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Original

Management of vitamin D deficiency in clinical practice: results of a nationwide multidisciplinary study

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Abstract

Introduction: in recent years, there has been considerable interest in vitamin D, both regarding its physiological aspects and its deficiency, the need for supplementation, recommended doses, and even the type of metabolite that should be used.

Material and methods: given the lack of universally accepted criteria among all scientific societies and the significant heterogeneity observed in clinical practice regarding these issues, we conducted a survey of a sample of 698 doctors in Spain from the specialties of Primary Care, Internal Medicine, Rheumatology, Traumatology, Endocrinology, Gynecology, and Geriatrics to understand their opinions on various aspects of vitamin D management.

Results: there is a notable disparity in the responses to the 8 questions related to their usual clinical practice, both in the likelihood of requesting a vitamin D determination and in how it is prescribed.

Conclusion: finally, the recommendations of the expert panel that developed the survey and analyzed its results are presented.

Keywords:
Vitamin D.
Survey. Spanish doctors.

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INTRODUCTION

The significant role of vitamin D in the prevention and treatment of clinical conditions, both skeletal and extraskeletal, as well as chronic diseases, along with the high prevalence of its deficiency worldwide, including developed countries with high solar exposure like Spain (1), has led to an increase in the demand for its analysis in recent years, both nationally and internationally (2-6). Additionally, there has been an increase in the prescription of vitamin D treatments (4-8). However, there is no unanimous consensus among medical societies, which provide different guidelines and recommendations depending on the degree of deficiency and the patient's profile (9-14), nor is there consensus on the optimal level of vitamin D, evaluated by the serum level of 25-hydroxyvitamin D (25[OH]D) (2,15,16), with ongoing debate about the cutoff value for defining deficiency, insufficiency, or overdose (17,18). Ultimately, although the decision on how to manage vitamin D deficiency is left to the health care professional's discretion, the determinants and characteristics of vitamin D prescription in routine clinical practice have been poorly investigated.

With this study, we aimed to evaluate the knowledge and prescription characteristics of vitamin D in the routine clinical practice of healthcare professionals in Spain and to assess whether there are differences in management among the various related specialties: Primary Care, Internal Medicine, Endocrinology, Traumatology, Gynecology, Rheumatology, and Geriatrics. To achieve this, we conducted a national survey with specific questions on the diagnosis, treatment, and monitoring of vitamin D deficiency.

MATERIALS AND METHODS

We conducted a non-interventional study based on an online quantitative survey from September through November 2022.

PARTICIPANTS

Medical specialists in Primary Care, Internal Medicine, Rheumatology, Traumatology, Endocrinology, Gynecology, or Geriatrics who practiced in the public or private national health care system and had, at least, 1 year of experience in managing patients with vitamin D deficiency. To participate, they were required to sign a consent form for the study.

QUESTIONNAIRE AND DATA MINING

The questionnaire included 8 closed-ended questions (some with multiple-choice options) on the diagnosis, treatment, and monitoring of vitamin D deficiency (Table I). This questionnaire was designed and agreed upon by a group of expert physicians in bone mineral metabolism and the specialties included in this study. Sociodemographic characteristics of the participants (specialty, age, gender, practice setting, and location) were also collected.

Health care professionals who met the inclusion criteria were contacted through a database of healthcare professionals (OneKey, IQVIA). Those who agreed to participate in the study accessed the questionnaire through the CAWI-NET platform.

The study was conducted in full compliance with the protocol, the principles established in the Declaration of Helsinki (19), the clinical practice guidelines on good pharmacoepidemiological practice, and quality procedures, and in compliance with relevant clinical practice guidelines on the treatment and protection of personal data. The study protocol was approved by Hospital Universitario Puerta de Hierro de Majadahonda Research Ethics Committee in Madrid, Spain (47/770284.9/22).

SAMPLE SIZE

Considering the universe of specialists, with a 95 % confidence level (p = q = 50 %), and the goal of not exceeding a 10 % sampling error in any of the consulted specialties, a total of 698 surveys were required: 110 in Primary Care, 100 in Internal Medicine, 98 in Endocrinology, 100 in Traumatology, 100 in Gynecology, 95 in Rheumatology, and 95 in Geriatrics. The representativeness of all geographical regions of the country was ensured. The national distribution by autonomous communities (ACs) was made proportionally to the universe under study. Subsequently, a geographical division into 5 zones (north, northeast, center, east, and south) was made for the corresponding subgroup analysis.

STATISTICAL ANALYSIS

All participants were identified with an anonymized code. Incomplete questionnaires were invalidated and replaced until the total sample of 698 was reached. No imputation of missing values was performed for any variable.

Both the number of cases and the percentage were used to describe categorical variables. The mean, standard deviation, median, quartiles (Q1 and Q3),

Table I. Questionnaire on the diagnosis, treatment, and monitoring of vitamin D deficiency

Questions	Answers
Q1. In your routine clinical practice, how relevant do you consider the identification of vitamin D deficiency states to be?	A. Very relevant B. Slightly relevant C. Not relevant at all D. DK/DA
Q2. If you decided to request a lab test for vitamin D levels…:	A. I could do it without any problem B. I could do it with difficulty, requiring justification and filling out forms C. I could not do it even if I wanted to D. DK/DA
Q3. When dealing with a patient who presents risk factors for vitamin D deficiency, when do you measure 25(OH) vitamin D levels to initiate treatment?	A. Always, to verify vitamin D deficiency before starting treatment B. Never. I treat suspected vitamin D deficiency without measuring 25(OH) blood levels C. Occasionally, depending on clinical circumstances or the metabolite being used D. DK/DA
Q4. At what levels of 25(OH)D do you consider vitamin D deficiency to be treated?	A. < 30 ng/mL B. < 20 ng/mL C. < 10 ng/mL D. DK/DA
Q5. What levels of 25(OH)D would you consider risky for adverse effects due to excess vitamin D activity (e.g., hypercalcemia, hypercalciuria, etc.)?	A. > 50 ng/mL B. > 60 ng/mL C. > 90 ng/mL D. DK/DA
Q6. Which of the following doses do you usually use? You may select multiple options:	A. Calcifediol 0.266 mg/month B. Calcifediol 0.266 mg/biweekly C. Calcifediol 0.266 mg/weekly D. Cholecalciferol 25,000 IU/month E. Cholecalciferol 25,000 IU/biweekly F. Cholecalciferol 25,000 IU/weekly G. Cholecalciferol 50,000 IU/weekly H. DK/DA
Q7. Do you think it is necessary to monitor vitamin D levels after starting treatment?	A. Only with calcifediol B. Only with cholecalciferol C. With either of the two D. With neither of the two E. DK/DA
Q8. If monitoring 25(OH)D levels, how often do you request a follow-up after the initial measurement?	A. Around 4 months B. Around 6 months C. Between 6 and 12 months D. I do not request follow-up tests E. DK/DA

DK/DA: does not know/does not answer.

minimum, and maximum were used to express continuous variables (age).

We conducted a descriptive analysis for the overall sample, as well as for each specialty. A comparative analysis was conducted between specialties, as well as between all specialties and Primary Care using the chi-square test. Within each specialty, sub-analyses were performed using the same methodology based on demographic characteristics: age (< 40 years / ≥ 40 years), gender, practice setting, and geographic location. Statistical analysis was performed using the Gandía BarbWin program. A *p*-value < 0.05 was considered statistically significant.

RESULTS

A total of 698 health care professionals successfully completed the survey and were included in the analysis. Table II shows the participants' sociodemographic characteristics. The participants' mean (standard deviation) age was 42 years (10.4), 56 % of whom were women, with some variations depending on the specialty. A total of 66.9 % practiced exclusively in the public sector, 7.4 % in the private sector, and 25.7 % in both sectors.

The answers to each question asked to respondents are shown in figure 1 and table III for the overall sample and broken down by specialties, respectively.

Most specialists surveyed stated that identifying states of vitamin D hypovitaminosis was very relevant (overall, 81 %). This consideration was significantly lower in Primary Care (72 %), Traumatology (69 %), and Gynecology (69 %) vs the other specialties (86 % up to 92 %) ($p < 0.05$).

