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Cost-Effectiveness of Vitamin D Screening Compared to Universal Supplementation to Prevent Falls Among Community-Dwelling Older Adults

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Abstract

Objectives—To evaluate the cost-effectiveness of population screening for vitamin D insufficiency, compared to universal vitamin D supplementation, among community-dwelling, older adults.

Design—A Markov decision model, simulating follow-up over a 36-month period. Published data were used to estimate values for the model, including costs (measured in 2011 U.S. dollars), utilities (measured in quality-adjusted life years [QALYs]), and probabilities.

Setting—Decision analysis simulation from a societal perspective

Participants—Hypothetical cohort of community-dwelling women and men between age 65 and 80 years.

Measurements—Net monetary benefit (NMB) was calculated by subtracting the incremental cost of the strategy from the product of the incremental QALYs and the willingness-to-pay threshold. A higher NMB indicates greater cost-effectiveness.

Results—Among women age 65 to 80 years, population screening was slightly more cost-effective than universal supplementation, with an incremental NMB of $224 compared to $189 ($P < 0.001$). Population screening among men was also more cost-effective than universal supplementation (incremental NMB: $298 vs. $260, $P < 0.001$). However, results differed by age group. Among those age 65 years, population screening had similar cost-effectiveness to universal supplementation in women ($59 vs. $71) and men ($114 vs. $120, respectively). Among those age

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Conflict of Interest

Cathleen Colón-Emeric is a consultant for Novartis and Amgen and has received research funding from Novartis, Wyeth, and Pfizer for work unrelated to that presented in the manuscript. She is a co-owner of Biscardia LLC and co-inventor of US patent application, “Bisphosphonate compositions and methods for treating heart failure.”

Author Contributions:

Richard H. Lee: Study concept and design, acquisition of subjects and/or data, analysis and interpretation of data, preparation of manuscript

Thomas Weber: Acquisition of subjects and/or data, analysis and interpretation of data Cathleen Colón-Emeric: Study concept and design, acquisition of subjects and/or data, analysis and interpretation of data, preparation of manuscript

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80 years, population screening was substantially more cost-effective than universal supplementation in women ($563 vs. $428) and men ($703 vs. $571, respectively).

Conclusion—Both population screening and universal supplementation for vitamin D insufficiency are cost-effective strategies among community-dwelling older women and men. Among the oldest old, population screening may be more cost-effective than universal supplementation.

Keywords

Cost-effectiveness; vitamin D; accidental falls

INTRODUCTION

Approximately one-third of adults age 65 years and older and half of those age 80 years and older fall at least once per year.(1) With more than 39 million older individuals in the U.S., it is estimated that approximately 13 million falls occur each year and that 2.2 million require medical attention.(2) Approximately 1 in 10 falls among older adults result in a fracture.(3, 4) Fall-related injuries in older adults are a significant source of morbidity and mortality, costing over $19 billion in direct medical expenditures.(3, 5, 6)

The United States Preventative Services Task Force has supported vitamin D supplementation for the prevention of falls.(7) Recent meta-analyses suggest that vitamin D supplementation reduces the rate of accidental falls among community-dwelling older adults when targeted to patients with low serum 25-hydroxyvitamin D levels, but not in patients with normal levels.(8-10) However, identifying individuals with vitamin D insufficiency would require population screening. The diagnosis of vitamin D insufficiency requires a laboratory assay and repeated measurements over time. In contrast, vitamin D supplements may be obtained over-the-counter inexpensively, and are associated with few adverse effects. Current guidelines recommend vitamin D supplementation for adults over age 65, but do not consider the option of population screening and targeted treatment, in part due to the lack of cost-effectiveness data.(7, 11)

Therefore, we performed a cost-effectiveness analysis to compare a strategy of population screening for vitamin D insufficiency to that of universal supplementation for the prevention of falls in community-dwelling older adults. We hypothesized that the strategy selection would vary by age and gender, as the risk of falls is higher in women and at older ages.

METHODS

Decision Model

A Markov decision model was constructed to simulate accidental falls over a 36-month period in hypothetical cohorts of older adults.(12) A societal perspective was adopted in which all costs are considered regardless of who bears them. The time horizon was selected to be consistent with the randomized, controlled trials included in meta-analyses.(8-10, 13-15)Participants were simulated for both male and female cohorts based on data from the 2010 Current Population Survey for the distribution of older adults age 65 to 80 years. (16)Subgroup analyses were performed limiting cohorts for specific age and gender selection: 1) Women, age 65 years, 2) women, age 80 years, 3) men, age 65 years, 4) men, age 80 years. Only Caucasians were considered due to the lack of published data among individuals of other races or ethnicities. Figure 1 depicts the Markov model with the possible health states and transitions. Four health states were modeled: No falls; history of falls with fear of falling; history of falls without fear of falling; and death.

