

A Cost Analysis of Systematic Vitamin D Supplementation in the Elderly versus Supplementation based on Assessed Requirements

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Abstract

Hypovitaminosis D is common among older people and treatment with vitamin D is associated with reduced risk of falls and fractures. This paper provides a cost analysis of assessing the vitamin D status of and providing the pharmaceuticals for elderly citizens in Kalmar County, Sweden (population approximately 230,000). Four hypothetical interventions were analyzed: (a) systematic vitamin D/calcium supplementation to all elderly (≥ 75 years), (b) assessment of vitamin D status in elderly and supplementation to those with insufficient levels, (c) systematic vitamin D/calcium supplementation to all nursing-home residents, and (d) assessment of vitamin D status in nursing-home residents and supplementation to those with insufficient levels. The calculations were based on an estimated reduction in overall costs due to the assessed number of hip fractures after vitamin D/calcium supplementation. The annual net economic benefit of vitamin D/calcium supplementation was estimated at (a) €304,000, (b) €860,000, (c) €755,000, and (d) €740,000. The provision of systematic vitamin D supplementation to nursing-home residents would provide a substantial net economic benefit to society and assessment of the vitamin D status before starting supplementation does not seem to be necessary. Although assessment of all elderly citizens would be more comprehensive, the true proportion with insufficient vitamin D levels in the general population is uncertain and to reaching consensus on the most advantageous daily vitamin D intake, vitamin D blood levels are necessary. Also, systematic supplementation to all elderly would result in other outcomes that could be worth the cost, but that remains to be evaluated.

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Introduction

Vitamin D is essential for skeletal metabolism, muscle function, calcium homeostasis, and the immune system (1). It has also been presented as a preventive factor for chronic diseases such as cardiovascular disease, type 2 diabetes, autoimmune diseases, and various cancers (2-4), and for non-vertebral and hip fractures in older patients (2,3,5). Furthermore, low vitamin D levels are reported to be associated with increased mortality among the elderly in Sweden (6,7).

The main source of vitamin D is from sensible sun exposure, and other sources are food and dietary supplements (1,8). People at risk of insufficient vitamin D levels include the elderly and individuals with limited sun exposure, such as those in nursing homes (9). Moreover, the elderly often avoid direct sunlight and also have a reduced capacity to synthesize vitamin D in their skin (10).

The level of total serum 25-hydroxyvitamin D (S-25(OH)D; calcidiol) is usually considered the best indicator of vitamin D status (1,2). However, there is no consensus on optimal S-25(OH)D levels and what should be the appropriate level for defining vitamin D deficiency. Consequently, there are numerous guidelines/recommendations on the management of vitamin D status (1,3,4,8,11-14). Most of the recent guidelines/recommendations suggest that S-25(OH)D levels ≥ 50 nmol/L reflect sufficient vitamin D (1,4,11,13,14). However, in fragile older adults with an elevated risk of falls and fractures, it has been suggested that the minimum S-25(OH)D level should be ≥ 75 nmol/L (8,13). S-25(OH)D levels were recently reported to be < 50 nmol/L in $> 65\%$ of elderly patients (aged ≥ 75 years) with hip fractures (15).

Falls and fractures are common among the elderly. Some studies have found that vitamin D supplementation reduces the incidence of falls and fractures (2). Others have found that vitamin D alone does not seem to prevent fractures (16,17), whereas supplements of vitamin D plus calcium reduce the risk of falls (18) and hip fractures in the elderly (16). In a pooled analysis of studies on fracture prevention, high-dose vitamin D supplementation (≥ 800 IU daily) appeared to reduce the risk of hip fracture by 30% in people aged ≥ 65 years (19). Vitamin D supplementation has therefore been suggested as a cost-effective intervention for reducing falls, hip fractures and

healthcare costs (20-22) in the elderly. In addition, combining vitamin D with calcium has been shown to be cost-effective in the prevention of osteoporotic fractures (23,24).

Previous randomized trials and official guidelines have indicated that there is a correlation between vitamin D supplementation, adequate vitamin D levels in the blood, and reduced risk of osteoporotic hip fractures. Therefore, the objective of this study was to compare systematic supplementation with vitamin D/calcium with assessment of vitamin D levels and subsequent supplementation, if required among the elderly, from a cost perspective. It was hoped that the study would provide a basis for planning and implementing public guidelines for screening for vitamin D deficiency and providing vitamin D treatment for the elderly.

Methods

Cost analysis

A prevalence-based approach was used. The calculations involved both bottom-up estimates, where the costs for a defined subpopulation were assessed and then extrapolated to represent the entire population, and top-down estimates, where national frequencies and events were assessed (25).

