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Research and Evaluated Service Improvement

Vitamin D assessment in primary care: changing patterns of testing

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Key messages

- The number of vitamin D tests requested by primary care, and the associated cost, is rapidly increasing.
- More cases of vitamin D deficiency were detected each year, but the odds of detecting deficiency decreased.
- Repeat tests form a significant proportion of total requests, and should be performed after three to six months.
- Seasonal variation in vitamin D levels should always be considered when requesting tests and interpreting results. Clinicians should consider risk factors for vitamin D deficiency to ensure targeted testing of patients.

Why this matters to us

There is increasing awareness of the importance of vitamin D for maintaining musculoskeletal health by both the medical profession and the public. The number of requests for vitamin D testing from primary care is consequently increasing. Testing is expensive and can amount to a substantial financial burden, particularly if testing and retesting are performed inappropriately. There is a need to develop clear guidance for assessing vitamin D status in primary care. We believe our observations and recommendations will inform to improve the cost-effectiveness of vitamin D testing, its ability to influence management and thus make a real impact within primary care practice and patient care. Although this study was carried out in Liverpool, conclusions remain relevant to London given its greater black, Asian and minority ethnic population who are at increased risk of vitamin D deficiency.

ABSTRACT

Background Over recent years there has been increased interest in the disease burden associated with vitamin D deficiency. This, combined with recognition that the prevalence of vitamin D deficiency is high in the UK, has led to increased requests for vitamin D assessment from primary care clinicians.
Setting A primary care cohort in Liverpool.
Question How has the usefulness of vitamin D testing changed over time in identifying deficiency?
Methods Vitamin D results from primary care practices in Liverpool were collected between 2007 and 2012, inclusive. Results were allocated to six cohorts based on year of request and each was grouped into three categories (adequate, insufficient and deficient).
Results Vitamin D results of 9460 (74%) first tests and 3263 (26%) retests were analysed. Total number of requests increased 11-fold, from 503 in 2007 to 5552 in 2012. Overall 42% of first-test results were deficient (< 30 nmol). With each incremental year, more cases of vitamin D deficiency were detected – but the odds of detecting vitamin D deficiency decreased.
Conclusions An exponential increase in the number of vitamin D requests was observed over this six-year period. Although more patients with vitamin deficiency were identified, the increased number of tests represents a significant cost to health services. Moreover, the practice of retesting too soon after treatment can be inappropriate. There is a need to develop clear guidance for assessing vitamin D status in primary care.

Keywords: primary care, supplementation, testing, treatment, vitamin D

Introduction

There is increasing awareness of the importance of vitamin D for maintaining musculoskeletal health by both the medical profession and the public. The recent re-emergence of rickets and osteomalacia has received much media attention,[1] and there is growing interest in vitamin D deficiency as a potential risk factor for cardiovascular, autoimmune and some malignant diseases.[2]

Most vitamin D is obtained by UVB exposure of the skin and little is ingested from dietary sources. The UK receives adequate UVB radiation for vitamin D synthesis only during late spring and summer.[3] In addition, cloud cover, the use of sunblock, the amount of skin exposure, obesity and skin pigmentation all influence an individual's ability to generate and utilise vitamin D.[3,4] The UK population is therefore at risk of suboptimal vitamin D for much of the year, particularly if they have been unable to build up high concentrations during the summer months.

The National Diet and Nutrition Survey reported vitamin D deficiency (defined as < 25 nmol/L) in 18% of adults aged 19–64 years and 20% of children aged 11–18 years.[5] At even greater risk are black and minority ethnic (BME) groups who, due to increased skin pigmentation, require greater exposure to UVB radiation to produce vitamin D and who may be more likely to cover their skin for cultural or religious reasons. Deficiency was reported in up to 94% of an Asian cohort in Birmingham, UK.[6] Although Liverpool does not have a large BME population, vitamin D deficiency has been noted as a health issue in its Somali community since 2003.[7,8]

Consequently, the frequency of vitamin D testing is increasing, particularly in primary care. Because the cost of measuring vitamin D is relatively expensive (ranging between £12 and £20 per test), this places a substantial financial burden on health services, particularly if testing is performed indiscriminately with inappropriate retesting. Concerns regarding over-testing have been recognised by regional bodies as well as the National Osteoporosis Society (NOS) in their guidance.[9,10] The rise of inappropriate testing in primary care, particularly in low-risk groups, was also raised at the 2014 Royal College of General Practitioners conference.[11]

The prevalence of vitamin D deficiency is high, while supplementation and treatment are relatively cheap and rarely associated with significant adverse effects. The aim of this study was, therefore, to assess how the usefulness of vitamin D testing has changed over time in identifying deficiency. A study of vitamin D deficiency in Liverpool, which has a predominantly white Caucasian population, highlights the need for increased awareness in areas with substantial black, Asian and minority ethnic populations such as London.[12,13]

Methods

Fully anonymised vitamin D results from primary care requests in Liverpool were identified from 2007 to 2012, inclusive. All were processed in one laboratory based at the Royal Liverpool University Hospital. Vitamin D assessments in children aged below 16 years were excluded since most requests were not initiated in primary care.

