamin D
B	total potential net economic benefits yet to be realised from use of a calcium + vitamin D food supplement
BMD	Bone Mineral Density
S/Pop	Benefit per User
C	Total cost of an calcium + vitamin D regimen
CBA	Cost-benefit analysis
CI	Confidence interval
d	The expected per person cost of calcium + vitamin D utilisation per year
EFSA	European Food Safety Authority
EU	European Union
g	gram
h	The expected cost of a osteoporosis-attributed event
µg/day	microgram
mg	Milligram
N*	Number needed to treat
Pop	Target Population
PPP	Purchasing Power Parity
RCT	Randomised controlled trials
RRR	Relative risk reduction
S	Total potential savings from reduced hospital service utilisation following osteoporosis-attributed bone fractures that are realisable if the entire target population were to sufficiently utilise a calcium + vitamin D food supplement
S/C	Benefit Cost Ratio
U.S.	United States of America
UL	Tolerable Upper Intake Level
WHO	World Health Organization

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