Analysis

Vitamin D supplementation and testing in the UK: costly but ineffective?

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KEY MESSAGES

- Vitamin D supplementation and testing has increased dramatically over the past 20 years
- Costs were more than £130 million/year in 2018, and more than £1 billion between 2009 and 2018.
- Despite these very large costs, the characteristic vitamin D deficiency diseases, rickets and osteomalacia, have not declined over this period.
- Current guidance on vitamin D testing and supplementation and the evidence on which it is based should be reconsidered
- Different strategies for preventing these defining vitamin D deficiency diseases should be implemented, such as food fortification.

Contributors and sources

MB, AA, AG, and MW are clinical academics with an interest in vitamin D deficiency. The article arose out of discussions between the authors on the role of vitamin D supplements during a sabbatical by MB where he visited the research groups of AA and MW. All authors designed the research. MB performed the analyses. MB drafted the paper. All authors critically reviewed and improved it. MB is the guarantor for the article. All authors had access to all the data. MB takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Patient involvement

No patients were involved in the writing of this article.

Conflicts of Interest

We have read and understood [BMJ policy on declaration of interests](#) and have the following interests to declare: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: MB is the recipient of an HRC Clinical Practitioner Fellowship; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. MB, AG, AA, and MW have all co-authored reports of randomised controlled trials and systematic reviews of vitamin D supplementation.

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Vitamin D supplementation and testing in the UK: costly but ineffective?

Standfirst

Costs of vitamin D supplementation and blood testing to the UK NHS have risen 10-fold over the last 20 years to more than £130 million/year in 2018, totalling more than £1 billion between 2009-18, but cases of rickets and osteomalacia have not declined, suggesting that current public health strategies to prevent these rare diseases resulting from vitamin D deficiency are costly but ineffective.

Vitamin D supplementation is a hot topic, both in scientific literature, where it arouses passionate debates,¹ and in the media, where it is often portrayed as a panacea for disease.^{2,3} Since 2013, vitamin D has been one of the 20 most frequently prescribed medications in the English NHS. This prominence is relatively recent. Of the top 20 agents in 2018, vitamin D had the fourth largest increase in both prescriptions and costs since 2008. Figure 1A shows that vitamin D prescriptions in the UK have increased about 14-fold from 2 to 27 million/year over the past 18y. Likewise, prescription costs have increased from £13 to £111 million/year (Figure 1B). These trends differ from those for prescriptions of osteoporosis medications suggesting the increase is not because of co-prescription of vitamin D with those drugs. Vitamin D is also widely available in over-the-counter preparations and the costs of those supplements are not included in these Figures.

Figure 1: Panel A shows the number of prescriptions by year in the UK for vitamin D (colecalciferol and ergocalciferol preparations) monotherapy, co-administered calcium and vitamin D, and the total number of vitamin D prescriptions. Panel B shows the costs of these prescriptions in the UK, by year. Data were obtained from the relevant government websites.

Measuring vitamin D stores (as serum 25-hydroxyvitamin D) is a large additional NHS cost.^{4,5} Very large increases in test requests have been reported from primary care practices in England,^{6,7} and data from four laboratories in each country of the UK show at least 10-fold increases in tests performed since 2001 (Figure 2). Collectively, these four laboratories serve about 8.4 million people for vitamin D measurement. If these data are extrapolated to

the UK population and an average cost to the NHS of £15/test⁶ is assumed, estimated annual testing costs increased from about £1million to £17 million between 2001 and 2018. Given variations in local testing practice and assay cost, there is considerable uncertainty in these estimates for the UK population. These cost estimates are substantially lower than those in Canada and Australia,⁴ and may therefore be a considerable underestimate if indirect costs of testing and appointments are factored in. Thus, the total costs of NHS vitamin D testing and prescriptions have increased from £14 million/year in 2001 to about £130 million/year in 2018. In the ten years between 2009 and 2018, the total cost to the NHS was more than £1 billion.

Figure 2: The number of 25-hydroxyvitamin D tests per year in four laboratories in the UK. Approximate estimates of the populations served by each laboratory were: Glasgow ~ 5.5 million, Belfast ~ 1.9 million, Cardiff ~ 500,000, Cornwall ~ 450,000.