Risk and probability estimation

Transition probabilities between health states (i.e. the probability a hypothetical subject will move from one state to another) were obtained from the peer reviewed literature and accounted for the influence of age, gender, vitamin D status (insufficient or not), and prior falls history. The incidence of falls was obtained from the 2006 Behavioral Risk Factor Surveillance System survey results.(17) The incidence of fall-related hospitalizations in the United States was obtained from an analysis of the National Electronic Injury Surveillance System.(18) The risk of recurrent falls was obtained from a published systematic review.(19) Gender and age-specific mortality estimates were based on Life Tables from the US Census Bureau.(20) Base case probability estimates are given in Table 1.

Model Assumptions

For the baseline comparison, subjects were neither screened for vitamin D insufficiency nor supplemented with vitamin D. “Vitamin D insufficiency” was defined as a serum 25-hydroxyvitamin D level less than 25ng/mL, consistent with the majority of trials included in the meta-analysis.(8-10) “Vitamin D deficiency” was defined as a serum 25-hydroxyvitamin D level less than 15ng/ml. Subjects with insufficient vitamin D levels were at increased risk for falls, consistent with the published meta-analysis of randomized, controlled trials of vitamin D supplementation. Population prevalence for low vitamin D levels, varied by age and gender, were derived from published results of NHANES 2003-2006.(21)

Figure 2 illustrates the decision tree constructed for analysis. For the population screening strategy, all subjects were assumed to have serum 25-hydroxyvitamin D levels measured. The dose (and therefore cost) of vitamin D provided was varied based on the baseline vitamin D level. For those with sufficient levels (> 25 ng/ml), no vitamin D supplements were assumed. For those with vitamin D insufficiency (15-25 ng/ml), a regimen of supplementation with cholecalciferol 1000 IU daily was assumed. For those with vitamin D deficiency (<15 ng/ml), a strategy of cholecalciferol 2000 to 4000 IU daily was assumed (i.e. 2 to 4-times supplement cost). The maximum dose was limited to 4000 IU, consistent with recommendations from the Institute of Medicine.(11, 22) Adherence to supplementation was modeled at 80%(range 50-90%), and effectiveness of therapy was assumed to begin after 6 months of supplementation (range 3-9 months).(23)

For the universal supplementation strategy, all hypothetical subjects were assigned a regimen of cholecalciferol 1000 IU daily, regardless of underlying 25-hydroxyvitamin D status. Subjects with sufficient levels would incur costs of supplementation; however, the risk of falls would not change. Subjects with vitamin D insufficiency (15-25 ng/ml) would incur costs of supplementation, and their risk of falls was assumed to return to that of subjects with sufficient levels. However, subjects with vitamin D deficiency (<15 ng/ml) would incur cost of supplementation, but their risk of falls was assumed to remain elevated, because a sufficient 25-hydroxyvitamin D level would not be attained with standard supplementation doses. Adherence to supplementation was modeled at 80%(range 50-90%), and effectiveness of therapy was assumed to begin after 6 months of supplementation (range 3-9 months).(23)

All cohorts were assumed to have no prior history of falls at the beginning of the time horizon. Adverse events from vitamin D supplementation alone are rare, though an increased incidence of renal calculi have been reported with combined calcium and vitamin D supplementation.(15, 24-26) Analyses including this potential adverse event were performed with negligible change in results and therefore not included in this report. The efficacy of vitamin D supplementation was assumed to be the same for all age and gender groups.

Incremental cost estimation

Direct medical costs for the model were collected and estimated from a variety of sources. All costs were updated to 2011 dollars according to the Consumer Price Index.(27) The direct costs of falls (i.e. costs directly related to falls care including emergency department, hospital, or outpatient clinic care) were obtained froma published systematic review and an analysis of the MarketScan Medicare Supplemental database.(28, 29) Information regarding the indirect costs (i.e., costs related to lost productivity, need for informal caregivers, etc.) of falls is limited.(28, 30) Therefore, cost estimations were conservatively limited to direct costs only. This costing method underestimates the total societal cost of a falls event and results in underestimation of the total cost-effectiveness for each strategy.

The cost for vitamin D supplementation was calculated from the average retail cost of a single vitamin D (cholecalciferol) 1000 IU capsule from 5 retail pharmacy chains in July 2011. Serum 25-hydroxyvitamin D testing cost (e.g., 2011 U.S. $41.66) was derived from published reimbursement schedules provided from the Centers for Medicare and Medicaid Services.(31) Health costs were discounted at a rate of 3% per year.

By convention, the willingness-to-pay (WTP) threshold was set at $50,000/QALY.(32) This reflects the amount of money society is generally willing to pay to obtain 1 quality-adjusted life-year (QALY) from a medical treatment or prevention strategy. Cost estimates for the base case, as well as estimates for variability utilized in sensitivity analyses, are shown in Table 1.

