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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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.\textsuperscript{4,5} Very large increases in test requests have been reported from primary care practices in England,\textsuperscript{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/test$^6$ is assumed, estimated annual testing costs increased from about £1 million 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**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Age/ Population group</th>
<th>Recommended Nutrient Intake for Vitamin D (µg/d, IU/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMA 1991&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0-6m</td>
<td>8.5, 340</td>
</tr>
<tr>
<td></td>
<td>6m-3y</td>
<td>7, 280</td>
</tr>
<tr>
<td></td>
<td>4-50y with summer sun exposure</td>
<td>0, 0</td>
</tr>
<tr>
<td></td>
<td>4-50y without summer sun exposure</td>
<td>10, 400</td>
</tr>
<tr>
<td></td>
<td>50+y</td>
<td>10, 400</td>
</tr>
<tr>
<td></td>
<td>Pregnant and lactating women</td>
<td>10, 400</td>
</tr>
<tr>
<td>SACN 2016</td>
<td>&lt;1y</td>
<td>8.5-10, 340-400</td>
</tr>
<tr>
<td></td>
<td>1-3y</td>
<td>10, 400</td>
</tr>
<tr>
<td></td>
<td>4+y</td>
<td>10, 400</td>
</tr>
</tbody>
</table>

<sup>a</sup> 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. 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. 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. These updated meta-analyses differ from the originals, with none showing a beneficial effect of vitamin D. For falls, contemporaneous meta-analyses to the SACN report and subsequent RCTs and more comprehensive meta-analyses and trial sequential analyses do not show benefits of vitamin D supplementation. 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).
A retrospective survey of cases of symptomatic vitamin D deficiency in children in Glasgow identified an average of 23 cases/year between 2002 and 2008, with a clear annual trend of increasing cases. Only 2/3 of cases had clinical features of rickets. Two recent surveys of 3500 paediatricians in the UK and Republic of Ireland using the British Paediatric Surveillance Unit reported low numbers of children with hypocalcaemia and rickets. In the first survey, 91 cases of hypocalcaemic seizures were reported over 2 years between 2011 and 2013. In the second survey, 125 cases of rickets that met a standard, predefined definition were reported over 2 years between 2015 and 2017. These figures may be underestimates because rickets may be under-recognised or non-skeletal complications, such as hypocalcaemic seizures or cardiomyopathy, may not be attributed to vitamin D deficiency. Nevertheless, the findings from these three reports are consistent with the hospital statistics, and collectively show that neither rickets nor osteomalacia admissions have decreased substantially. However, the incidence of rickets might have increased over the past 20 years in some areas.

No impact of UK recommendations

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

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

A different approach

Even though the current strategies are very costly and have not lowered the rates of rickets or osteomalacia, the UK government has indicated that there is unlikely to be any change. Rickets and osteomalacia are preventable and others have argued that the UK should be
able to prevent these conditions through public health policy.\textsuperscript{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,\textsuperscript{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.\textsuperscript{25,26} Mandatory margarine fortification continued until 2013.\textsuperscript{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.\textsuperscript{28}

Although SACN\textsuperscript{8} and most reviews\textsuperscript{29,30} have not found evidence of benefits of vitamin D supplements on non-musculoskeletal outcomes, a few individual meta-analyses have reported benefits\textsuperscript{31} in subgroups with 25-hydroxyvitamin D <25nmol/L, but these have not changed guidance.\textsuperscript{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.\textsuperscript{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,\textsuperscript{33} and could be combined with targeted supplementation programmes in at-risk populations, if necessary.
### Box 2: strategies for prevention of osteomalacia and rickets from vitamin D deficiency

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case finding</td>
<td>Identify individuals at risk and supplement</td>
<td>Focuses on individuals at highest risk. Few people take supplements for no benefits.</td>
<td>Unlikely to prevent all cases, especially in those with decreased health care access.</td>
</tr>
<tr>
<td>Targeted supplementation</td>
<td>Identify population groups at risk and supplement</td>
<td>Focuses on groups at highest risk. Supplement programmes can be modified for different cultures, religious groups, education levels etc</td>
<td>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.</td>
</tr>
<tr>
<td>Universal supplementation</td>
<td>Whole population is supplemented</td>
<td>Theoretically could prevent almost all cases</td>
<td>Disadvantages those with decreased health care access. Large number of people take supplements for no benefit. Substantial costs.</td>
</tr>
<tr>
<td>Increased sun exposure</td>
<td>Encourage greater summer sun exposure</td>
<td>Inexpensive</td>
<td>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</td>
</tr>
<tr>
<td>Food fortification</td>
<td>Mandatory fortification of certain foods</td>
<td>Theoretically could prevent almost all cases Historically successful Practised in other countries Lower cost</td>
<td>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</td>
</tr>
</tbody>
</table>


