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Temporal and regional variability in the request of vitamin D from general practitioners in Spain

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Abstract

Background: Our main goal is to study the inter-practice regional variability and the temporal evolution in the request of 25-hydroxyvitamin D (25[OH]D) by general practitioners (GPs) in Spain.
Methods: Clinical laboratories in different autonomic communities (AACCs) were invited to report the number of 25(OH)D test requested by GPs during 2012 and 2014. The number of 25(OH)D requested per 1000 inhabitants and the index of variability were calculated, and compared between regions and time periods. We calculated the number of tests that could have been potentially saved in regions where 25(OH)D could be requested from primary care without restrictions taking into account the request in those where it is restricted, and the potential economical savings.
Results: Seventy-six laboratories participated in the 2012 edition, and 110 in 2014, corresponding to 17,679,195 and 27,798,262 inhabitants (59.8% Spanish population). The number of 25(OH)D requested per 1000 inhabitants increased from 1.1 in 2012 to 3.4 in 2014 ($p < 0.001$). The variability index also increased from 51.7 to 68. There was a significantly variability among the different AACCs, ranging from 0.94 to 21.24 ($p = 0.002$). 173,885 tests could have been not measured from primary care in regions without ordering restrictions, resulting in potential 886,813.5€ savings.
Conclusions: There was a high variability in the request of 25(OH)D by GPs in Spain, which significantly increased in a 2 year period. The demand was higher in areas where the request of 25(OH)D was not restricted in primary care, with potential savings if the request would approach to regions with ordering restrictions.

Keywords: appropriateness; demand management; primary care; vitamin D.

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Introduction

Vitamin D is a secosteroid hormone responsible for normal calcium homeostasis and bone health [1] and is increasingly recognized as an important sterol hormone with ubiquitous expression of the vitamin D receptor throughout the body's organs [2]. While the effects of vitamin D on bone are well recognized there is increasing appreciation of its extra skeletal effects. It also modulates transcription of cell cycle proteins that decrease cell proliferation and increase cell differentiation of a number of specialized cells of the body [3]. Finally, vitamin D possesses immunemodulatory properties that may alter responses to infections in vivo [4].

Vitamin D status is evaluated by measuring the serum concentration of 25(OH)D. However, despite its involvement in the above metabolic processes, there is no evidence regarding the benefits of screening of vitamin D deficiency. Its measurement is only recommended to investigate the status of individuals at risk of vitamin D deficiency [5].

Lately there has been an exponential growth in the volume of data created in the clinical laboratories along with increasing health care demands. REDCONLAB studies have focused in comparing the request for laboratory testing in primary care in Spain [6–8]; a great variability exists, and also a generalized lack of appropriateness in laboratory testing [9–11] by general practitioners (GPs).

The aim of this research was, first, to study the interpractice regional variability in the request of 25(OH)D by GPs in Spain; second, to compare its temporal evolution in its request in two different annual REDCONLAB studies, and finally study the economic impact of a potential inappropriate ordering. We hypothesized that the significant advertising of the effects of vitamin D that occurred in recent years would generate a variability and misuse of 25(OH)D.

Materials and methods

Setting

Spain is divided in 17 Autonomous Communities (AACCs). Every Spanish citizen possesses the Individual Health Care Card, which provides access to public health services as a healthcare user throughout the National Health System. The Health system in every AACC is divided into Health Departments (HDs). Each HD covers a geographic area and its population. It is composed by several primary care centers and usually a unique hospital. The laboratory located at the hospital attends the needs of every HD inhabitant.

Data collection

In REDCONLAB 2012, a call for data was posted via email. As in the previous edition [7], Spanish laboratories willing to participate were invited to fill out an enrollment form and submit their results online. The dissemination of the questionnaire was addressed to the participants of previous studies of the REDCONLAB group that recommended to other laboratories to join the current edition. In 2014, the dissemination of the questionnaire was also addressed to the participants of previous REDCONLAB studies and also a LinkedIn group was created (https://www.linkedin.com/in/redconlab-grupo-a5663bb7). In this edition, laboratories located in each AACC reported whether the request of 25(OH)D was easily available/requested or not (strict criteria for 25(OH)D request) in primary care.

The numbers of 25(OH)D requested by the GPs for the years 2012 and 2014 from laboratories at different HD across Spain were reported in both studies. As in the previous editions [6, 7] each participating laboratory was required to deliver data from local Laboratory Information Systems Patient's databases and also to provide data of the organization. Annual hours of sunshine in each HD [12] were also recorded.

Data processing

After collecting the data, test-utilization rates were calculated by standardization with the population attended by each laboratory. Rates were expressed as tests per 1000 inhabitants. Inhabitants were the residents in each public HD. Also the index of variability was calculated, as the top decile divided by the bottom decile (90th percentile/10th percentile). Both editions results were compared.

