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NICE

An Economic Evaluation of Interventions to Improve the Uptake of Vitamin D Supplements in England and Wales

Report

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26 MARCH 2014

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Section 1: Introduction

1.1 BACKGROUND

Vitamin D is an essential nutrient that is needed to help maintain calcium and phosphate levels in the body and also to develop healthy bones and promote skeletal growth. Although the main source of vitamin D is from exposure to sunlight, it is also found in a number of foods, such as: eggs, powdered milk, oily fish and fortified fat spreads and breakfast cereals.

There are groups of the population that may be at risk of vitamin D deficiency, including pregnant and breastfeeding women, children under the age of 5 and adults aged over 65 years, people who are not exposed to much sun (such as those who cover up their skin when they are outdoors or those who are confined indoors for a considerable amount of time) and people who have darker skin including people of African, African-Caribbean and South Asian origin.

Although there are initiatives such as Healthy Start vitamins, a low uptake of these vitamin supplements among the population who qualify for the Healthy Start Scheme has been reported. This report outlines the methods and results of an economic model aimed at estimating the cost-effectiveness of interventions to promote the uptake of vitamin D.

1.2 AIMS OF THE MODELLING

Of the four key questions outlined in the scope it was intended that the economic modelling work would be relevant to the first two, shown below.

Question 1: How effective and cost effective are interventions to increase awareness and implementation of existing guidance on vitamin D among health professionals or others working with at-risk populations? What are the implications for professional training and practice?

Question 2: How effective and cost effective are interventions to increase awareness and uptake of existing guidance on vitamin D among at-risk groups (with special consideration given to those eligible for the Healthy Start scheme)?

In order to answer these two questions it was intended that a decision-analytic model would be developed to estimate the expected costs and health benefits of various interventions to increase uptake of vitamin D supplements. The costs and consequences of various interventions could then be directly compared in order to assess which are most effective and cost-effective.

In order to assess the cost-effectiveness of a particular intervention a standard unit of benefit is required in order to compare across treatment areas. For example, if we cure a certain number of cases in one disease area and avert a certain number of events in another we need a common unit in order to decide which of these outcomes is more desirable. Health economics uses the quality-adjusted life year (QALY) for this purpose. The QALY incorporates the life years gained from a treatment strategy, adjusted for the quality of life that the person experiences during those years. Quality of life is determined using measures of utility, which describe health-related quality of life, such as mobility, pain, ability to carry out usual functions, depression, on a scale of 0 to 1, with 1 being full health and 0 being dead. For example, if a person lives for 10 years with a utility of 0.5 they will gain 5 QALYs. If they live for 4 years with a utility of 0.75 they will gain 3 QALYs.

Cost-effectiveness analysis is based on the comparison of one intervention with another, such as standard care or no intervention. In order to do this it is the *incremental* QALYs and *incremental* costs that are considered. Most new interventions are more costly and also provide more health benefits. In order to decide whether the extra health benefits are worth the extra costs of the intervention, the incremental cost-effectiveness ratio is calculated. The ICER subtracts the cost of the current strategy from the cost of the new strategy, divided by the benefits of the current strategy subtracted from the benefits of the new strategy in order to determine the incremental cost per unit of benefit. The formula for calculating the ICER is shown below:

$$ICER = \frac{Cost_{New\ strategy} - Cost_{Old\ strategy}}{Benefit_{New\ strategy} - Benefit_{Old\ strategy}}$$

The higher the ICER, the higher the cost per QALY gained. NICE currently uses an ICER threshold of £20,000 to £30,000, above which an intervention is not deemed to be an efficient use of NHS resources.

Questions 1 and 2 are concerned with the cost-effectiveness of interventions to increase the uptake of vitamin D supplementation. In order to assess the costs and benefits of these interventions in the traditional way it is necessary to assess the costs and benefits of vitamin D supplementation itself. An intervention to improve the uptake of vitamin D supplement usage is only beneficial in so far as use of vitamin D supplements is useful. To do this a targeted literature review was conducted in order to identify those diseases more likely to occur given a vitamin D deficiency. The costs and QALY impacts of those diseases could then be quantified.

In order to align with anticipated guidance from the Scientific Advisory Committee on Nutrition (SACN) it was decided that the model should focus on the relationship between vitamin D deficiency and rickets and osteomalacia, as this is where the strongest evidence lies. When investigating this evidence it was found that whilst there was evidence that those with rickets or osteomalacia have low vitamin D levels, there was a lack of evidence demonstrating the prevalence of rickets amongst people who are vitamin D deficient and those who aren't vitamin D deficient. This information is required to demonstrate the benefit of treating vitamin D deficiency, i.e. of reducing an individual's risk of developing rickets or osteomalacia by transferring them from the vitamin D deficient group to the sufficient group, and thereby assigning them a lower prevalence. For example, in the minutes from SACN's 9th meeting it was noted that "members agreed with their previous conclusion that there was a lack of evidence from RCTs for beneficial effects of vitamin D on bone health markers." In the minutes from the 8th meeting "it was noted that in the tabulated studies on vitamin D and rickets, it was uncertain if the cause of rickets was vitamin D deficiency or low calcium intake."

Therefore, it was decided that this aspect of the analysis would be excluded from the model. Rather than using the traditional approach of cost per QALY the model would instead be based on a simplified analysis, assessing the cost per additional person using vitamin D supplements. This would be based on the expected additional costs for a campaign to increase the uptake of vitamin D supplementation, per additional person using vitamin D supplements. Two cost-consequences analyses were conducted:

Analysis 1: An assessment of an intervention carried out in Birmingham by Heart of Birmingham PCT to increase the uptake of vitamin D supplementation among pregnant and breastfeeding women and children under five.

Analysis 2: A cost-comparison of universal provision of vitamin D supplements (assuming 100% uptake) versus provision of vitamin D supplements only to those who have tested positive for vitamin D deficiency.

As there was a great deal of uncertainty around the inputs to both of the models, extensive sensitivity analyses were carried out. The base case results reported should be read in conjunction with the results of these sensitivity analyses.

There were five subgroups of interest specified in the scope, which were as follows:

1. All pregnant and breastfeeding women;
2. Infants and young children aged less than 5 years;
3. Older people aged 65 and over;
4. People who have low (or no exposure) to the sun. For example, those who cover their skin for cultural reasons, and those who are housebound or confined indoors all year round (such as people in care homes or in prison);
5. People with dark skin, for example, people of African, African-Caribbean, Middle Eastern and South Asian origin (because their bodies cannot make as much vitamin D as those with paler skins).

In the current analysis it was not possible to collect the required data on the fourth and fifth subgroups, as explained in Section 2.1.2 below. Therefore, the current report focuses on the following subgroups:

1. All pregnant and breastfeeding women;
2. Infants and young children aged less than 5 years;
3. Older people aged 65 and over (in Analysis 2);
4. People with darker skin (Analysis 2).

Section 2: Economic Model

2.1 ANALYSIS 1: BIRMINGHAM INTERVENTION

2.1.1 Model Structure

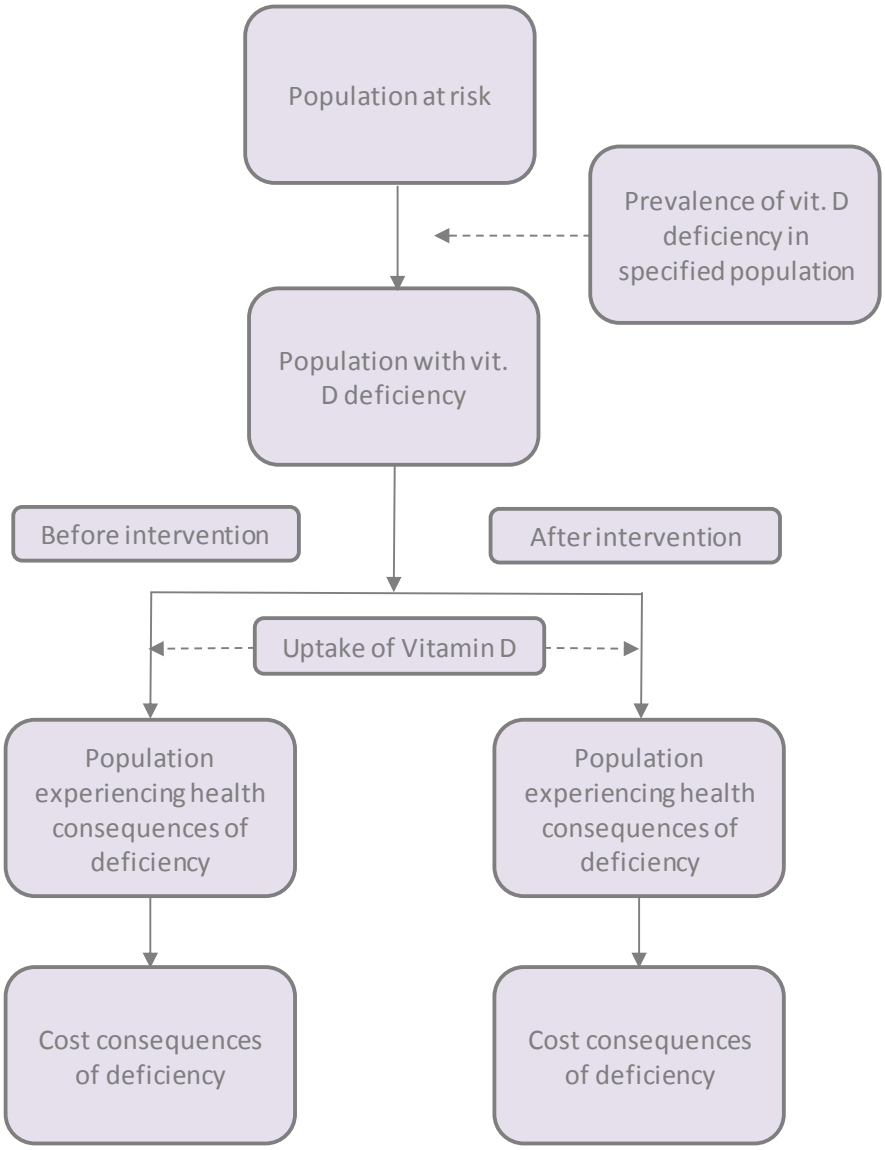
An economic model was constructed in *Microsoft Excel* to conduct a cost-consequence analysis of a campaign carried out in Birmingham to promote universal uptake of vitamin D supplementation among pregnant and breastfeeding women and children under the age of five years. This model compared two scenarios: before the intervention was implemented and after the intervention was implemented. The structure of the model is shown in Figure 2.1.