Samples were processed by tandem mass spectrometry. Vitamin D (25-OHD) levels are reported as a sum of 25-hydroxyvitamin D_2 and D_3 levels. The lower limit of quantification was 10 nmol/L. For the purpose of statistical analysis, levels < 10 nmol/L values were substituted as 5 nmol/L.

Summary statistics were calculated for the number of tests by gender, age categories and over months of the year.

Results were classified into three categories based on cut-offs from the NOS and Institute of Medicine (IOM) consensus guidelines.[9] These include vitamin D deficiency (< 30 nmol/L), insufficiency (30–50 nmol/L) and adequacy (> 50 nmol/L). Changes in the relative proportions of these categories were summarised by month and year.

Repeat tests (retests) were likely to be performed after supplementation or treatment and therefore were analysed separately from first tests. First and repeat tests were linked prior to full anonymisation.

Six cohorts were identified for the analysis of first tests, based on year of testing. The proportion with vitamin D deficiency was compared using multivariate logistic regression adjusting for age and gender.

Changes in vitamin D levels between first test and first retest were analysed using Wilcoxon's signed-rank test. The Wilcoxon rank-sum test was used for non-parametric comparisons and a chi-squared test used for proportions. $P < 0.05$ was taken to be statistically significant. Statistical analysis was performed using STATA12.

Results

Over the six-year period 12 723 samples were sent from primary care practices across Liverpool: 9460 (74%) were first tests and 3263 (26%) were retests.

Five hundred and three tests were requested in 2007, compared with 5552 in 2012 (Figure 1) – an 11-fold increase. The number of requests for repeat tests also increased, from 61 to 931 over the six-year period.

The median age of the whole cohort was 50 years [interquartile range (IQR) 34–66]; 75% of requests were for females and 25% were for males. The median age of females tested was 47 years (IQR 32–63), which was significantly lower than the median age observed in males (57 years, IQR 41–71) ($P < 0.001$). Females were tested more frequently than males in each age category with the gender difference most marked during reproductive years.

The number of requests varied sporadically throughout each month of the year, with request numbers lowest from December to February (data not shown).

