

# BMJ Open Cost-effectiveness and budget impact of Empirical vitamin D therapy on unintentional falls in older adults in the UK

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## ABSTRACT

**Objectives:** To evaluate the health outcomes and economics associated with the current guidance relating to the prevention of falls in the elderly through vitamin D supplementation.

**Setting:** UK.

**Participants:** UK population aged 60 years and above.

**Interventions:** A Markov health state transition model simulated patient transitions between key fall-related outcomes using a 5-year horizon and annual cycles to assess the costs and benefits of empirical treatment with colecalciferol 800 iu daily.

### Primary and secondary outcome measures:

Costs and health outcomes attributable to fall prevention following vitamin D supplementation.

**Results:** Our model shows that treating the UK population aged 60 years and above with 800 iu colecalciferol would, over a 5-year period: (1) prevent in excess of 430 000 minor falls; (2) avoid 190 000 major falls; (3) prevent 1579 acute deaths; (4) avoid 84 000 person-years of long-term care and (5) prevent 8300 deaths associated with increased mortality in long-term care. The greatest gains are seen among those 75 years and older. Based on reduction in falls alone, the intervention in all adults aged 65+ is cost-saving and leads to increased quality adjusted life years. Treating all adults aged 60+ incurs an intervention cost of £2.70bn over 5 years, yet produces a –£3.12bn reduction in fall-related costs; a net saving of £420M. Increasing the lower bound age limit by 5-year increments increases budget impact to –£1.17bn, –£1.75bn, and –£2.06bn for adults 65+, 70+ and 75+, respectively.

**Conclusions:** This study shows that treatment of the elderly UK population with colecalciferol 800 iu daily would be associated with reductions in mortality and substantial cost-savings through fall prevention.

## INTRODUCTION

Vitamin D is increasingly recognised as an important sterol hormone with ubiquitous expression of the vitamin D receptor throughout the body's organs.<sup>1</sup> While the

## Strengths and limitations of this study

- Age-group specific determination of health costs related to falling.
- A conservative health economic model which interprets current guidance on prevention of falls using vitamin D therapy is highly cost effective in the treatment of adults over a 5-year time horizon.
- Conservative estimation of costs of falls presenting to accident and emergency (A+E) only.
- Fall prevention with empirical vitamin D 800 iu daily is associated with a reduced mortality comparable to that found in meta-analyses.
- The role of vitamin D in fall prevention remains controversial.

effects of vitamin D on bone are well recognised there is increasing appreciation of its extraskelatal effects.<sup>2</sup> Indeed, vitamin D deficiency is implicated in diseases beyond calcium metabolism such as diabetes, multiple sclerosis and cancer.<sup>2</sup> With a high prevalence of vitamin D deficiency and insufficiency in the general population, increasing attention is turning to the positive impact of vitamin D replacement therapy.

Meta-analytic data reveal that vitamin D treatment is associated with reduced risk of fractures in the elderly only in doses at or above roughly 800 iu daily.<sup>3</sup> Yet, these conclusions are disputed, as others argue that aetiological mechanisms such as bone mineralisation is unchanged through vitamin D intervention.<sup>4</sup> However, falls are a particularly important event in the aetiology of fractures, as well as contributing to other morbidities, hospitalisation and institutionalisation in the elderly. Again, the data regarding falls has been confounded by inclusion of data relating to different doses, additional calcium supplementation and length of study.<sup>5</sup> A meta-analytic study suggested a significant reduction in the risk of falls in

elderly participants only in studies using doses of 700 iu of vitamin D or above.<sup>6</sup> Again, the study has been criticised, yet a more recent review of the data by the American and British Geriatric Societies conclude that vitamin D therapy should be given to elderly participants at risk of falls and at a dose of at least 800 iu per day.<sup>7</sup> They conclude that the number needed to treat (NNT) to prevent one fall is 10 compared with a NNT of 13 associated with exercise training. While evidence points to doses of at least 800 iu daily in fall prevention strategies in elderly participants, a letter from the Chief Medical Officers in the UK recommends a smaller dose of 400 iu daily for all participants over 65 years of age at risk of vitamin D deficiency.<sup>8</sup>