Utility estimation

The impact of falls on health-related quality of life (HRQoL) was taken from a published study that pooled HRQoL data from 2 clinical trials and 1 prospective cohort study. (33)Baseline health state utility values were obtained from a published systematic review. (34)Utility values can range between 0 (death) and 1 (perfect health), and reflect patients' relative valuation of different health states.(12)Population-derived utility data by age and gender were drawn from cross-sectional surveys of the US population.(35) As with costs, utilities were discounted at 3% per year. Table 1 shows base case utilities and ranges used in sensitivity analyses.

Cost-effectiveness analysis

Model analysisutilized the fixed, base case parameters for 36 Markov cycles, each representing one-month. Mean costs and utilities accrued over this time were used to estimate the net monetary benefit (NMB) of each strategy. The NMB is a summary statement used in health economic evaluations, calculated as effectiveness (measured in quality adjusted life years, or QALYs) multiplied by the willingness to pay threshold (defined a priori as $50,000 per QALY) minus the cost of the strategy.(36) Strategies with the NMB greater than zero cost less than the societal willingness-to-pay threshold, and the most cost-effective strategy is that with the highest NMB. The advantage of the NMB is that statistical calculations with small mean differences in effectiveness (such as the change in QALYs from vitamin D supplementation) remain stable, unlike traditional summary estimates such as the incremental cost-effectiveness ratio (cost per QALY).(36-38) Analyses were performed using decision analysis software (TreeAge Pro Suite 2011; TreeAge Software, Inc., Williamstown, MA).

One-way sensitivity analyses were performed on all probabilities, costs, and utilities to explore the effect of variations in model parameters on the NMB of each strategy. Probability, utility, and cost parameters were tested over the entire range of minimum and maximum values from the literature. Probabilistic sensitivity analysis was performed using

100,000 simulations. For each simulation, parameter values were randomly sampled from the distributions of each variable to account for uncertainty in the parameter estimates. Distributions were parameterized as normal, log-normal, triangular, or beta distributions using base case estimates and ranges, consistent with consensus recommendations.(39)

RESULTS

Cost-effectiveness analysis – Female

After 36-months of follow-up in a hypothetical cohort of older adult females, a strategy of population screening resulted in incremental costs of $112.82 and effectiveness of 0.007 QALYs, and universal supplementation resulted in incremental costs of $51.44 and effectiveness 0.005 QALYs. Consequently, at the willingness-to-pay (WTP) threshold of $50,000 per QALY, vitamin D screening among older adult women results in an incremental net monetary benefit (NMB) of $224, compared to $189 for universal supplementation ($P < 0.001$) [Figure 3].

Among females age 65 years, a strategy of population screening resulted in incremental costs of $116.59 and incremental effectiveness of 0.004 QALYs, and universal supplementation resulted in incremental costs of $53.40 and incremental effectiveness of 0.002 QALYs. Universal supplementation was statistically different from population screening, though the absolute magnitude was small with an incremental NMB of $71, compared to $59 ($P < 0.001$) [Figure 4].

Among females age 80 years, a strategy of population screening resulted in incremental costs of $105.80 and incremental effectiveness of 0.013 QALYs, and universal supplementation resulted in incremental costs of $47.57 and incremental effectiveness of 0.010 QALYs. Population screening was significantly more cost-effective than universal supplementation with an incremental NMB of $563, compared to $428 ($P < 0.001$) [Figure 4].

Sensitivity analyses – Female

In univariate sensitivity analysis, the falls risk reduction due to vitamin D supplementation and the cost of serum 25-hydroxyvitamin D testing had the largest impact on the NMB estimate. Both population screening and universal supplementation were cost-effective for values of falls risk reduction greater than 11%, though population screening remained more cost-effective for risk reduction values greater than 27%. Both strategies were cost-effective across the range of testing costs, but population screening was more cost-effective for testing costs less than $51.

At the WTP threshold of $50,000 per QALY, population screening among older adult women was most cost-effective in 52.8% of the simulations, compared to 36.3% for universal supplementation. Limiting the cohort to only women age 65 years, universal supplementation was the most cost-effective strategy in 37.2% of the simulations, compared to 42.6% of the simulations for population screening. Among women age 80 years, population screening was the most cost-effective strategy in 73.4% of the simulations, compared to 23.4% of the simulations for universal screening.

Cost-effectiveness analysis -Male

After 36-months of follow-up in a hypothetical cohort of older adult men, a strategy of population screening resulted in incremental costs of $105.46 and incremental effectiveness of 0.008 QALYs, whereas universal supplementation resulted in incremental costs of $52.55 and incremental effectiveness 0.006 QALYs. Consequently, at the WTP threshold, vitamin

D screening among older adult men resulted in an incremental NMB of $298, compared to $260 for universal supplementation ($P < 0.001$) [Figure 3].