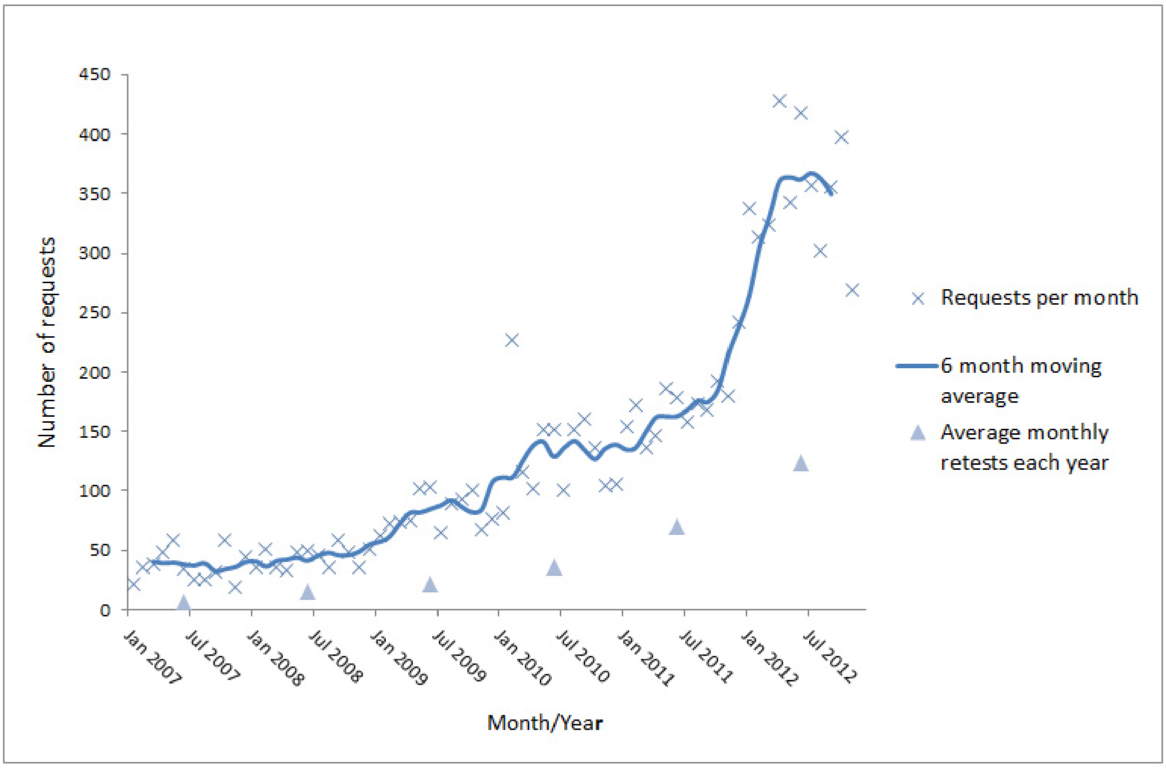

Figure 1 The total number of requests for vitamin D tests each month over six years. Triangles show the average monthly number of retests each year.

First-test vitamin D results

Over the six-year period, 40% of results from initial requests demonstrated vitamin D deficiency, 26% were insufficient and 34% were adequate. The overall median vitamin D result was 40.3 nmol/L (IQR 23.5–63.5 nmol/L) and the mean was 46.8 nmol/L (SD 33.3 nmol/L). The distribution of vitamin D results was strongly skewed towards deficiency; 186 tests (2%) had vitamin D levels > 150 nmol/L.

Median 25-OHD levels increased from 27.5 nmol/L (IQR 16.3–46.5) in 2007 to 42.7 nmol/L (IQR 25–65.1) in 2012 ($P < 0.001$). Figure 2 shows the proportion of tests demonstrating adequate vitamin D results, which rose from 21% in the first year to 40% in the final year of the study. Adjusted for age and sex, the odds of finding a deficient result was 2.41 times higher in 2007 than in 2012 (Table 1).

The proportion of results identified as deficient decreased from 55% to 36% over the six-year period. The absolute numbers of tests demonstrating vitamin D-deficient results increased from 237 in the first year to 1367 in the sixth year of this study. The proportion with insufficiency remained relatively stable over the period of study.

Median vitamin D levels showed a peak of 49.1 nmol/L (IQR 29.7–71nmol/L) in August and a trough of 27.9 nmol/L (IQR 17.7–45.8 nmol/L) in February (Figure 3).

The proportion with vitamin D deficiency each month also followed a sinusoidal pattern. Deficiency was detected at higher levels in winter (December to February) than in summer (June to August) (50% versus 29%, $P = 0.003$). Median vitamin D levels were 31 nmol/L in winter (IQR 17.6–51.7 nmol/L) compared with 46.3 nmol/L in summer (IQR 27.5–67.3 nmol/L) ($P < 0.001$). There were no significant differences in the proportions of deficiency, insufficiency and adequacy between genders ($P = 0.74$).

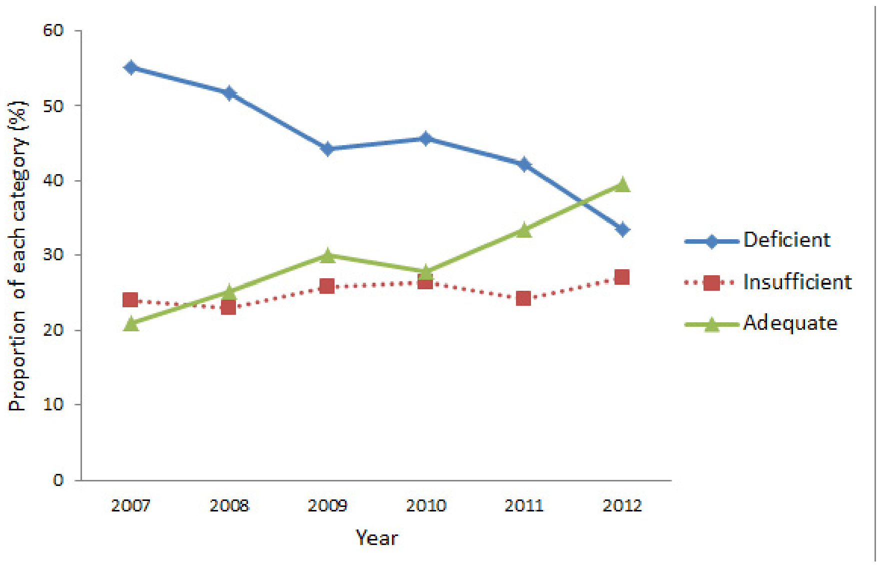

Figure 2 The proportion of each vitamin D category over six years as defined by the National Osteoporosis Society.