Almost all professionals can request an analysis to determine 25(OH)D levels without restriction (overall, 95 %). Primary Care stands out as the specialty with the most difficulty in performing this determination: 12 % could do so with difficulty, while 1 % indicated they could not ($p < 0.05$ compared to other specialties).

Most specialties typically measure vitamin D levels before initiating treatment (always, 74 %; occasionally, 23 %; and never, 3 %).

Table II. Sociodemographic characteristics

	Primary Care (n = 110)	Internal Medicine (n = 100)	Endocrinology (n = 98)	Traumatology (n = 100)	Gynecology (n = 100)	Rheumatology (n = 95)	Geriatrics (n = 95)
Age	47.0 [10.3]	39.3 [8.4]	40.8 [9.7]	40.0 [9.0]	37.8 [9.3]	42.1 [10.7]	47.0 [11.0]
< 40 years	30 %	*67 %*	52 %	54 %	*71 %*	50 %	28 %
≥ 40 years	*70 %*	33 %	48 %	46 %	29 %	51 %	*72 %*
Gender							
Female	59 %	58 %	60 %	25 %	*78 %*	60 %	52 %
Male	41 %	42 %	40 %	*75 %*	22 %	40 %	48 %
Sector							
Public	*87 %*	72 %	66 %	48 %	55 %	73 %	65 %
Private	6 %	6 %	11 %	4 %	14 %	4 %	7 %
Mixed	7 %	22 %	22 %	*48 %*	31 %	23 %	27 %

Data are express as n *(%) or mean [standard deviation].*

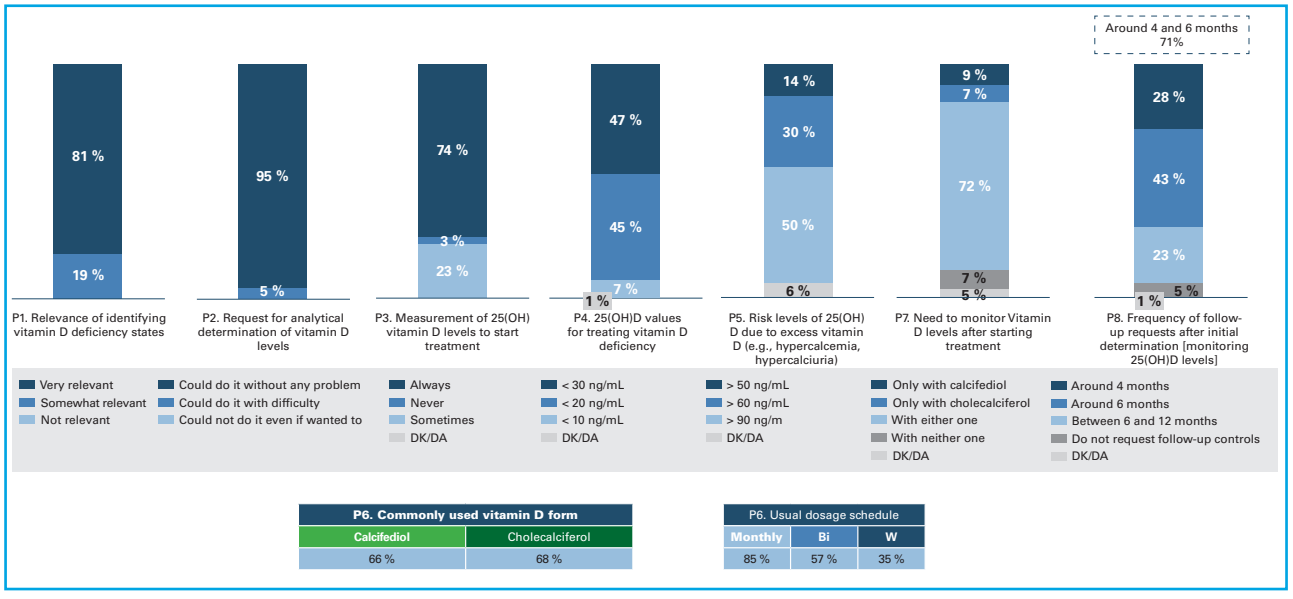

Figure 1. Issues related to the diagnosis, treatment, and monitoring of vitamin D deficiency. The results are presented for the total sample. Data are shown as a percentage. #Significant differences between periods ($p < 0.05$): W = weekly; Qi = biweekly; NS/NC: does not know/does not answer.

Table III. Issues related to the diagnosis, treatment, and monitoring of vitamin D deficiency

Survery	Primary Care (*n* = 110) A	Internal Medicine (*n* = 100) B	Endocrinology (*n* = 98) C	Traumatology (*n* = 100) D	Ginecology (*n* = 100) E	Rheumatology (*n* = 95) F	Geriatrics (*n* = 95) G
P1. Relevance of identifying vitamin D deficiency states							
- Very relevant	79 (72 %)	86 (86 %)*A,D,E	90 (92 %)*A,D,E	69 (69 %)	69 (69 %)	86 (91 %)*A,D,E	86 (91 %)*A,D,E
- Somewhat relevant	31 (28 %)*B,C,F,G	13 (13 %)	8 (8 %)	31 (31 %)	31 (31 %)	9 (9 %)	9 (9 %)
- Not relevant	0 (0 %)	1 (1 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 %	0 %
- DK/DA	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 %	0 %
P2. Request for analytical determination of vitamin D levels							
- Could do it without any problem	96 (87 %)	99 (99 %)*A	94 (96 %)*A	95 (95 %)	95 (95 %)	91 (96 %)*A	94 (99 %)*A
- Could do it with difficulty	13 (12 %)*B,C,F,G	1 (1 %)	4 (4 %)	5 (5 %)	5 (5 %)	4 (4 %)	1 (1 %)
- Could not do it even if wanted to	1 (1 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
- DK/DA	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
P3. Measurement of 25(OH) vitamin D levels to start treatment							
- Always	91 (83 %)*D,E	87 (87 %)*D,E,G	85 (87 %) *D,E,G	43 (43 %)	64 (64 %)*D	80 (84 %)*D,E,G	68 (72 %)*D
- Never	19 (17 %)	12 (12 %)	1 (1 %)	14 (14 %)*A,B,C,E,F,G	4 (4 %)*A,B,F	15 (16 %)	1 (1 %)
- Sometimes	0 (0 %)	1 (1 %)	12 (12 %)	43 (43 %)* A,B,C,F,G	32 (32 %)*A,B,C,F	0 (0 %)	26 (27 %)*B,C
- DK/DA	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
P4. 25(OH)D values for treating vitamin D deficiency							
- < 30 ng/mL	51 (46 %)*D	35 (35 %)	54 (55 %)*B,D	30 (30 %)	57 (57 %)*B,D	53 (56 %)*B,D	51 (54 %)*B,D
- < 20 ng/mL	52 (47 %)*G	56 (56 %)*E,F,G	43 (44 %)	54 (54 %)*E,G	36 (36 %)	39 (41 %)	31 (33 %)
- < 10 ng/mL	7 (7 %) *C	7 (7 %)	1 (1 %)	9 (9 %)*C	6 (6 %)	3 (3 %)	12 (13 %)*C,F
- DK/DA	0 (0 %)	2 (2 %)	0 (0 %)	7 (7 %)*A,C,E,F,G	1 (1 %)	0 (0 %)	0 (0 %)
P5. Risk levels of 25(OH)D due to excess vitamin D							
- > 50 ng/mL	20 (18 %)*D,F	19 (19 %)*D,F	12 (12 %)	6 (6 %)	12 (12 %)	8 (8 %)	22 (23 %)*C,D,E,F
- > 60 ng/mL	33 (30 %)*F	29 (29 %)	21 (21 %)	45 (45 %)*A,B,C,F,G	35 (35 %)*C,F	17 (18 %)	27 (28 %)
- > 90 ng/mL	48 (44 %)	46 (46 %)	64 (65 %)*A,B,D,E,G	35 (35 %)	41 (41 %)	68 (72 %)* A,B,D,E,G	44 (46 %)
- DK/DA	9 (8 %)*C	6 (6 %)	1 (2 %)	14 (14 %)*C,F,G	12 (12 %)* C,F,G	2 (2 %)	2 (2 %)