With such large increases in testing and supplementation, it is important to ask whether the investment by the NHS has been accompanied by improvements in health outcomes

attributable to vitamin D deficiency. Or could these very large sums of money have been spent more effectively?

Recent UK Guidance on Vitamin D supplementation (see Box 1)

For most of the last 30 years UK guidance was essentially unchanged, and focused on vitamin D supplementation for groups at high risk of vitamin D deficiency. That changed in 2016, when new recommendations considerably expanded the scope of vitamin D testing and treatment. At that time, the Scientific Advisory Committee on Nutrition (SACN), made new recommendations for reference nutrient intakes (RNIs) for vitamin D based upon musculoskeletal outcomes (Box 1).⁸ The RNI for children >1y and adults was set at 10 µg/d. SACN suggested that because the equivalent of this intake cannot be achieved through sunlight exposure in winter in the UK, dietary strategies to achieve these RNIs should be considered. As a result, Public Health England recommended that the entire population 'should consider taking' vitamin D supplements in autumn and winter, and adults at risk of vitamin D deficiency and children <5y should take vitamin D supplements year round.⁹ This change in guidance was adopted by equivalent bodies in Wales, Scotland and Northern Ireland. Subsequently, in late 2016, the National Institute for Health and Care Excellence (NICE) released detailed clinical knowledge summaries which included discussion of when to measure vitamin D, how to diagnose vitamin D deficiency, and when and how to provide vitamin D supplements.^{10,11}

Box 1: UK guidance on reference nutrient intake for vitamin D

Recommendation	Age/ Population group	Recommended Nutrient Intake for Vitamin D (µg/d, IU/d)
COMA 1991 ^a	0-6m	8.5, 340
	6m-3y	7, 280
	4-50y with summer sun exposure	0, 0
	4-50y without summer sun exposure	10, 400
	50+y	10, 400
	Pregnant and lactating women	10, 400
SACN 2016	<1y	8.5-10, 340-400
	1-3y	10, 400
	4+y	10, 400

COMA- Committee on Medical Aspects of Food and Nutrition Policy. SACN- Scientific Advisory Committee on Nutrition, which superseded COMA

^a COMA suggested that people confined indoors, people ≥65y, pregnant and lactating women, infants and children up to 4y, and Asian women and children who cover their skin, may need supplements to achieve the recommended nutrient intake.

Are the changes in guidance justified?

The 2016 SACN report concluded that only the musculoskeletal outcomes of rickets, osteomalacia, falls, muscle strength and function should be used for setting RNIs for vitamin D.⁸ There was insufficient evidence of beneficial effects of vitamin D supplementation on bone density, markers of bone turnover, fracture prevention and all non-musculoskeletal outcomes to justify consideration of these outcomes in its deliberations.⁸ SACN did not provide any quality assessment of studies they reviewed, nor a formal assessment of the strength of their recommendations, for example by using the GRADE tool, nor an economic evaluation of potential impact on health services.

Since the SACN report was released, the meta-analyses SACN relied on to support vitamin D supplementation for improved muscle strength and function have been independently updated with the removal of three retracted and unreliable trials.¹² These updated meta-analyses differ from the originals, with none showing a beneficial effect of vitamin D.¹² For falls, contemporaneous meta-analyses to the SACN report¹³⁻¹⁵ and subsequent RCTs and more comprehensive meta-analyses and trial sequential analyses do not show benefits of vitamin D supplementation.¹⁶ Thus, the only two outcomes now for which there is unequivocal evidence on which to make vitamin D recommendations are the classical vitamin D deficiency diseases of bone mineralization: rickets (children) and osteomalacia (adults). Each is best diagnosed from bone histology, but in clinical practice is usually diagnosed from clinical features, radiology and biochemistry that includes low serum calcium and phosphate, increased serum parathyroid hormone and increased serum markers of osteoblast activity, such as alkaline phosphatase.

Given that the rationale for changes in guidance from SACN in 2016 is to prevent rickets and osteomalacia, how commonly do these occur? What evidence is there that the incidence of these conditions has changed? Figure 3A shows that the rates of hospital admissions for osteomalacia and rickets in England have remained very low from 1998 to 2018, each between 30 and 100/year. There were possible small increases in rickets prior to 2008, and possible small decreases in both conditions from 2008 to 2014. In stark contrast, the admission rate for the broader diagnostic category of vitamin D deficiency was low until 2007, increased four-fold in 4 years, and then stabilised (Figure 3B). It cannot be determined from these data whether the increase between 2007 and 2011 represents a true increase in prevalence of symptomatic vitamin D deficiency but the apparent decreases in rates of admissions for rickets and osteomalacia during this time argue against it resulting from a change in disease prevalence. More likely, it occurred because of changes in coding

practices, such as coding an isolated 25-hydroxyvitamin D concentration of <25 nmol/L as vitamin D deficiency.