Among men age 65 years, a strategy of population screening resulted in incremental costs of $108.38 and effectiveness of 0.004 QALYs, while universal supplementation resulted in incremental costs of $54.07 and mean effectiveness of 0.003 QALYs. Universal supplementation was statistically different from population screening, though the absolute magnitude was small with an incremental NMB of $120 compared to $114 ($P < 0.001$) [Figure 4].

Among men age 80 years, a strategy of population screening resulted in incremental costs of $97.96 and effectiveness of 0.016 QALY, and universal supplementation resulted in incremental costs of $48.13 and effectiveness of 0.012 QALY. Population screening was significantly more cost-effective than universal supplementation with an incremental NMB of $703 compared to $571 (P < 0.001) [Figure 4].

Sensitivity analyses – Male

In univariate sensitivity analysis, the falls risk reduction due to vitamin D supplementation and the cost of serum 25-hydroxyvitamin D testing had the largest impact on the NMB estimate. Both population screening and universal supplementation were cost-effective across the range of falls risk reduction, though population screening remained more cost-effective for risk reduction values greater than 25%. Similarly, both strategies were cost-effective across the range of testing costs, but population screening was more cost-effective for testing costs less than $53.

At the WTP threshold of $50,000 per QALY, population screening among older adult men was most cost-effective in 54.3% of the simulations, compared to 38.2% for universal supplementation. Limiting the cohort to only men age 65 years, universal supplementation was the most cost-effective strategy in 44.2% of the simulations, compared to 42.5% of the simulations for population screening. Among men age 80 years, population screening was the most cost-effective strategy in 71.5% of the simulations, compared to 26.2% for universal screening.

DISCUSSION

This cost-benefit analysis demonstrates that both universal supplementation and population screening for vitamin D deficiency among both older adult women and men are cost-effective from a societal perspective. Population screening for vitamin D insufficiency may be more cost-effective than universal supplementation at older ages. This result is likely driven by the earlier identification of subjects with vitamin D deficiency (serum 25-hydroxyvitamin D levels < 15 ng/ml) in whom cholecalciferol 1000 IU daily would not likely raise levels sufficiently. Consequently, these persons are able to achieve target levels and reduce their falls risk earlier. This is especially true among the oldest old who are at higher risk for vitamin D deficiency.

This analysis has several implications for clinicians and researchers. While a strategy of universal supplementation with a current standard dose vitamin D (1000 IU daily) is cost-effective at a population level, our model suggests that an additional clinical and cost benefit is obtained by screening for and treating vitamin D deficiency among persons at highest risk. Clinical controversy remains over the safety and efficacy of higher daily doses (i.e. >1500 IU daily), and high intermittent dosing (e.g. 50,000 IU monthly to 500,000 IU annually).(40-45)Changes in standard recommended doses for vitamin D supplements may have an impact on whether population screening or universal supplementation is most cost-effective.

Additional research is needed to identify supplementation regimens that optimize the clinical benefits.

We were unable to identify prior cost-effectiveness analyses in the published literature comparing population screening to universal vitamin D supplementation. A prior cost-utility analysis of falls prevention programs showed that vitamin D supplementation was less costly than standard care ($1800 vs. $1400) and increased QALYs among older adults at high risk for falls.(46) Supplementation was the most cost-effective strategy in over 29% of simulations at a WTP threshold of $50,000/QALY. However, that analysis did not evaluate the strategy of targeted supplementation after serum testing, but assumed universal supplementation within a population of adults older than 65 years. Moreover, it utilized efficacy data from a meta-analysis that included trials of nursing home residents who have a substantially higher prevalence of vitamin D insufficiency than community-dwelling older adults.

The current results depend on the cost of vitamin D testing not increasing more than the current Medicare reimbursement rate. As testing for serum 25-hydroxyvitamin D becomes more automated and available, we anticipate that the distribution of costs will narrow and likely approach the current reimbursement rate. The results were robust to variations in the other parameter estimates. We note that the probability, utility, and cost estimates in the current study were obtained from several high quality meta-analyses, pooled analyses,analyses of national databases, or large population-based cohort studies. The base values and ranges represent the most conservative estimation of the intervention effect.

Several limitations to this analysis should be considered. This study focused on Caucasian older adults due to limited published data on other ethnicities to define the transition probabilities. Cost estimates were taken from published data of analyses of large Medicare datasets, inflated to 2011 dollars, and may not accurately reflect the actual cost in today’s practice. Only direct costs were considered, given limited data regarding indirect costs of falls. This approach represents a conservative underestimation of the cost-effectiveness for the strategy. The cost of the serum 25-hydroxyvitamin D test was based on the current CMS reimbursement rate, which may underestimate the true societal cost for testing; to account for this we incorporated wide distributions of costs in the sensitivity analyses.