The intervention used in Birmingham is described by Moy *et al.* (2012)[1] and McGee and Shaw (2013)[2]. The intervention rolled out the universal supplementation of vitamin D to the whole of Birmingham for women during pregnancy and up until their child was 12 months old, and to all children under 5 years old. The supplements were provided free of charge to all mothers and children at Health Centres, Children's Centres and at some GP practices and pharmacies. Information was provided to the public through Asian media networks and Asian shops. Posters and leaflets (in eight community languages) were placed in health centres and surgeries, and logo-branded materials such as shopping bags, supermarket trolley keys, baby sunhats and t-shirts were available in local shops. Adverts were also placed on buses.

[1] Moy, R.J., McGee, E., Debelle, G. D., Mather, I. & Shaw, N. J. 2012. Successful public health action to reduce the incidence of symptomatic vitamin D deficiency. *Archives of Disease in Childhood*, 97 (11), 952-4.

[2] McGee,E. & Shaw, D. 2013. Vitamin D supplementation: Putting recommendations into practice. *Journal of Health Visiting*, 1 (3), 2-7.

Figure 2.1: Model structure



To allow flexibility, throughout the model, there are options built in to enable the user to change the input parameters, which will automatically be applied in the model. Specific inputs included in the model will be discussed in more detail in Sections 2.1.2 to 2.1.5.

In the set-up phase of the model, population figures and prevalence of vitamin D deficiency have been used to calculate the total population of subgroups one and two (all pregnant and breastfeeding women and infants and young children aged less than 5 years) and the number within each subgroup that are vitamin D deficient. The model aims to follow, for both subgroups, a cohort of people through the pre- or post-intervention phase and to calculate the cost of each pathway. The cost of the cohort of patients in the pre-intervention pathway can then be calculated and compared to the cost of the same cohort in the post-intervention pathway to determine the cost difference created by implementing the intervention.

For each pathway, the difference in uptake of vitamin D is used to determine the number of people experiencing health consequences of vitamin D deficiency. The cost of these consequences is then applied. The uptake also impacts upon the number of people incurring the costs of the vitamin D supplements.

The model compares the results for pre- and post-intervention. The outputs of the model (for both subgroups) show the incremental:

- Number of people taking vitamin D;
- Number of people at risk of vitamin D deficiency taking vitamin D;
- Number of people with symptomatic vitamin D (see Section 2.1.4.1 for symptomatic vitamin D explanation);
- Cost of symptomatic vitamin D (see Section 2.1.4.1 for symptomatic vitamin D explanation);
- Cost of intervention;
- Total costs.

The model also reports the extra cost per extra person taking vitamin D (the number of extra people taking vitamin D divided by the incremental cost) and a total cost difference overall, for both sub-groups.

2.1.2 Epidemiology

The total population of pregnant and breastfeeding women was taken from the Office for National Statistics (2012)[3] and was based on the number of live births (729,674) minus the number of multiple births (11,441; assumed to all be twins), to give 718,233 pregnancies.[3] As the number of pregnant and breastfeeding women was based on the annual incident population it was not necessary to add in the number of breastfeeding women in addition to the pregnant women as these were already accounted for. The prevalence of vitamin D in this population was taken from McAree *et al.* (2012)[4]. These figures were used to calculate the total vitamin D deficient population for this subgroup, shown in Table 2.1.

The population of children under five was obtained from ONS (2012)[5] data and the prevalence of vitamin D deficiency was determined by taking a weighted average of vitamin D deficiency from the available data of children aged 4 to 18 months[6]. An assumption was made that this prevalence figure applied to children up to the age of five in the absence of data more specific to this subgroup. These figures were used to calculate the total vitamin D deficient population for this subgroup, shown in Table 2.1.

[3] http://www.ons.gov.uk/ons/rel/vsob1/characteristics-of-birth-2--england-and-wales/2012/sb-characteristics-of-birth-2.html

[4] McAree et al. Vitamin D deficiency in pregnancy - still a public health issue. Maternal and child nutrition. 2013; 9: 23-30.

[5] http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-england-and-wales/mid-2012/sty-population-estimates.html

[6] Alison Lennox, Jill Sommerville, Ken Ong, Helen Henderson and Rachel Allen. Diet and Nutrition Survey of Infants and Young Children. Cambridge: MRC, 2011.

Table 2.1: Population and prevalence figures by subgroup

Subgroup	Total population	Prevalence of vitamin D deficiency	Total vitamin D deficient population
Pregnant/breast feeding women	718,233	36%	258,564
Children under 5	3,573,205	3.42%	122,204

2.1.3 Cost Inputs

The Birmingham intervention on which the model inputs are based was a campaign to promote universal access to vitamin D supplements within the pregnant and breastfeeding women and children under 5 years subgroups. The data are based on three publications from the same intervention published over a number of years[7] [8] [9]. The author of these publications has been contacted and the breakdown of costs of the intervention was provided. The cost of the intervention for the Heart of Birmingham PCT was supplied (£25,000) and this was multiplied by the number of PCTs in England at that time to give a population cost of the intervention of £3.8 million. Of this £3.8 million we assumed that 50% of the budget went towards promotion to pregnant and breastfeeding women and 50% on promoting uptake in children, giving a cost of £1.9 million for each subgroup. By using this figure we have assumed that the costs of promoting the intervention will average the same for all other PCTs as for the cost of promoting the intervention in the Heart of Birmingham PCT. We have also assumed that the number of women and children are the same proportion of the population in the other PCTs.

The costs per unit of vitamin D were supplied by the Department of Health. The annual cost was calculated in the model using the number of units supplied multiplied by the cost per unit. This figure was divided by the number of years the vitamins would be supplied for to calculate the average annual cost. These figures are shown in Table 2.2 below.

Table 2.2: Costs of provision of vitamin D supplements

	Cost of vitamins (per unit)	Weeks eligible	Number of units (for whole time eligible)	Total cost per patient (for whole time eligible)	Average annual cost
Pregnant / breast feeding women	£0.83	82	11	£9.13	£5.82
Children under 5	£1.68	204	26	£43.68	£10.92

[7] McGee, E. 2010. Prevention of rickets and vitamin D deficiency in Birmingham: The case for universal supplementation, Birmingham, National Health Service.

[8] Moy, R.J., McGee, E., Debelle, G. D., Mather, I. & Shaw, N. J. 2012. Successful public health action to reduce the incidence of symptomatic vitamin D deficiency. Archives of Disease in Childhood, 97 (11), 952-4.

[9] McGee,E. & Shaw, D. 2013. Vitamin D supplementation: Putting recommendations into practice. Journal of Health Visiting, 1 (3), 2-7.

2.1.4 Uptake of the Intervention

In this analysis ‘uptake’ refers to the percentage of people receiving vitamin D supplements and does not specify the percentage of people actually taking the vitamin supplements.

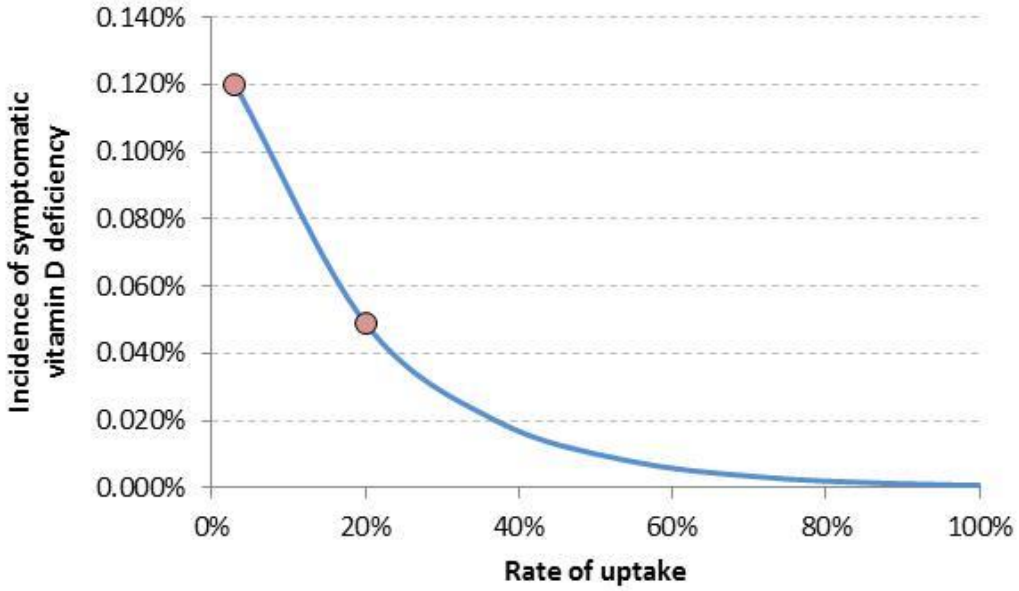
2.1.4.1 Pregnant and breastfeeding women, and children under five years subgroups

The before-intervention percentage uptake is taken from Moy *et al*. (2012)[8] which states that the 'estimated uptake of the vitamin D supplement component is extremely low with no more than 2% to 4% of those eligible receiving the supplement (unpublished data made available to primary care trusts)' (p. 954). The average of these estimates was used in the model.

The post-intervention uptake was taken from the later McGee and Shaw (2013)[9] report which states that uptake in the area in which the intervention was implemented reached 23% for pregnant and breastfeeding women and 20% for children under five in 2012-13.

Modelling of the consequences of increased uptake in these two subgroups was based on the prevalence of presenting cases of symptomatic vitamin D deficiency, before and after the intervention, and was taken from Moy *et al.* (2012)[8]. The annual incidence of symptomatic vitamin D deficiency was 0.12% before the intervention and 0.049% after the intervention[8]. These data were only available for children, so in the absence of any other data, the assumption was made that the same effects applied to women. Based on these two data points, an exponential function was applied to the percentage of patients with symptomatic vitamin D deficiency based on the percentage uptake of vitamin D. Although the true relationship is it not known for the whole curve, it is arguable that there will be a decrease in the marginal rate of return since the first people to uptake might be those most in need (i.e. most deficient) and therefore receive most benefit, whilst the last people to uptake vitamin D may be those with the least need. If this is the case an exponential function might be appropriate. This assumed function was only used to test the impact of varying the post-intervention rate of uptake in the sensitivity analysis, and was not used in the base case. The relationship is shown below, in Figure 2.2.