Figure 3: Hospital admissions per year for England showing the number of individuals admitted with vitamin D deficiency (E55), rickets (E55.0) and osteomalacia (M83).

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210 A retrospective survey of cases of symptomatic vitamin D deficiency in children in Glasgow
211 identified an average of 23 cases/year between 2002 and 2008, with a clear annual trend of
212 increasing cases.¹⁷ Only 2/3 of cases had clinical features of rickets.¹⁷ Two recent surveys of
213 3500 paediatricians in the UK and Republic of Ireland using the British Paediatric
214 Surveillance Unit reported low numbers of children with hypocalcaemia and rickets. In the
215 first survey, 91 cases of hypocalcaemic seizures were reported over 2 years between 2011
216 and 2013.¹⁸ In the second survey, 125 cases of rickets that met a standard, predefined
217 definition were reported over 2 years between 2015 and 2017.¹⁹ These figures may be
218 underestimates because rickets may be under-recognised or non-skeletal complications,
219 such as hypocalcaemic seizures or cardiomyopathy, may not be attributed to vitamin D
220 deficiency.¹⁹⁻²¹ Nevertheless, the findings from these three reports are consistent with the
221 hospital statistics, and collectively show that neither rickets nor osteomalacia admissions
222 have decreased substantially. However, the incidence of rickets might have increased over
223 the past 20 years in some areas.

224

225 **No impact of UK recommendations**

226 Figures 1-3 show no obvious impact of the UK guidance. Vitamin D supplementation and
227 testing increased steadily from 2001 onwards, in the absence of guidance recommending
228 such changes. Conversely, after the guidance changed substantially in 2016 to recommend
229 consideration of vitamin D supplementation in winter for the entire population, there was no
230 demonstrable increase in supplementation. Given the dramatic increases in vitamin D
231 testing, and the change in recommendations from targeting of high-risk groups to
232 supplementation of more of the population, the incidence of osteomalacia and rickets would
233 have been expected to have fallen over time. As this has not occurred, the current guidance
234 on vitamin D should be reassessed.

235

236 If vitamin D supplementation and testing increases were unrelated to UK guidance, what
237 were the causes? We can only speculate, noting that vitamin D is relentlessly but uncritically
238 promoted in the media for numerous indications,²² and that many medical articles claim
239 widespread benefits from vitamin D supplements, often based on weak, observational
240 evidence.²³

241

242 **A different approach**

243 Even though the current strategies are very costly and have not lowered the rates of rickets
244 or osteomalacia, the UK government has indicated that there is unlikely to be any change.²⁴
245 Rickets and osteomalacia are preventable and others have argued that the UK should be

able to prevent these conditions through public health policy.^{18,19,24} Box 2 shows five possible broad strategies and their advantages and disadvantages. The public health strategy that is most likely to be effective is food fortification. Historically, food fortification in the UK largely eliminated rickets caused by vitamin D deficiency,^{25,26} but this practice was mostly stopped during the 1950s after cases of infantile hypercalcaemia occurred, possibly because of inappropriately high doses of vitamin D used to fortify food.^{25,26} Mandatory margarine fortification continued until 2013.²⁷ A number of countries, such as Finland, have national vitamin D food fortification programmes that have largely eliminated rickets caused by vitamin D deficiency, without safety concerns.²⁸

Although SACN⁸ and most reviews^{29,30} have not found evidence of benefits of vitamin D supplements on non-musculoskeletal outcomes, a few individual meta-analyses have reported benefits³¹ in subgroups with 25-hydroxyvitamin D <25nmol/L, but these have not changed guidance.³² Food fortification is likely to prevent the development of such levels in the population. NICE recommends that patients with osteoporosis should have a measurement of vitamin D and, if deficient, be co-prescribed vitamin D supplements with their osteoporosis medication.¹⁰ Again, food fortification would largely remove the need to measure vitamin D and co-prescribe vitamin D in this situation.