In conclusion, this study demonstrates that population screening for vitamin D insufficiency is cost-effective among older adults. Moreover, among the oldest old, population screening was more cost-effective than universal supplementation. Future studies should focus on the efficacy of higher vitamin D doses and the indirect costs and benefits of supplementation among this age group. The result of this study should help inform clinical practice as well as guideline development for preventative services.

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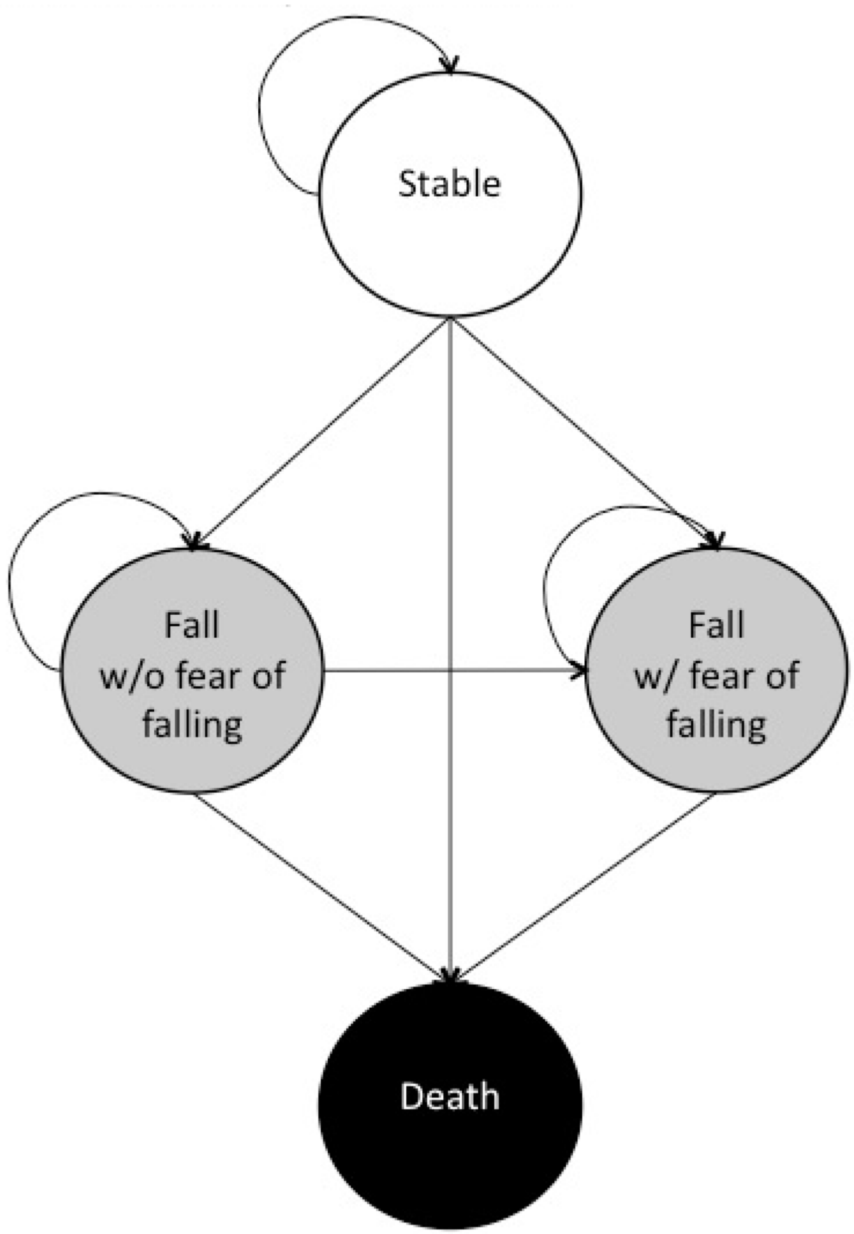

Figure 1.

Flow chart depicting possible health states and transitions for Markov model construction to simulate progression of events. At the start of each simulation, all subjects were assumed to be *No Falls* (without prior falls). Fall event outcomes include: 1) no injury, 2) injurious fall without hospitalization, and 3) injurious fall with hospitalization. *Grey* circles represent health states with lower age- and gender-specific utilities related to fall history. *Death* is a terminal node.