Figure 2.2: Assumed relationship between vitamin D uptake and symptomatic vitamin D deficiency (for sensitivity analysis only)



2.1.5 Costs of Vitamin D Deficiency

In the pregnant and breastfeeding women, and children under 5 years, subgroups the impact of vitamin D deficiency was modelled as the number of presenting cases of symptomatic vitamin D deficiency (see Section 2.1.4.1). The cost of treating symptomatic vitamin D deficiency was taken from Zipitis *et al.* (2006)[10] and was £2,505 per case.

2.2 ANALYSIS 2: TESTING VERSUS NO TESTING

In this analysis two alternative scenarios were compared:

Scenario 1: Universal testing within each subgroup and provision of vitamin D supplements only to those who are found to be deficient.

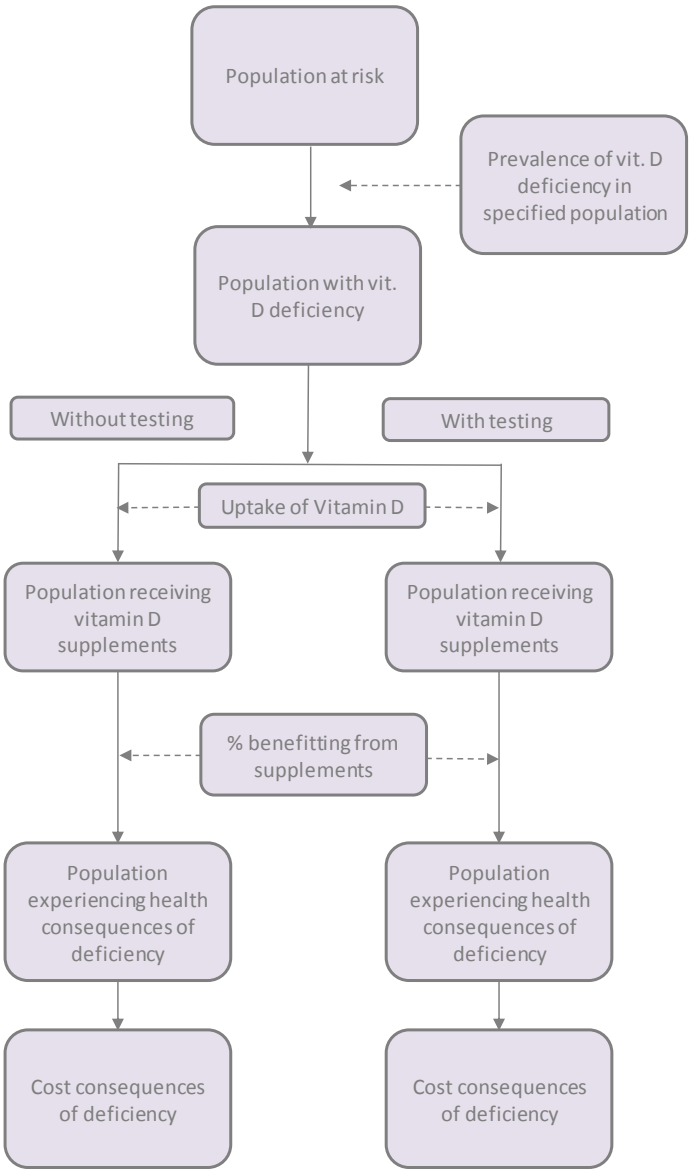
Scenario 2: No testing and universal provision of vitamin D supplements within each subgroup, regardless of vitamin D status.

(It has been assumed for simplicity that the test was 100% accurate.)

The structure of the model used in Analysis 2 is shown in Figure 2.3 below.

[10] Zipitis, C.S., Markides, G.A., & Swann, I.L. 2006. Vitamin D deficiency: prevention or treatment? Archives of Disease in Childhood, 91, 1011-1014.

Figure 2.3: Model structure



The population size, vitamin D deficiency prevalence and cost inputs used for the two subgroups in Analysis 1 were also applied in Analysis 2. Analysis 2 also considered an additional two subgroups: (1) those aged over 65 years and (2) people with darker skin. The population and prevalence of deficiency data were taken from Census 2011 data[11] and included all ethnic groups excluding those categorised under 'white' and data from the D-Fines study. The population of people over the age of 65 was obtained from ONS (2012)[5] data and was the sum of males and females over the age of 65. The prevalence of vitamin D deficiency in this group was taken from Health Survey for England 2005[12] data and was a weighted average across all age groups above 65 and across males and females.

[11] http://www.nomisweb.co.uk/census/2011/LC2101EW/view/2092957703?rows=c_ethpuk11&cols=c_sex
[12] http://www.hscic.gov.uk/pubs/hse05olderpeople

Table 2.3: Population and prevalence figures by subgroup

Subgroup	Total population	Prevalence of vitamin D deficiency	Total vitamin D deficient population
Aged 65 and over	9,176,882[5]	11.21%[12]	1,028,728

2.2.1 Cost Inputs

In addition to the cost inputs used in Analysis 1, a cost of testing was also applied. Two sources were found that reported the cost of testing for vitamin D deficiency. The Royal National Orthopaedic Hospital give a cost of £20[13] and a statement from NHS Derby City and NHS Derbyshire County reports a cost of £13 per test[14]. For the basecase model an average of the two was used, £16.50, and was explored in the sensitivity analyses.

The cost per dose of vitamin D also remained the same as in Analysis 1 for the women and children subgroups. However, this makes the assumption that all patients are given the same dose of vitamin D. It was discussed that in the testing scenario, patients that are identified as deficient may be given a higher 'treatment' dose (which is likely to have different effectiveness too). However, the data were not available to model this in this subgroup.

The cost per dose of vitamin D for the over 65's subgroup was taken from a document summarising the vitamin D supplements available to pharmacy services[15] and the cheapest cost per tablet was selected. The dose for universal supplementation was assumed to be 1000IU (costing £20.70 per annum) and a treatment dose was 3000IU (costing £62.09 per annum), both of which were taken from Lee et al. (2013)[16]. The cost per tablet was then multiplied by the number necessary for a yearly dose.

Due to a lack of data the cost of supplementation in the subgroup with darker skin was assumed to be equal to the cost for the over 65 years' subgroup.

As in Analysis 1, the cost of treating symptomatic vitamin D deficiency was taken from Zipitis *et al.* (2006)[17] and was £2,505 per case.

[13] Royal National Orthopaedic Hospital: http://www.rnoh.nhs.uk/clinical-services/paediatric-adolescents/vitamin-d-children. Accessed 12th February 2014.

[14] NHS Derby City and NHS Derbyshire County: http://www.derbyshiremedicinesmanagement.nhs.uk/images/content/files/Prescribing%20Guidelines/Vitamin%20D%20Position%20Statment%20(with%20test%20cost%20change).pdf. Accessed 12th February 2014.

[15] East and South East Specialist Pharmacy Services. Vitamin D deficiency and insufficiency: Updating available products.

[16] Lee et al. 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. 2013; 61:5.

[17] Zipitis, C.S., Markides, G.A., & Swann, I.L. 2006. Vitamin D deficiency: prevention or treatment? Archives of Disease in Childhood, 91, 1011-1014.

In the over 65 years subgroup the impact of vitamin D deficiency was modelled as the number of non-vertebral fractures. The cost of a non-vertebral fracture in this age-group was taken from Dolan and Torgerson (1998)[18] and was converted to 2012/2013 costs using the Hospital and Community Health Services Index from PSSRU's Unit Costs of Health and Social Care 2013[19].

2.2.2 Effectiveness

In the basecase analyses for Analysis 2 it was assumed that both Scenarios 1 and 2 would result in a reduction of symptomatic vitamin D deficiency by 50%. The assumption of 50% is used because although 100% of deficient people are receiving supplements, it is not clear what the adherence will be and that some people may not benefit sufficiently from the supplement due to other reasons. Therefore, the Committee felt that 50% would be a more realistic and conservative assumption. This assumption is explored further in sensitivity analyses.

As it is not known how many people in the women and children subgroup would actually benefit from supplementation in each of the 'with testing' and 'without testing' scenarios, a number of exploratory analyses were conducted. In the pregnant and breastfeeding women and children under 5 years, the relationship between uptake and reduction in symptomatic cases used in Analysis 1 (see Section 2.1.4.1) was applied. For example, in the basecase it was assumed that only 50% of deficient people would actually receive a benefit and so 50% uptake was used as a proxy for 50% receiving a benefit. This gave a probability of experiencing symptomatic vitamin D deficiency of 0.015%, calculated using the exponential formula described in Section 2.1.4.1. These data are from a general population, rather than a deficient population. In reality it may be that the relationship between uptake and prevalence of symptomatic deficiency is stronger in a deficient population than a general population as the capacity to benefit is greater. Therefore, sensitivity analyses were conducted to test the impact of these assumptions.

In the over 65's subgroup the baseline risk of fracture due to falls in a vitamin D deficient population was taken from Pfeifer *et al*. (2000)[20] and was 9%. It should be noted that this figure applies to a calcium monotherapy subgroup, not a placebo group. A relative risk for fractures due to falls following vitamin D supplementation in a deficient population was then applied to this to give the risk of fractures in those deficient people who have received supplementation following testing. The relative risk applied was 0.56 and was taken from the subgroup in Bischoff-Ferrari *et al*. (2012)**Error! Bookmark not defined.** with a vitamin D level of <30nmol/litre subgroup and aged over 65. Applying this relative risk to the baseline risk gives a risk of fractures of 5.04% in vitamin D deficient people who are receiving supplements. The 'before intervention' risk was applied to 50% of the deficient people and the 'after intervention' risk was applied to the other 50% of deficient people in both the 'with testing' and 'without testing' scenarios in the basecase model.

[18] Dolan and Torgerson (1998). The cost of treating osteoporotic fractures in the United Kingdom female population. Osteoporosis Int. 1998; 8: 611-617.

[19] Curtis L. Unit Costs of Health and Social Care 2012. In: Unit PSSR, editor. Kent 2012.

[20] **Pfeifer et al. 2000. Effects of a short-term vitamin D and calcium supplementation on body sway and** secondary hyperparathyroidism in elderly women. Journal of Bone and Mineral Research, 15, 1113-1118.