Universal vitamin D supplementation in older adults has been found to be a cost-effective strategy for fall prevention in the USA,<sup>9</sup> and also in Western European populations (including the UK) but using fractures as the primary modifiable outcome.<sup>10–12</sup>

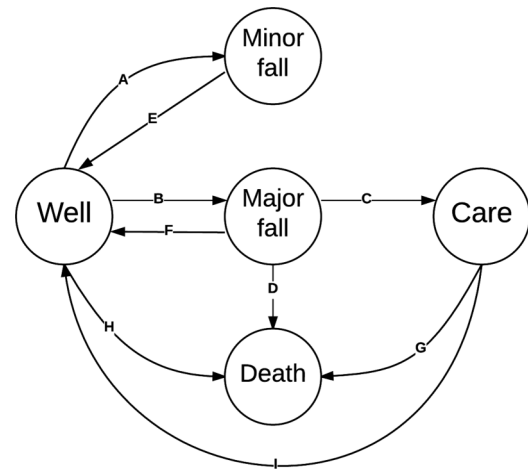
While the data suggest a positive impact of vitamin D therapy on fall prevention, there are no data which interpret the financial impact of vitamin D treatment on the UK population. Thus, based on the American Geriatrics Society/British Geriatrics Society (AGS/BGS) guidance<sup>7</sup> in terms of a dose of at least 800 iu daily together with recommendations of the CMOs of the UK<sup>8</sup> supporting treatment of a UK elderly population, we evaluated the cost-effectiveness and budget impact of treating the older adult (age 60 years and above) UK population with at least 800 iu of vitamin D daily with regard to its impact on falls.

## METHODS

A Markov health state transition model was constructed in Microsoft Excel to simulate patient transitions through a simplified patient pathway representing the key fall-related outcomes described in a detailed audit of UK accident and emergency department (A&E) records.<sup>13</sup> The model conservatively used a 5-year horizon and annual cycles to assess the costs and benefits of treatment with colecalciferol 800 iu daily. The payer perspective was that of the UK taxpayer taking National Health Service (NHS) and Social Care expenditure into account.

### Health states

As described in figure 1, patients enter the model in the 'Well' state, and during each cycle it was assumed they lived in an independent community setting. During each cycle patients could experience either: (1) a 'Minor fall', necessitating A&E attendance but no admission and either no follow-up, outpatient follow-up or general practitioner (GP) follow-up; or (2) a 'Major fall' with admission to hospital via A&E and either discharge to home with follow-up or transfer to postacute care; or (3) death. Those experiencing a minor fall were assumed to make a full recovery as were those who had



**Figure 1** Markov health state transition model representing unintentional falls in older people. Key: 'Well', No fall in cycle and living at home; 'Minor fall', Fall resulting in A&E attendance but no admission; 'Major fall', Fall resulting in hospital admission; 'Care', No fall in cycle and living in care facility; and 'Death', from any cause. A&E, accident and emergency.

a major fall but did not require postacute care or died in hospital. Patients transferred to postacute care could return to independent living in their first year, thereafter the remainder were assumed to require long-term residential or nursing care.

### Health state transitions

Annual rates of accident and emergency admission were used to define age-group dependent probability of minor and major unintentional falls.<sup>13</sup> These were derived by Scuffham *et al*, from a detailed analysis of UK sentinel databases are used to record mode of arrival at A&E, circumstances of the accident (cause), injury sustained, and deployment (eg, referral to GP). It was conservatively assumed that: each patient experiences just one fall event in a given year; and that future probability of falling is not conditional on fall history. Acute phase outcomes following admission for a major fall (death and discharge to post-acute care) were also defined.<sup>13</sup> Age-group dependent all-cause mortality was applied equally to those remaining fall-free and those recovering fully from either a minor or major fall.<sup>14</sup> For those in long-term care, the death rate observed by Bebbington *et al*<sup>15</sup> during their longitudinal survey of 2540 admitted residents from 18 local authorities was conservatively applied. The probability of returning home in the first year after admission to long-term care was also applied from the Bebbington study. The transitions are summarised in table 1.