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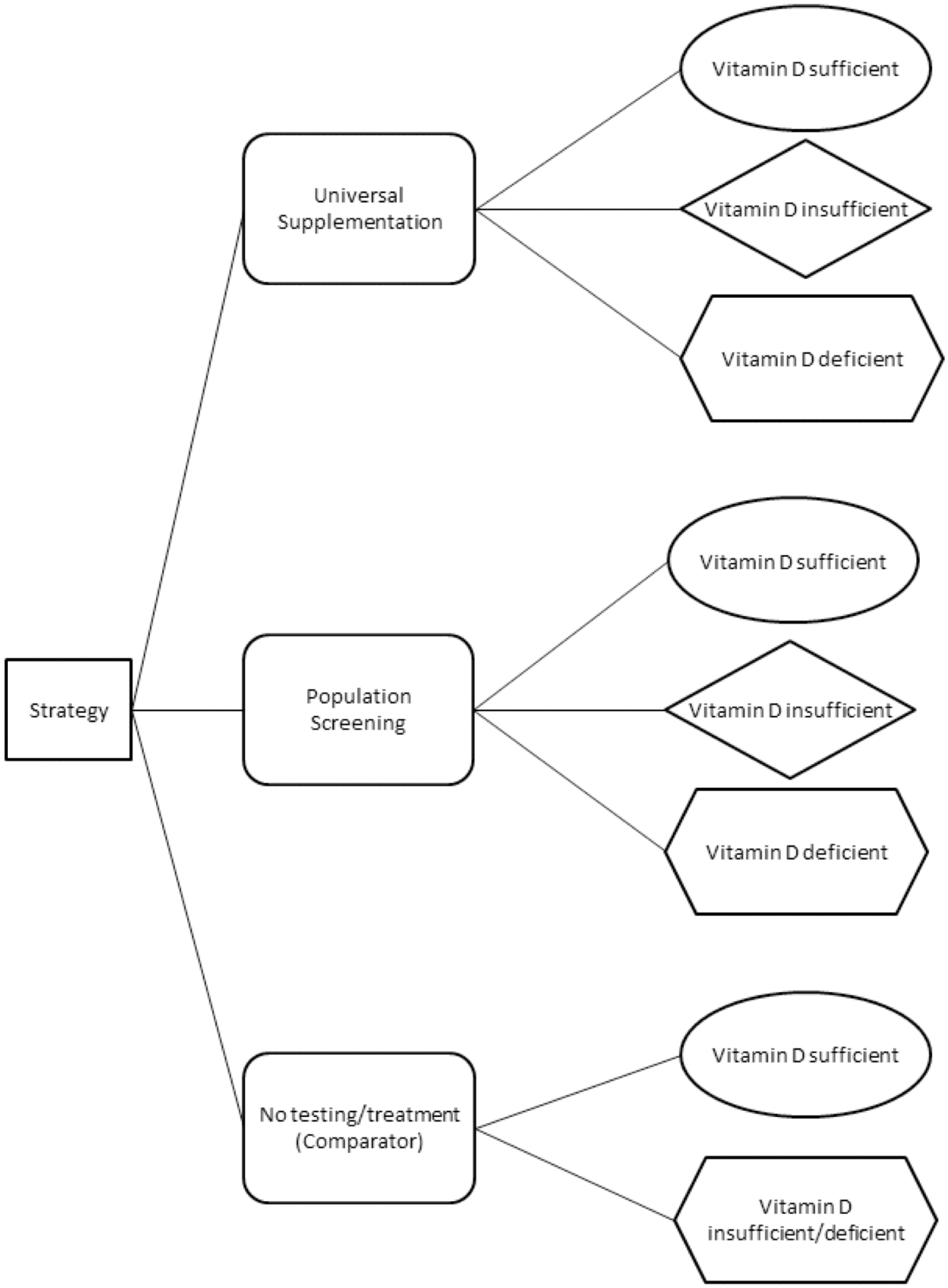

Figure 2.

Decision tree illustrating the 3 modeled strategies and cohort constituents by vitamin D status. *Ovals* represent cohort with lowest falls risk. *Diamonds* represent cohort with improvement in falls risk due to vitamin D supplementation. *Hexagons* represent cohort with highest risk of falls. *Note*: For “No testing/treatment” strategy vitamin D insufficient and deficient groups combined, as falls risk assumed to be higher, given no vitamin D supplementation in either group.