In all three subgroups modelled in Analysis 2 it was assumed in the basecase that 50% of people would benefit, in both the universal supplementation and testing scenarios. However, it is likely that in the universal supplementation scenario, if 50% of the general population are taking or benefiting from vitamin D, fewer of the vitamin D deficient people will be getting the supplement than in the testing scenario in which 50% of the vitamin D *deficient* people will be receiving the supplement. Further, those people testing positive for vitamin D deficiency would be likely to be given a treatment dose, whereas those people in the universal supplementation scenario who are deficient would not be given a treatment dose as it is not known that they are deficient. It is possible that some people who are vitamin D deficient would not benefit in the universal supplementation group (due to the dose not being high enough). In addition, it is not clear whether those people in the universal supplementation scenario who actually take the vitamins would be those most in need (e.g. because they have identified their risk of deficiency) or those least in need (e.g. due to a high level of awareness and proactive behaviour around health issues). For these reasons, two-way sensitivity analysis varying the number of people benefiting from supplementation in each scenario has been carried out and is reported in the results section.

Section 3: Results

3.1 ANALYSIS 1: BIRMINGHAM INTERVENTION

This section presents the costs of the pre- and post-intervention phases of Analysis 1, testing the cost impact of implementing the Birmingham intervention. First the base case results are presented using the base case input data, which is outlined in Section 2.1. The univariate sensitivity analysis results are then presented to explore the quantitative uncertainty in the model.

3.1.1 Basecase Results

Table 3.1 shows the results for pregnant and breastfeeding women. It shows that after the intervention there are more people taking vitamin D, more people at risk taking vitamin D and fewer people with symptomatic vitamin D deficiency and, therefore, lower costs associated with symptomatic vitamin D. The incremental cost of intervention (including supplying vitamins and the cost of the campaign) is over £2.7million. This is offset somewhat by the costs saved by treating fewer symptomatic vitamin D women; however, this results in an incremental cost of over £1.2 million for this group. This is equivalent to a cost increase of £10.15 per extra person taking vitamin D. The intervention improved the uptake of vitamin D which led to symptomatic vitamin D cases being averted. The cost per case averted is £2,859.

Table 3.1: Model outputs for the pregnant and breastfeeding women subgroup

Pregnant / breast feeding women	**Before intervention**	**After intervention**	**Incremental**
No. taking vitamin D	21,547	165,194	143,647
No. at risk taking vitamin D	7,757	59,470	51,713
No. with symptomatic vit. D def.	862	352	-510
Cost of symptomatic vitamin D	£2,159,328	£881,726	-£1,277,602
Cost of intervention	£125,302	£2,860,648	£2,735,346
Total cost	**£2,284,630**	**£3,742,374**	**£1,457,744**
Cost per extra person taking vitamin D			**£10.15**
Cost per deficiency averted			**£2,859**

Table 3.2 shows the results for the children-under-5-years subgroup. As with the scenario above, it is seen that after the intervention there are more people taking vitamin D, more people at risk taking vitamin D and fewer people with symptomatic vitamin D deficiency and, therefore, lower costs associated with symptomatic vitamin D. The intervention costs are over £8.5 million higher for post-intervention. The reason the intervention costs are much

higher for children is that the price of vitamin D is higher for children than adults (£1.68 vs £0.86). Overall there is an increased cost per person of £4.62. The cost per case of symptomatic vitamin D averted for children was £1,229.

Table 3.2: Model outputs for the children under five years subgroup

Children under 5	Before intervention	After intervention	Incremental
No. taking vitamin D	107,196	714,641	607,445
No. at risk taking vitamin D	3,666	24,441	20,775
No. with symptomatic vit. D def.	4,288	2,003	-2,285
Cost of symptomatic vitamin D	£10,742,643	£5,017,343	-£5,725,301
Cost of intervention	£1,170,582	£9,703,880	£8,533,298
Total cost	£11,913,225	£14,721,222	**£2,807,997**
Cost per extra person taking vitamin D			**£4.62**
Cost per deficiency averted			**£1,229**

Table 3.3 shows the results for both subgroups combined. The model estimates an overall increased cost of over £4 million.

Table 3.3: Total costs for all subgroups

Grand total	Before intervention	After intervention	Incremental
Total cost (all subgroups)	£14,197,855	£,18,463,596	£4,256,741

3.1.2 Sensitivity Analysis

Univariate sensitivity analyses were carried out on the key parameters within the model, for each population.

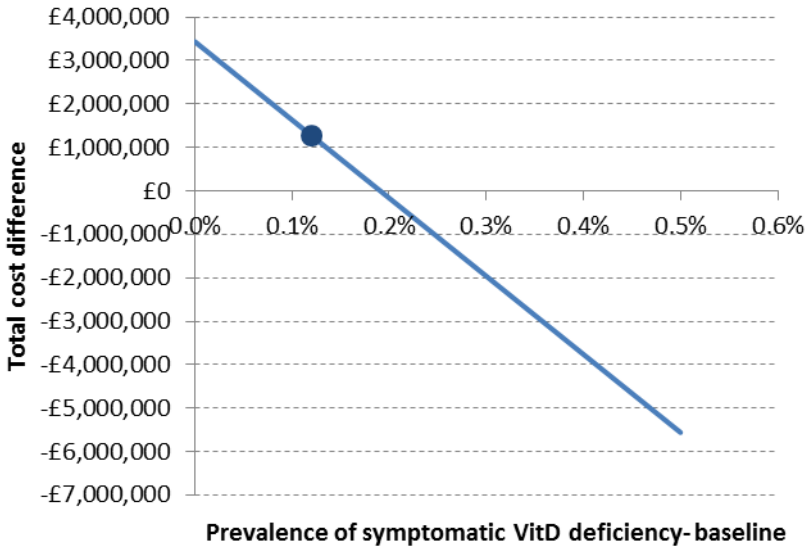
3.1.2.1 Pregnant and breastfeeding women and children under 5 years

The key sensitivity analyses reported here are for the subgroup of pregnant and breastfeeding women. The directions observed in each graph are the same for the corresponding graph in the children subgroup (however, the threshold of when it is cost-saving differ). To avoid repetition and for clarity, only the pregnant and breastfeeding women subgroup is reported here.

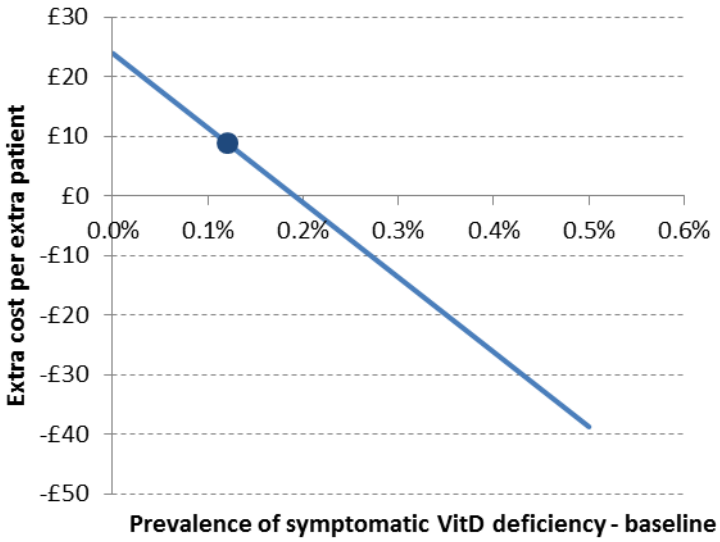
Graphs 3.1 and 3.2 demonstrate that, as expected, increasing the baseline prevalence of symptomatic vitamin D deficiency increases the cost savings overall and per patient. This is due to there being more people that are able to benefit from the vitamin D supplement. Similarly the sensitivity analyses for the prevalence of vitamin D deficiency *after* the

intervention (Graphs 3.3 and 3.4) also show that, as expected, the lower the prevalence after the intervention, the larger the cost savings.

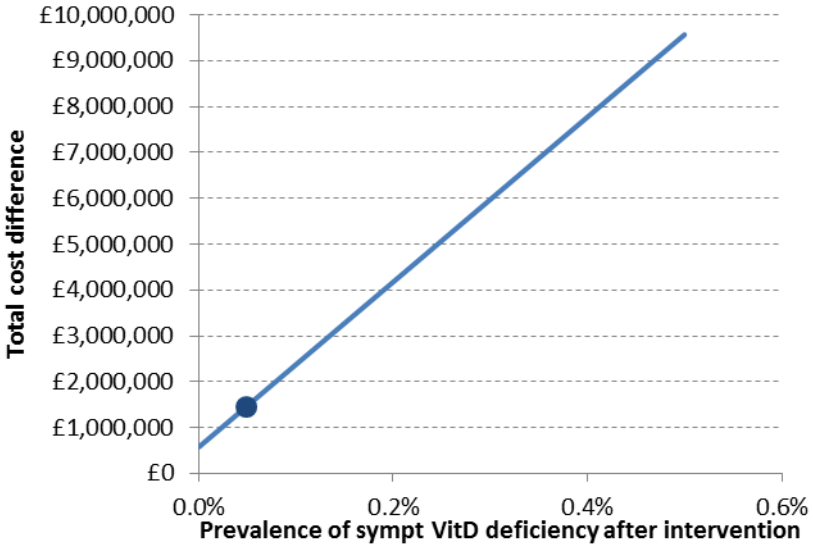
Graph 3.1: Sensitivity analysis for baseline prevalence of symptomatic vitamin D deficiency on total cost difference



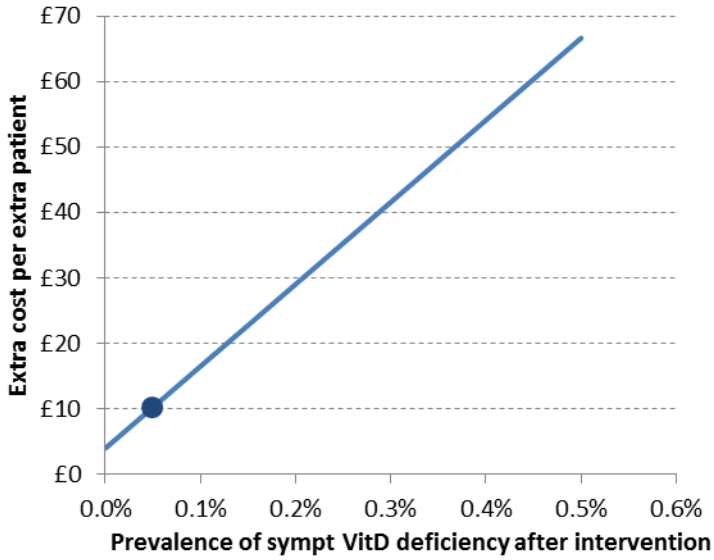
Graph 3.2: Sensitivity analysis for baseline prevalence of symptomatic vitamin D deficiency on per patient cost



Graph 3.3: Sensitivity analysis for prevalence of symptomatic vitamin D deficiency after intervention on total cost difference