Table 1 Logistic regression comparing the odds of finding a deficient result in each year cohort compared with the index year 2012, adjusted for age and sex

Year	Odds of finding deficient result	95% confidence interval
2012	Index	
2011	1.44	1.28, 1.61
2010	1.70	1.51, 1.92
2009	1.50	1.30, 1.74
2008	2.16	1.80, 2.60
2007	2.41	1.96, 2.95

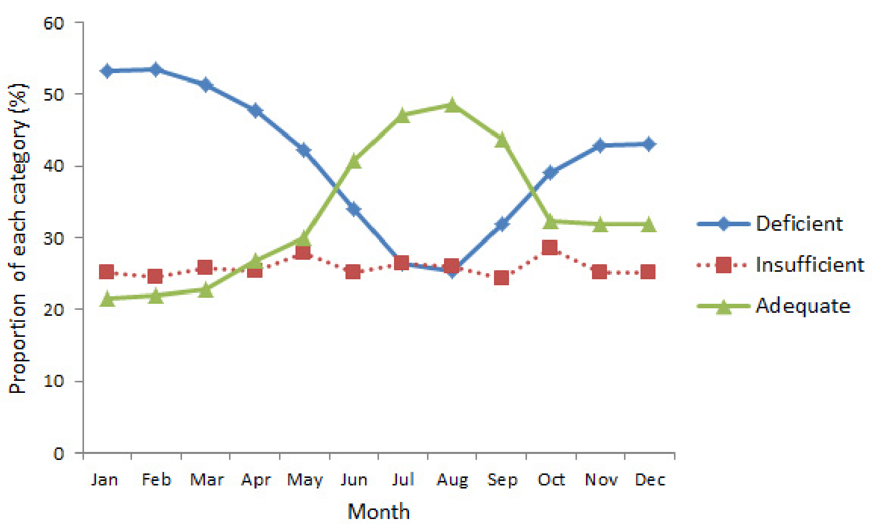

Figure 3 The proportion of each vitamin D category over months of the year as defined by the National Osteoporosis Society.

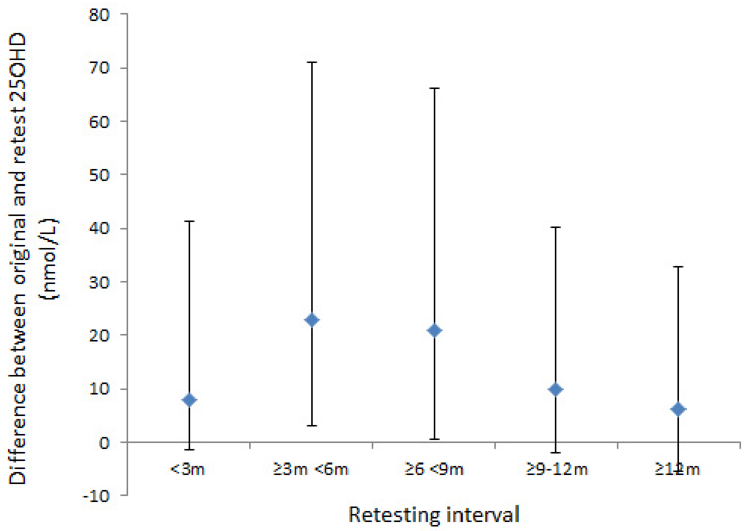

Figure 4 Difference in median and interquartile range of vitamin D levels between the first test and first repeat test at different intervals.

Repeat test results

Of the tests, 3272 were repeats. The absolute number of retests increased exponentially over the study period (Figure 1). The number of retests as a percentage of the total number of tests also increased, from 15% in 2007 to 27% in 2012. Some patients had multiple retests, therefore only the first retests (n = 2120) are analysed below.

Twenty percent of retests were performed within three months of the first test and 32% were performed after one year. Although all medians shown in Figure 4 were statistically different from the first test, those retests performed between three and nine months afterwards (36.9%) showed the largest increase in vitamin D levels. Retesting within four weeks (7%) showed no statistical difference in vitamin D levels from the first test (data not shown). Ninety-two retest results (4%) showed levels above 150 nmol/L.