### Treatment

The intervention under consideration is empiric treatment of all older adults aged 60 years and over with colecalciferol 800 iu daily. While this considers the older adult cohort preceding that recommended by the UK

**Table 1** Transition probabilities between Markov health states (see figure 1)

Transition	Description	Source	Age group (%)			
			60–64	65–69	70–74	≥75
A	Probability of minor fall	Scuffham	2.4	2.4	2.8	5.8
B	Probability of major fall	Scuffham	0.3	0.5	0.9	3.7
C	Probability of long-term care following major fall	Scuffham	0.0	0.0	8.6	27.4
D	Probability of death following major fall	Scuffham	0.2	0.4	0.7	1.0
E	Recovery following minor fall	Assumption	100.0	100.0	100.0	100.0
F	Recovery following major fall	1-C-D	99.8	99.6	90.7	71.7
G	Probability of death while in care	Bebbington*	–	–	20.6	20.6
H	Probability of death from independent living	ONS	0.6	0.6	1.6	7.5
I	Probability of return to independent living	Bebbington†	–	–	3.8	3.8

\*Conservatively estimated as that applicable to residential care.

†93/2450 older adults admitted to institutional care observed over 42 months. As the survival distribution of ‘returners’ is unknown the model conservatively estimates that they occur in the first year only following a major fall.

chief medical officers,<sup>8</sup> it takes in the age cohorts examined by Scuffham *et al*<sup>13</sup> with respect to falling, thus providing evidence to where the economic boundary of ‘older’ adulthood may lie with respect to fall prevention. The daily dose of colecalciferol administered is higher than the 400 iu jointly recommended by the UK CMOs because daily doses less than 700 iu have been shown to be ineffective in preventing falls in older adults, while patients treated with between 700 and 1000 iu have a shown a lower relative risk of falling (RR 0.81 (95% CI 0.71 to 0.92)).<sup>6</sup> This treatment effect was applied equally to falls of any severity. The comparator was assumed to be current standard of care.

In terms of adverse effects of treatment we assumed none associated with vitamin D 800 iu daily treatment in line with the recent US Preventative Services Task Force finding of adequate evidence that the harms of treatment of vitamin D deficiency are small to none.<sup>16</sup>

### Costs

Within our model, we selected the price of only licensed 800 iu vitamin D formulations available for prescription in the UK. We chose these preparations as there is a specific NHS tariff making calculations straightforward but also the Medicines and Healthcare Products Regulatory Agency (MHRA) stipulate that where a licensed product exists, unlicensed products should not be used.<sup>17</sup>

Therefore daily colecalciferol 800 iu treatment was assumed to be met by proprietary oral capsules as the lowest cost option in the British National Formulary (BNF).<sup>18</sup> Fall-related costs were those listed<sup>13</sup> and indexed to 2014 prices.<sup>19</sup> All costs are summarised in table 2.

### Utilities

Baseline utility in the ‘Well’ state was defined according to 5-year age group and the UK value set for the EQ-5D-3 L.<sup>20</sup> Falls were assumed to confer a disutility associated with severe fear of falling.<sup>21</sup> Postacute institutional care was also associated with disutility compared to age-gender matched counterparts reported in a study of

Australian older adults.<sup>22</sup> Hospital admission following a major fall was conservatively assumed to incur the same disutility as postacute care for 10 days, the average length of stay for HRG R29.6, *Tendency to fall, not elsewhere classified*.<sup>23</sup> Utilities are summarised in table 3.