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Table III. Issues related to the diagnosis, treatment, and monitoring of vitamin D deficiency

Survery	Primary Care (*n* = 110) A	Internal Medicine (*n* = 100) B	Endocrinology (*n* = 98) C	Traumatology (*n* = 100) D	Ginecology (*n* = 100) E	Rheumatology (*n* = 95) F	Geriatrics (*n* = 95) G
P6A. Commonly used vitamin D form							
- Calcifediol 0.266 mg/month	62 (56 %)*,D,E	48 (48 %)*,D,E	63 (64 %)*,B,D,E	23 (23 %)	13 (13 %)	63 (66 %)*,B,D,E	60 (63 %)*,B,D,E
- Calcifediol 0.266 mg/Bi	38 (35 %)*,D,E	50 (50 %)*,A,D,E	64 (65 %)*,A,B,D,E	13 (13 %)	8 (8 %)	56 (59 %)*,A,D,E	58 (61 %)*,A,D,E
- Calcifediol 0.266 mg/W	14 (13 %)	20 (20 %)*,D,E	23 (24 %)*,A,D,E,F	8 (8 %)	6 (6 %)	12 (13 %)	14 (15 %)*,E
- Cholecalciferol 25,000 IU/month	46 (42 %)*,B,G	29 (29 %)	41 (42 %)*,G	35 (35 %)*,G	43 (43 %)*,B,G	51 (54 %)*,B,D,G	21 (22 %)
- Cholecalciferol 25,000 IU/Bi	38 (35 %)*,D	26 (26 %)	49 (50 %)*,A,B,D,E,G	18 (18 %)	30 (30 %)*,D	60 (63 %)*,A,B,D,E,G	24 (25 %)
- Cholecalciferol 25,000 IU/month	30 (27 %)*,B,G	12 (12 %)	24 (25 %)*,B	34 (34 %)*,B,F,G	44 (44 %)*,A,B,C,F,G	18 (19 %)	14 (15 %)
- Cholecalciferol 50,000 IU/month	10 (9 %)	8 (8 %)	9 (9 %)	6 (6 %)	3 (3 %)	6 (6 %)	4 (4 %)
- DK/DA	1 (1 %)	2 (2 %)	0 (0 %)	4 (4 %)*,C,F,G	2 (2 %)	0 (0 %)	0 (0 %)
P6B. Usual dosage schedule							
- Monthly	81 (74 %)*D,E,#,Q,S	64 (64 %)*,D,E,#,S	71 (72 %)*D,E,#,S	49 (49 %)#,Q	50 (50 %)#,Q	76 (80 %)*,B,D,E,G,#,S	64 (67 %)*,D,E,#,S
- Bi	59 (54 %)*D,E,#S	64 (64 %)*,D,E,#,S	78 (80 %)*,A,B,D,E,#,S	26 (26 %)	35 (35 %)	74 (78 %)*A,B,D,E,#,S	65 (68 %)*,A,D,E,#,S
- W	40 (36 %)	28 (28 %)	37 (38 %)	43 (43 %)*,B,F,G,#,Q	47 (47 %)*,B,F,G,#,Q	25 (26 %)	25 (26 %)
P7. Need to monitor Vitamin D levels after starting treatment							
- Only with calcifediol	7 (6 %)	9 (9 %)	9 (9 %)	9 (9 %)	6 (6 %)	9 (10 %)	15 % *E
- Only with cholecalciferol	8 (7 %)	9 (9 %)*C	22 (%)	15 (15 %)*C,G	9 (9 %)*C	6 (6 %)	3 %
- With either one	84 (76 %)*D,E	77 (77 %)*D,E	84 (86 %)*D,E	54 (54 %)	55 (55 %)	74 (78 %)*D,E	77 %*D,E
- With neither one	7 (6 %)*B	1 (1 %)	3 (3 %)	12 (12 %)*B,C	18 (18 %)*A,B,C,F,G	5 (5 %)	5 %
- DK/DA	5 (5 %)	4 (4 %)*C,G	0 (0 %)	10 (10 %)*C,F,G	12 (12 %)*A,B,C,F,G	1 (1 %)	0 %
P8. Frequency of follow- up requests after initial determination							
- Around 4 months	21 (19 %)	36 (36 %)*A	33 (34 %)*A	25 (25 %)	30 (30 %)	23 (24 %)	27 (28 %)
- Around 6 months	51 (46 %)*E	48 (48 %)*E	52 (53 %)*D	36 (36 %)	29 (29 %)	44 (47 %)*E	38 (40 %)
- Between 6 and 12 months	36 (33 %)*B,C,D	15 (15 %)	52 (13 %)	19 (19 %)	25 (25 %)*C	26 (27 %)*B,C	27 (28 %)*B,C
- > 12 months	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
- Do not request follow- up controls	1 (1 %)	0 (0 %)	0 (0 %)	16 (16 %)*A,B,C,F,G	15 (15 %)*A,B,C,F,G	0 (0 %)	3 (3 %)
- DK/DA	1 (1 %)	1 (1 %)	0 (0 %)	4 (4 %)*C	1 (1 %)	2 (2 %)	1 (1 %)
P1. Relevance of identifying excessive states of vitamin D							
- It is very important	79 (72 %)	*86 (86 %)*A,D,E*	*90 (92 %)*A,D,E*	69 (69 %)	69 (69 %)	*86 (91 %)*A,D,E*	*86 (91 %)*A,D,E*
- It is not that important	*31 (28 %)*B,C,F,G*	13 (13 %)	8 (8 %)	31 (31 %)	31 (31 %)	9 (9 %)	9 (9 %)
- It is not importat at all	0 (0 %)	1 (1 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 %	0 %
- DK/DA	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 %	0 %

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Table III. Issues related to the diagnosis, treatment, and monitoring of vitamin D deficiency

Survery	Primary Care (*n* = 110) A	Internal Medicine (*n* = 100) B	Endocrinology (*n* = 98) C	Traumatology (*n* = 100) D	Ginecology (*n* = 100) E	Rheumatology (*n* = 95) F	Geriatrics (*n* = 95) G
P2. Request for analytical determination of vitamin D levels							
- Could do it without any problem	96 (87 %)	*99 (99 %)*A*	*94 (96 %)*A*	95 (95 %)	95 (95 %)	*91 (96 %)*A*	*94 (99 %)*A*
- Could do it with difficulty, justifying it and filling out forms	*13 (12 %)*B,C,F,G*	1 (1 %)	4 (4 %)	5 (5 %)	5 (5 %)	4 (4 %)	1 (1 %)
- Could not do it even if wanted to	1 (1 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
- DK/DA	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
P3. Measurement of 25(OH) vitamin D levels to start treatment							
- Always, to verify that there is vitamin D deficiency before starting treatment	*91 (83 %)*D,E*	*87 (87 %)*D,E,G*	*85 (87 %)*D,E,G*	43 (43 %)	*64 (64 %)*D*	*80 (84 %)*D,E,G*	*68 (72 %)*D*
- Never. I treat the suspicion of vitamin D deficiency without measuring 25(OH) levels in blood	19 (17 %)	12 (12 %)	1 (1 %)	*14 (14 %)*A-G*	*4 (4 %)*A,B,F*	15 (16 %)	1 (1 %)
- In certain occasions, depending on clinical circumstances or the metabolite to be used	0 (0 %)	1 (1 %)	12 (12 %)	*43 (43 %)*A-G*	*32 (32 %)*A,B,C,F*	0 (0 %)	*26 (27 %)*B,C*
- DK/DA	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
P4. 25(OH)D values for treating vitamin D deficiency							
- < 30 ng/mL	*51 (46 %)*D*	35 (35 %)	*54 (55 %)*B,D*	30 (30 %)	*57 (57 %)*B,D*	*53 (56 %)*B,D*	*51 (54 %)*B,D*
- < 20 ng/mL	*52 (47 %)*G*	*56 (56 %)*E,F,G*	43 (44 %)	*54 (54 %)*E,G*	36 (36 %)	39 (41 %)	31 (33 %)
- < 10 ng/mL	*7 (7 %)*C*	7 (7 %)	1 (1 %)	9 (9 %)*C	6 (6 %)	3 (3 %)	*12 (13 %)*C,F*
- DK/DA	0 (0 %)	2 (2 %)	0 (0 %)	7 (7 %)*,A,C,E,F,G	1 (1 %)	0 (0 %)	0 (0 %)
P5. Risk levels of 25(OH)D due to excess vitamin D							
- > 50 ng/mL	*20 (18 %)*D,F*	*19 (19 %)*D,F*	12 (12 %)	6 (6 %)	12 (12 %)	8 (8 %)	*22 (23 %)*C,D,E,F*
- > 60 ng/mL	*33 (30 %)*F*	29 (29 %)	21 (21 %)	*45 (45 %)*A,B,C,F,G*	*35 (35 %)*C,F*	17 (18 %)	27 (28 %)
- > 90 ng/mL	48 (44 %)	46 (46 %)	*64 (65 %)*A,B,D,E,G*	35 (35 %)	41 (41 %)	*68 (72 %)*A,B,D,E,G*	44 (46 %)
- DK/DA	*9 (8 %)*C*	6 (6 %)	1 (2 %)	*14 (14 %)*C,F,G*	*12 (12 %)*C,F,G*	2 (2 %)	2 (2 %)

