PROGETTO ALIMENTAZIONE E VITAMINA D

Roma - Hotel Mediterraneo via Cavour 5

27 maggio 2022

Responsabile Scientifico: Professor R. Nuti

Board: I. Chiodini, A. Falchetti, B. Frediani, A. Gaudio, L. Gennari, S. Giannini, A. Giusti, S. Gonnelli, G. Iolascon, G. Letizia Mauro, M. Mazzantini, S. Migliaccio, A. Migliore, G. Minisola, S. Minisola, M. Rossini, F. Silveri, F. Vescini

Utilità del dosaggio del 25OHD

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OUTLINE

- **Assessment of vitamin D status and related limitations**

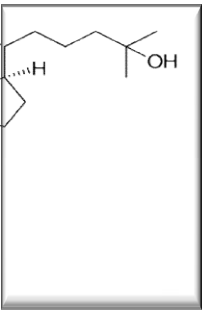
- **Measurement of 25OH vitamin D levels**

  - Patient Settings:
    - *General population*
    - *Istitutionalized patients*
    - *Before Antiresorptive/Osteoanabolic treatment*

- SIOMMMS Guidelines
- Indications from Nota 96

DETERMINATION OF VITAMIN D STATUS

Serum $1,25(OH)_2D$

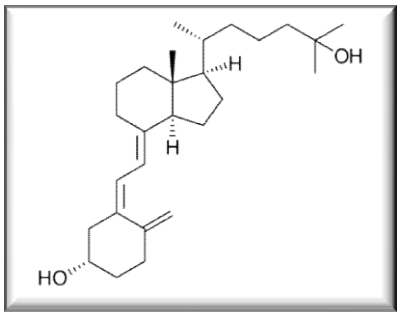


- tightly regulated by PTH
- *Normal level may be maintained even in the setting of hypocalcemia*
- *Short Half-Life (4-6 hours)*

urement of 1,25(OH)2D may be useful in
d and inherited disorders in the
lism of 25(OH)D and phosphate, including:

ronic kidney disease
reditary phosphate-losing disorders
cogenic osteomalacia
eudovitamin D-deficiency rickets
amin D-resistant rickets
ronic granuloma forming
g. sarcoidosis and some lymphomas)

Serum 25(OH) D



- *Long Half-Life (2-3 week*

➢ Serum concentration of **25(OH)D**, the main circulating metabolite of vitamin D, has bee accepted since 1997 by the Panel on Calciu and Related Nutrients of the Food and Nutrition Board (IOM–NAS) **as** **the correct functional indicator of vitamin D status**

IOM=Institute of Medicine; NAS=National Academy of Sciences

Adapted from Lips P. In: *Advances in Nutritional Research*, Vol 9. New York: Plenum Press, 1994:151–165; Webb AR et a 1990;51:1075–1081; Lips P *Endocr Rev* 2001;22:477–501; Boonen S et al *Osteoporos Int* 2004;15:511–519; *Dietary Refe Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: Institute of Medicine, National Academy Pre

Holick MF et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline J Clin Endocrinol Metab 2011:96(7):1911–1930

DOCRINE SOCIETY | THE AMERICAN GERIATRICS SOCIETY | NATIONAL OSTEOPOROSIS FOUNDATION | SIOMMMS | IOF International Osteoporosis Foundation | AACE

25(OH)D (ng/mL)	25(OH)D (nmol/L)	
<20	<50	Deficiency
20-30	50-75	Insufficiency
30-100	75-250	Sufficiency
>100	>250	Excess
>150	>375	Toxicity

Reference Intakes for Calcium and Vitamin D

November 30, 2010

INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMIES

als were at risk of **vitamin D deficiency** when their serum levels were less than **12 ng/mL (30 nmol/L)**.

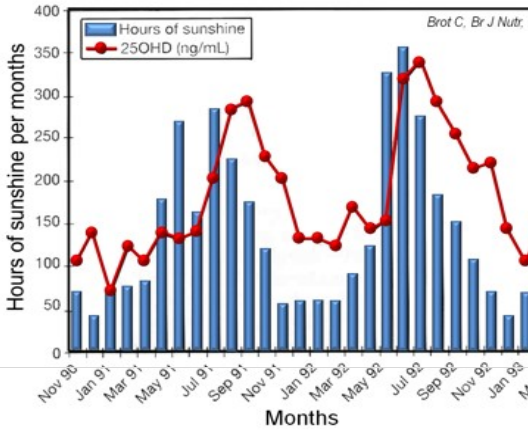
-but not all—individuals were at risk of **vitamin D uacy** when their serum 25OHD levels were **between 12 ng/mL** (30–50 nmol/L).

lly all individuals were **vitamin D replete when their 25OHD levels were 20 ng/mL or greater** (50 nmol/L).

Dietary reference intakes for calcium and vitamin D. In: Washington, DC: The National Academies Press 2011

Challenges and limitations of measuring 25OHD and establishing a threshold for Vitamin D sufficie

- Variations in calcium Intake
- Duration of 25OHD depletion
- Racial and Ethnic differences
- Seasonal variation in 25OHD levels



- Differences in 25OHD Assays (*substantial variability*)
- Differences in Study Design *(cross-sectional, statistical approa*

- **GOLD STANDARD TECHNIQUE**: Liquid Chromatography T Mass Spectrometry
  - **DEQAS** (Vitamin D External Quality Assessment Scheme)
  - **VDSP** (Vitamin D Standardization Program)

MEASUREMENT OF VITAMIN D LEVELS

Should the biochemical assessment of serum 25(OH)D levels be done in the **general population**?

Should the biochemical assessment of serum 25(OH)D levels be done in the **population at risk of hypovitaminosis D**?

Is baseline serum 25(OH)D testing necessary in subjects candidates for **pharmacological treatment for osteoporosis**?

ng requests for vitamin D measurement: costly, ng, and without credibility

	Why important for vitamin D?	Examples
ng l g	Many risk factors are related to both low 25OHD and poor health outcomes; statistical models might be incomplete if such factors are not measured, or measured imprecisely	Little physical activity (outdoor activity often related to sunlight exposure); low socioeconomic status; obesity; smoking; season
sality	Sunlight exposure is a major determinant of circulating-25OHD concentrations; pain or illness can limit sunlight exposure through inactivity, and thus disease could cause inadequacy rather than the reverse	Clinical diagnosis of many disorders (eg, multiple sclerosis) can be preceded by a period of preclinical disease when little time is spent outdoors; acute inflammation can drive down circulating 25OHD concentrations so that in acute illnesses or many hospitalised patients, low measurements are secondary to an acute-phase response
and s	Null or negative findings are less likely to be published, especially when overwhelming perception is of a positive association; thus, investigators are less likely to pursue publication or persist after manuscript rejection than if results were positive; null findings that are published are not frequently cited and result in little media interest, and therefore perception of the weight of evidence can be heavily skewed	Marniemi and colleagues' 2005 report[8] of no association of 25OHD with 130 cases of myocardial infarction in elderly people has been cited 33* times in Web of Science; by contrast, Wang and co-workers' 2008 article[9] reporting 25OHD inadequacy associated with 120 cases of cardiovascular disease in Framingham offspring has been cited 409* times

m 25-hydroxyvitamin D. *As of Nov 28, 2011.