Discussion

This study has demonstrated a marked increase in the number of requests for vitamin D measurement by primary care providers over a recent six-year period. Although the absolute number of deficient individuals increased each year, the odds of finding a deficient result was 2.41 times higher in 2007 than in 2012. Using the current quoted cost of £20 for measurement of vitamin D, this relates to an increase in annual primary care spending on this investigation of over £100 000 over a six-year period. Twenty percent of retests were performed too soon after the first test.

The increase in requests for vitamin D tests reflects both increased public awareness of vitamin D deficiency and a response among clinicians to recent publications.[10,14–16] To improve the usefulness of vitamin D tests, GPs could, while awaiting future guidance from the National Institute for Health and Care Excellence (NICE), follow the available guidelines, which emphasise targeted testing.[10,16]

Vitamin D levels showed sinusoidal seasonal variation that closely follows hours of sunlight. Winter levels will not reflect the year-round vitamin D status, thus it may not be necessary to treat those identified as borderline deficient in winter. Conversely, an individual with insufficient vitamin D over late summer is likely to become deficient over the winter. Clinicians should take this into consideration when deciding their thresholds for treatment. Patients with equivocal or minor symptoms of deficiency might be advised to improve their vitamin D intake via diet, over-the-counter supplements and increased sun exposure during the summer.

A significant proportion of requests were retests. Despite guidelines recommending retesting after three to six months,[10,17] 20% of retests were performed within three months. Our results suggest that retesting soon after intervention may not allow sufficient time for serum levels to respond. By contrast, retesting within four weeks of a large loading dose may give a false picture of over repletion.

Timely retesting after three to six months can confirm adequate treatment and prevent potential toxic over-treatment. Although recommended dosing regimens are rarely associated with toxicity, vitamin D treatment can unmask previously undiagnosed primary hyperparathyroidism.[9] Daily supplements of 800–1000 IU cholecalciferol have been shown to raise serum levels by 24–29 nmol/L, reaching a steady-state after a minimum of three months, but most likely after six months.[18] Retesting after nine months also showed comparatively little change in median vitamin D levels, which may suggest inadequate ongoing maintenance or poor compliance.

Vitamin D deficiency, whether overtly symptomatic or subclinical, has been endemic and will continue to rise with the demographic shift of the UK. It is a significant public health issue, but as yet lacks centralised and standardised guidance. There is a clear need for education of the public and healthcare professions, especially in issues of prevention through supplementation, diagnosis through targeted testing particularly in at risk groups, adequate treatment, ongoing maintenance and monitoring.

The Department of Health Healthy Start programme aims to supplement low-income pregnant women and their young children.[19,20] This should, if fully implemented with an accompanying public awareness campaign, reduce the burden of symptomatic vitamin D deficiency. Although there may be justified concerns over the low doses used in supplements, a recent study of universal supplementation reported considerable reduction in the incidence of symptomatic vitamin D deficiency in a child population.[21] As a result, NICE is considering the cost-effectiveness of the Healthy Start vitamin programme becoming universal.[22]

Vitamin D deficiency is an important public health issue. However, care also needs to be taken not to over attribute non-specific symptoms to it and over-medicalise mild insufficiency. While programmes to widen the availability of vitamin D supplementation are awaited, patients may be encouraged to use relatively inexpensive vitamin D supplements widely available over the counter. It is important to note, however, that supplemental doses will not be sufficient for those with frank deficiency.

Improving understanding of vitamin D assessment in the adult primary care population is essential to improve quality and cost-efficiency of care delivery. Understanding that the UK elderly and other high-risk populations are likely to be vitamin D deficient for much of the year reduces the need for vitamin D testing in these patients.[11] An argument to retest after a three-month period of vitamin D therapy may improve cost-efficiency, but this needs to be explored in further studies.

Limitations

Although conclusions cannot be drawn about vitamin D status at a population level, the results from this inherently biased sample are an interesting indication of testing trends in primary care. However, there are several limitations due to the use of anonymous data. It is not known whether any first tests were performed after supplementation or treatment, and retesting may have been performed without altering management. Both will influence data and interpretation. It was also not possible to categorise vitamin D results by ethnicity (as a proxy for skin tone and cultural skin covering).

Conclusion

The number of vitamin D tests performed in primary care, and the associated cost, is increasing. GPs should consider risk factors for vitamin D deficiency to ensure targeted testing of patients. Retesting after treatment should be performed after three to six months. Clear national guidelines are needed for a prevention and treatment strategy for vitamin D deficiency in primary care.

GOVERNANCE

Research Ethics Committee approval was not required for the use of fully anonymised data collected for routine clinical and audit purposes. This study was registered and approved by the clinical audit department, Aintree University Hospital, Liverpool (ref: 2873).

CONFLICT OF INTEREST

None.

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