### Budget impact population

Budget impact calculations were based on the older adult population of the UK at the 2011 census.<sup>24</sup>

## RESULTS

### Outcomes

Over the 5-year model horizon, our model suggests that empiric colecalciferol treatment at 800 iu daily among

**Table 2** Costs to NHS relating to falls and vitamin D treatment

Description	GBP2014	Source
Annual cost of daily vitamin D	£43.83	BNF
800 IU supplementation		
Ambulance journey	£306	Scuffham
GP consultation	£31	
A&E attendance	£111	
Return to residence, attend OP	£116	
Return to residence, attend GP	£31	
Long-term care (6 months)	£16 388	
Minor fall (weighted)		
60–64	£442	
65–69	£456	
70–74	£466	
≥75	£462	
Major fall (weighted HRG acute costs)		
60–64	£2622	
65–69	£2766	
70–74	£3603	
≥75	£3537	

A&E, accident and emergency; BIM, Budget Impact Model; BNF, British National Formulary; GP, general practitioner; HRG, Healthcare Resource Group; NHS, National Health Service; ONS, Office of National Statistics; OP, outpatients.

**Table 3** Health state utilities by age-group

Health state	Source	Age group			
		60–64	65–69	70–74	≥75
Well	Kind <i>et al</i> <sup>20</sup>	0.800	0.780	0.780	0.730
Minor fall	Thiem <i>et al</i> <sup>21</sup>	0.783	0.763	0.763	0.713
Major fall		0.768	0.748	0.748	0.698
Long-term care	Couzner <i>et al</i> <sup>22</sup>	0.606	0.586	0.586	0.536

older adults aged 60 years and over in the UK would: (1) prevent in excess of 430 000 minor falls; (2) avoid 190 000 major falls; (3) prevent 1579 acute deaths; (4) avoid 84 000 person-years of long-term care; and (5) avoid a further 8300 deaths associated with increased mortality in long-term care (table 4). The greatest gains are seen among those aged 75 years and older which would account for 51% of preventable minor falls, 75% of preventable major falls, 96% of person years in care avoided and 94% avoidable attributable mortality.

### Cost-effectiveness

Compared to current care, treating all adults aged 60 years and over with colecalciferol 800 iu daily would have an incremental cost-effectiveness ratio of £19 759 per quality adjusted life year (QALY) gained based on a reduction in falls alone. The same intervention in all adults aged 65 years and over, as recommended by the

**Table 4** Comparison of 5-year fall-related outcomes for current care versus empiric vitamin D maintenance therapy

Age group	Current	Vitamin D	Δ
<b>Minor falls</b>			
60–64	449 271	363 910	85 360
65–69	350 460	283 875	66 585
70–74	328 891	266 484	62 407
≥75	1 190 867	968 252	222 615
<b>Major falls</b>			
60–64	64 769	52 463	12 306
65–69	77 452	62 737	14 715
70–74	109 630	88 828	20 802
≥75	761 374	619 046	142 328
<b>Deaths from falls</b>			
60–64	149	121	28
65–69	333	270	63
70–74	713	577	135
≥75	7233	5881	1352
<b>Person-years in care</b>			
60–64	–	–	–
65–69	–	–	–
70–74	18 338	14 857	3481
≥75	426 696	346 408	80 288
<b>Deaths from care</b>			
60–64	–	–	–
65–69	–	–	–
70–74	1932	1566	367
≥75	42 586	34 625	7961

UK CMOs<sup>8</sup> dominates current care, by being cost-saving and leading to increased QALYs (table 5).

### Budget impact

The costs and net budget impact of alternative age-bound strategies for use of empiric maintenance treatment with colecalciferol 800 iu daily are shown in table 6. Treating all adults aged 60 years and over, would incur an intervention cost of £2.70bn over 5 years, yet over the same period a –£3.12bn reduction in fall-related costs would produce a net saving of £420M. Increasing the lower bound age limit by 5-year increments increases budget impact to –£1.17bn, –£1.75bn and –£2.06bn for intervention strategies applied to all adults aged 65+, aged 70+ and aged 75+, respectively (figure 2).