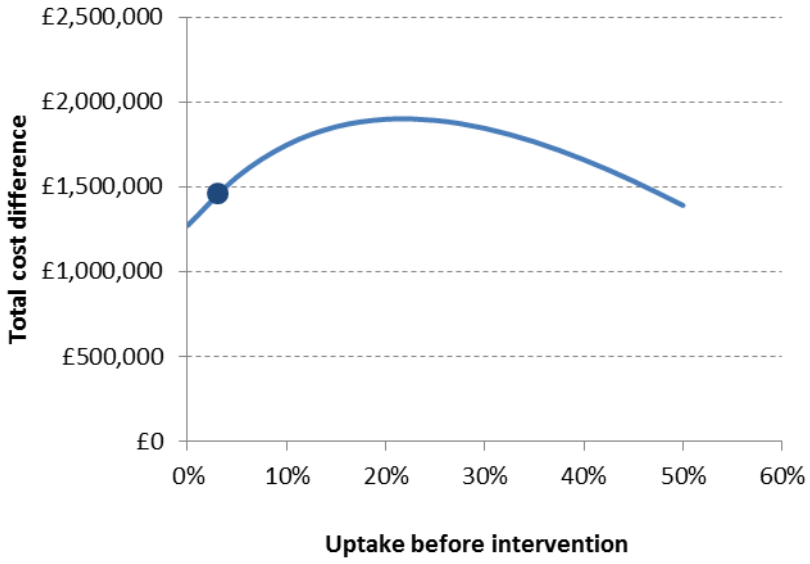


Graph 3.4: Sensitivity analysis for prevalence of symptomatic vitamin D deficiency after intervention on per patient cost



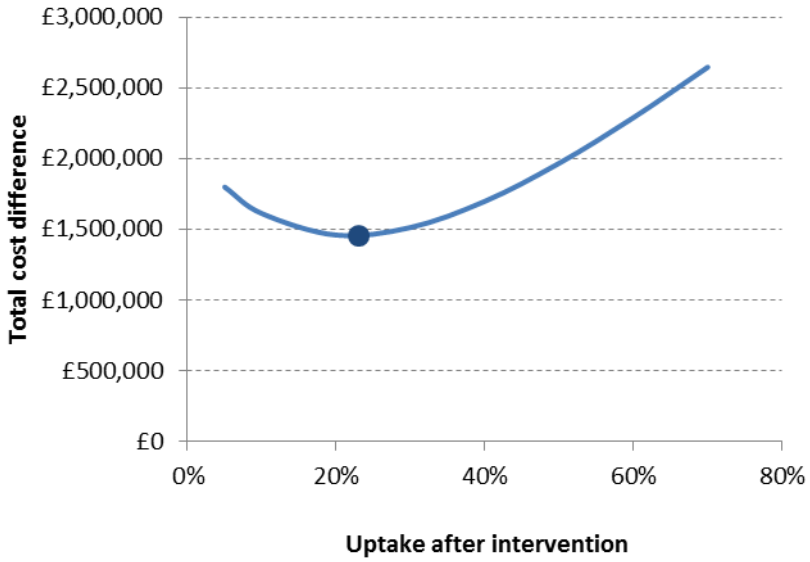
Graph 3.5 shows that even if the uptake of supplementation is 0% before the intervention, the intervention is still not cost saving. As the uptake before the intervention increases, so the costs incurred by the intervention increase, up to a certain point. Past this point, further increasing the before intervention uptake results in greater costs before the intervention, as more people are taking supplements, but only marginal increases in health benefits, as the majority of the deficient population are already taking supplements. This means that the incremental costs of the intervention reduce past this point. However, even with an uptake of 50% of the population before the intervention, it is still not cost saving.

Graph 3.5: Sensitivity analysis for uptake of vitamin D before intervention on total cost

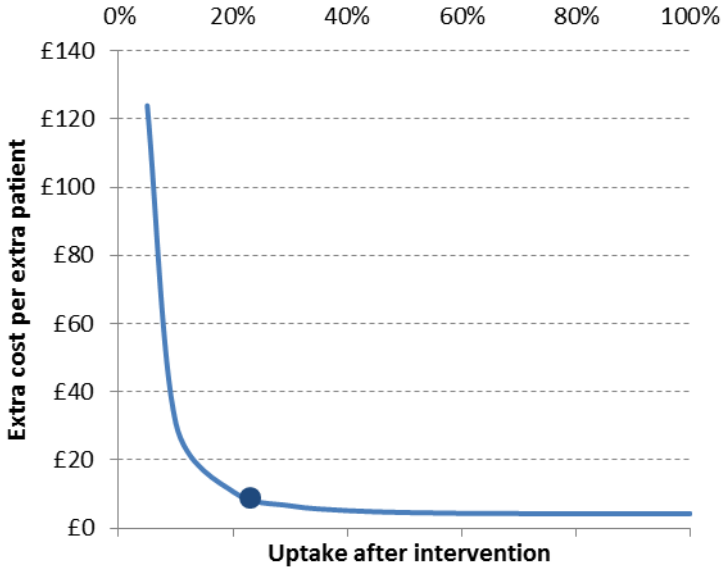


Graphs 3.6 and 3.7 demonstrate the impact of varying the post-intervention uptake rates on the total costs and the extra cost per extra uptake. Graph 3.6 shows the total cost different for the whole subgroup while Graph 3.7 shows the extra cost per extra patient. These graphs show that, initially, improving the uptake rate after the intervention increases cost savings. This is because more people are receiving vitamin D supplementation and so there are fewer cases of *symptomatic* deficiency. However, after a certain point, the cost savings start to reduce. This is due to the fact that most symptomatic patients have already been accounted for, and so increasing the coverage (i.e. providing supplements to patients who are not vitamin D deficient) incurs additional costs whilst accruing only a marginal associated benefit.

Graph 3.6: Sensitivity analysis for uptake of vitamin D after intervention on total cost difference

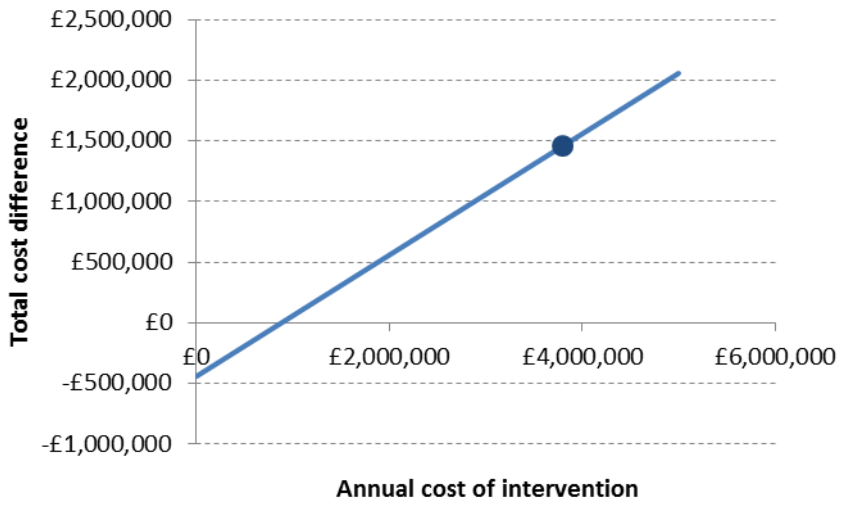


Graph 3.7: Sensitivity analysis for uptake of vitamin D after intervention on per patient cost

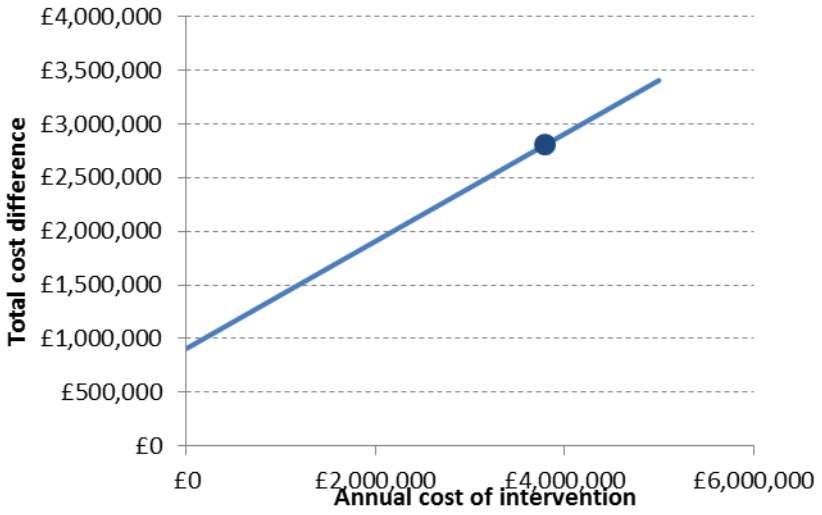


Graph 3.8 varies the intervention cost. It shows that the intervention is cost saving up to an intervention cost of around £1.5 million. However, it is worth noting that for the children under 5 years subgroup (see Graph 3.9) the results demonstrate a cost increase across all modelled ranges of the intervention cost.

Graph 3.8: Sensitivity analysis for cost of intervention on total cost difference



Graph 3.9: Sensitivity analysis for cost of intervention on total cost difference for children subgroup



3.2 ANALYSIS 2: TESTING VERSUS NO TESTING

This section presents the costs of providing universal vitamin D supplementation to the whole population versus testing the whole population for vitamin D deficiency and providing supplementation only to those who are deficient. First, the base case results are presented using the base case input data, which are outlined in Section 2.1. Then, two-way sensitivity analyses are presented. Finally, univariate sensitivity analysis results are presented to explore the quantitative uncertainty in the model.

3.2.1 Basecase Results

Table 3.4 shows the results for the pregnant and breastfeeding women subgroup. There is no incremental cost difference between these two approaches for symptomatic vitamin D deficiency costs because in both scenarios, all deficient people have been supplied with vitamin D supplementation and 50% of people benefit in both scenarios. The results show that, with these assumptions, testing to identify the deficient population costs more than supplying vitamin D universally, resulting in an incremental cost of almost £10 million and a per person cost of £12.78.

Table 3.4: Analysis 2 outputs for women subgroup

Pregnant/breast feeding women	**Without testing for deficiency**	**With testing for deficiency**	**Incremental**
Number tested	0	718,233	718,233
Number taking vitamin D	718,233	258,564	-459,669
No. with symptomatic Vit D def.	38	38	0
Cost of testing	£0	£11,850,845	£11,850,845
Cost of intervention	£4,176,731	£1,503,623	-£2,673,108
Cost of symptomatic vitamin D	£94,734	£94,734	£0
Total cost	**£4,271,465**	**£13,449,202**	**£9,177,737**
Cost per person			**£12,78**

Table 3.5 shows the results for the children aged under 5 subgroup. Similarly to the subgroup above, this table shows that the costs of testing the whole population is higher than providing universal vitamin D supplementation to the whole population, resulting in an incremental cost of over £21 million for this subgroup, and a net cost per person of £5.95 for take the testing approach.