tial limitations in making causal inferences from observational epidemiology for vitamin D

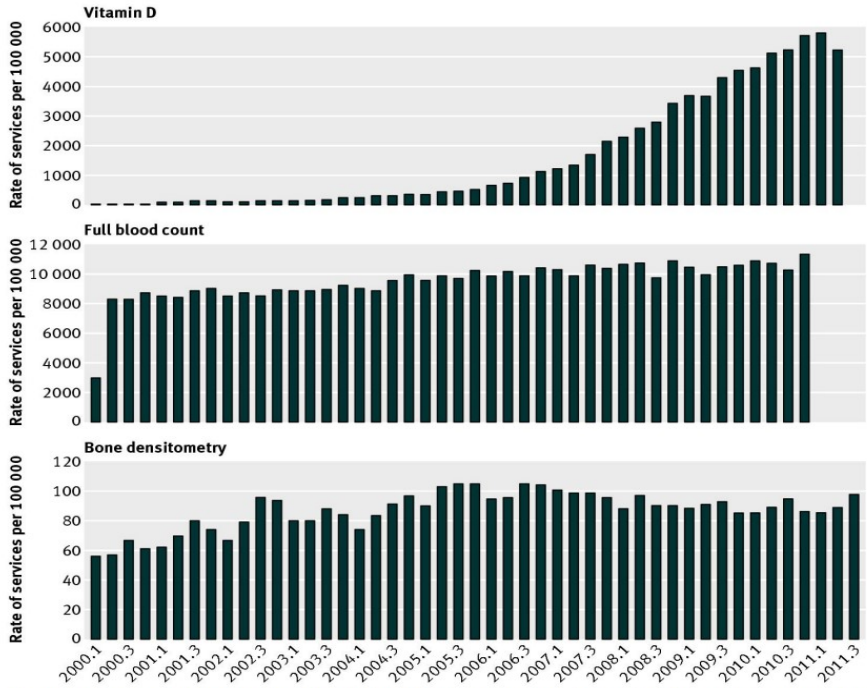
Sattar N, Welsh P, Panarelli M, Forouhi NG. Lancet 2012;379:95–6

BMJ

PREVENTING OVERDIAGNOSIS

The rise and rise of vitamin D testir

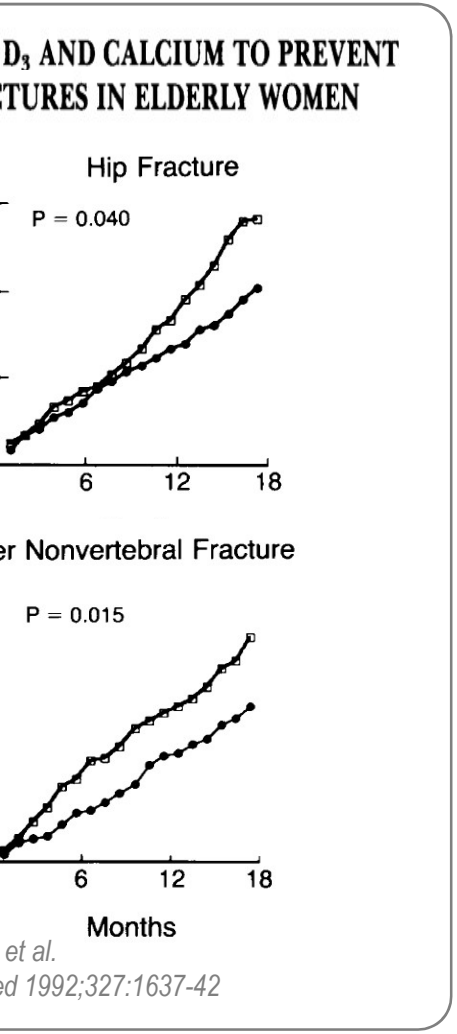
Similar concerns exist for overdiagnosis and overtreatment of vitamin D deficiency.[2 3] Currently, the appropriate timing and frequency of testing for the diagnosis of vitamin D deficiency is unclear. The cost of testing in Australia increased from $A1m (£0.66m; €0.83m; $1m) in 2000 to $95.6m in 2010, on average 59% each year.[2] Similarly, in Ontario, Canada, testing increased 25-fold from 2004 to 2010. Projections suggest that $C150m (£95m; €120m; $147m) will be spent on vitamin D testing in 2012, up from $38m in 2009.[4] Similarly, the UK has seen a sixfold increase in such tests between 2007 and 2010.[5]



Requests per 100 000 for vitamin D, full blood count, and bone densitometry between 2000 and 20

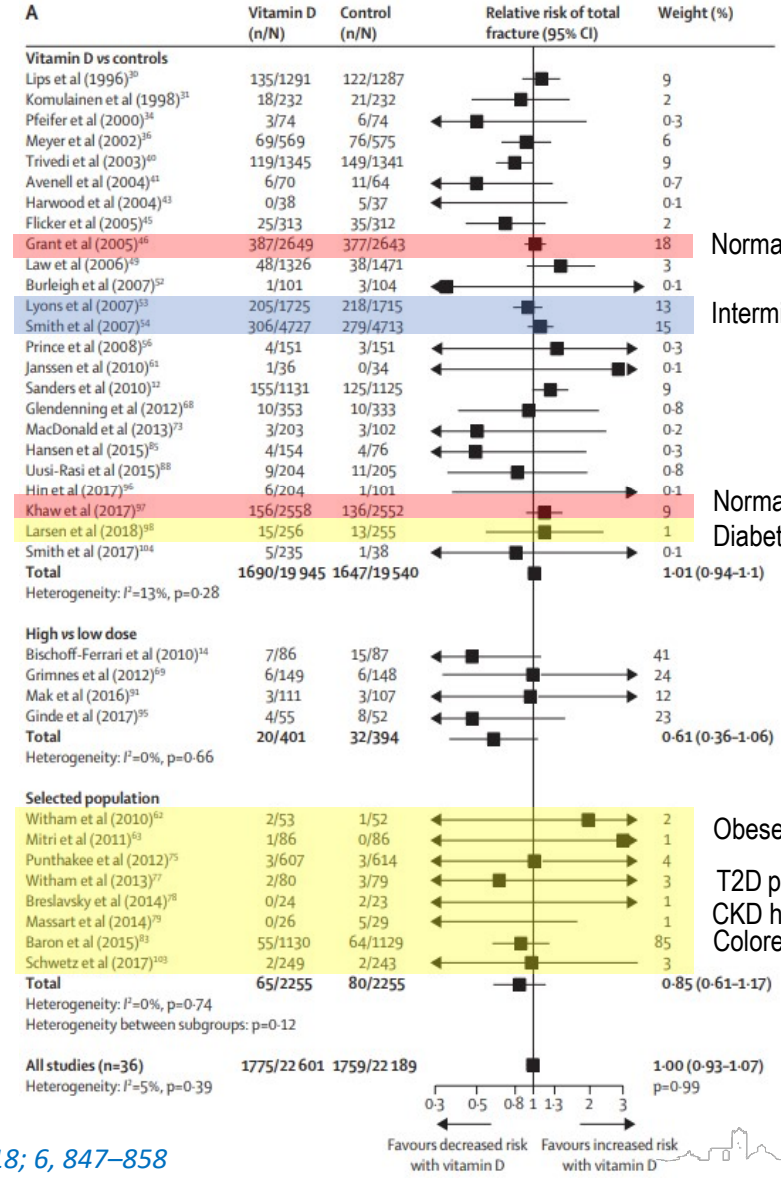
Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis

Mark J Bolland, Andrew Grey, Alison Avenell



	All trials (n=81)
Population unselected for underlying illness	61 (75%)
Treatment studied	
Vitamin D *vs* controls	39 (48%)
Vitamin D with agent *vs* agent	26 (32%)
Calcium	20 (25%)
Exercise	2 (2%)
Calcium and exercise	1 (1%)
Other	3 (4%)
High-dose *vs* low-dose vitamin D	16 (20%)
Vitamin D dose >800 IU per day	55 (68%)
Frequency of vitamin D dose	
Daily	44 (54%)
Intermittent	36 (44%)
Mixed	1 (1%)
Trial duration ≤1 year	55 (68%)
>200 participants	39 (48%)
Community-dwelling participants	69 (85%)
Majority of participants female	62 (77%)
Baseline mean age <65 years	33 (41%)
Baseline mean BMI <30 kg/m²	58 (72%)
Baseline 25-hydroxyvitamin D concentration	
<25 nmol/L	4/72 (6%)
<50 nmol/L	41/72 (57%)
<75 nmol/L	71/72 (99%)
Achieved 25-hydroxyvitamin D concentration	
≥50 nmol/L	69/76 (91%)
≥75 nmol/L	44/76 (58%)
Outcome data	
Fracture	42 (52%)
Falls	37 (46%)
Bone mineral density	41 (51%)

Data are n (%) or n/N (%), since some characteristics were not reported in all trials. See appendix (pp 4–9) for full details of trial characteristics.



Bolland MJ et al. Lancet Diabetes Endocrinol 2018; 6, 847–858

NATURE REVIEWS | RHEUMATOLOGY

NEWS & VIEWS

BONE

Falls, fractures and vitamin D: a never-ending story?

Iacopo Chiodini and Luigi Gennari

Vitamin D is important for skeletal metabolism and calcium homeostasis, but conflicting evidence exists as to whether vitamin D supplementation has a protective effect on musculoskeletal outcomes. Do the results of a new meta-analysis bring clarity or increase confusion?

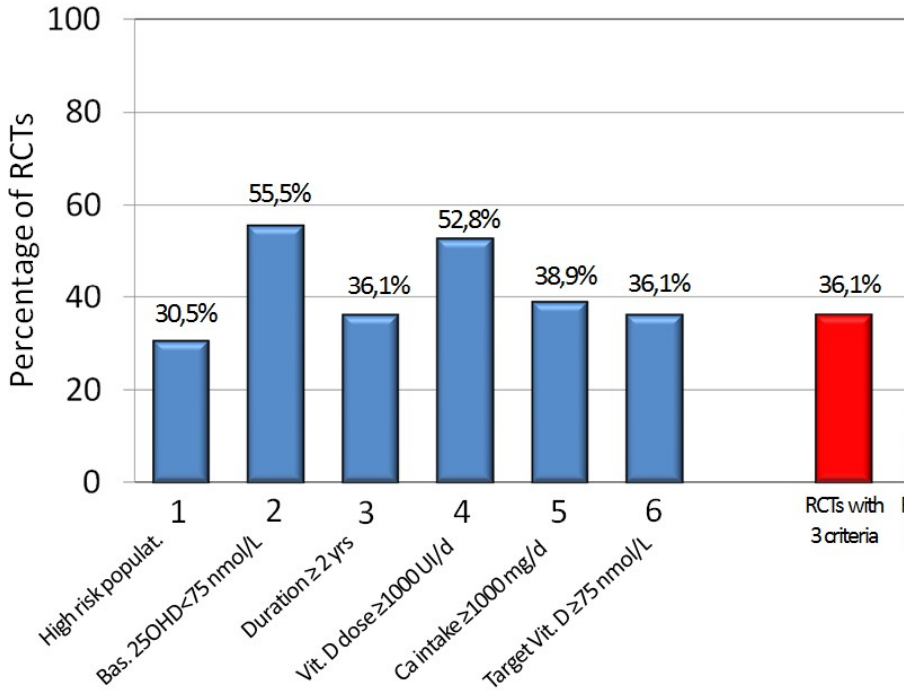
Refers to Bolland, M. J. et al. Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analyses, and trial-sequential analyses. *Lancet Diabetes Endocrinol.* **6**, 847–858 (2018).

Box 1 | **Proposed recommendations for vitamin D trials on musculoskeletal outcomes**

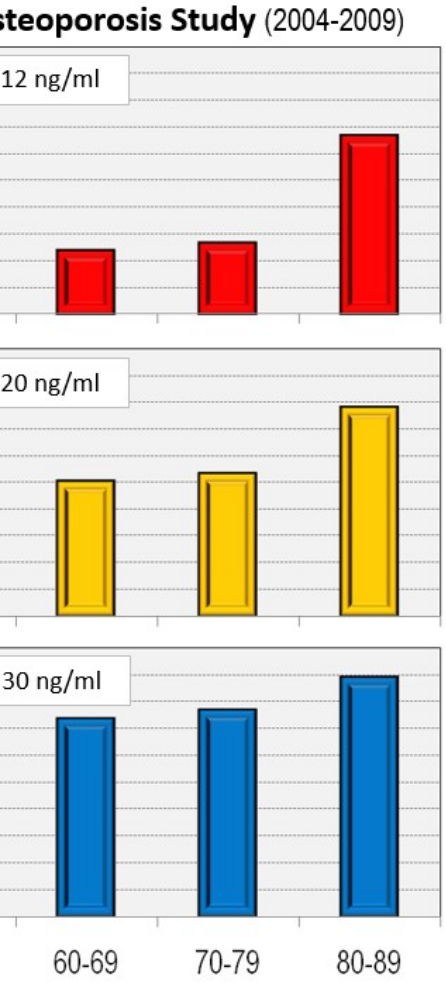
The usefulness of data from trials of vitamin D supplementation for musculoskeletal outcomes could be improved by adhering to the following proposed recommendations:

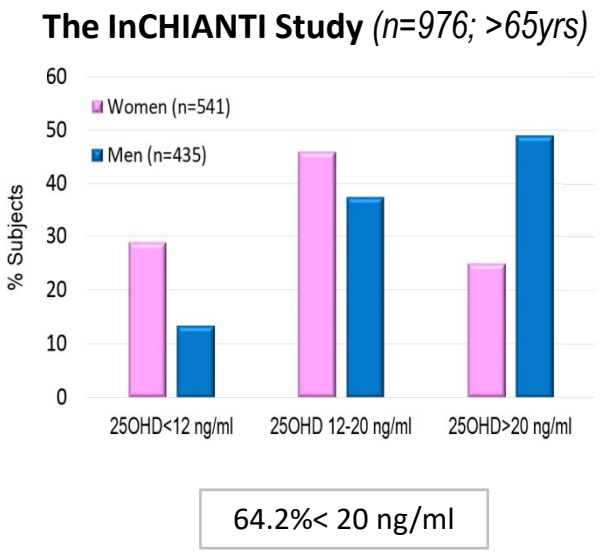
- the inclusion of patients from high-risk populations (such as patients who have become institutionalized or individuals with a bone mineral density (BMD) within the osteopenic range);
- the inclusion of patients with a baseline 25-hydroxyvitamin D (25(OH)D) concentration of <75 nmol/l;
- the use of cholecalciferol doses equivalent to ≥1,000 IU per day (either daily or monthly regimens[a]);
- the use of calcium supplements for individuals with a calcium intake ≤1,000 mg per day;
- a target 25(OH)D concentration of ≥75 nmol/l for the duration of the study;
- a study duration of ≥2 years for the evaluation of BMD and fractures;
- the registration of all major comorbidities.

[a]Depending on the baseline 25(OH)D concentration, consider using a cumulative high dose to rapidly achieve a healthy vitamin D status (≥75 nmol/l) during the entry phase of the study.



1. Should serum 25OHD assessment be done in the general population?





64.2%< 20 ng/ml

- as recently outlined by an update report and systematic review for t US Preventive Services Task Force study published to date evaluated the efficacy and safety of vitamin supplementation according to a randomization performed on screening versus non-screening fo vitamin D deficiency

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Vitamin D Deficiency in Adults

US Preventive Services Task Force Recommendation Statement

min D is a fat-soluble vitamin that performs an important role in calcium one metabolism and also affects many other cellular regulatory functions al system. Vitamin D requirements may vary by individual; thus, no one evel cutpoint defines deficiency, and no consensus exists regarding the els of vitamin D that represent optimal health or sufficiency.

ate its 2014 recommendation, the US Preventive Services Task Force sioned a systematic review on screening for vitamin D deficiency, including arms of screening and early treatment.

munity-dwelling, nonpregnant adults who have no signs or symptoms of cy or conditions for which vitamin D treatment is recommended.

MENT The USPSTF concludes that the overall evidence on the benefits of min D deficiency is lacking. Therefore, the balance of benefits and harms of min D deficiency in asymptomatic adults cannot be determined.

N The USPSTF concludes that the current evidence is insufficient to assess nefits and harms of screening for vitamin D deficiency in asymptomatic nt)

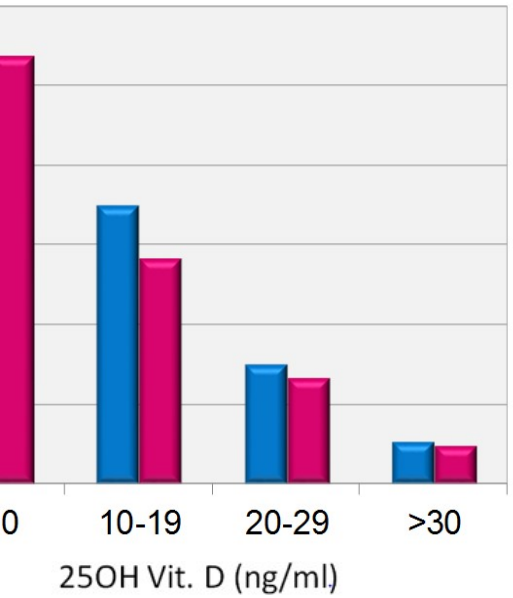
436-1442. doi:10.1001/jama.2021.3069

Figure. Clinician Summary: Screening for Vitamin D Deficiency in Adults

What does the USPSTF recommend?	**For asymptomatic, community-dwelling, nonpregnant adults:** The USPSTF found that the **evidence is insufficient** to assess the balance of benefits and harms of screening for vit deficiency. More research is needed. **I statement**
To whom does this recommendation apply?	Community-dwelling, nonpregnant adults who have no signs or symptoms of vitamin D deficiency or conditions fo vitamin D treatment is recommended. It does not apply to persons who are hospitalized or living in institutions such as nursing homes.
What's new?	This recommendation is consistent with the 2014 USPSTF statement.
How to implement this recommendation?	There is insufficient evidence to recommend for or against screening for vitamin D deficiency.
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org) to read the full recommendation state This includes more details on the rationale of the recommendation, including benefits and harms; supporting evide and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but in decision-making to the specific patient or situation.

uld serum 25OHD assessment be done in the population at risk of hypovitamino

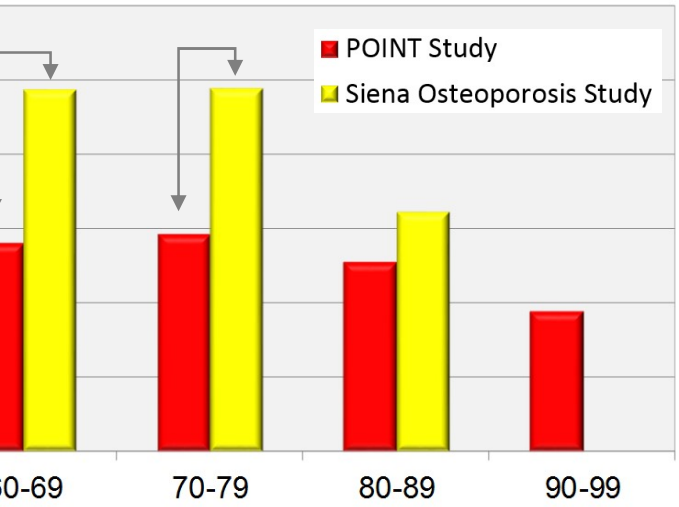


POINT Study

<20 ng/ml

Males 79.8% *(88.7% in winter)*

Females 81.9% *(87.3% in winter)*



SIOMMMS Società Italiana dell'Osteoporosi del Metabolismo Minerale e delle Malattie dello Scheletro