The calculations included direct medical costs, such as the cost of assessing vitamin D status (total S-25(OH)D were used as an indicator of vitamin D status) and the cost of pharmaceuticals, and direct non-medical costs, such as transportation. However, indirect costs such as production loss due to sick leave or early retirement were not included (as the study population was of retirement age). Intangible costs such as pain and suffering were not included as these costs are generally difficult to determine, nor were the costs of premature mortality or decreased quality of life included because of lack of data. The calculations were based on Swedish registries, reports and databases, and published literature. Supplementary information regarding vitamin D management not found in the literature was given by experts from the main study: clinicians, nurses, pharmacologists, and care department staff/unit heads. All costs were taken from published literature and official databases.

Study population

The data were from a Swedish study (15) on vitamin D status in individuals aged ≥ 75 years selected from groups with a frailty phenotype and a control

group. All participants were residents of Kalmar County, a combined urban and rural area in south-eastern Sweden with a population of approximately 230,000. A detailed description of the study design and the main results have been published elsewhere (15).

Control group

The control group in the main study (n = 169) (15) consisted of community dwelling elderly. A variety of strategies was used for recruitment, including advertising in local newspapers, supermarkets, and pensioner's associations. No one in the control group had vitamin D prescribed. These older adult controls were enrolled in the study only if they considered themselves to be in good health despite their age. The exclusion criteria were a history of dementia, low-energy fractures and stroke. Subjects in the control group who were prescribed antidiabetic medication, vitamin D or calcium by a physician were also excluded. The mean (SD) and median (range) S-25(OH)D levels in the control group were 73.9 (22.3) and 74 (22–154) nmol/L, respectively, and 13% had insufficient S-25(OH)D levels (<50 nmol/L).

Nursing homes

This group included individuals aged ≥ 75 years living in nursing homes. The number of nursing-home residents in Sweden was obtained from the Swedish National Board of Health and Welfare (26) and two municipalities in Kalmar County. The mean (SD) and median (range) of S-25(OH)D levels among the nursing-home residents were 46.5 (26.7) and 38 (15–132) nmol/L, respectively, and 76% had insufficient S-25(OH)D levels (<50 nmol/L).

Study design

The cost analysis was based on the following hypothetical interventions:

- a. Systematic vitamin D/calcium supplementation for all individuals aged ≥ 75 years (n = 25,545) in Kalmar County (total population approximately 230,000).
- b. Assessment of the vitamin D status of all individuals aged ≥ 75 years (n = 25,545) in Kalmar County and vitamin D/calcium supplementation for those with insufficient levels (<50 nmol/L).

- c. Systematic vitamin D/calcium supplementation for all nursing-home residents aged ≥ 75 years (n = 2418) in Kalmar County.
- d. Assessment of the vitamin D status of all nursing-home residents aged ≥ 75 years (n = 2418) in Kalmar County and vitamin D/calcium supplementation for those with insufficient levels (<50 nmol/L).

Hip fractures

The number of hip fractures in Kalmar County was obtained from the Swedish National Registry of hip fracture patient care (27) (Table 1). The proportion of hip fractures sustained by nursing-home residents was estimated at 40%, corresponding to 151 hip fractures per year (27-31).

We hypothesized that vitamin D supplementation, with or without calcium, could reduce the number of hip fractures by 30%, according to a published analysis on fracture prevention (19).

Resource units and costs

All costs were estimated in Swedish Crowns (SEK) using 2014 prices and were then converted to euros (€1.00 = SEK9.097); where applicable, the consumer price index was applied as the conversion factor.

The hip fracture cost was based on two previous Swedish studies (32,33) (Table 1).

The personnel costs were based on the average hourly wage of Swedish nurses and biomedical laboratory scientists (34). The time required to take one venous blood sample was estimated at 5 minutes for an experienced nurse (personal communication, healthcare staff). The cost of a laboratory S-25(OH)D test was obtained from a medical price list from the Kalmar County Council (Table 1).

The cost of pharmaceutical treatment was based on the weighted mean of the costs of vitamin D3 (800 IU) alone and vitamin D3 (800 IU) plus calcium (500 mg) (ratio 10/90). Henceforth in this paper the pharmaceutical treatment will be written as "vitamin D supplementation" in either case. The costs of systematic supplementation of all citizens aged ≥ 75 years in Kalmar County was based on the costs of over-the-counter

pharmaceuticals. Pharmaceutical prices were taken from Pharmaceutical Specialties in Sweden (35) (Table 1).