In 2014, laboratories were classified within AACC (when more than four participants); HD were classified into three groups regarding annual average of sunshine hours (<2000, 2000–2999 and more than 3000), and finally into two groups named vitamin D availability and restricted-availability depending if 25(OH)D could be ordered in primary care with or without restrictions. The demand of 25(OH)D per 1000 inhabitants was compared in each group.

A call of data was sent to every 2014 participant asking for the price of a 25(OH)D test (reagent), and the average price was calculated. We also calculated how many tests would have been not ordered if in regions where the request if 25(OHD) is restricted would have had the same figures as the ones where it is not. We finally calculated the potential economical savings through the average price of the reagent.

In both REDCONLAB editions all participants laboratories used immunoassays to measure 25(OH)D except three where high performance liquid chromatography was used. There were no changes in the method employed between editions.

Statistical analysis

All analyses were performed using SPSS Inc. for Windows, Version 21.0. (SPSS Inc., Chicago, IL, USA). Descriptive statistics were generated for test-utilization rates. The analysis of the distribution of the number of test requests per 1000 inhabitants was conducted by way of the Kolmogorov-Smirnov test. In order to explore the variability through test-utilization rates comparison the index of variability was used. The differences in the indicator results according to the REDONLAB edition, AACC, sunshine hours and 25(OH)D order restriction were calculated by way of a U Mann-Whitney test or Kruskal-Wallis test analysis, as appropriate. A two-sided $p \le 0.05$ rule was utilized as the criterion for rejecting the null hypothesis of no difference.

Results

Seventy-six laboratories participated in the 2012 REDCONLAB edition, corresponding to a catchment area of 17,679,195 inhabitants. One hundred and ten laboratories from 16 AACCs participated in the 2014 REDCONLAB edition, corresponding to a catchment area of 27,798,262 inhabitants, or 60% of the Spanish population. Table 1 shows the demographic data of all participants, the 10 AACCS with more than four participants are codified by number to preserve confidentiality (in alphabetical order: Andalucía, Canarias, Castilla La Mancha, Castilla Leon, Extremadura, Galicia, Madrid, Murcia, País Vasco and Valencia), and the eleventh group with those AACCs that did not reach the four participants (in alphabetical order: Aragon, Asturias, Baleares, Cantabria and Cataluña).

Figure 1 displays the high dispersion of the ratio of 25(OH)D requests per 1000 inhabitants for both study editions. Table 2 shows the descriptive analysis of the ratio 25(OH)D per 1000 inhabitants, again for both REDCONLAB editions; the ratio was significantly higher for year 2014 than for 2012 (3.4 vs. 1.1, $p<0.001$). The variability

Table 1: Descriptive characteristics of the hospitals/health care departments that participated in the 2014 study.

Health Departments, n	110
Patients, n	27.434.262
Population/department, mean (95% CI)	2,31,969.8 (198,487.5–265,452.0)
Autonomous Community, n (%)	
1	20 (18.2%)
2	16 (14.5%)
3	10 (9.1%)
4	11 (10.1%)
5	12 (10.9%)
6	5 (4.5%)
7	5 (4.5%)
8	6 (5.5%)
9	6 (5.5%)
10	5 (4.5%)
Rest	14 (12.7%)
Management, n (%)	
Public	104 (94.5%)
Private	6 (5.5%)
Setting, n (%)	
Urban	18 (16.4%)
Rural	5 (4.5%)
Urban-rural	87 (79.1%)

index was also higher in 2014 than in 2012 (68 vs. 51.7, $p<0.001$).

Figure 2 shows how the ratio was significantly different in the different AACCs, ranging from 0.94 to 21.24 ($p=0.002$).

The results of 25(OH)D/1000 inhabitants in the three groups regarding the annual average of sunshine are shown in Figure 3; there was a statistically difference ($p=0.011$).

GPs in AACCs codified as 2, 3 and 8 can only order 25(OH)D in primary care following restricted criteria, and such AACCs conform the restricted-availability vitamin D group. The rest of AACCs represent the availability group. Figure 4 shows the request of 25(OH)D in both groups, with median of 25(OH)D/1000 inhabitants of 2.35 and 6.1, respectively ($p<0.001$).

Sixty laboratories reported the price of the reagent. The average price was €5.08. Taking into account this price, €258,988.60 and €1,390,914.20 were spent in 2012 and 2014, respectively in 25(OH)D measurement from primary care, only taking into account reagent cost.

173,885 25(OH)D tests could have been not measured in 2014 if the demand in the availability group would have been the same as in the restricted-availability counterpart, with potential savings of €886,813.50, only in reagent costs.