Populations/conditions at risk of hypovitaminosi

- **Old people** *(≥ 75 yrs)*
- **Institutionalized pts** or conditions associated with inadequate solar exposu
- **Obesity**
- **Pregnancy** and breastfeeding
- **Metabolic bone diseases** and other skeletal disorders
- Vegan diet
- Nervous anorexia
- **Chronic renal failure**
- Cancer (in particular breast, prostate, and colon)
- **Type 2 diabetes mellitus**
- **Intestinal malabsorption** and bariatric surgery
- **Drugs** that interfere with the absorption or hepatic metabolism of vita (antiepileptics, glucocorticoids, antiviral AIDS, antifungal agents, cholestyra
- Cystic fibrosis

uld serum 25OHD assessment be done in the population at risk of hypovitamino

A. *Is there any direct evidence that basal 25(OH)D levels represent an essential parameter for prescribing vitamin D supplementation?*

B. *In a population at risk of hypovitaminosis D is there evidence that the a basal 25(OH)D measurement may contribute in preventing potential toxicity?*

C. *In a population at risk of hypovitaminosis D, is baseline 25(OH)D measurement cost-effective?*

uld serum 25OHD assessment be done in the population at risk of hypovitamino

- Theoretically, the **goal of 25(OH)D testing** should be to facilitate the normalization of 25(OH)D levels, with potential skeletal, muscular or extra-skeletal benefits.

- Although the majority guidelines consider the measurement of serum 25(OH)D levels as highly recommendable, at least in subjects defined at risk of hypovitaminosis D, **there is no direct evidence supporting a clear advantage** in performing an assessment of the basal vitamin D status

(2014) 53:367–374
07/s00394-013-0634-3

REVIEW

min D supplementation, body weight and human serum droxyvitamin D response: a systematic review

Zittermann · Jana B. Ernst · Gummert · Jochen Börgermann

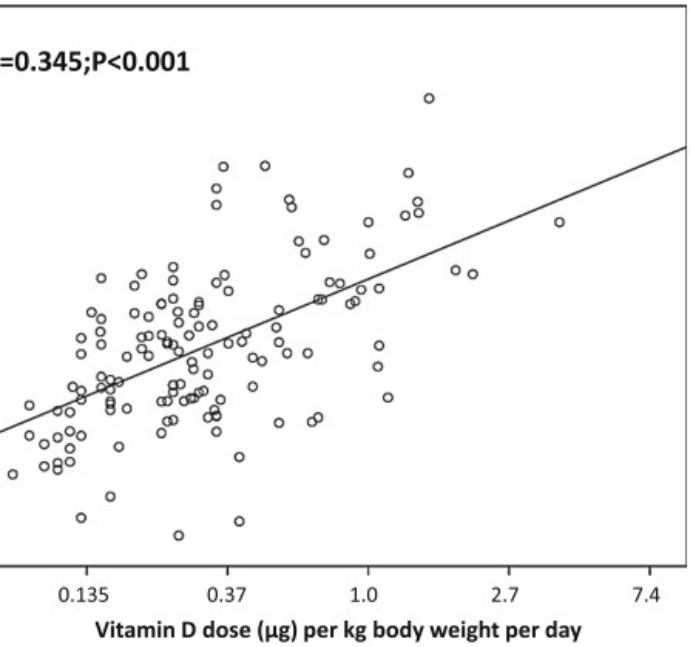


Table 2 Determinants of change in circulating 25-hydroxyvitamin D (in nmol/l) in 144 cohorts on vitamin D

Variables	Regression coefficient	95 % confidence interval		*P* value
		Lower bound	Upper bound	
Intercept	49.4	42.5	56.2	<0.001
Ln dose in µg/kg body weight/day	16.03	13.3	18.8	<0.001
Age (years)	0.22	0.12	0.31	<0.001
Type of supplement				
D_2	−20.19	−26.4	−14.0	
D_3	Ref.			<0.001
Calcium supplements				
No	Ref.			
Yes	−6.34	−10.9	−1.75	0.007
Baseline 25OHD (per nmol/l)	−0.13	−0.23	−0.03	0.012

Variables included in analysis: age, ethnicity, diseases, Ln vitamin D dose, frequency and duration of intake, type of vitamin D supplement, method of 25OHD measurement, baseline 25OHD level, co-administration of calcium supplement or other nutrients and vitamin D producer

Table 3 Calculated daily vitamin D_3 dose for achie D-deficient individuals a target 25-hydroxyvitami 50 nmol/l and 75 nmol/l, respectively

	30-year-old person	70-y
Baseline 25OHD level 25 nmol/l; target 25OHD leve		
50 kg body weight	9 µg (360 IU)	5
75 kg body weight	13.5 µg (540 IU)	7.7
100 kg body weight	18 µg (720 IU)	10
Baseline 25OHD level 25 nmol/l; target 25OHD leve		
50 kg body weight	42 µg (1,680 IU)	24
75 kg body weight	63 µg (2,520 IU)	36.5
100 kg body weight	84 µg (3,360 IU)	49

IU international unit

Zittermann A, Ernst JB, Gummert JF, Börgermann J. Vitamin D supplementation, body weight and human serum 25-hydroxyvitamin D response: a systematic review. Eur J Nutr 2014;53:367–74.

Serum 25(OH)D response to vitamin D_3 supplementation: A meta-regression analysis

analysis for DM from baseline of serum 25(OH)D

	DM	95% CI	*P*-value
D dose (IU/d)			
	32.5	28.1–37	<0.001
	39.3	42.4–57.4	
	34.2	32.6–43.2	
n (mo)			
	25.6	18.1–33.1	<0.001
	41.7	33.8–49.5	
	39.5	36.5–52.5	
serum 25(OH)D (nmol/L)			
mol/L	39.6	34.0–45.2	<0.001
mol/L	30.8	25.6–36	
	28.4	23.6–33.2	<0.001
	35.5	28.1–51	
	40.5	32–49	