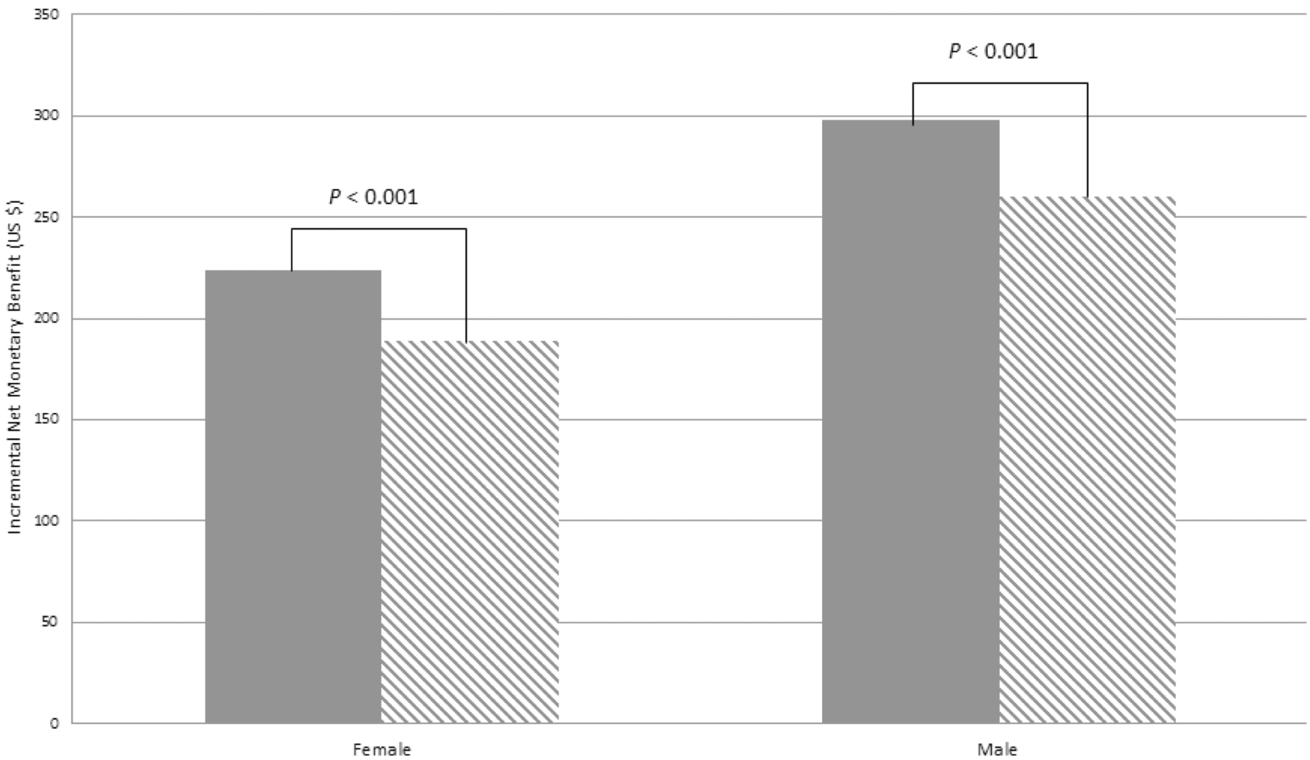

Figure 3.
Incremental net monetary benefit among older adults age 65 to 80 years, by gender. Willingness-to-pay threshold = US $50,000. Population screening (*solid bars*) and universal supplementation (*striped bars*). *Note*: more cost-effective strategy demonstrates higher incremental net monetary benefit.