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Table III. Issues related to the diagnosis, treatment, and monitoring of vitamin D deficiency

Survery	Primary Care (*n* = 110) A	Internal Medicine (*n* = 100) B	Endocrinology (*n* = 98) C	Traumatology (*n* = 100) D	Ginecology (*n* = 100) E	Rheumatology (*n* = 95) F	Geriatrics (*n* = 95) G
P6A. Commonly used vitamin D form							
- Calcifediol 0.266 mg/month	*62 (56 %)*D,E*	*48 (48 %)*D,E*	*63 (64 %)*B,D,E*	23 (23 %)	13 (13 %)	*63 (66 %)*B,D,E*	*60 (63 %)*B,D,E*
- Calcifediol 0.266 mg/Bi	*38 (35 %)*D,E*	*50 (50 %)*A,D,E*	*64 (65 %)*A,B,D,E*	13 (13 %)	8 (8 %)	*56 (59 %)*A,D,E*	*58 (61 %)*A,D,E*
- Calcifediol 0.266 mg/W	14 (13 %)	*20 (20 %)*D,E*	*23 (24 %)*A,D,E,F*	8 (8 %)	6 (6 %)	12 (13 %)	*14 (15 %)*E*
- Cholecalciferol 25,000 IU/month	*46 (42 %)*B,G*	29 (29 %)	*41 (42 %)*G*	*35 (35 %)*G*	*43 (43 %)*B,G*	*51 (54 %)*B,D,G*	21 (22 %)
- Cholecalciferol 25,000 IU/Bi	*38 (35 %)*D*	26 (26 %)	*49 (50 %)*A,B,D,E,G*	18 (18 %)	*30 (30 %)*D*	*60 (63 %)*A,B,D,E,G*	24 (25 %)
- Cholecalciferol 25,000 IU/month	*30 (27 %)*B,G*	12 (12 %)	*24 (25 %)*B*	*34 (34 %)*B,F,G*	*44 (44 %)*A,B,C,F,G*	18 (19 %)	14 (15 %)
- Cholecalciferol 50,000 IU/month	10 (9 %)	8 (8 %)	9 (9 %)	6 (6 %)	3 (3 %)	6 (6 %)	4 (4 %)
- DK/DA	1 (1 %)	2 (2 %)	0 (0 %)	*4 (4 %)*C,F,G*	2 (2 %)	0 (0 %)	0 (0 %)
P6B. Usual dosage schedule							
- W	*81 (74 %)*D,E,#,Q,S*	*64 (64 %)*D,E,#,S*	*71 (72 %)*D,E,#,S*	*49 (49 %)#,Q*	50 (50 %)#,Q	*76 (80 %)*B,D,E,G,#,S*	*64 (67 %)*D,E,#,S*
- Bi	*59 (54 %)*D,E,#,S*	*64 (64 %)*D,E,#,S*	*78 (80 %)*A,B,D,E,#,S*	26 (26 %)	35 (35 %)	*74 (78 %)*A,B,D,E,#,S*	*65 (68 %)*A,D,E,#,S*
- W	40 (36 %)	28 (28 %)	37 (38 %)	*43 (43 %)*B,F,G,#,Q*	*47 (47 %)*B,F,G,#,Q*	25 (26 %)	25 (26 %)
P7. Need to monitor Vitamin D levels after starting treatment							
- Only with calcifediol	7 (6 %)	9 (9 %)	9 (9 %)	9 (9 %)	6 (6 %)	9 (10 %)	*15 %*E*
- Only with cholecalciferol	8 (7 %)	*9 (9 %)*C*	22 (%)	**15 (15 %)*C,G**	*9 (9 %)*C*	6 (6 %)	3 %
- With either one	*84 (76 %)*D,E*	*77 (77 %)*D,E*	*84 (86 %)*D,E*	54 (54 %)	55 (55 %)	*74 (78 %)*D,E*	*77 %*D,E*
- With neither one	*7 (6 %)*B*	1 (1 %)	3 (3 %)	*12 (12 %)*B,C*	*18 (18 %)*A,B,C,F,G*	5 (5 %)	5 %
- DK/DA	5 (5 %)	*4 (4 %)*C,G*	0 (0 %)	*10 (10 %)*C,F,G*	*12 (12 %)*A,B,C,F,G*	1 (1 %)	0 %
P8. Frequency of follow- up requests after initial determination							
- Around 4 months	21 (19 %)	*36 (36 %)*A*	*33 (34 %)*A*	25 (25 %)	30 (30 %)	23 (24 %)	27 (28 %)
- Around 6 months	*51 (46 %)*E*	*48 (48 %)*E*	*52 (53 %)*D*	36 (36 %)	29 (29 %)	*44 (47 %)*E*	38 (40 %)
- Between 6 and 12 months	*36 (33 %)*B,C,D*	15 (15 %)	52 (13 %)	19 (19 %)	25 (25 %)*C	*26 (27 %)*B,C*	*27 (28 %)*B,C*
- Do not request follow- up controls	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
- DK/DA	1 (1 %)	0 (0 %)	0 (0 %)	*16 (16 %)*A,B,C,F,G*	*15 (15 %)*A,B,C,F,G*	0 (0 %)	3 (3 %)
	1 (1 %)	1 (1 %)	0 (0 %)	*4 (4 %)*C*	1 (1 %)	2 (2 %)	1 (1 %)

*The results are presented by specialty. The data are shown as percentages of the total number of respondents in each specialty. *A-G: Statistically significant differences between specialties (p < 0.05); #Significant differences between periods (p < 0.05); W: weekly; Bi: biweekly; DK/DA: does not know/does not answer.*

Traumatology and Gynecology stand out as the specialties that less frequently determine 25(OH)D levels systematically before starting treatment (Traumatology: 43 % occasionally and 14 % never; Gynecology: 32 % occasionally and 4 % never; $p < 0.05$ compared to other specialties).

Overall, a lack of consensus is evident regarding the cutoff point for treating vitamin D deficiency. A total of 47 %, 45 %, and 7 % consider 25(OH)D values of 30 ng/mL, 20 ng/mL, and 10 ng/mL, respectively, as the cutoff points for initiating treatment. In other words, 99 % would treat at levels < 10 ng/mL, 92 % < 20 ng/mL, and 47 % < 30 ng/mL. These percentages vary depending on the specialty consulted. Endocrinology, Gynecology, Rheumatology, and Geriatrics predominantly consider the value of 30 ng/mL (> 50 %). In contrast, internists and traumatologists more frequently (> 50 %) establish the threshold value at 20 ng/mL. Of note that 7 % of traumatologists indicated they did not know how to answer this question.