### DISCUSSION

Our study shows that treating all adults over the age of 65 with vitamin D at doses of 800 iu daily would result in a substantial cost-saving to the UK NHS of £1.2 billion over 5 years through prevention of some 530 000 falls, 84 000 person-years in long-term care, and almost 10 000 premature deaths. Additionally, the empiric treatment of younger seniors from the age of 60 would also be cost-saving, albeit less so. The main relief of burden on health and social care expenditure would arise from avoidance of long-term care following a fall in those aged 70 years and over. These data are consistent with cost-effectiveness assessments of universal vitamin D supplementation in older adults in the USA<sup>9</sup> and also in Western European populations but using fractures as the primary modifiable outcome.<sup>10 11</sup>

The ‘memory-less’ property of our Markov model structure introduced a conservative assumption that fall history does not influence future risk of falling. Additionally, falls among those receiving long-term care was not modelled. Our model also applied all-cause mortality as the background death rate, which include deaths from unintentional falls, effectively reducing the

**Table 5** Cost-effectiveness results of alternative treatment strategies (per person treated)

Strategy	Incremental costs	Incremental QALYs	ICER
Treat all adults ≥60 years	£23.52	0.0012	£19 759
Treat all adults ≥65 years	–£34.19	0.0014	Dominant
Treat all adults ≥70 years	–£147.01	0.0018	Dominant
Treat all adults ≥75 years	–£419.88	0.0027	Dominant

ICER, incremental cost-effectiveness ratio; QALY, quality adjusted life year.

**Table 6** Budget impact on NHS for alternative age-bound empiric vitamin D maintenance therapy strategies

Strategy	Well	Minor fall	Major fall	Care after major fall	Long-term care	Total	Net BIM
Current care							
All 60+	£ M	£1062 M	£3472 M	£3540 M	£9378 M	£17 451 M	
All 65+	£ M	£863 M	£3302 M	£3540 M	£9378 M	£17 083 M	
All 70+	£ M	£703 M	£3088 M	£3540 M	£9378 M	£16 709 M	
All 75+	£ M	£550 M	£2693 M	£3386 M	£8994 M	£15 623 M	
Empiric vitamin D maintenance							
All 60+	£2703 M	£944 M	£2857 M	£2886 M	£7642 M	£17 032 M	–£420 M
All 65+	£1903 M	£767 M	£2717 M	£2886 M	£7642 M	£15 915 M	–£1168 M
All 70+	£1270 M	£626 M	£2540 M	£2886 M	£7642 M	£14 963 M	–£1746 M
All 75+	£771 M	£490 M	£2216 M	£2761 M	£7330 M	£13 567 M	–£2056 M