The cost of transportation to and from Swedish healthcare units was obtained from a previous study (36). The cost of transportation to and from Swedish nursing homes was calculated as the average wage during an estimated one-hour trip with additional travel expenses (€0.203 per km) as per the Swedish public reimbursement policies (Table 1).

Assessment of vitamin D status

We chose a S-25(OH)D level of <50 nmol/L as the cut-off point to indicate insufficient vitamin D levels (1,4,11). In the latest Nordic Nutrition Recommenda-

tions, published in 2013 (4), a S-25(OH)D concentration of ≥ 50 nmol/L was used as an indicator of sufficient vitamin D status. The frequently referenced report from the American Institute of Medicine (IOM) from 2011 (11) also recommended that a S-25(OH)D level of at least 50 nmol/L would be sufficient to optimize bone health.

Since the control group consisted of individuals aged ≥ 75 years and who considered themselves healthy, the proportion (13%) of individuals with insufficient S-25(OH)D levels (<50 nmol/L) was probably not representative of the entire elderly population. We therefore doubled the proportion of individuals aged ≥ 75 years with S-25(OH)D levels <50 nmol/L to 25%. This was considered not to be an exaggeration since a recent

Table 1. Data sources

Resource unit	No.	Unit cost (€)	Sources
Inhabitants of Kalmar County (aged ≥ 75 years)	25,545	n.a.	(34)
Nursing-home residents (aged ≥ 75 years)	2418	n.a.	(26)
Hip fractures	378	20,574	(27,32,33)
Average hourly wage ^a	n.a.	17.81	(34)
S-25(OH)D laboratory test		21.99	Kalmar County Council
S-25(OH)D sampling ^b		1.48	
Pharmaceuticals	n.a.	73.98 ^c	(35)
Transportation personnel ^d	50 ^e	19.79	Personal communication; (34)
Transportation citizens ^f		15.72	(36)

a .Swedish nurses and biomedical laboratory scientists.

b. Estimated to take 5 min per sample; wage costs.

c .Weighted mean of the costs of vitamin D3 (800 IU) alone and vitamin D3 (800 IU) plus calcium (500 mg) supplementation (ratio 10/90); treatment during 1 year.

d .Estimated to take 1 hr; 10 km.

e .No. of nursing homes in Kalmar County.

f .One-way trip.

study investigating vitamin D status in healthy Swedish blood donors (aged 18–65 years) showed that 50% had S-25(OH)D levels of <50 nmol/L for 50% of the year (37).

The assessment of the vitamin D status differed between the groups and the calculations were based on different scenarios, as described below.

Control group

Measurement of S-25(OH)D levels in the control group included the cost of a laboratory S-25(OH)D test, transportation costs to and from the healthcare units, and personnel costs in terms of working time. General assessment of the entire population would be performed similarly.

Nursing homes

The healthcare personnel would arrange organized sampling at each nursing home. The costs included were the laboratory S-25(OH)D test, transportation to and from the nursing homes, and personnel costs in terms of working time.

Results

Systematic supplementation versus pretreatment assessment

The annual cost of systematic vitamin D supplementation versus assessment of S-25(OH)D status and supplementation only for those with insufficient levels (<50 nmol/L) in individuals aged ≥ 75 years living in Kalmar County is shown in Table 2. The net economic benefit of systematic vitamin D supplementation in all elderly individuals was estimated at €303,679, whereas that of supplementing only those with insufficiency was estimated at €858,826 (including the cost of assessment). Among nursing-home residents, these net economic benefits were estimated at €753,136 and €738,313, respectively.

Hip fracture cost

The total annual cost of hip fractures ($n = 378$) among older adults (aged ≥ 75 years; $n = 25,545$) in Kalmar County was estimated at €7,776,902. Approximately 40% of the total hip fracture cost stemmed from nursing-home residents (Table 2).

Discussion

The provision of systematic vitamin D supplementation to nursing-home residents would

provide a substantial net economic benefit to society, and assessment of the vitamin D status before starting supplementation does not seem to be necessary in this high-risk group for vitamin D deficiency.

The intervention with the largest net economic benefit (Table 2) was assessment of the vitamin D status in all individuals aged ≥ 75 years in Kalmar County followed by supplementation of those who had insufficient S-25(OH)D levels (<50 nmol/L). The economic benefit associated with this intervention was approximately 80% larger than that associated with supplementing all individuals aged ≥ 75 years without previous assessment of the vitamin D status, but it was only 14–16% larger than either of the interventions in residents of nursing homes (Table 2). However, the true proportion of individuals with insufficient vitamin D levels in the population is uncertain.