There is also a lack of consensus on the consideration of the risk of adverse effects due to excess vitamin D activity (e.g., hypercalcemia or hypercalciuria). Overall, the maximum acceptable 25(OH)D level is established at 50, 60, or 90 ng/mL by 14 %, 30 %, and 50 % of prescribers, respectively, that is, 14 % would warn of the risk of adverse effects due to excess vitamin D activity with values > 50 ng/mL, 44 % > 60 ng/mL, and 94 % > 90 ng/mL. Again, of note that 6 % of specialists did not know the answer to this question. These values vary depending on the specialty consulted. Rheumatology and Endocrinology predominantly consider the value of 90 ng/mL (> 50 %).

Both cholecalciferol and calcifediol are widely used molecules for the treatment of vitamin D deficiency (66 % and 68 % of professionals use them, respectively); the monthly regimen (65 %) is the most widely used vs the biweekly (57 %) and weekly (35 %) regimens ($p < 0.05$). Traumatology and Gynecology preferentially use cholecalciferol as the active ingredient ($p < 0.05$ vs calcifediol). They also make greater use of the weekly regimen ($p < 0.05$ vs other specialties) vs specialties such as Internal Medicine, Endocrinology, or Geriatrics. It is observed that among specialists who treat suspected vitamin D hypovitaminosis without measuring 25(OH)D levels in the blood, the use of cholecalciferol is significantly higher than that of calcifediol ($p < 0.05$).

In all specialties, it is considered necessary to monitor vitamin D levels after starting treatment (88 %, regardless of the active ingredient), generally between 4 and 6 months (71 %). However, Gynecology and Traumatology are the specialties that show the most divergence (15 % and 16 %, respectively, do not request follow-up checks; $p < 0.05$ vs other specialties).

Subgroup analyses were conducted based on the demographic characteristics of the participants (Annex 1). Some specialists aged ≥ 40 years showed divergences in certain aspects of vitamin D management vs their younger colleagues. Certain groups reported greater difficulty in requesting 25(OH)D tests, which was correlated with a significantly higher rate of empirical treatment (in the absence of testing).

DISCUSSION

Vitamin D deficiency is recognized as a major public health issue and is highly prevalent worldwide (20,21), even in Mediterranean countries like Spain (1). This has led to the implementation of food fortification programs and recommendations for supplementation and treatment of deficiency. Food fortification with vitamin D offers an opportunity to improve vitamin D intake in the population. However, in many countries, including Spain, fortification is voluntary and not widely implemented (22). The dosing of vitamin D can be complex due to different indications, various threshold values for treatment, available active ingredients, galenic instructions, dosages, and diverse clinical settings. This study aimed to evaluate the prescription practices of various medical specialties throughout Spain. A total of 698 specialists from 7 medical specialties participated in the study.

First, the results of our study demonstrate that medical specialists in Spain are aware of the clinical relevance of vitamin D deficiency (81 % consider hypovitaminosis D to be very relevant). The development of guidelines and growing scientific evidence have increased medical awareness of vitamin D and its possible supplementation to support general health and improve certain clinical conditions and chronic diseases observed in multiple specialties (8).

Nearly all professionals can request a test to determine 25(OH)D levels without restriction (overall, 95 %). This finding is certainly surprising, considering the screening protocols and strategies to limit vitamin D determinations (23,24), which can vary depending on the health care area. Although some specialties experienced greater difficulty in conducting determinations based on geographic location, these results did not follow a conclusive pattern.

Most specialties usually measure vitamin D levels to start treatment (74 % always, 26 % in certain cases or never). This finding highlights that vitamin D deficiency treatment is generally associated with analytically confirmed hypovitaminosis. The rate obtained is lower than similar studies conducted with primary care physicians on the treatment of institutionalized elderly patients (94 % began treatment after confirm-

ing hypovitaminosis D vs 83 % in our study) (25) or for the management of COVID-19 (26), but higher than a previous study conducted in Spain (55 % of *n* = 50 primary care physicians) (27).

However, there is a certain percentage of health care professionals who administer treatment in the absence of testing (empirical treatment). This result is similar to the work of Machattou et al. (30 % empirical treatment) (27). In this regard, various medical societies and health organizations already recommend starting vitamin D supplementation without testing in different populations, including the recommendations of the working group of the European Society of Clinical and Economical Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) (28). The underlying reasons for these recommendations are that there is sufficient evidence of the benefits, and this strategy is generally simple, effective, and economical. Examples include supplementation in individuals with insufficient sun exposure, children and adolescents, pregnant and breastfeeding women to meet the recommended daily amounts (28-31). The American Geriatrics Society indicates that 25(OH)D testing before starting treatment is unnecessary in older adults (≥ 65 years), especially if sun exposure is insufficient, as is the case with institutionalized elderly individuals (28,30,32,33). Various national and international societies also state that routine vitamin D screening may be unnecessary in patients with osteoporosis or fragility fractures, who should be prescribed vitamin D (often with calcium) as an adjunct to antiresorptive therapy (28,34). Cholecalciferol is recommended as the molecule of choice in cases where treatment is initiated without 25(OH)D testing (35,36).

Overall, a lack of consensus is evident regarding the threshold value for treating vitamin D deficiency. 47 %, 45 %, and 7 % of specialists consider 25(OH)D levels of 30 ng/mL, 20 ng/mL, and 10 ng/mL, respectively, as the thresholds for initiating treatment.

Heterogeneity in the responses aligns well with the lack of consensus among various organizations and scientific societies, which establish different concentrations for defining deficiency, insufficiency, or optimal vitamin D levels, also depending on the patient's profile (2,18,28,37). Regarding the minimum recommended value, an association has been described between serum 25(OH)D levels, bone mineral density (BMD), and musculoskeletal parameters. Some studies suggest that with levels < 20 ng/mL, there is an increased risk of fractures (28,38,39). Other studies point to 25(OH)D levels > 24 ng/mL to reduce the risk (40,41). From 30 ng/mL, parathyroid hormone (PTH) levels stabilize (42), significantly reducing the risk of falls and fractures (43). Higher levels may be necessary to achieve benefits beyond musculoskeletal health.

The controversy surrounding the definition of vitamin D deficiency and the maximum levels of 25(OH)D is partly due to the reporting of non-standardized results (44). Although it is widely accepted that measuring circulating 25(OH)D is the best indicator of an individual's vitamin D status (45), it is recognized that the 25(OH)D value obtained from a single sample can vary substantially depending on the assay used. Historically, 25(OH)D measurements were performed in research centers using high-pressure liquid chromatography (HPLC) or competitive protein-binding methods. In the 1990s, validated radioimmunoassays and other methods, such as enzyme-linked immunosorbent assay (ELISA) or chemiluminescence, were developed. The recent clinical availability of liquid chromatography-tandem mass spectrometry (LC-MS/MS) and HPLC technologies has improved the performance of 25(OH)D assays (46,47). Various standardization programs have also been developed: vitamin D External Quality Assessment Scheme (DEQAS) (48) or the Vitamin D Standardization Program (VDSP) (44). Despite these efforts, significant variability between and within assays persists to this day.

Of note that a considerable percentage of specialists believe that vitamin D deficiency should only be treated when values fall < 10 ng/mL, a level widely recognized as severe vitamin D deficiency and a patient risk (9,13,49-51).

Similarly, the maximum acceptable 25(OH)D level for considering the risk of adverse effects (e.g., hypercalcemia or hypercalciuria) was established at 50, 60, or 90 ng/mL by 14 %, 30 %, and 50 % of prescribers, respectively. There is also divergence in clinical practice guidelines, going from 50 up to 100 ng/mL, depending on the reference consulted (9,13,36,37,42,49,51,52). Although vitamin D toxicity is rare, it can present with severe hypercalcemia, hypercalciuria, and potential clinical signs, such as confusion, apathy, recurrent vomiting, abdominal pain, polyuria, polydipsia, or dehydration. This is related to excessive long-term vitamin D intake, the use of certain metabolites (as will be discussed later), metabolic pathway dysfunctions of vitamin D, or the presence of a concomitant disease that locally produces $1,25(OH)_2D$ (47). In addition to the described vitamin D toxicity, various clinical trials have shown that the risk of falls or mortality starts to increase moderately when 25(OH)D levels rise > 40-60 ng/mL, similar to what happens in deficiency situations (42,53,54). These observations are commonly referred to as the J or U curve effect and are already noted as non-physiological or "possibly harmful" levels by various national and international societies (13,28).