ence interval

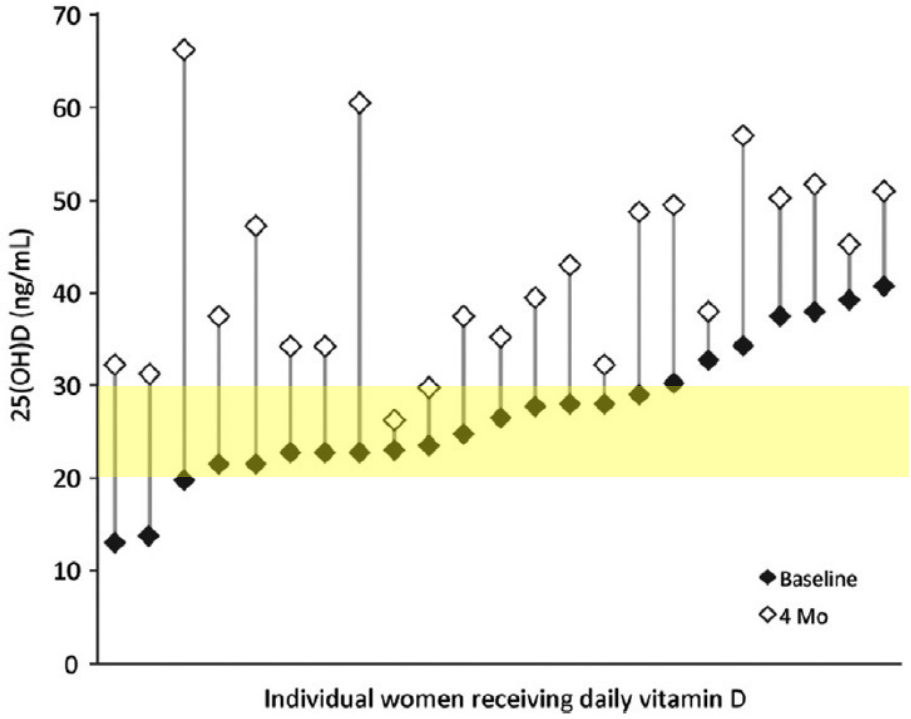
Summary of meta-regression analysis between PMD and dose, duration 25(OH)D and age

	Slope	(95% CI)
Dose (IU/d)	0.006	0.005–0.007
Duration (mo)	0.21	0.14–0.27
Baseline 25(OH)D (nmol/L)	−0.19	−0.21 to −0.18
Age (y)	0.42	0.40–0.46

Bidar S, et al. Nutrition 2014;30:975–85

Variable response to vitamin D supplementation

(Increases in 25OHD following 2300 IU vitamin D daily for 4 months)



Is repeating 25OHD measurement at 4-6 months after starting vitamin D supplementation a reasonable approach?

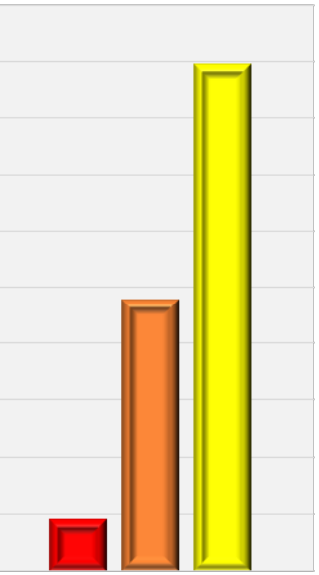
➢ Some patients experience little or no increase in serum 25OHD even following what is generaly considered a high dose vitamin D-supplementation.

kley N and Carter DG. Endocrinol Metab Clin N Am 2017;46:885–899

Preoperative severe vitamin D deficiency is a significant independent risk factor for poorer functional outcome and quality of life after surgery for hip fractures

N= 664 pts

Age (77±9 yrs)



Variable		6 months Mean	6 months Std. deviation	6 months One-way ANOVA p-value	Baseline Mean	Baseline Std. deviation	Baseline One-way ANOVA *p*-value
Parker Mobility Score	Normal	4.15	2.841	.003	6.26	2.842	.002
	Insufficiency	4.63	2.650		6.67	2.555	
	Deficient	4.50	2.583		6.47	2.609	
	Severe deficiency	3.17	2.307		5.27	2.510	
	Total	4.41	2.642		6.42	2.625	
Harris Hip Score	Normal	72.96	17.155	.181	Not available		
	Insufficiency	75.70	14.394				
	Deficient	76.01	14.734				
	Severe deficiency	71.59	14.616				
	Total	75.19	14.881				
SF36 PF	Normal	35.63	33.040	.047	51.23	30.370	.014
	Insufficiency	35.95	29.214		54.48	30.731	
	Deficient	35.67	28.362		52.76	30.378	
	Severe deficiency	23.73	27.474		40.33	32.402	
	Total	34.79	29.289		52.20	30.888	

	Regression estimate (95% confidence interval) Parker Mobility Score	*p*-value	Regression estimate (95% confidence interval) SF36 Physical Functioning	*p*-value
Preoperative serum total 25-hydroxyvitamin D (severe vitamin D deficiency as reference)				
Normal vitamin D	1.05 (0.16 to 1.94)	.021	12.85 (2.72 to 22.97)	.013
Vitamin D insufficiency	1.25 (0.52 to 1.98)	.001	10.07 (1.78 to 18.35)	.017
Vitamin D mild deficiency	1.15 (0.42 to 1.89)	.002	10.23 (−1.90 to 18.56)	.016
Age	−0.10 (−0.12 to −0.08)	<.002	−1.06 (−1.30 to -0.83)	<.001

Sim DS et al. Osteoporos Int 2021;32:2217–2224

3. Is baseline 25OHD assessment necessary in patients candidates for pharmacological treatment for osteoporosis ?

Indeed, the **verification of the achievement of ”optimal” 25(OH)D levels** before the start of anti-fracture therapy, where standard doses are used, **might have some benefit for the effectiveness of the therapy itself and eventually prevent possible complications** (i.e. hypocalcemia and, in case of intravenous regimens of bisphosphonates acute phase reaction).

However, the cost-effectiveness of this approach remains to be demonstrated. Similar indications can be drawn in case of bone antiresorptive or anabolic treatment for other skeletal diseases.

e 25(OH)D level needed to maintain a favorable phosphonate response is ≥33 ng/ml

of non-response to bisphosphonate therapy was
EUROFORS study, which identified patients for
erapy after "failing" anti-resorptive agents (me-
of bisphosphonate treatment was 36 months)
onse included any of the following:

f<−3.0 at the lumbar spine, femoral neck, total
ochanter despite >24 months of bisphosphonate

of >3.0% in BMD at the lumbar spine, bilat-
oral neck, total hip, or trochanter between the
and follow-up DEXA scans

low-trauma fracture despite >12 months of
honate therapy

S, et al. Osteoporos Int 2012;23:2479–87.

Table 3 Predictive performance for response of various vitamin D cut points

	N (Ref/Exp)[a]	Odds ratio	95% CI	*P* value
Unadjusted models				
25(OH)D (ng/ml)				
≥20	26/184	1.81	0.77–4.27	0.18
≥30	66/144	5.35	2.72–10.53	<0.0001
≥33	85/125	5.06	2.74–9.32	<0.0001
≥40	134/76	3.65	2.02–6.62	<0.0001
Adjusted models[b]				
25(OH)D (ng/ml)				
≥20	26/184	1.001	0.35–2.83	0.999
≥30	66/144	4.45	1.98–9.99	0.0003
≥33	85/125	4.53	2.17–9.48	<0.0001
≥40	134/76	4.32	1.96–9.52	0.003

P values in reference to OR=1

CI confidence interval

[a] The 25 (OH)D levels were selected based on their frequent use as clinically relevant cut points.