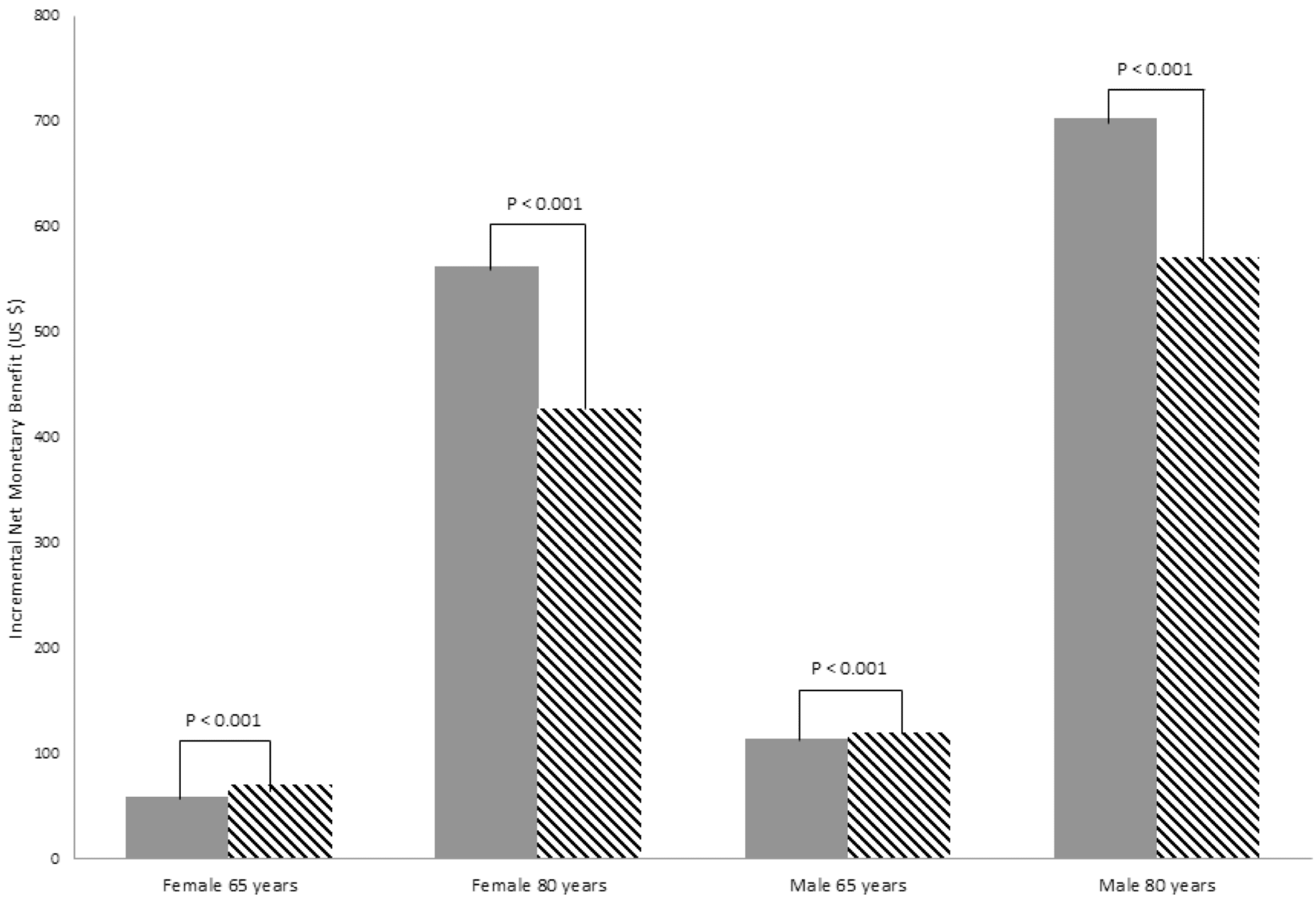

Figure 4.

Incremental net monetary benefit by sub-group of age and gender. Willingness-to-pay threshold = US $50,000. Population screening (*solid bars*) and universal supplementation (*striped bars*).

Table 1

Base Case Values and Ranges for Cost, Utility, and Probability Estimates by Gender

Parameter	Gender	
	Female	**Male**
Costs		
Fall, mean(SD)		
Outpatient		
Age 65 – 69	$656 (2282)	
Age 70 – 74	491 (1558)	
Age 75 – 79	533 (1431)	
Age 80+	406 (583)	
Hospitalization		
Age 65 – 69	$19114 (13652)	
Age 70 – 74	17363 (11595)	
Age 75 – 79	22981 (27369)	
Age 80+	23113(32493)	
25-hydroxyvitamin D	$41.66	
Vitamin D capsule, mean(SD)	$0.077 (0.062)	
Utilities		
HRQoL, mean (95% CI)		
Age 65 - 69	0.811 (0.800 – 0.822)	0.840 (0.827 – 0.852)
Age 70 – 79	0.771 (0.758 – 0.784)	0.802 (0.788 – 0.816)
Age 80+	0.724 (0.701 – 0.747)	0.782 (0.757 – 0.807)
Health utility loss		
Fall	0.044 (0 – 0.075)	
Fall with fear of falling	0.161 (0.105 – 0.253)	
Probabilities		
Falls, % (95% CI)		
Age 65 - 69	13.6 (12.6 – 14.5)	13.9 (12.6 – 15.1)
Age 70 - 74	14.3 (13.2 – 15.5)	13.2 (11.9 – 14.5)
Age 75 - 79	16.1 (14.9 – 17.4)	14.2 (12.6 – 15.7)
Age 80+	20.1 (18.8 – 21.4)	21.0 (19.2 – 22.8)
Injurious fall, % of All falls (95% CI)		
Age 65 - 69	35.5 (31.9 – 39.1)	20.8 (17.2 – 24.4)
Age 70 - 74	36.8 (32.4 – 41.3)	22.6 (18.5 – 26.7)
Age 75 - 79	34.9 (30.9 – 39.0)	23.0 (18.6 – 27.4)
Age 80+	33.6 (30.3 – 36.9)	26.8 (22.5 – 31.1)
Death, %		
Age 65 - 69	1.07	1.66
Age 70 - 74	1.65	2.50
Age 75 - 79	2.82	4.13
Age 80+	4.86	6.78

[a]Costs reflect adjustment to 2011 U.S. dollar

[b]Utility values can range between 0 (death) and 1 (perfect health)

[c]HRQoL: Health-related quality-of-life