Conclusion

Costs of UK vitamin D supplementation and testing have increased dramatically over the past 20 years, exceeding £130 million/year in 2018 and totalling >£1 billion in the last decade. These changes in prescribing and testing do not appear to be related to changes in UK guidance on vitamin D. Despite this considerable investment, there is no evidence of reductions in the clinical manifestations of vitamin D deficiency, namely rickets and osteomalacia, suggesting that the current approaches are both expensive *and* ineffective. Current vitamin D guidance and the evidence upon which it is based should be revisited. Food fortification is likely to be both cheaper and more effective,³³ and could be combined with targeted supplementation programmes in at-risk populations, if necessary.

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Box 2: strategies for prevention of osteomalacia and rickets from vitamin D deficiency

Strategy	Description	Advantages	Disadvantages
Case finding	Identify individuals at risk and supplement	Focuses on individuals at highest risk. Few people take supplements for no benefits.	Unlikely to prevent all cases, especially in those with decreased health care access.
Targeted supplementation	Identify population groups at risk and supplement	Focuses on groups at highest risk. Supplement programmes can be modified for different cultures, religious groups, education levels etc	Current strategy which has not reduced cases. Disadvantages those with decreased health care access. Moderate costs. Moderate number of people take supplements for no benefit.
Universal supplementation	Whole population is supplemented	Theoretically could prevent almost all cases	Disadvantages those with decreased health care access. Large number of people take supplements for no benefit. Substantial costs.
Increased sun exposure	Encourage greater summer sun exposure	Inexpensive	Complex message (skin cancers vs vitamin D) Unlikely to prevent all cases. Conflict with religious beliefs or cultural practices. May not be sufficient for individuals with very deeply pigmented skin
Food fortification	Mandatory fortification of certain foods	Theoretically could prevent almost all cases Historically successful Practised in other countries Lower cost	Resistance to mandatory food fortification. Fortified food needs to be consumed by at risk groups in sufficient quantities to ensure adequate intake of vitamin D

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References

1. Bolland MJ, Avenell A, Grey A. Should adults take vitamin D supplements to prevent disease? *BMJ* 2016;355:i6201.
2. <https://www.webmd.com/food-recipes/features/vitamin-d-vital-role-in-your-health#1> [Accessed 1/11/2019].
3. <https://www.theguardian.com/society/2019/may/26/top-uk-scientist-urges-people-to-take-vitamin-d-supplements> [Accessed 1/11/2019].
4. Bilinski K, Boyages S. The rise and rise of vitamin D testing. *BMJ* 2012;345:e4743.
5. Sattar N, Welsh P, Panarelli M, et al. Increasing requests for vitamin D measurement: costly, confusing, and without credibility. *Lancet* 2012;379(9811):95-6.
6. Basatemur E, Hunter R, Horsfall L, et al. Costs of vitamin D testing and prescribing among children in primary care. *Eur J Pediatr* 2017;176(10):1405-09.
7. Crowe FL, Jolly K, MacArthur C, et al. Trends in the incidence of testing for vitamin D deficiency in primary care in the UK: a retrospective analysis of The Health Improvement Network (THIN), 2005-2015. *BMJ Open* 2019;9(6):e028355.
8. Scientific Advisory Committee on Nutrition (SACN). *Vitamin D and Health*. London: TSO, 2016.
9. <https://www.gov.uk/government/news/phe-publishes-new-advice-on-vitamin-d> [accessed 1.11.2019].
10. National Institute for Health and Clinical Excellence (NICE). Clinical Knowledge Summary: Vitamin D deficiency in adults - treatment and prevention. 2016.
11. National Institute for Health and Clinical Excellence (NICE). Clinical Knowledge Summary: Vitamin D deficiency in children. 2016.
12. Avenell A, Bolland MJ, Grey A. Population vitamin D supplementation in UK adults: too much of nothing? *Drug Ther Bull* 2020:epublished 20/11/2020.
13. Cameron ID, Gillespie LD, Robertson MC, et al. Interventions for preventing falls in older people in care facilities and hospitals. *Cochrane database of systematic reviews* (Online) 2012;12:CD005465.
14. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane database of systematic reviews* (Online) 2012;9:CD007146.
15. Bolland MJ, Grey A, Gamble GD, et al. Vitamin D supplementation and falls: a trial sequential meta-analysis. *Lancet Diabetes Endocrinol* 2014;2(7):573-80.
16. Bolland MJ, Grey A, Avenell A. Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis. *Lancet Diabetes Endocrinol* 2018;6(11):847-58.