Comparisons were made as follows: <20 vs. ≥20, <30 vs. ≥30, <33 vs. ≥33, and <40 vs. ≥40. Thus, each level of 25(OH)D uses all the subjects with lower values (reference [ref]) vs. those at and above the cutoff value (experimental [exp])

[b] Adjusted for age, BMI, race, baseline T-score at the lumbar spine, oral bisphosphonate vs. iv-zoledronate, concurrent calcium supplementation, history of SERM use, history of HRT use, study site, Charlson index, total duration of bisphosphonate therapy, duration between DEXA scans, and 25(OH)D level

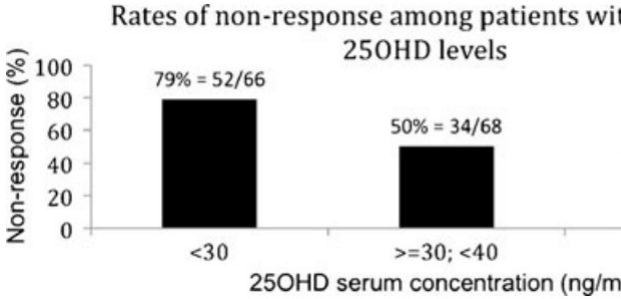
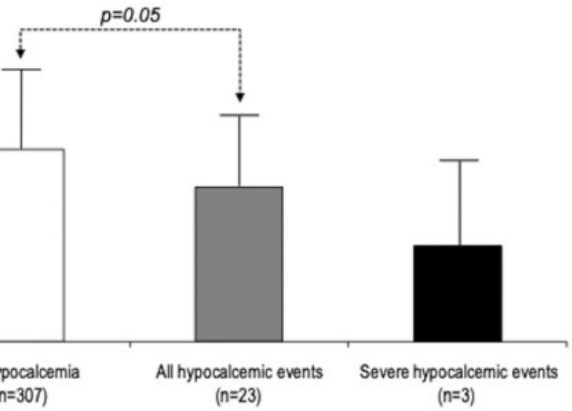
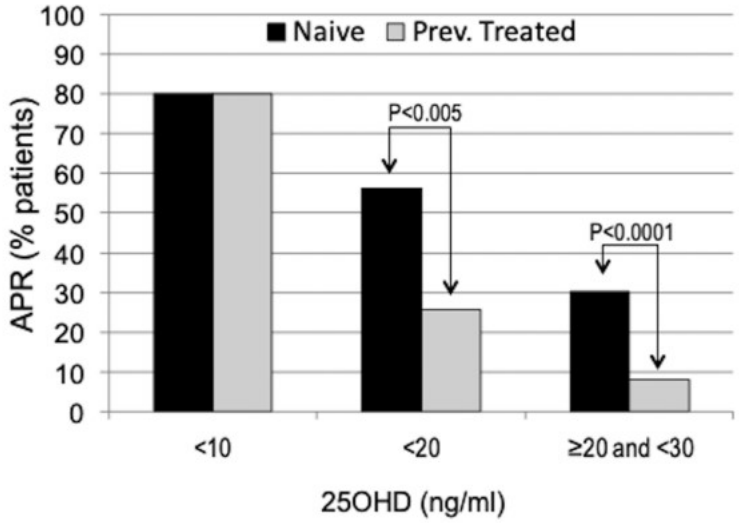


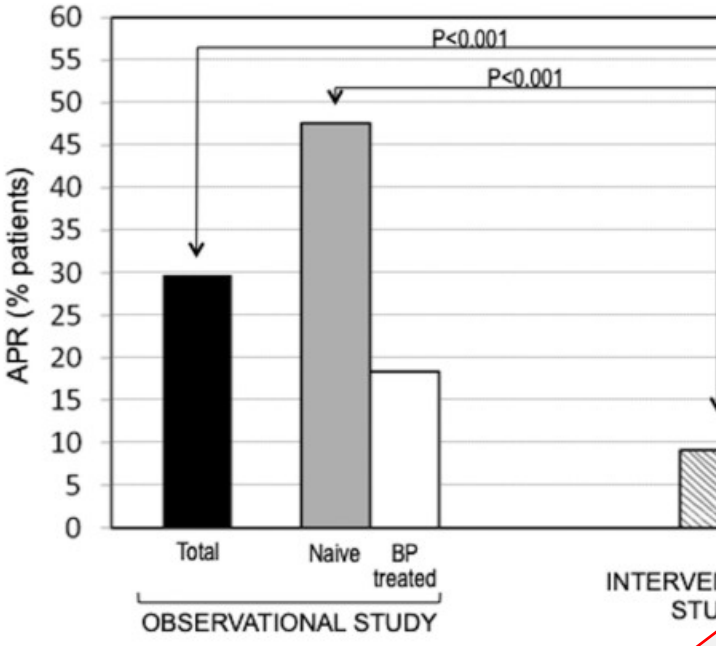
Fig. 2 Association between 25OHD level and bisp
sponse. When patients are stratified by 25OHD level,
response decreases as vitamin D level increases

eventive Role of Vitamin D Supplementation for ute Phase Reaction after Bisphosphonate Infusion in get's Disease

	Zoledronate IV (n = 219)	Neridronate IV (n = 111)
eaction, n (%)	67 (30.6)	31 (27.9)
ke illness	40 (18.3)	29 (26.1)
	38 (17.3)	28 (25.2)
	40 (18.3)	29 (26.1)
	18 (8.2)	13 (11.7)
	15 (6.8)	10 (9.0)
%)	5 (2.3)	3 (2.7)
, n (%)	13 (11.7)	10 (9.0)
%)	1 (0.46%)	0
on, n (%)	0	0
of the jaw	0	0







Choleca
50000 IU
for 8 w
(before N-E

Merlotti D et al. J Clin Endocrinol Metab, March 2020, 105(3):e466–e476

NOTA 96

Agenzia Italiana del Farmaco

Farmaci inclusi nella Nota AIFA: - colecalciferolo - colecalciferolo/Sali di calcio - calcifediolo	*La prescrizione a carico del SSN dei farmaci con indicazione "**prevenzione e trattamento della carenza di vitamina D**" nell'adulto (>18 anni) è limitata alle seguenti condizioni:* Prevenzione e trattamento della carenza di vitamina D nei seguenti scenari clinici : indipendentemente dalla determinazione della 25(OH) D • persone istituzionalizzate • donne in gravidanza o in allattamento • persone affette da osteoporosi da qualsiasi causa o osteopatie accertate non candidate a terapia remineralizzante (vedi nota 79) previa determinazione della 25(OH) D (vedi algoritmo allegato) • persone con livelli sierici di 25OHD < 20 ng/mL e sintomi attribuibili a ipovitaminosi (astenia, mialgie, dolori diffusi o localizzati, frequenti cadute immotivate) • persone con diagnosi di iperparatiroidismo secondario a ipovitaminosi D • persone affette da osteoporosi di qualsiasi causa o osteopatie accertate candidate a terapia remineralizzante per le quali la correzione dell'ipovitaminosi dovrebbe essere propedeutica all'inizio della terapia * • una terapia di lunga durata con farmaci interferenti col metabolismo della vitamina D • malattie che possono causare malassorbimento nell'adulto * Le terapie remineralizzanti dovrebbero essere iniziate dopo la correzione della ipovitaminosi D.