Table 3.5: Analysis 2 outputs for children subgroup

Children under 5	**Without testing for deficiency**	**With testing for deficiency**	**Incremental**
Number tested	0	3,573,205	3,573,205
Number taking vitamin D	3,573,205	122,204	-3,451,001
No. with symptomatic vit. D def.	18	18	0
Cost of testing	£0	£58,957,883	£58,957,883
Cost of intervention	£39,019,399	£1,334,463	-£37,684,935
Cost of symptomatic vitamin D	£44,774	£44,774	£0
Total cost	**£39,064,172**	**£60,337,120**	**£21,272,947**
Cost per person			**£5.95**

Table 3.6 shows the results for the aged 65 and over subgroup. The results confirm the same effect in this subgroup. The incremental cost of testing for deficiency rather than providing universal supplementation is over £114 million. The incremental cost is much

larger in this group due to the population being much larger than the first two subgroups (over 9 million). However, these results rest on the assumption that both groups are benefitting equally. It is likely that the group with testing will benefit more, due to it being targeted at those who actually need supplementation, and due to treatment doses being applied. There are no data suggesting how much the testing group may benefit by. Therefore, the impact of varying the effectiveness of supplementation in each scenario (universal testing versus universal supplementation) has been explored using two-way sensitivity analyses. These are reported in Section 3.2.2 overleaf.

Table 3.6: Analysis 2 outputs for aged 65+ subgroup

Aged 65 and over	**Without testing for deficiency**	**With testing for deficiency**	**Incremental**
Number tested	0	9,176,882	9,176,882
Number taking vitamin D	9,176,882	1,028,728	-8,148,154
No. with fractures	72,217	72,217	0
Cost of testing	£0	£151,418,553	£151,418,553
Cost of intervention	£189,934,355	£68,874,924	-£126,059,431
Cost of fractures	£262,788,783	£262,788,783	£0
Total cost	**£452,723,138**	**£478,082,259**	**£25,359,122**
Cost per person			**£2.76**

Table 3.7 shows the results for the 'people with darker skin' subgroup. These results do not include any health outcomes, or the costs associated with these health outcomes, as the data were not available. In this analysis, the cost of vitamin D supplementation was assumed to be the same as for the over 65's subgroup.

Table 3.7: Analysis 2 outputs for 'people with darker skin' subgroup

People with darker skin	**Without testing for deficiency**	**With testing for deficiency**	**Incremental**
Number tested	0	15,733,034	15,733,034
Number taking vitamin D	15,733,034	10,929,739	-4,803,295
Cost of testing	£0	£259,595,061	£259,595,061
Cost of intervention	£325,627,339	£226,213,312	-£99,414,027
Total cost	**£325,627,339**	**£485,808,373**	**£160,181,034**
Cost per person			**£10.18**

Table 3.8 shows the results for all three subgroups combined (not including the 'people with darker skin' subgroup as this analysis did not account for health benefits). Combining the results shows that compared to providing universal supplementation, testing the whole population to identify those that are deficient and providing these people with vitamin D supplements would result in an incremental cost of over £56 million.

Table 3.8: Total costs for all subgroups

Grand total	Without testing for deficiency	With testing for deficiency	Incremental
Total cost (all subgroups)	£495,058,775	£551,868,581	£56,809,806

3.2.2 Two-Way Sensitivity Analysis

In the basecase model it was assumed that 50% of people would receive and benefit from the supplements in both the universal supplementation and testing scenarios. However, there are a number of reasons why this assumption may be inappropriate.

If 50% of the general population are taking or benefiting from vitamin D, fewer of the vitamin D deficient people will be getting the supplement than in the testing scenario, in which 50% of the vitamin D *deficient* people will be receiving the supplement.

Further, those people testing positive for vitamin D deficiency would be likely to be given a treatment dose, whereas those people in the universal supplementation scenario who are deficient would not be given a treatment dose as it is not known that they are deficient. It is possible that some people who are vitamin D deficient would not benefit sufficiently in the universal supplementation group (due to the dose not being high enough). The same deficient person might in reality receive a higher dose in the 'testing' scenario than in the 'universal supplementation' scenario.

In addition, not everybody who receives the supplements will actually take them. It is not clear whether those people in the universal supplementation scenario who actually take the vitamins would be those most in need (e.g. because they have identified their risk of deficiency) or those least in need (e.g. due to a high level of awareness and proactive behaviour around health issues).

Also, different individuals receiving the same dosage may differ in the benefit they receive from that dosage if their underlying need is different. It is unclear how people will benefit depending on their underlying deficiency levels. For example, it is not known what benefit an individual who is very deficient may experience from supplementation compared to someone who is only mildly deficient. It is not clear if an individual with low vitamin D levels but not deemed to be deficient would benefit from supplementation or in what ways they may benefit.

Lee *et al*. (2013)[16] attempted to address these issues. However, their analysis did not take into account all of the factors above. For example, whilst they categorised a patient by level of deficiency (deficient, insufficient and sufficient) these categories are arbitrarily selected and in reality the relationship between level of deficiency and response to supplementation would be much more granular. To account for the great uncertainty in the current model, in the effectiveness of each of the two scenarios (universal supplementation and testing) in reducing the impact of vitamin D deficiency, sensitivity analysis was conducted. This sensitivity analysis varied the health outcomes in each of the two scenarios simultaneously, allowing the impact of each of them, individually and collectively, to be explored. This method allows the factors above to be incorporated into the analysis, as well as any factors that are not known.

In the women and children subgroups this was implemented by varying the prevalence of symptomatic vitamin D deficiency in the two scenarios.

In the over 65s' subgroup, the number of people benefiting from vitamin D supplementation in the two scenarios (universal supplementation and testing) was varied. This was done by altering the proportion of people with the before supplementation fracture rate (9%) and the proportion of people with the after supplementation fracture rate (5.04%). For example, if the proportion of people benefiting was 50%, this meant that 50% of people were exposed to the before supplementation fracture rate and 50% were exposed to the after intervention fracture rate.

It is likely that the people in the testing scenario would benefit more from supplementation than those in the universal supplementation scenario. Therefore, the analyses (displayed below) focus on those combinations where the health outcomes of the testing scenario are better than those of the universal supplementation scenario. In all three analyses the green cells indicate that the testing scenario is cost saving compared to the universal supplementation scenario. The red cells indicate that it is not cost saving.

Tables 3.9, 3.10 and 3.11 show the results of the two-way sensitivity analyses for the women, children and over 65s' subgroups, respectively. The tables display the incremental cost of universal provision compared to testing for deficiency, so a positive number suggests that testing will cost more than universal provision and a negative number shows that .testing will cost less than universal provision.

For the pregnant and breastfeeding women, even if the prevalence of symptomatic deficiency were 0% after testing and treatment of those who were found to be deficient, the prevalence of deficiency in the universal supplementation scenario would need to be as high as 2% after supplementation in order for the testing scenario to be cost saving. For the children under 5 years, even if the prevalence of symptomatic deficiency were 0% after testing and treatment of those who were found to be deficient, the prevalence of deficiency in the universal supplementation scenario would need to be as high as 7% after supplementation in order for the testing scenario to be cost saving. In the over 65s' group it was estimated that the proportion of people benefitting from supplementation in the testing

scenario would need to be 20% percentage points higher than the proportion benefitting in the universal supplementation scenario in to be cost saving. Table 3.11 shows the results in the opposite direction to the tables displaying the sensitivity analysis for the women and children subgroups. This is because the percentage increase in the women and children subgroup indicates an increase in symptomatic vitamin D while a percentage increase in the over 65s subgroup indicates an increase in the number of people benefitting. The percentage increase for women and children is a negative change whereas the percentage increase for the over 65s is a positive change.

Table 3.9: Two-way sensitivity analysis of uptake in women – total population 718,233

		Percentage of women with symptomatic vitamin D deficiency - Testing scenario									
		0.000%	0.50%	1.000%	1.500%	2.00%	2.500%	3.000%	3.50%	4.000%	4.500%
Percentage of women with symptomatic vitamin D deficiency - Universal scenario	0.000%	£9,177,737									
	0.50%	£5,938,746	£9,177,737								
	1.000%	£2,699,755	£5,938,746	£9,177,737							
	1.500%	-£539,236	£2,699,755	£5,938,746	£9,177,737						
	2.00%	-£3,778,227	-£539,236	£2,699,755	£5,938,746	£9,177,737					
	2.500%	-£7,017,218	-£3,778,227	-£539,236	£2,699,755	£5,938,746	£9,177,737				
	3.000%	-£10,256,209	-£7,017,218	-£3,778,227	-£539,236	£2,699,755	£5,938,746	£9,177,737			
	3.50%	-£13,495,200	-£10,256,209	-£7,017,218	-£3,778,227	-£539,236	£2,699,755	£5,938,746	£9,177,737		
	4.000%	-£16,734,191	-£13,495,200	-£10,256,209	-£7,017,218	-£3,778,227	-£539,236	£2,699,755	£5,938,746	£9,177,737	
	4.500%	-£19,973,182	-£16,734,191	-£13,495,200	-£10,256,209	-£7,017,218	-£3,778,227	-£539,236	£2,699,755	£5,938,746	£9,177,737

Table 3.10: Two-way sensitivity analysis of uptake in children – total population 3,573,205

		Percentage of children with symptomatic vitamin D deficiency - Testing scenario									
		0.00%	1.00%	2.00%	3.00%	4.00%	5.00%	6.00%	7.00%	8.00%	9.00%
Percentage of children with symptomatic vitamin D deficiency - Universal scenario	0.00%	£21,272,947									
	1.00%	£18,211,295	£21,272,947								
	2.00%	£15,149,642	£18,211,295	£21,272,947							
	3.00%	£12,087,990	£15,149,642	£18,211,295	£21,272,947						
	4.00%	£9,026,337	£12,087,990	£15,149,642	£18,211,295	£21,272,947					
	5.00%	£5,964,684	£9,026,337	£12,087,990	£15,149,642	£18,211,295	£21,272,947				
	6.00%	£2,903,032	£5,964,684	£9,026,337	£12,087,990	£15,149,642	£18,211,295	£21,272,947			
	7.00%	-£158,621	£2,903,032	£5,964,684	£9,026,337	£12,087,990	£15,149,642	£18,211,295	£21,272,947		
	8.00%	-£3,220,274	-£158,621	£2,903,032	£5,964,684	£9,026,337	£12,087,990	£15,149,642	£18,211,295	£21,272,947	
	9.00%	-£6,281,926	-£3,220,274	-£158,621	£2,903,032	£5,964,684	£9,026,337	£12,087,990	£15,149,642	£18,211,295	£21,272,947