Both cholecalciferol and calcifediol are commonly used molecules for treating vitamin D deficiency (66 % and 68 % of professionals use them, respectively), with varying doses and regimens; the monthly regimen is the most used (65 %). The preference for the monthly regimen may reflect the dosing indications of national clinical practice guidelines for the treatment of

non-severe vitamin D deficiency (13,51). International clinical practice guidelines tend to recommend weekly treatment more often (11,34,52). However, the variety of reported doses and regimens indicates that physicians may adjust their choice based on the degree of deficiency, following recommendations (12,13,49,51).

It is observed that among specialists who treat suspected vitamin D deficiency without measuring 25(OH)D levels, the use of cholecalciferol is significantly higher than calcifediol ($p < 0.05$), possibly justified by its pharmacokinetic and safety profile. Pharmacokinetic studies have determined that the half-life of cholecalciferol is 60 days, as its lipophilic and fat-soluble nature allows for tissue storage (55-57). This characteristic of cholecalciferol would favor 25(OH)D production from tissue cholecalciferol according to the body's requirements (55).

The conversion rate of cholecalciferol to 25(OH)D follows a non-linear increase, resulting in a plasma 25(OH)D curve that plateaus at levels of approximately 30 to 50 ng/mL (56,59-64). In other words, there is a more significant increase (steeper curve) in serum 25(OH)D in cases of more severe vitamin D deficiency, and a lower conversion rate is observed once 25(OH)D levels approach a certain threshold or in patients with sufficient levels (58,59,61-64). This pharmacokinetic profile also prevents fluctuations in serum 25(OH)D after individual administrations; instead, sustained 25(OH)D levels are achieved over time (60). Overall, the hepatic hydroxylation stage (63,65), along with the non-linear production of 25(OH)D, can prevent an indefinite increase in serum values once under treatment and result in more predictable and stable levels over time at a given target level. In other words, evidence suggests that the efficacy of cholecalciferol supplementation in sufficient patients is physiologically reduced by the body, possibly to prevent overdose and toxicity.

Finally, all specialties consider it necessary to monitor vitamin D levels after starting treatment, generally between 4 and 6 months (71 %). This result is consistent with clinical practice guideline recommendations, which suggest monitoring serum concentrations every 3-4 months (13,14,32). A significant percentage delays this monitoring (6-12 months or does not request follow-up checks: 28 %). According to some clinical practice guidelines, monitoring may be deemed unnecessary in certain populations, as long as treatment is administered within recommended limits (13,32,34,66,67). Cases in which monitoring cannot be performed, medical societies have recommended the use of cholecalciferol (13,32), justified by the metabolism described earlier.

As far as we know, this survey is the first of its size at the national level, and also the first of international scope: these are its main strengths. The study design and sample size have ensured the geographic representativeness of specialists nationwide, as well as of each of the specialties included. However, it also presents limitations, as it did not include other specialties such as pediatrics, nor did it evaluate co-prescription with other treatments.

RECOMMENDATIONS FROM A MULTIDISCIPLINARY PANEL OF EXPERTS

Vitamin D deficiency has been widely linked to bone diseases such as rickets, osteomalacia, osteopenia, or osteoporosis. Various clinical trials evaluating the extra-skeletal effects of vitamin D have shown variable results, which have been associated with the inclusion of patients with sufficient levels. In fact, analyses in deficient patients have shown favorable outcomes in extra-skeletal conditions, such as cardiovascular risk, autoimmune diseases, diabetes, etc. Therefore, it seems generally advisable to maintain adequate vitamin D levels in the population (47).

Based on the results obtained in the present study, as well as the available scientific evidence, the multidisciplinary panel of experts made the following recommendations:

- At a multidisciplinary level, there are high-risk populations for vitamin D deficiency (49), such as people with muscle weakness or at risk of fractures/falls, in whom it would be indicated to determine 25(OH)D levels.
- There are patients who, due to their characteristics and clinical condition, could receive vitamin D treatment without the need for prior determination: limited sun exposure, insufficient vitamin D intake, pigmented skin, children and adolescents, pregnant and lactating women, older adults (≥ 65 years), and the elderly (especially if they are at risk of fractures), institutionalized individuals, subjects at risk of or diagnosed with osteoporosis, especially those receiving anti-osteoporotic treatment and those with fragility fractures, obese patients and those before/after bariatric surgery, malabsorption, and documented hypovitaminosis D, among others.
- Overall, intervals of 25(OH)D can be established to indicate vitamin D deficiency at < 20 ng/mL (< 50 nmol/L), insufficiency at 20-30 ng/mL (50-75 nmol/L), and an optimal range at 30-50 ng/mL (75-125 nmol/L). In any case, the target level may vary depending on the population group and the underlying clinical condition being treated with vitamin D. In the overall population, but especially in high-risk patients such as older adults, postmenopausal women, or patients with bone pathologies such as osteoporosis, it is suggested to maintain 25(OH)D levels above 30 ng/mL to maximize bone health benefits.
- Since mortality risk tends to increase slightly, it does not seem advisable to raise levels > 60 ng/mL.

– In general, either cholecalciferol or calcifediol can be used to treat patients with 25(OH)D deficiency, as both molecules have distinct pharmacokinetic and pharmacodynamic properties.
  • Due to the fact that treatments with cholecalciferol administered daily, weekly, or monthly are equally effective in achieving target serum concentrations, physicians should discuss with their patients which dosage regimen will achieve the best adherence. This equivalence has not been demonstrated for treatments based on calcifediol.
  • Calcitriol and active analogs of vitamin D should be reserved for populations with special pathologies, such as advanced renal failure or secondary hyperparathyroidism.
– If the health care professional decides to monitor 25(OH)D levels, it is recommended to do so 3-4 months after starting treatment and then every 6-12 months. If 25(OH)D levels are not determined or monitored, or if monitoring occurs at intervals > 6 months, treatment with cholecalciferol may be preferable due to its metabolism and plasma profile.
– Monitoring the levels of patients under treatment is advisable in the following situations: symptomatic vitamin D deficiency, use of metabolites other than cholecalciferol (e.g., calcifediol or calcitriol), supplementation in high doses (> 2000 IU/day in patients taking drugs that interfere with the absorption or metabolism of vitamin D or cause side effects), patients with poor adherence to treatment, a history of hypervitaminosis D, hypo- or hypercalcemia or hypercalciuria and hyperphosphatemia, malabsorption syndromes and bariatric surgery, obesity (body mass index > 30 kg/m^2), chronic granulomatous, liver, and renal diseases, metabolic bone diseases, particularly patients on anti-osteoporotic treatments or with a history of falls and fractures, hyperparathyroidism and hyperthyroidism, and patients hypersensitive to vitamin D, among others.
  • To maximize bone health, along with vitamin D supplementation, it is necessary to ensure a daily calcium intake of 1000-1200 mg, especially in patients with osteoporosis or at risk of falls or fractures. We suggest the combined use of calcium and vitamin D as an adjunct therapy to osteoporosis treatments.

CONCLUSION

In conclusion, the number of requests and treatments for vitamin D has increased in recent years. This study highlights the awareness that healthcare professionals already have regarding vitamin D deficiency. In turn, the survey identified some knowledge gaps among physicians and heterogeneity in the management of the deficiency, especially regarding threshold values and treatment monitoring. The results of this study offer insights for the development of national clinical guidelines, with recommendations based on scientific evidence.

ANNEX 1.

SUB-ANALYSIS OF GROUPS BASED ON DEMOGRAPHIC CHARACTERISTICS: AGE, GENDER, CLINICAL PRACTICE SETTING, AND GEOGRAPHICAL LOCATION

Some specialists aged 40 years or older show differences in certain aspects of vitamin D management vs their younger colleagues. In Rheumatology, a significantly higher proportion always measures levels before initiating treatment (94 % ≥ 40 years vs 75 % < 40 years; $p < 0.05$). In Traumatology, establishing 10 ng/mL (17 % ≥ 40 years vs 2 % < 40 years, $p < 0.05$) and 90 ng/mL (48 % ≥ 40 years v. 24 % < 40 years, $p < 0.05$) as cut-off points for treating vitamin D deficiency and a possible occurrence of adverse effects, respectively, is significantly more common.