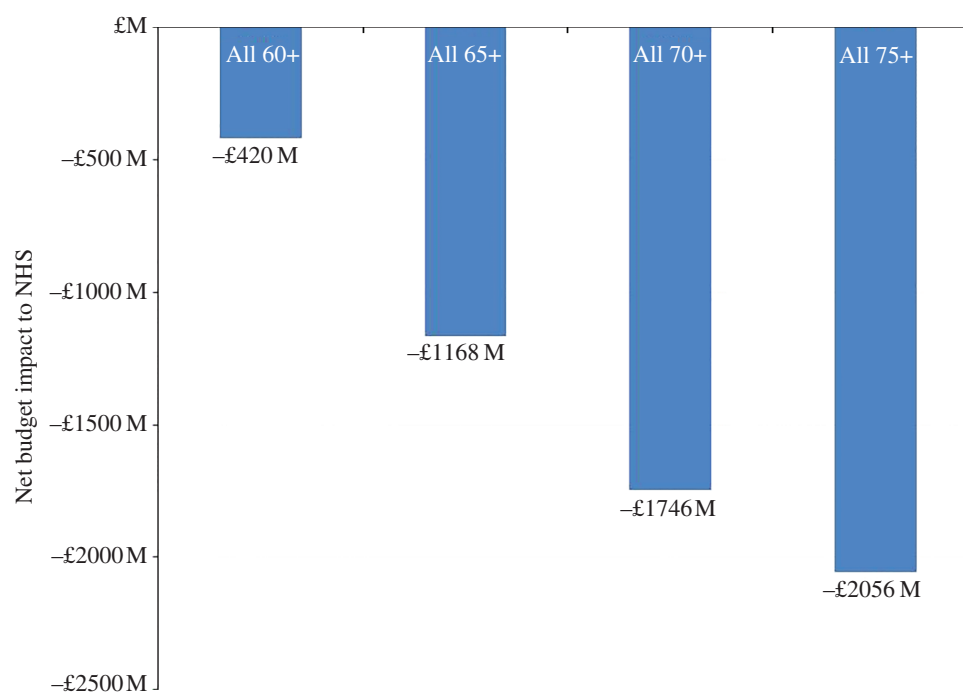
NHS, National Health Service.

‘at-risk’ population. Therefore our estimates of cost-effectiveness are likely conservative.

Sustainability of treatment effect is an important consideration in any economic analysis. Active forms of vitamin D, including colecalciferol, do not need hydroxylation in the kidney, so their effect on falls should be influenced less by age-related decline in kidney function than the effect of supplemental vitamin D. The duration of the eight randomised controlled trials included in the primary efficacy meta-analysis we modelled,<sup>6</sup> was 2, 3, 5, 12, 20, 24 and 36 months suggesting that the pooled effect is consistent over longer time periods. In addition we conservatively set a model horizon of 5 years to avoid speculative extrapolation of long-term benefits with increasing uncertainty.

Falls are a particularly common problem in the elderly person accounting for 10% of emergency hospital visits and 6% of hospital admissions with risk increasing with increasing age.<sup>25</sup> Rather than a benign

process, falls are a predictor of increasing morbidity, mortality and importantly institutionalisation. In consequence, falls present a significant risk to health and are costly. We based our calculations on the health economic evaluation of falls in the UK.<sup>13</sup> This data included the cost of falls to the NHS and social care budgets. While our calculated cost-savings are great, the estimates used to support these calculations have been conservative. Indeed, the older person who has fallen suffers greater decline in activities of daily living as well as greater risk of institutionalisation.<sup>26</sup> Those who return to independent living following a fall often require domestic care support, costs we did not factor in our evaluation. With this in mind, we have demonstrated that 800 iu colecalciferol daily is a cost-effective treatment purely based on fall prevention in individuals 60 years and over. The cost per QALY of £19 759 is within the expected economic cost per QALY threshold of £20 000 advocated by the National Institute of Care Excellence

**Figure 2** Budget impact results for alternative treatment strategies.

(NICE). This is comparable to evaluations for the prevention of ischaemic heart disease with statin therapy.<sup>27</sup> Similarly, dominant QALY costs, (indicating that there are net savings accrued through fall prevention with vitamin D treatment), were noted with the application of the recommendations of the CMOs letter<sup>8</sup> for the treatment of all patients aged 65 years and over (table 5).