Whithout measure

After 25(measurer

Agenzia Italiana del Farmaco

Nota 96 - Allegato 1

(adattato da NICE 2018)

1. Esiste almeno un sintomo persistente fra quelli elencati suggestivo per carenza di vitamina D ?
   - Sintomi di osteomalacia come dolenzia in sedi ossee o dolore (anche pulsante) lombosacrale, pelvico o agli arti inferiori; senso di impedimento fisico; dolori o debolezza muscolare (anche di grado elevato) soprattutto ai quadricipiti ed ai glutei con difficoltà ad alzarsi da seduto o andatura ondeggiante;
   - Dolori diffusi di lunga durata;
   - Propensione alle cadute immotivate.
2. È prevista una terapia di lunga durata con farmaci interferenti col metabolismo della vitamina D (ed es. antiepilettici, glucocorticoidi, anti-retrovirali, anti-micotici, colestiramina, orlistat etc.) oppure esiste una condizione di malassorbimento (ad es. fibrosi cistica, celiachia, m. Crohn, chirurgia bariatrica, etc) ?
3. Esiste una patologia ossea accertata (osteoporosi, osteomalacia o malattia di Paget) che può beneficiare dal trattamento con vitamina D oppure necessita di terapia remineralizzante?
4. Esiste un riscontro di PTH elevato con calcemia normale o bassa?

SI

È appropriata la prescrizione di una determinazione della 25(OH) D.
Nell'interpretazione dei risultati considerare che il laboratorio potrebbe NON condividere i medesimi intervalli di normalità.

NO

La determinazione della 25(OH) D, NON è appropriata.

Livelli di 25 (OH D		
0 – 12 ng/mL (0-30 nmol/L)	13-20 ng/mL (30-50 nmol/L)	>20 ng/mL (50 nmol/L)
Prescrizione di: colecalciferolo in dose cumulativa di 300.000 UI somministrabile in un periodo massimo di 12 settimane, suddivisibili in dosi giornaliere, settimanali o mensili (non oltre le 100.000 UI/dose per motivi di sicurezza)	Prescrizione di: colecalciferolo in dose giornaliera di 750-1.000 UI o in alternativa dosi corrispondenti settimanali o mensili.	Considerare altre possibili cause dei sintomi. Con l'eccezione di patologie ossee riconosciute, la supplementazione con vitamina D non è raccomandata e pertanto non rimborsata dal SSN.
Prescrizione di: calcifediolo 1cps 2 volte al mese	Prescrizione di: calcifediolo 1cps/mese	

Verifica dei livelli della 25OH D a tre mesi nel caso non vi sia risoluzione del quadro clinico di partenza

La supplementazione con vitamina D, dopo la eventuale fase intensiva iniziale di 3 mesi, prevede:
- l'interruzione del trattamento a correzione avvenuta dei sintomi da carenza salvo ricomparsa degli stessi
- la prosecuzione per tutta la durata delle terapie remineralizzanti,
- la prosecuzione per la durata delle terapie interferenti col metabolismo della vitamina D (antiepilettici etc.)
- la prosecuzione in caso di osteomalacia, osteoporosi e malattia di Paget

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E

CrossMark

f insufficient serum vitamin D status in older alidated model

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oped an externally validated simple prediction model to predict serum 25(OH)D levels < 30, < 40, < 50 and women with risk factors for fractures. The benefit of the model reduces when a higher 25(OH)D threshold is

in D deficiency is associated with increased fracture risk in older persons. General supplementation of all itamin D could cause medicalization and costs. We developed a clinical model to identify insufficient serum D (25(OH)D) status in older women at risk for fractures.

le of 2689 women ≥ 65 years selected from general practices, with at least one risk factor for fractures, a dministered and serum 25(OH)D was measured. Multivariable logistic regression models with backward loped to select predictors for insufficient serum 25(OH)D status, using separate thresholds 30, 40, 50 and and external model validations were performed.

n the models were as follows: age, BMI, vitamin D supplementation, multivitamin supplementation, calcium ily use of margarine, fatty fish ≥ 2×/week, ≥ 1 hours/day outdoors in summer, season of blood sampling, the l and smoking. The AUC was 0.77 for the model using a 30 nmol/L threshold and decreased in the models lds to 0.72 for 60 nmol/L. We demonstrate that the model can help to distinguish patients with or without 5(OH)D levels at thresholds of 30 and 40 nmol/L, but not when a threshold of 50 nmol/L is demanded.

xternally validated model can predict the presence of vitamin D insufficiency in women at risk for fractures. al benefit of this tool is highly dependent of the chosen 25(OH)D threshold and decreases when a higher

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Research and Applications

AMIA

Research and Applications

Decrease in unnecessary vitamin D testing using clinical decision support tools: making it harder to do the wrong thing

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ABSTRACT

Objective: To evaluate the impact of clinical decision support (CDS) tools on rates of vitamin D testing. Screen ing for vitamin D deficiency has increased in recent years, spurred by studies suggesting vitamin D's clinica benefits. Such screening, however, is often unsupported by evidence and can incur unnecessary costs.

Materials and Methods: We evaluated how rates of vitamin D screening changed after we implemented 3 CD tools in the electronic health record (EHR) of a large health plan: (1) a new vitamin D screening guideline, (2) a alert that requires clinician acknowledgement of current guidelines to continue ordering the test (a "hard stop" and (3) a modification of laboratory ordering preference lists that eliminates shortcuts. We assessed rates o overall vitamin D screening and appropriate vitamin D screening 6 months pre- and post-intervention.

Results: Vitamin D screening rates decreased from 74.0 tests to 24.2 tests per 1000 members ($P < .0001$). The pro portion of appropriate vitamin D screening tests increased from 56.2% to 69.7% ($P < .0001$), and the proportion o inappropriate screening tests decreased from 43.8% pre-implementation to 30.3% post-implementation ($P < .0001$

Discussion: To our knowledge, this is the first demonstration of how CDS can reduce rates of inappropriate vita min D screening. We used 3 straightforward, inexpensive, and replicable CDS approaches. We know of no pre vious research on the impact of removing options from a preference list.

Conclusion: Similar approaches could be used to reduce unnecessary care and decrease costs without reducin quality of care.