

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	COST-EFFECTIVENESS AND BUDGET IMPACT OF EMPIRICAL VITAMIN D THERAPY ON UNINTENTIONAL FALLS IN OLDER ADULTS IN THE UNITED KINGDOM
<b>AUTHORS</b>	Poole, Christopher; Smith, Jamie; Davies, John

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Parijat De Department of Diabetes & Endocrinology City Hospital Dudley Road Birmingham UK
<b>REVIEW RETURNED</b>	22-Mar-2015

<b>GENERAL COMMENTS</b>	<p>The authors review and address a very pertinent and topical area in the world of medicine today.</p> <p>As stated, that although the exact dose and mode of benefit from Vitamin D supplementation is somewhat controversial, nevertheless, this paper addresses the cost modelling exercise of falls prevention and it's effect on morbidity and mortality in a wide ranging age group of elderly population.</p> <p>The statistical modelling is robust and takes into account a number of factors that influence and affect falls related factors and it's impact on the economy and nicely shows the substantial financial gains from cholecalciferol 800 IU supplementation. The findings are clearly tabulated and presented nicely and should be easy enough to understand even for those readers who are not very statistically oriented with cost modelling exercises.</p> <p>The limitations I would say for this paper are that it does not state whether these gains are sustainable in the long term or not and the fact that the authors assume the modelling around A&amp;E attendances only. To be fair, and as mentioned also by the authors, if every fall is taken into account in the community and hospital (assuming all such patients were not on Vitamin D treatment), the savings, if this model were to be replicated, would be even greater.</p> <p>Otherwise, the paper is very well written and addresses an important public health problem in our cash-strapped NHS.</p>
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<b>REVIEWER</b>	Peter Eibich Health Economics Research Centre Nuffield Department of Population Health University of Oxford UK
<b>REVIEW RETURNED</b>	16-Apr-2015

<p><b>GENERAL COMMENTS</b></p>	<p>Summary: The manuscript evaluates the cost-effectiveness and budget impact on the NHS of vitamin D therapy for fall prevention in the elderly in the UK. The results indicate that vitamin D therapy in adults aged 60+ can be considered cost-effective, while vitamin D therapy in the elderly above 65 dominates the alternative of no treatment.</p> <p>Fall prevention in the elderly is a topic of major interest, and the study offers a number of contributions to the literature. In particular, it provides evidence on the cost-effectiveness of a vitamin D dose that has been suggested as effective for fall prevention in the UK. The model used for the analysis is simple and intuitive, yet the conclusions should be fairly robust given that most of the assumptions involved seem very conservative.</p> <p>However, there are a number of points in the manuscript that require further clarification and could benefit from a revision:</p> <p>1.) In the introduction the authors state (p.4 line 35) that “there are no data which interpret the financial impact of vitamin D treatment on the UK population”. However, there seem to be a few published articles on the cost-effectiveness of vitamin D treatments, which might be of interest to the reader, even though the treatment is not exactly the same as in this manuscript or the population is a different one. Furthermore, their results might serve as a comparison for the results presented in this paper.</p> <p>Examples are:</p> <ul style="list-style-type: none"> <li>- Hiligsmann et al., 2014 : Cost-effectiveness of vitamin D and calcium supplementation in the treatment of elderly women and men with osteoporosis, European Journal of Public Health</li> <li>- Zarca et al., 2014: Cost-effectiveness analysis of hip fracture prevention with vitamin D supplementation: a Markov micro-simulation model applied to the French population over 65 years old without previous hip fracture, Osteoporosis International</li> <li>- Lee et al., 2013: Comparison of cost-effectiveness of vitamin D screening with that of universal supplementation in preventing falls in community-dwelling older adults, Journal of the American Geriatrics Society</li> <li>- Jansen et al., 2008: Cost-effectiveness of a fixed dose combination of alendronate and cholecalciferol in the treatment and prevention of osteoporosis in the United Kingdom and The Netherlands. Current Medical Research and Opinion</li> </ul> <p>2.) P. 6, l. 18 &amp; 19: The phrase “over a five year period” appears twice in this sentence.</p> <p>3.) P. 7 l. 19: Here the authors state that social care costs are not included, whereas on page 4 l. 52 they state that social care expenditures were taken into account. It should be clarified which one of these two statements is true.</p> <p>4.) P. 7 l.33-39: Here the choice of the prices for 800iu vitamin D is discussed. As this is an important input in the model, it would be more fitting to state this in the methods section.</p> <p>5.) The discussion could benefit from putting the focus onto the policy implications of the study rather than underlining the medical consequences of vitamin D deficiency, which are already discussed in the introduction.</p> <p>6.) While the data sources are mentioned in Table 1, and are referenced throughout the text, the manuscript might benefit from a short discussion of the underlying data sources in the main body of text.</p>
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	<p>7.) Table 3 is missing a reference to the data source.</p> <p>8.) There is a typo in Table 4, section minor falls, age group 70-74. The shown delta does not correspond to the difference of "Current" and "Vit D".</p>
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## VERSION 1 – AUTHOR RESPONSE