Table 3.11: Two-way sensitivity analysis in over-65s – total population 9,176,882

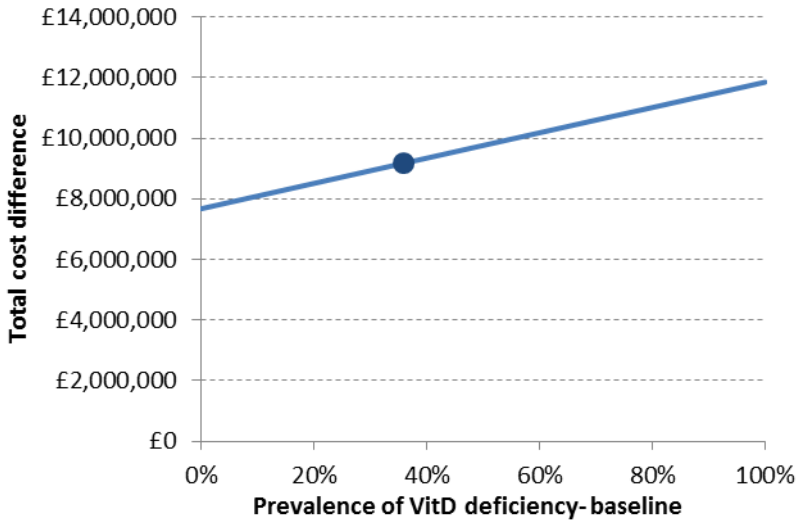
% benefitting from supplementation in universal scenario	% benefitting from supplementation in testing scenario										
	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
0%	£25,359,122	£10,535,139	-£4,288,844	-£19,112,826	-£33,936,809	-£48,760,792	-£63,584,774	-£78,408,757	-£93,232,739	-£108,056,722	-£122,880,705
10%		£25,359,122	£10,535,139	-£4,288,844	-£19,112,826	-£33,936,809	-£48,760,792	-£63,584,774	-£78,408,757	-£93,232,739	-£108,056,722
20%			£25,359,122	£10,535,139	-£4,288,844	-£19,112,826	-£33,936,809	-£48,760,792	-£63,584,774	-£78,408,757	-£93,232,739
30%				£25,359,122	£10,535,139	-£4,288,844	-£19,112,826	-£33,936,809	-£48,760,792	-£63,584,774	-£78,408,757
40%					£25,359,122	£10,535,139	-£4,288,844	-£19,112,826	-£33,936,809	-£48,760,792	-£63,584,774
50%						£25,359,122	£10,535,139	-£4,288,844	-£19,112,826	-£33,936,809	-£48,760,792
60%							£25,359,122	£10,535,139	-£4,288,844	-£19,112,826	-£33,936,809
70%								£25,359,122	£10,535,139	-£4,288,844	-£19,112,826
80%									£25,359,122	£10,535,139	-£4,288,844
90%										£25,359,122	£10,535,139
100%											£25,359,122

3.2.3 Sensitivity Analyses

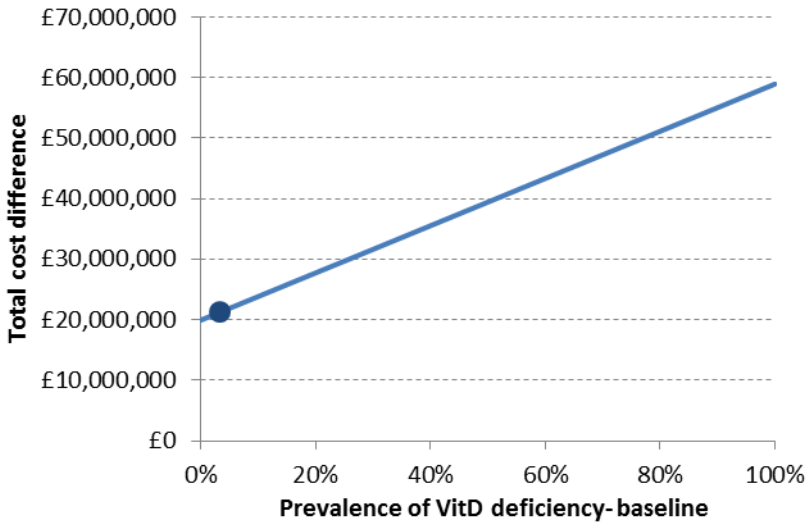
Univariate sensitivity analyses were carried out on uncertain parameters within the model for each population. The key sensitivity analyses reported for Analysis 2 are prevalence of vitamin D deficiency (in the general subgroup population) and the cost of testing for vitamin D.

Graphs 3.10, 3.11 and 3.12 demonstrate that, as the prevalence of vitamin D deficiency in the baseline population of each subgroup increases, the more the incremental cost of 'with testing' compared to 'without testing' increases. This is because an increase in the prevalence of deficiency results in an increase in the number of people receiving supplements in the 'with testing' scenario, whereas the number of people receiving supplements in the 'without testing' scenario is constant.

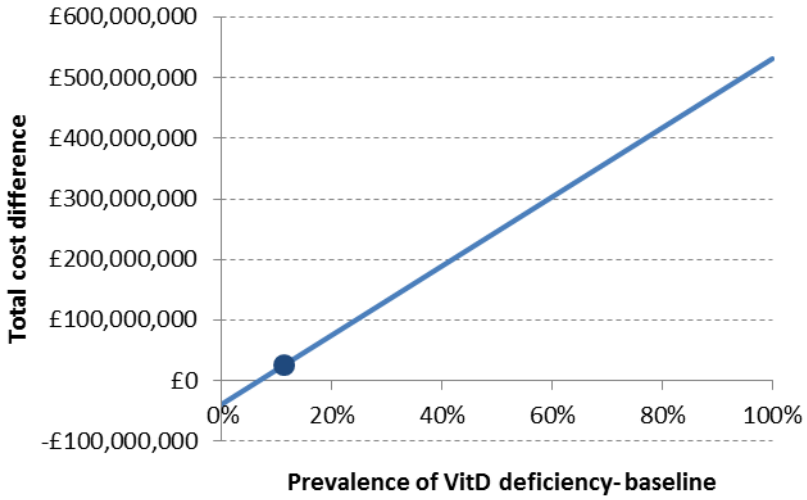
Graph 3.10: Sensitivity analysis for prevalence of vitamin D deficiency – Women



Graph 3.11: Sensitivity analysis for prevalence of vitamin D deficiency – Children

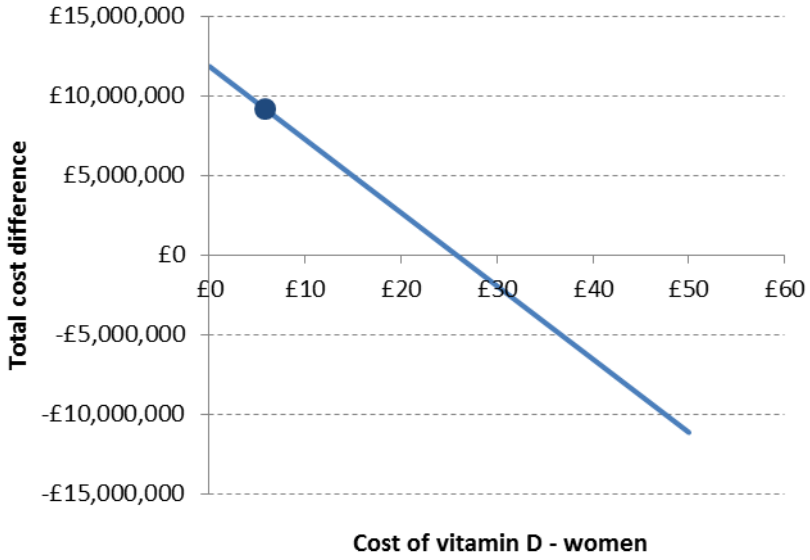


Graph 3.12: Sensitivity analysis for prevalence of vitamin D deficiency – Aged 65+

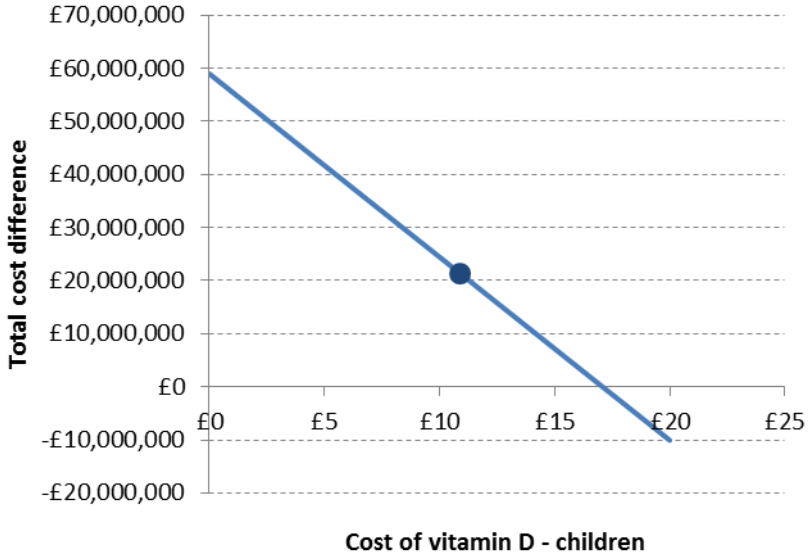


Graphs 3.13 to 3.14 show that as the annual cost of vitamin D supplementation increases the incremental costs of testing reduces. This is because fewer people are taking supplements in the testing scenario, and so increasing the supplement costs has a smaller impact in this scenario. The per-person annual cost of supplementation would need to be over around £25, £15 and £23 for the women, children and over 65s' subgroups, respectively.