Discussion

The request of 25(OH)D in Spain showed a great regional variability and increased significantly over time. Close to €1.5 million were spent during 2014 on reagent to measure 25(OH)D in a primary care, on a cohort covering 60% of the total Spanish population. The request was lower in HDs with higher sunshine hours and in AACCs with a restricted policy regarding the test demand. Should the laboratories in the remaining AACCs approach the request in the latter regions, close to €1 million would have been saved, only in reagent costs.

Indications for the measurement of 25(OH)D are very specific [5]. In general population without any pathology in vitamin D metabolism its request is not recommended. It is even accepted to treat with low doses of vitamin D3 supplements (cholecalciferol), without any previous 25(OH)D measurement [13]. In patients with chronic diseases

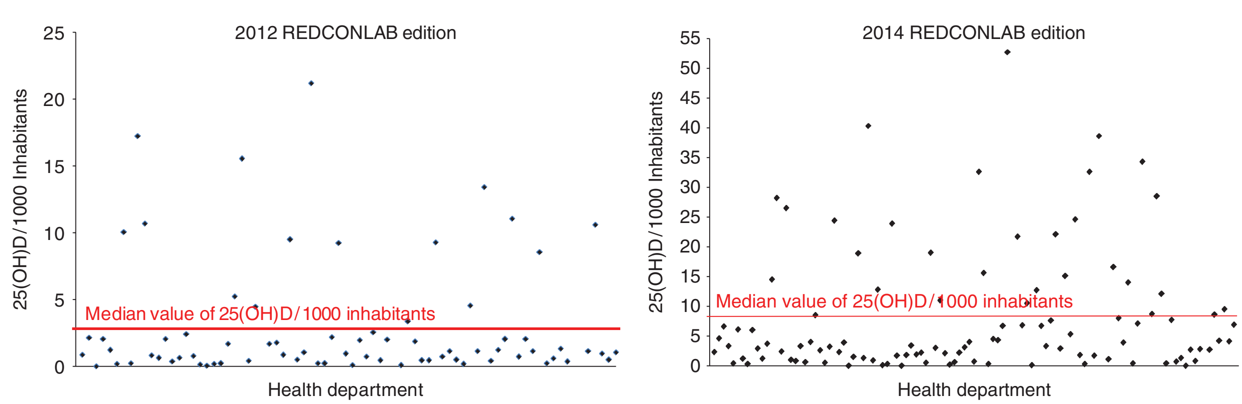

Figure 1: Scattered plots showing the 25(OH)D/1000 inhabitants indicator results for each REDCONLAB edition.
Scattered plots showing the 25(OH)D/1000 inhabitants indicator results for each REDCONLAB edition (2012 and 2014). Horizontal line displays the median value of indicator.

Table 2: Descriptive analysis of 25(OH)D request in both REDCONLAB editions.

	REDCONLAB 2012	REDCONLAB 2014
Health Departments, n	76	110
Inhabitants	17.679.195	27.434.262
Number of 25(OH)D tests, n	50.982	273.802
25(OH)D/Health Department	670.8	2489.1
25(OH)D/1000 inhabitants, median (IQR)[a]	1.1 (1.8)	3.4 (8.8)
Variability index	51.7	68

[a]$p < 0.001$. IQR, interquartile range.

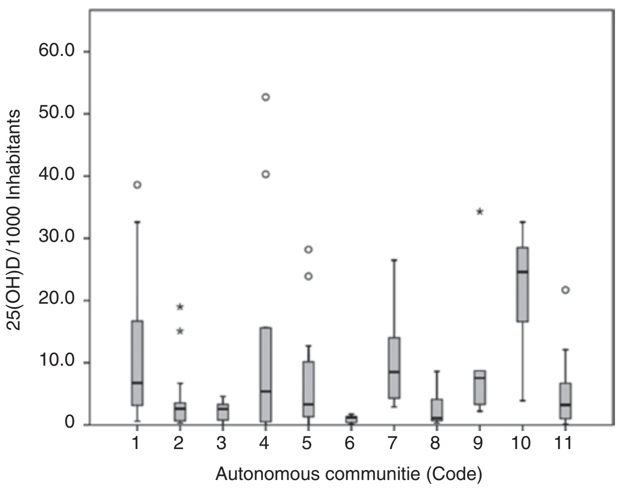

Figure 2: 25(OH)D/1000 inhabitants indicator in different autonomous communities.
Boxplot for 25(OH)D/1000 inhabitants regarding autonomous communities.