### Reviewer 1:

The limitations I would say for this paper are that it does not state whether these gains are sustainable in the long term or not and the fact that the authors assume the modelling around A&E attendances only.

Again, we would like to thank the reviewer for the request for clarification. The duration of the eight randomised controlled trials included in the primary efficacy analysis we modelled<sup>1</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 greater uncertainty. This is now included in the discussion.

To be fair, and as mentioned also by the authors, if every fall is taken into account in the community and hospital (assuming all such patients were not on Vitamin D treatment), the savings, if this model were to be replicated, would be even greater.

We concur thank you.

### Reviewer 2

1.) In the introduction the authors state (p.4 line 35) that "there are no data which interpret the financial impact of vitamin D treatment on the UK population". However, there seem to be a few published articles on the cost-effectiveness of vitamin D treatments, which might be of interest to the reader, even though the treatment is not exactly the same as in this manuscript or the population is a different one. Furthermore, their results might serve as a comparison for the results presented in this paper.

Examples are:

- Hiligsmann et al., 2014 : Cost-effectiveness of vitamin D and calcium supplementation in the treatment of elderly women and men with osteoporosis, European Journal of Public Health
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- Lee et al., 2013: Comparison of cost-effectiveness of vitamin D screening with that of universal supplementation in preventing falls in community-dwelling older adults, Journal of the American Geriatrics Society
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We thank the reviewer for these helpful citations to which we now refer in the introduction and discussion sections of the manuscript.

2.) P. 6, l. 18 & 19: The phrase "over a five year period" appears twice in this sentence. Second use of phrase now deleted. Thankyou.

3.) P. 7 l. 19: Here the authors state that social care costs are not included, whereas on page 4 l. 52 they state that social care expenditures were taken into account. It should be clarified which one of these two statements is true.

The latter statement is true with respect to inclusion of institutional care costs from social care budgets. Not included were domestic care support costs for those who return to independent living following a fall, another conservative design factor in our analysis. Discussion now updated accordingly.

4.) P. 7 l.33-39: Here the choice of the prices for 800iu vitamin D is discussed. As this is an important input in the model, it would be more fitting to state this in the methods section.  
Agree. Thank you for the suggestion.

5.) The discussion could benefit from putting the focus onto the policy implications of the study rather than underlining the medical consequences of vitamin D deficiency, which are already discussed in the introduction.

Thank you for the suggestion. The following has been added to the discussion.

With respect to UK public health policy regarding vitamin D supplementation in older adults [8], we believe, in light of the clinical and economic evidence, that the current advice is flawed. Firstly, the recommendation of universal supplementation of colecalciferol 400iu (10ug) daily has been shown to be ineffective in the prevention of either falls [6] or fractures[3]. Expert guidelines suggest a minimum daily supplement of 800iu in those at risk [7]. Secondly 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 [18] but also as a means of improving patient compliance with treatment [19] and ensuring equity of access to all older adults who remain exempt from prescription charges across the UK.

6.) While the data sources are mentioned in Table 1, and are referenced throughout the text, the manuscript might benefit from a short discussion of the underlying data sources in the main body of text.

Good suggestion thank you. Implemented accordingly.

7.) Table 3 is missing a reference to the data source.

Good suggestion thank you. Implemented accordingly.

8.) There is a typo in Table 4, section minor falls, age group 70-74. The shown delta does not correspond to the difference of "Current" and "Vit D".

Should read 62,407. Well spotted, thank you.