- 320 17. Ahmed SF, Franey C, McDevitt H, et al. Recent trends and clinical features of
321 childhood vitamin D deficiency presenting to a children's hospital in Glasgow. Arch
322 Dis Child 2011;96(7):694-6.
- 323 18. Basatemur E, Sutcliffe A. Incidence of hypocalcemic seizures due to vitamin D
324 deficiency in children in the United Kingdom and Ireland. J Clin Endocrinol Metab
325 2015;100(1):E91-5.
- 326 19. Julies P, Lynn RM, Pall K, et al. Nutritional rickets under 16 years: UK surveillance
327 results. Arch Dis Child 2020;105(6):587-92.
- 328 20. Aul AJ, Fischer PR, O'Grady JS, et al. Population-Based Incidence of Potentially Life-
329 Threatening Complications of Hypocalcemia and the Role of Vitamin D Deficiency. J
330 Pediatr 2019;211:98-104 e4.
- 331 21. Uday S, Fratzl-Zelman N, Roschger P, et al. Cardiac, bone and growth plate
332 manifestations in hypocalcemic infants: revealing the hidden body of the vitamin D
333 deficiency iceberg. BMC Pediatr 2018;18(1):183.
- 334 22. Caulfield T, Clark MI, McCormack JP, et al. Representations of the health value of
335 vitamin D supplementation in newspapers: media content analysis. BMJ Open
336 2014;4(12):e006395.
- 337 23. Autier P, Boniol M, Pizot C, et al. Vitamin D status and ill health: a systematic review.
338 Lancet Diabetes Endocrinol 2014;2(1):76-89.
- 339 24. Uday S, Hogler W. Prevention of rickets and osteomalacia in the UK: political action
340 overdue. Arch Dis Child 2018;103(9):901-06.
- 341 25. Samuel HS. Infantile Hypercalcaemia, Nutritional Rickets, and Infantile Scurvy in
342 Great Britain. A British Paediatric Association Report. Br Med J 1964;1(5399):1659-
343 61.
- 344 26. Stewart WK, Mitchell RG, Morgan HG, et al. The Changing Incidence of Rickets and
345 Infantile Hypercalcaemia as Seen in Dundee. Lancet 1964;1(7335):679-82.
- 346 27. [https://www.gov.uk/government/consultations/spreadable-fats-and-milk-and-milk-](https://www.gov.uk/government/consultations/spreadable-fats-and-milk-and-milk-products)
347 [products](https://www.gov.uk/government/consultations/spreadable-fats-and-milk-and-milk-products) [accessed 1.11.2019].
- 348 28. Pilz S, Marz W, Cashman KD, et al. Rationale and Plan for Vitamin D Food
349 Fortification: A Review and Guidance Paper. Front Endocrinol (Lausanne)
350 2018;9:373.
- 351 29. Theodoratou E, Tzoulaki I, Zgaga L, et al. Vitamin D and multiple health outcomes:
352 umbrella review of systematic reviews and meta-analyses of observational studies
353 and randomised trials. BMJ 2014;348:g2035.
- 354 30. Autier P, Mullie P, Macacu A, et al. Effect of vitamin D supplementation on non-
355 skeletal disorders: a systematic review of meta-analyses and randomised trials.
356 Lancet Diabetes Endocrinol 2017;5(12):986-1004.

- 357 31. Martineau AR, Jolliffe DA, Hooper RL, et al. Vitamin D supplementation to prevent
358 acute respiratory tract infections: systematic review and meta-analysis of individual
359 participant data. BMJ 2017;356:i6583.
- 360 32. Torjesen I. Evidence does not support vitamin D for reducing respiratory infections,
361 reviews conclude. BMJ 2020;369:m2629.
- 362 33. Aguiar M, Andronis L, Pallan M, et al. The economic case for prevention of
363 population vitamin D deficiency: a modelling study using data from England and
364 Wales. Eur J Clin Nutr 2019:electronic publication 20/8/19.
- 365