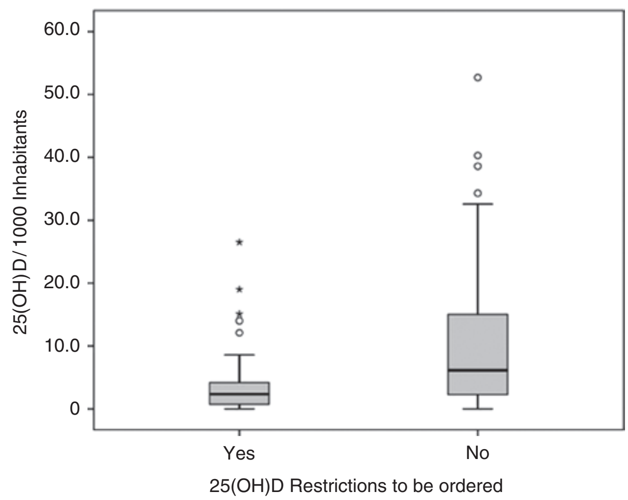

Figure 4: Comparison of 25(OH)D/1000 inhabitants indicator between autonomous communities depending on the existence of 25(OH)D restrictions to be ordered.
Boxplot for 25(OH)D/1000 inhabitants depending on the existence of 25(OH)D restrictions to be ordered in autonomous communities.

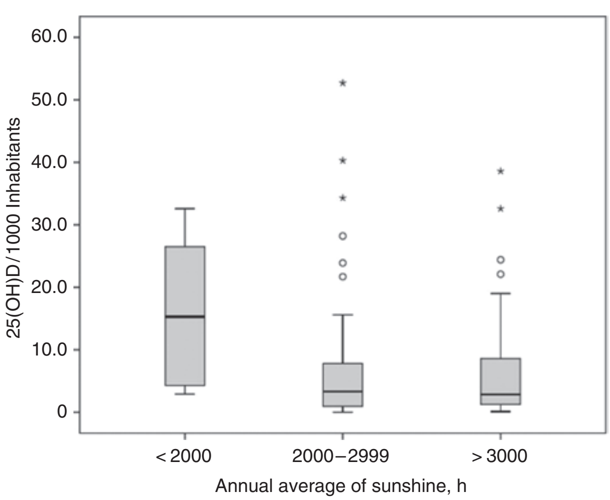

Figure 3: Comparison of 25(OH)D/1000 inhabitants indicator regarding annual sunshine hours.
Boxplot for 25(OH)D/1000 inhabitants regarding annual average of sunshine.

affecting the metabolism of vitamin D, measuring 25(OH)D is indicated; if vitamin supplementation, the test should be done after 3 months of vitamin D supplementation [14]. Its overuse may be related to the initial testing and also to inappropriate retesting [15]. Moreover, an increase in vitamin therapy consumption could happen thanks to this over-prescription. In fact, the number of vitamin D prescriptions has increased considerably over the last decade [16].

Additionally to the exponential growth in the request of 25(OH)D, our study shows great regional variability. Although González-Molero et al. [17] concluded that one third of the Spanish population may be at risk of vitamin D deficiency, it would be difficult to find a single reason to explain the differences between the HDs at the different AACCs, as there are few indications for the test to be requested. One reason is the difference in sunshine hours, as we have found in the study. However, in addition to weather considerations, it seems unlikely that the number of 25(OH)D requests is so much higher in certain AACCs than in others.

The comparison between different geographical areas is a relatively easy way to study variability, but also to indirectly infer a potential an over- or under-request [18]. In fact through previous REDCONLAB studies some tests that were under- [6, 11] and over-request [6, 9, 10, 19, 20] have been detected, and that has led to the design and establishment of subsequent strategies for a better laboratory test demand [21–24].

Taking into account our study results that show the high expenditure generated by the request of a single test in primary care, the very specific indications to be requested this test, the Spanish sunny weather, it seems that at least AACCs with more tests demand could show a potential degree of test request inappropriateness and consequently would need to get closer to the less demanding. In fact, the savings would have been around €1 million. Strategies to reduce the demand for this test could be designed and established as in other settings [25].

Vitamin D supplementation is safe an inexpensive [26]. Empiric vitamin D supplementation can be justified for elderly population, and this measure can be cost effective [27].

The study had certain limitations. First, the differences in 25(OH)D request between health care regions in Spain could be explained because the voluntary participation in the study that could generate a substantial selection bias, the percentage of repeat tests in different areas or by regional different degrees in the management of vitamin D disorders in primary care as we do not know the indications and 25(OH)D concentrations for each request. Second, the calculated economic savings have only been calculated on the basis of reagent price without considering other costs as staff, instruments, maintenance and may not apply to other countries or settings, since our laboratories belong to the Public Health Network, where reagent prices are very low. And lastly, our results in terms of number of tests requested per inhabitants could be difficult to export to other non-Public Health Care models.

In conclusion, there is a high variability in the request of 25(OH)D by GPs in Spain and this demand has significantly increased in a 2-year period. The request is lower in regions with sunny weather and in such areas where 25(OH)D request is restricted in primary care, suggesting a potential over-request in the HDs with more demand. Significant economic savings could be achieved if the request of 25(OH)D in the latter regions would approximate to those with lower demand.

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