Among nursing-home residents, who are a known risk group for vitamin D insufficiency, the annual net economic benefit of the two interventions was similar. Thus, in the nursing-home group, assessment of the vitamin D status prior to vitamin D supplementation does not seem to be necessary. An expert group from the French Group of Geriatrics and Nutrition has also suggested that, given the probable cost-effectiveness and safety of the intervention, a population-based rather than an individual-based approach to vitamin D supplementation, without the need of preliminary monitoring of S-25(OH)D levels, would be acceptable for nursing-home residents (38). Furthermore, the American Geriatrics Society has recently revised its recommendations, stating that routine laboratory testing for 25(OH)D levels before starting supplementation is not necessary in nursing-home populations (8), which also supports our findings.

While the results for the total elderly population were somewhat uncertain, the data for nursing-home residents were more robust. Thus, limiting systematic vitamin D supplementation to known risk groups such as the elderly and individuals who have limited exposure to the sun might be preferable. However, in addition to the economic aspects, there is also an ethical point of view. Assessment of the vitamin D status among all individuals aged ≥ 75 years would reach a larger population, leading to prevention of a higher number of hip fractures with associated reduced pain and suffering, and this would

also affect the quality of life of this population. On the other hand, elderly citizens who consider themselves to be in good health may not need vitamin D supplementation (15). It appears that further studies are needed to determine the actual vitamin D status in the general population.

The calculations include some key figures and altering these figures would alter the outcome. The

major cost driver was the 30% risk reduction of hip fracture. If this risk reduction was lower (16) the net benefit would also be lower. In the control group of the main study, only 13% had insufficient vitamin D levels (15). As a sensitivity analysis, we doubled this percentage to 25% in our calculations. There are several known risk groups in the general population who are predisposed to insufficient vitamin D levels (9), and the

Table 2. The annual costs of systematic vitamin D supplementation and assessment of S-25(OH)D levels in individuals aged ≥ 75 years in Kalmar county

Costs (€)							
	Individuals (n)	Hip fracture	Vitamin D assessment	Vitamin D supplementation	Assessment + supplementation	Cost reduction (€) ^a	Net benefit (€)
All older individuals	25,545	7,776,902				2,333,071	
Systematic supplementation	25,545			2,029,391	2,029,391		303,679
Pretreatment assessment	6386 ^b		1,001,952	472,293	1,474,245		858,826
All nursing-home residents	2418	3,106,646 ^c				931,994	
Systematic supplementation	2418			178,858	178,858		753,136
Pretreatment assessment	1828 ^d		57,748	135,932	193,681		738,313

a. Based on 30% reduction in the risk of hip fracture (19)

b. The proportion of individuals with S-25(OH)D levels < 50 nmol/L was estimated to be 25%, that is, approximately twice as many as in the control group in the main study

c. The no. of hip fractures was estimated to be 151, based on 40% of hip fracture patients living in nursing homes or institutions (27-31)

d. The proportion of nursing-home residents with S-25(OH)D levels < 50 nmol/L was 76% (15)

control group consisted of community dwelling elderly who considered themselves healthy. Hypothetically, if 50% of the individuals aged ≥ 75 years had insufficient vitamin D levels, the net benefit would be halved (approximately €385,000). Furthermore, in real life non-adherence to medication can also influence the outcome.

Among the nursing-home residents, as many as 76% had a S-25(OH)D level < 50 nmol/L (15). A high prevalence of insufficient vitamin D in nursing-home residents has been reported previously (38). In addition, a Swedish study examining the vitamin D status of the elderly in nursing homes found that this highly prevalent vitamin D deficiency was associated with increased mortality (7).

Our decision to use 50 nmol/L as the cut-off point for insufficient S-25(OH)D levels (4,11,13,14) is further supported by the findings of a Swedish study showing that elderly women who maintain 25(OH)D levels above 50 nmol/L between the ages of 75 and 80 years have a lower incidence of both hip and major osteoporotic fractures during the following 5 years (age 80–85 years). However, over a 10-year period, a reduction in the incidence of hip fractures was only seen at serum levels above 75 nmol/L (39). Therefore, a higher target level of vitamin D (75 nmol/L) has been suggested for older, more fragile adults (8,13).

The calculations were based on a vitamin D dose of 800 IU daily, which is in accordance with the Nordic Nutrition Recommendations (4). A study from the United Kingdom found that treating all adults aged ≥ 65 years with vitamin D 800 IU daily reduced the incidence of hip fractures and the number of deaths. From a health economic perspective, the greatest savings were seen following the treatment of individuals aged ≥ 70 years, with similar reductions in mortality (22). Another study showed that treatment of the elderly population (aged ≥ 60 years) with vitamin D3 800 IU daily was associated with reductions in mortality and substantial cost-savings through fall prevention (21).