Regarding the geographical location of health care professionals, of note that certain groups report greater difficulty in requesting 25(OH)D determinations: primary care providers in the northern and southern regions (14 % and 21 %, respectively, have difficulty; $p < 0.05$ vs other regions), as well as trauma specialists in the southern region (15 % have difficulty; $p < 0.05$ vs other regions). Consequently, different specialists perform empirical treatment (in the absence of determination) significantly more frequently: primary care providers in the northern region of Spain (36 % only measure levels on certain occasions), trauma specialists (30 % never), and gynecologists (55 % on certain occasions/never) in the southern region.

There were no statistically or clinically significant differences in other comparisons or categories.

REFERENCES

1. Navarro-Valverde C, Quesada-Gómez J. Deficiencia de vitamina D en España. ¿Realidad o mito? Rev Osteoporos Metab Miner 2014;6:S5-10. DOI: 10.4321/S1889-836X2014000500002
2. Carbonell Abella C. Vitamina D: indicaciones para el cribado y tratamiento. FMC 2019;26(8):441-7.
3. De la Fuente Cadenas J, López Mompó C, López Pavón I, Vedia Urgell C, Granada Ybern ML, Reina Rodríguez D. Adecuación de las solicitudes analíticas de vitamina D en Atención Primaria. Aten Prim Pract 2019;1(2):30-5. DOI: 10.1016/j.appr.2018.11.001
4. Enríquez Gutiérrez E, Sánchez Martín EM, Hernández Arroyo MJ, Díaz Madero AA, Martí Rodríguez C, Eugenio Almeida E. Indicación de la determinación de vitamina D y de la adecuación del tratamiento en función de los resultados. Med Gen Fam 2023;11(6). DOI: 10.24038/mgyf.2022.057
5. Appiah D, Kamrudin S, de Riese C. Factors Associated with Potentially Inappropriate Screening for Vitamin D Deficiency among Women in Medically Underserved Regions of West Texas. J Clin Med 2023;12(3). DOI: 10.3390/jcm12030993
6. Kahwati LC, LeBlanc E, Weber RP, Giger K, Clark R, Suvada K, et al. Screening for Vitamin D Deficiency in Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2021;325(14):1443-63. DOI: 10.1001/jama.2020.26498
7. Sanitarios DGdFyP. Vitamina D: Más allá de la latitud N 37° 51' 57.28"". Información Farmacoterapéutica de la Comunitat Valenciana 2023;8.
8. Cianferotti L, Parri S, Gronchi G, Rizzuti C, Fossi C, Black DM, et al. Changing patterns of prescription in vitamin D supplementation in adults: analysis of a regional dataset. Osteoporos Int 2015;26(11):2695-702. DOI: 10.1007/s00198-015-3187-x
9. Cucalón-Arenal J, Blay-Cortés MG, Zumeta-Fustero J, Blay-Cortés V. Actualización en el tratamiento con colecalciferol en la hipovitaminosis D desde Atención Primaria. MGYF 2019;8(2):68-78. DOI: 10.24038/mgyf.2019.014
10. Society NO. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. Royal Osteoporosis Society; 2018.
11. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int 2014;25(10):2359-81. DOI: 10.1007/s00198-014-2794-2
12. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96(7):1911-30. DOI: 10.1210/jc.2011-0385
13. Casado E QJ, Naves M, Peris P, Jódar E, Giner M, Neyro JL, et al. SEIOMM recommendations on the prevention and treatment of vitamin D deficiency. Rev Osteoporos Metab Miner 2021;13(2):84-97.
14. Dawson-Hughes B, Mithal A, Bonjour JP, Boonen S, Burckhardt P, Fuleihan GE, et al. IOF position statement: vitamin D recommendations for older adults. Osteoporos Int 2010;21(7):1151-4. DOI: 10.1007/s00198-010-1285-3
15. Cavalier E, Delanaye P, Chapelle JP, Souberbielle JC. Vitamin D: current status and perspectives. Clin Chem Lab Med 2009;47(2):120-7. DOI: 10.1515/CCLM.2009.036
16. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006;84(1):18-28. DOI: 10.1093/ajcn/84.1.18
17. Bouillon R, Carmeliet G. Vitamin D insufficiency: Definition, diagnosis and management. Best Pract Res Clin Endocrinol Metab 2018;32(5):669-84. DOI: 10.1016/j.beem.2018.09.014
18. Roth DE, Abrams SA, Aloia J, Bergeron G, Bourassa MW, Brown KH, et al. Global prevalence and disease burden of vitamin D deficiency: a roadmap for action in low- and middle-income countries. Ann N Y Acad Sci 2018;1430(1):44-79. DOI: 10.1111/nyas.13968
19. WMA. WMA Declaration of Helsinki-Ethical principles for medical research involving human subjects. updated 2018 July.
20. Cashman KD. Global differences in vitamin D status and dietary intake: a review of the data. Endocr Connect 2022;11(1). DOI: 10.1530/EC-21-0282
21. Mogire RM, Mutua A, Kimita W, Kamau A, Bejon P, Pettifor JM, et al. Prevalence of vitamin D deficiency in Africa: a systematic review and meta-analysis. Lancet Glob Health 2020;8(1):e134-e42. DOI: 10.1016/S2214-109X(19)30457-7
22. Niedermaier T, Gredner T, Kuznia S, Schottker B, Mons U, Lakerveld J, et al. Vitamin D food fortification in European countries: the underused potential to prevent cancer deaths. Eur J Epidemiol 2022;37(4):309-20. DOI: 10.1007/s10654-022-00867-4
23. Rodd C, Sokoro A, Lix LM, Thorlacius L, Moffatt M, Slater J, et al. Increased rates of 25-hydroxy vitamin D testing: Dissecting a modern epidemic. Clin Biochem 2018;59:56-61. DOI: 10.1016/j.clinbiochem.2018.07.005
24. Felcher AH, Gold R, Mosen DM, Stoneburner AB. Decrease in unnecessary vitamin D testing using clinical decision support tools: making it harder to do the wrong thing. J Am Med Inform Assoc 2017;24(4):776-80. DOI: 10.1093/jamia/ocw182
25. Buckinx F, Reginster JY, Cavalier E, Petermans J, Ricour C, Dardenne C, et al. Determinants of vitamin D supplementation prescription in nursing homes: a survey among general practitioners. Osteoporos Int 2016;27(3):881-6. DOI: 10.1007/s00198-015-3469-3
26. Jude EB, Tentolouris N, Rastogi A, Yap MH, Pedrosa HC, Ling SF. Vitamin D prescribing practices among clinical practitioners during the COVID-19 pandemic. Health Sci Rep 2022;5(4):e691. DOI: 10.1002/hsr2.691
27. Machattou M, Rusinovich Lovgach O, Lledó Delgado A, Molina Esteban N, Sazn Jardón M, Tovar Sugrañes AVE, et al. Encuesta profesional sobre el uso de preparados de vitamina D_3 en clínica en distintos ámbitos asistenciales. XLVIII Congreso Nacional de la Sociedad Española de Reumatología. Granada; 2022.
28. Chevalley T, Brandi ML, Cashman KD, Cavalier E, Harvey NC, Maggi S, et al. Role of vitamin D supplementation in the management of musculoskeletal diseases: update from an European Society of Clinical and Economical Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) working group. Aging Clin Exp Res 2022;34(11):2603-23. DOI: 10.1007/s40520-022-02279-6
29. Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium; Ross AC, Taylor CL, Yaktine AL, del Valle HB; editors. Dietary Reference Intakes for Calcium and Vitamin D. Washington (DC): National Academies Press; 2011.