Vitamin D is an important sterol hormone involved in calcium metabolism with recognition of its important role in musculoskeletal health. Evidence reveals that vitamin D deficiency is common in the UK with studies suggesting a prevalence as high as 50%<sup>28</sup> and even higher in certain populations such as the elderly and institutionalised.<sup>29</sup> Decreased bone mineralisation, increased fracture risk as well as increased risk of falls are associated with vitamin D deficiency<sup>30–32</sup> and evidence would point to the improvement in some of these parameters following treatment, particularly in the elderly.<sup>3 6 33</sup> However, not all studies conclude a reduction in falls and such discrepancies may be a consequence of the use of different formulations (ergocalciferol or colecalciferol), different doses of vitamin D, differing baseline vitamin D status and also differing populations.<sup>5 34</sup> However, guidelines on fall prevention has evaluated the evidence and support the treatment of individuals with deficiency, or potential deficiency, at risk of falls with at least 800 iu of vitamin D daily.<sup>7</sup> Similarly, UK CMOs also advocate vitamin D treatment, yet the 400 iu dose advocated may be ineffective in terms of preventing deficiency, falls and fractures in an elderly population.<sup>3 6</sup> In consequence, we elected an 800 iu dose as the minimal, guidance-advocated dose for fall prevention in the elderly.

The importance of vitamin D in an adult population can be seen at the extreme end of the clinical spectrum as osteomalacia, with pseudofractures and profound proximal muscle weakness. Symptoms and signs resolve following treatment and so it seems plausible that vitamin D therapy too has beneficial effects in non-osteomalacic vitamin D deficiency.<sup>35</sup> This is supported by studies revealing dose dependent reduction in falls and fractures<sup>3 6 33</sup> which may accrue only with vitamin D deficiency/insufficiency, a common problem in the elderly population. Factors contributing to the reduced risk of falls following vitamin D treatment include improved muscle strength<sup>36 37</sup> as well as improved balance.<sup>34</sup> Indeed, improved muscle mitochondrial oxidative function<sup>38</sup> as well as muscle energy metabolism<sup>39</sup> following vitamin D treatment may provide mechanistic explanations for improved strength and endurance. Histologically, reduced muscle fibre number and changes in muscle fibre type may contribute further to the sarcopaenia and myopathy found with aging and vitamin D deficiency<sup>40</sup> and may improve following treatment with vitamin D.<sup>41</sup>

Our study also shows that the reduced risk of falls associated with treating an elderly population with vitamin D

is associated with a substantial reduction in premature deaths. Studies reveal increased mortality associated with lower 25OHD concentrations although this relationship has been considered to be an epiphenomenon of illness. However, recent data support the role of reduced mortality following vitamin D treatment.<sup>42–45</sup> In particular, colecalciferol rather than ergocalciferol appears to offer superiority in mortality reduction.<sup>44</sup> The single figure per cent reduction in mortality seen in such studies is in keeping with that calculated in our study.

With respect to UK public health policy regarding vitamin D supplementation in older adults,<sup>8</sup> we believe, in light of the clinical and economic evidence, that the current advice is flawed. First, the recommendation of universal supplementation of colecalciferol 400 iu (10 µg) daily has been shown to be ineffective in the prevention of either falls<sup>6</sup> or fractures.<sup>3</sup> Expert guidelines suggest a minimum daily supplement of 800 iu in those at risk.<sup>7</sup> Second, the optimal method of procurement is not clearly stated, with OTC supply being given equal weighting to prescription. We contend that prescribed therapy should be favoured over OTC preparations, not just on the grounds of quality and safety<sup>18</sup> but also as a means of improving patient compliance with treatment<sup>19</sup> and ensuring equity of access to all older adults who remain exempt from prescription charges across the UK.

In conclusion, our data show that with only reference to fall prevention, the provision of empiric colecalciferol therapy to all older adults in the UK potentially offers considerable cost-saving to the UK NHS over a 5-year horizon. Accompanying such financial benefits, a reduction in attributable premature mortality and increase in quality-adjusted life years could also be expected.

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**Competing interests** JS Davies provides medical consultancy advice to Internis Pharmaceuticals and MEDA, the manufacturers of vitamin D products and has undertaken speaker meetings for Internis Pharmaceuticals. CDP has undertaken consultancy work for Internis Pharmaceuticals, the manufacturer of vitamin D products, Norgine and Sandoz. JS has nothing to declare.

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