Supplementation with vitamin D and calcium has been shown to reduce the risk of hip fractures (16). However, the elderly are often already taking many medications and the addition of yet another pharmaceutical to be taken daily could meet resistance among both physicians and patients.

The protective effect of vitamin D is most often seen in those with low basal 25(OH)D levels. The evidence for improvements in bone health, total mortality, and the risk of falling is only conclusive for treatment with vitamin D combined with calcium (4). In general, treatment with oral vitamin D alone does not seem to be associated with serious harm (12). However, there appears to be a small increased risk of gastrointestinal symptoms and renal disease for vitamin D plus calcium (16). It is recommended that calcium supplementation should not be systematically prescribed, but should only be given to those who do not reach desirable calcium levels despite diet modification (38). Since some individuals, especially among the elderly, may not be able to take vitamin D supplementation that includes calcium because of these adverse events, a proportion of the elderly are treated with vitamin D alone. This was taken into account in our calculations, as the cost of the pharmaceuticals included a weighted average of the costs of vitamin D and vitamin D plus calcium supplementation.

In the United States, no primary care professional organisation currently recommends population-wide screening for vitamin D deficiency. One of the problems associated with screening is that some people may be misclassified as having vitamin D deficiency because of uncertainty about the cut-off point for defining deficiency and variability in the available 25(OH)D assay results. Misclassification can result in over-diagnosis (which may lead to non-deficient people receiving unnecessary treatment) or under-diagnosis (which may lead to deficient people not receiving treatment) (12). Another disadvantage associated with screening (assessment) is that it is a burden on the healthcare organisation with respect to personnel time and resources, which otherwise could be used in more prioritised healthcare areas.

Limitations and method discussion

This analysis of the cost savings achieved by preventing hip fractures with vitamin D supplementation was based on the costs incurred during the first year after a fracture. However, the mean fracture-related costs 13–18 months after a hip fracture have been estimated at €2,422 (40). Thus, the cost-savings in our study were probably underestimated. The cost-savings in this analysis may have been further underestimated

by the exclusion from the analysis of other health benefits of vitamin D supplementation, such as reduced incidences of cancer (41) and infections (42).

However, while in our analysis, the vitamin D status was measured at only one occasion, there was no variation when measured seasonally (15). It has been recommended that follow-up measurements be made after a couple of months (38), which would mean that the cost of the intervention (which includes assessment of the vitamin D status) would be higher.

The calculations were based on treating all individuals who had vitamin D insufficiency with the same dose, despite their individual vitamin D levels. According to specific algorithms, individuals with more severe vitamin D deficiency and obese patients should be given larger vitamin D doses. However, in our study there were only 12 nursing-home residents with S-25 (OH)D levels <25 nmol/L (15) and, thus, the total cost was not influenced. Furthermore, we do not know the degree of non-adherence, but the adherence to treatment might be better at nursing homes where the personnel manage the medication.

None of the participants in the control group were prescribed vitamin D supplements whereas 14% of the nursing home residents were given supplements (15). However, half of these residents were given a low dose (400 IU) vitamin D. Furthermore, there was no information regarding intake of food sources rich in vitamin D or vitamins not prescribed by a physician, or about exposure to sunlight in either groups (15), which could be important aspects influencing the vitamin D status. The study was based on only one county in Sweden with a population of approximately 230,000 citizens.

Conclusion

The provision of systematic vitamin D supplementation to nursing-home residents would provide a substantial net economic benefit to society, and assessment of the vitamin D status before starting supplementation does not seem to be necessary in this high-risk group for vitamin D deficiency. This advice is in accordance with recommendations offering vitamin D (400–800 IU daily) to high risk individuals or populations without measurement of 25(OH)D (43). Further studies of the vitamin D status in the general population are needed. However, the results of future studies in

Sweden might differ from those of already published studies as the Swedish National Food Agency is currently revising its recommendations about fortified foods and has proposed an extension of the products subject to mandatory vitamin D fortification.

Although assessment of all elderly citizens would be more comprehensive, the true proportion with insufficient vitamin D levels in the general population is still uncertain and to reaching consensus on the most advantageous daily vitamin D intake, vitamin D blood levels are necessary. Also, systematic supplementation to all elderly would result in other outcomes that could be worth the cost, but that remains to be evaluated.

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