30. Health UDo. Vitamin D - advice on supplements for at risk groups; 2012.
31. Minisola S, Colangelo L, Pepe J, Occhiuto M, Piazzolla V, Renella M, et al. Vitamin D screening. J Endocrinol Invest 2020;43(8):1047-51. DOI: 10.1007/s40618-020-01220-w
32. American Geriatrics Society Workgroup on Vitamin DSfOA. Recommendations abstracted from the American Geriatrics Society Consensus Statement on vitamin D for Prevention of Falls and Their Consequences. J Am Geriatr Soc 2014;62(1):147-52. DOI: 10.1111/jgs.12631
33. Rolland Y, de Souto Barreto P, Abellan Van Kan G, Annweiler C, Beauchet O, Bischoff-Ferrari H, et al. Vitamin D supplementation in older adults: searching for specific guidelines in nursing homes. J Nutr Health Aging 2013;17(4):402-12. DOI: 10.1007/s12603-013-0007-x
34. Aspray TJ, Bowring C, Fraser W, Gittoes N, Javaid MK, Macdonald H, et al. National Osteoporosis Society vitamin D guideline summary. Age Ageing 2014;43(5):592-5. DOI: 10.1093/ageing/afu093
35. Tarazona-Santabalbina FJ, Cuadra L, Cancio JM, Carbonell FR, Garrote JMP, Casas-Herrero A, et al. Vitamin D supplementation for the prevention and treatment of COVID-19: a position statement from the Spanish Society of Geriatrics and Gerontology. Rev Esp Geriatr Gerontol 2021;56(3):177-82. DOI: 10.1016/j.regg.2021.02.001
36. Pludowski P, Takacs I, Boyanov M, Belaya Z, Diaconu CC, Mokhort T, et al. Clinical Practice in the Prevention, Diagnosis and Treatment of Vitamin D Deficiency: A Central and Eastern European Expert Consensus Statement. Nutrients 2022;14(7):1483. DOI: 10.3390/nu14071483
37. Rockwell M, Kraak V, Hulver M, Epling J. Clinical Management of Low Vitamin D: A Scoping Review of Physicians' Practices. Nutrients 2018;10(4). DOI: 10.3390/nu10040493
38. Holvik K, Gjesdal CG, Tell GS, Grimnes G, Schei B, Apalset EM, et al. Low serum concentrations of alpha-tocopherol are associated with increased risk of hip fracture. A NOREPOS study. Osteoporos Int 2014;25(11):2545-54. DOI: 10.1007/s00198-014-2802-6
39. Feng Y, Cheng G, Wang H, Chen B. The associations between serum 25-hydroxyvitamin D level and the risk of total fracture and hip fracture. Osteoporos Int 2017;28(5):1641-52. DOI: 10.1007/s00198-017-3955-x
40. Bischoff-Ferrari HA. Relevance of vitamin D in fall prevention. Geriatr Psychol Neuropsychiatr Vieil 2017;15(1):E1-7. DOI: 10.1684/pnv.2017.0650
41. Lv QB, Gao X, Liu X, Shao ZX, Xu QH, Tang L, et al. The serum 25-hydroxyvitamin D levels and hip fracture risk: a meta-analysis of prospective cohort studies. Oncotarget 2017;8(24):39849-58.
42. Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord 2017;18(2):153-65.
43. Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Hathcock J, Giovannucci E, Willett WC. Benefit-risk assessment of vitamin D supplementation. Osteoporos Int 2010;21(7):1121-32.
44. Sempos CT, Heijboer AC, Bikle DD, Bollerslev J, Bouillon R, Brannon PM, et al. Vitamin D assays and the definition of hypovitaminosis D: results from the First International Conference on Controversies in Vitamin D. Br J Clin Pharmacol 2018.
45. Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the institute of medicine: What clinicians need to know. J Clin Endocrinol Metab 2011;96(1):53-8.
46. Lensmeyer GL, Wiebe DA, Binkley N, Drezner MK. HPLC method for 25-hydroxyvitamin D measurement: comparison with contemporary assays. Clin Chem 2006;52(6):1120-6.
47. Giustina A, Bilezikian JP, Adler RA, Banfi G, Bikle DD, Binkley NC, et al. Consensus Statement on Vitamin D Status Assessment and Supplementation: Whys, Whens, and Hows. Endocr Rev 2024. DOI: 10.1210/endrev/bnae009
48. Carter GD, Berry J, Durazo-Arvizu R, Gunter E, Jones G, Jones J, et al. Hydroxyvitamin D assays: An historical perspective from DEQAS. J Steroid Biochem Mol Biol 2018;177:30-5.
49. Bleizgys A. Vitamin D Dosing: Basic Principles and a Brief Algorithm (2021 Update). Nutrients 2021;13(12).
50. Giustina A, Bouillon R, Dawson-Hughes B, Ebeling PR, Lazaretti-Castro M, Lips P, et al. Vitamin D in the older population: a consensus statement. Endocrine 2023;79(1):31-44.
51. Presa Lorite JC GAP, Martínez Medina M, Baró Mariné F, Fasero Laiz M, González Béjar M, González Rodríguez SP, et al. MenoGuía AEEM, segunda edición. Osteoporosis 2022.
52. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis- 2020 Update Executive Summary. Endocr Pract 2020;26(5):564-70.
53. Dawson-Hughes B, Wang J, Barger K, Bischoff-Ferrari HA, Sempos CT, Durazo-Arvizu RA, et al. Intra-trial Mean 25(OH)D and PTH Levels and Risk of Falling in Older Men and Women in the Boston STOP IT Trial. J Clin Endocrinol Metab 2022;107(5):e1932-e7.
54. Kojima G, Iliffe S, Tanabe M. Vitamin D supplementation as a potential cause of U-shaped associations between vitamin D levels and negative health outcomes: a decision tree analysis for risk of frailty. BMC Geriatr 2017;17(1):236.
55. Vieth R. Vitamin D supplementation: cholecalciferol, calcifediol, and calcitriol. Eur J Clin Nutr 2020;74(11):1493-7.
56. Jones G. Pharmacokinetics of vitamin D toxicity. Am J Clin Nutr. 2008;88(2):582S-6S.
57. Bilezikian JP, Formenti AM, Adler RA, Binkley N, Bouillon R, Lazaretti-Castro M, et al. Vitamin D: Dosing, levels, form, and route of administration: Does one approach fit all? Rev Endocr Metab Disord 2021;22(4):1201-18.
58. Fassio A, Adami G, Rossini M, Giollo A, Caimmi C, Bixio R, et al. Pharmacokinetics of Oral Cholecalciferol in Healthy Subjects with Vitamin D Deficiency: A Randomized Open-Label Study. Nutrients 2020;12(6).
59. Navarro Valverde C QGJ. Deficiencia de vitamina D en España. ¿Realidad o mito? Rev Osteoporos Metab Miner 2014;6:S5-10.
60. Charoenngam N, Kalajian TA, Shirvani A, Yoon GH, Desai S, McCarthy A, et al. A pilot-randomized, double-blind crossover trial to evaluate the pharmacokinetics of orally administered 25-hydroxyvitamin D3 and vitamin D3 in healthy adults with differing BMI and in adults with intestinal malabsorption. Am J Clin Nutr 2021;114(3):1189-99.
61. Jetter A, Egli A, Dawson-Hughes B, Staehelin HB, Stoecklin E, Goessl R, et al. Pharmacokinetics of oral vitamin D(3) and calcifediol. Bone 2014;59:14-9.
62. Bischoff-Ferrari HA, Dawson-Hughes B, Stocklin E, Sidelnikov E, Willett WC, Edel JO, et al. Oral supplementation with 25(OH)D3 versus vitamin D3: effects on 25(OH)D levels, lower extremity function, blood pressure, and markers of innate immunity. J Bone Miner Res 2012;27(1):160-9.

63. Quesada-Gómez JM, Bouillon R. Is calcifediol better than cholecalciferol for vitamin D supplementation? Osteoporos Int 2018;29(8):1697-711.
64. Gallagher JC, Sai A, Templin T, 2nd, Smith L. Dose response to vitamin D supplementation in postmenopausal women: a randomized trial. Ann Intern Med 2012;156(6):425-37.
65. Hall J. Parathyroid Hormone, Calcitonin, Calcium and Phosphate Metabolism, Vitamin D, Bone, and Teeth. In: Guyton and Hall Textbook of Medical Physiology. 14th edition. Elsevier; 2020.
66. Committee GPA. Vitamin D Testing. BCGuidelines.ca; 2019.
67. Committee AP. Treatment of Vitamin D Deficiency in Adults; 2020.