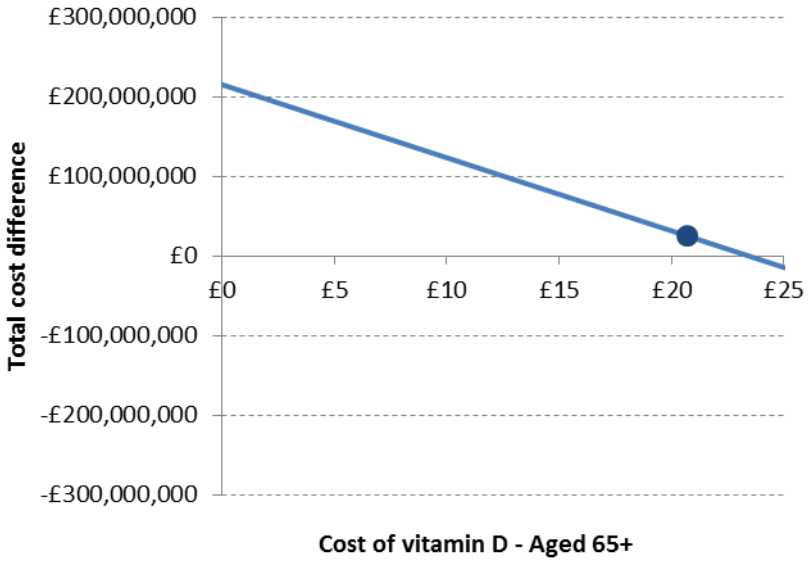
Graph 3.13: Sensitivity analysis for cost of vitamin D supplementation – Women



Graph 3.14: Sensitivity analysis for cost of vitamin D supplementation – Children

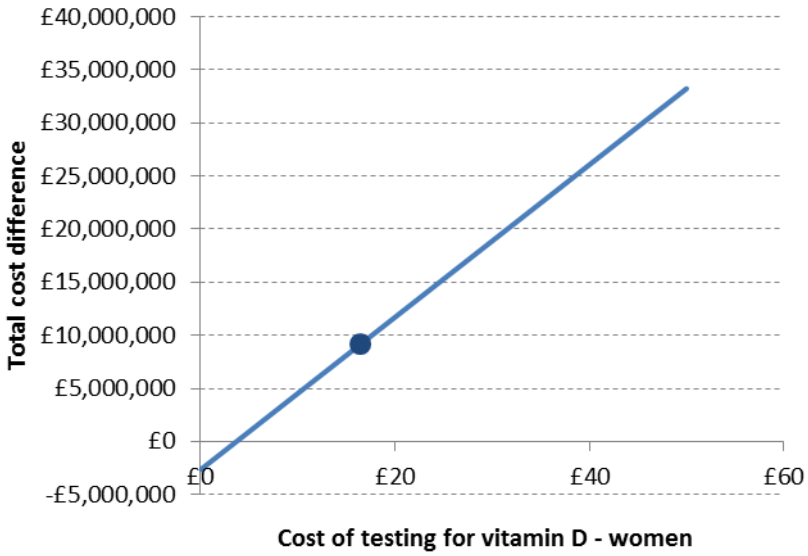


Graph 3.15: Sensitivity analysis for cost of vitamin D supplementation – Aged 65+

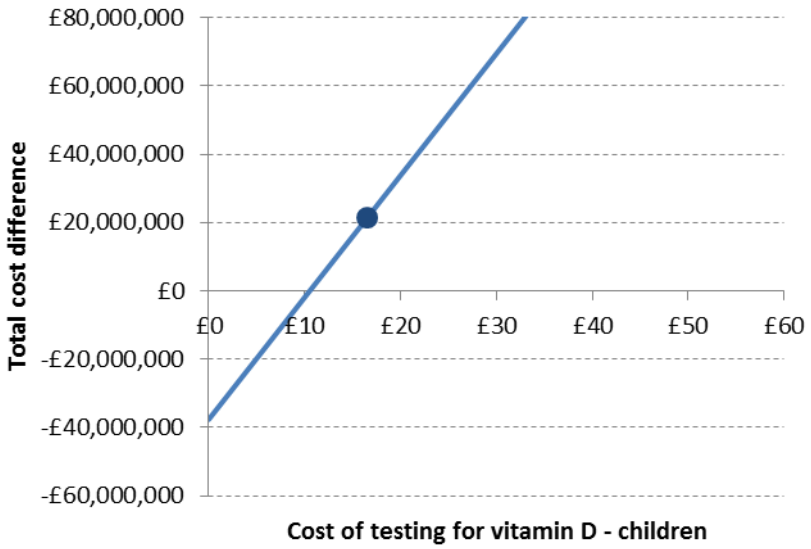


Graphs 3.16, 3.17 and 3.18 show that, as expected, as the cost of testing for vitamin D increases, the total cost difference increases. This is due to the 'with testing' approach costing more compared to the 'without testing' approach.

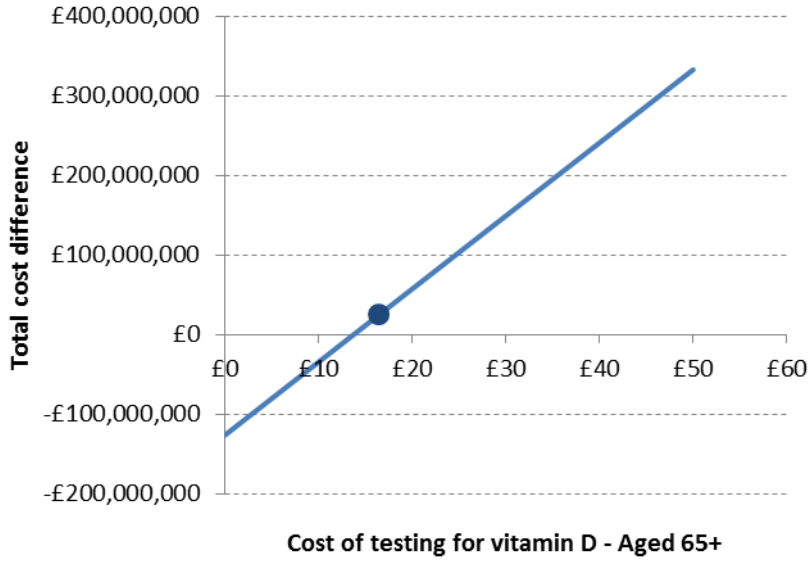
Graph 3.16: Sensitivity analysis for cost of testing for vitamin D deficiency – Women



Graph 3.17: Sensitivity analysis for cost of testing for vitamin D deficiency – Children



Graph 3.18: Sensitivity analysis for cost of testing for vitamin D deficiency – Aged 65+



Section 4: Discussion

4.1 SUMMARY

This analysis aimed to assess the cost-effectiveness of interventions to promote the uptake of vitamin D supplements, using the following two questions:

Question 1: How effective and cost effective are interventions to increase awareness and implementation of existing guidance on vitamin D among health professionals or others working with at-risk populations? What are the implications for professional training and practice?

Question 2: How effective and cost effective are interventions to increase awareness and uptake of existing guidance on vitamin D among at-risk groups (with special consideration given to those eligible for the Healthy Start scheme)?

It was originally intended that a traditional health economics approach would be taken, calculating the costs of each option and the health outcomes as quality-adjusted life years and using these to calculate an incremental-cost effectiveness ratio. This approach required that the costs and benefits of vitamin D supplementation be assessed and quantified. However, it was discovered that there was a lack of required data. For example, in the minutes from SACN's 9th meeting it was noted that "members agreed with their previous conclusion that there was a lack of evidence from RCTs for beneficial effects of vitamin D on bone health markers. However, it was agreed to check if the meta-analysis by Winzenberg *et al.* (2011) included any studies of vitamin D and calcium"[21] Therefore, rather than using the traditional approach of cost per QALY the model would instead be based on a simplified analysis, assessing the cost per additional person using vitamin D supplements. The following two analyses were conducted:

Analysis 1: An assessment of an intervention carried out in Birmingham by Heart of Birmingham PCT to increase the uptake of vitamin D supplementation among pregnant and breastfeeding women and children under five.

Analysis 2: A cost-comparison of universal provision of vitamin D supplements (assuming 100% uptake) versus provision of vitamin D supplements only to those who have tested positive for vitamin D deficiency.

[21] Note: This meta-analysis only includes effects on bone mineral density which was not useful for the traditional health economics approach as it is not linked to a health outcome. The meta-analyses concluded that vitamin D supplementation had no statistically significant effects on total body bone mineral content.

Due to a lack of information it was only possible to include the following three subgroups in this analysis:

1. Pregnant and breastfeeding women;
2. Children under the age of 5 years;
3. Adults over the age of 65 years.

In Analysis 1, assessing the Birmingham intervention, the model estimated that the intervention would be cost-saving in the pregnant and breastfeeding women, but cost-incurring in the children under 5 years subgroup. There was great uncertainty around many of the parameters in this analysis. The model appears to be driven by the following parameters: prevalence of vitamin D at baseline and after the intervention; uptake of vitamin D after the intervention; annual cost of supplying vitamin D and the cost of treating symptomatic vitamin D.

In Analysis 2, comparing testing for deficiency with no testing and universal provision, the model estimated that providing universal supplements to the whole population of each relevant subgroup was cost-saving in comparison with testing the whole population. However, this conclusion is based on the basecase inputs currently in the model. While the assumptions in the model are deemed to be the most appropriate there is still a lot of uncertainty surrounding some inputs, especially around the level of uptake and the effect this has on health, therefore, this conclusion should be read with the two-way sensitivity analysis (Section 3.2.2) in mind. This applied for all three subgroups. The key drivers in this analysis were the cost of testing for vitamin D deficiency, the cost of vitamin D supplements and the health outcomes expected in each scenario.

There was a great deal of uncertainty around many of the inputs used in the current analysis. For this reason a number of assumptions have had to be made and this should be taken into account when considering the results of the analysis. For example, two of the main drivers of Analysis, the cost of the intervention to promote uptake and the uptake that would result from the intervention, are very uncertain. In Analysis 2 it is very uncertain how uptake would differ in the two scenarios. It is possible that the uptake would differ between the two scenarios. For example, people who have tested positive for deficiency may be more likely to actually take the supplements they have been given than someone who has been given supplements through a universal scheme. In addition to this, it is likely that people who have tested positive for deficiency would be given a higher dose than those who receive supplements through a universal scheme. Therefore, a deficient person in the universal supplementation scenario may benefit less than an equally deficient person in the testing scenario. It is unclear how people will benefit depending on their underlying deficiency levels. It is possible that a very deficient person may benefit less than a less deficient person if given a universal supplementation dose, even though their need and capacity to benefit is greater. Sensitivity analyses have been conducted around the key inputs in the model in order to explore the impact of these uncertainties. The basecase results of the model should be considered alongside the sensitivity analyses.