# Screening for Vitamin D Deficiency in Adults

US Prevention Services Task Force Recommendation Statement


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# Importance

Vitamin D is a fat-soluble vitamin that performs an important role in calcium homeostasis and bone metabolism and also affects many other cellular regulatory functions outside the skeletal system.[1-3] Vitamin D requirements may vary by individual; thus, no one serum vitamin D level cutpoint defines deficiency, and no

that represent optimal health or sufficiency. According to the National Academy of Medicine, an estimated 97.5% of the population will have their vitamin D needs met at a serum level of 20 ng/mL (49.9 nmol/L) and risk for deficiency, relative to bone health, begins to occur at levels less than 12 to 20 ng/mL (29.9-

Health and Nutrition Examination Survey found that 5% of the population 1 year or older had very low 25-hydroxyvitamin D (25[OH]D) levels (<12 ng/mL) and 18% had levels between 12 and 19 ng/mL.[5]

## Patient Population Under Consideration

This recommendation applies to community-dwelling, nonpregnant adults who have no signs or symptoms of vitamin D deficiency, such as bone pain or muscle weakness, or conditions for which vitamin D treatment is recommended. This recommendation focuses on screening (ie, testing for vitamin D deficiency in asymptomatic adults and treating those found to have a deficiency), which differs from USPSTF recommendation statements on supplementation.

lower vitamin D levels. Low dietary vitamin D intake may be associated with lower 25(OH)D levels.[7] Little or no UV B exposure (eg, because of winter season, high latitude, or sun avoidance) and older age are also associated with an increased risk for low vitamin D levels.[8-12] Obesity is associated with lower 25(OH)D levels,[13] and people who are obese have a 1.3- to 2-fold increased risk of being vitamin D–deficient, depending on the threshold used to define deficiency.[8,9,13,14] The exact mechanism for this finding is not completely understood.

Depending on the serum threshold used to define deficiency, the prevalence of vitamin D deficiency is 2 to 10 times higher in non-Hispanic Black persons than in non-Hispanic White persons, likely related to differences in skin pigmentation.[7-9,14] However, these prevalence estimates are based on total 25(OH)D levels, and controversy remains about whether this is the best measure of vitamin D status among different racial and ethnic groups.

## Treatment and Interventions

Vitamin D deficiency is usually treated with oral vitamin D. There are 2 commonly available forms of vitamin D—vitamin $D_3$ (cholecalciferol) and vitamin $D_2$ (ergocalciferol). Both are available as either a prescription medication or an over-the-counter dietary supplement.

The goal of screening for vitamin D deficiency would be to identify and treat it before associated adverse clinical outcomes occur. Total 25(OH)D level is currently considered the best marker of vitamin D status.[4,19] A variety of assays can be used to measure 25(OH)D levels; however, levels can be difficult to measure accurately, and assays may underestimate or overestimate 25(OH)D levels. Additionally, the current evidence is inadequate to determine whether screening for and treatment of asymptomatic low 25(OH)D levels improve clinical outcomes in community-dwelling adults.

## Potential Harms

Screening may misclassify persons with a vitamin D deficiency because of the uncertainty about the cutoff for defining deficiency and the variability of available testing assays. Misclassification may result in overdiagnosis (leading to nondeficient persons receiving unnecessary treatment) or underdiagnosis (leading to deficient persons not receiving treatment).

A rare but potential harm of treatment with vitamin D is toxicity, which is characterized by marked hypercalcemia as well as hyperphosphatemia and hypercalciuria. However, the 25(OH)D level associated with toxicity (typically >150 ng/mL)[20] is well above the level considered to be sufficient. In general, treatment with oral vitamin D does not seem to be associated with serious harms.

## Other Related USPSTF Recommendations

The USPSTF has published recommendations on the use of vitamin D supplementation for the prevention of falls[22] and fractures[23] and vitamin supplementation for the prevention of cardiovascular disease or cancer.[24] These recommendations differ from the current recommendation statement in that they address vitamin D supplementation without first determining a patient's vitamin D status (ie, regardless of whether they have a deficiency).

## Harms of Screening and Treatment

The USPSTF found no studies that directly evaluated the harms of screening for vitamin D deficiency. The USPSTF found 36 studies that reported adverse events and harms from treatment with vitamin D (with or without calcium) compared with a control group. The absolute incidence of adverse events varied widely across studies; however, the incidence of total adverse events, such as gastrointestinal symptoms, fatigue, musculoskeletal symptoms, and headaches, and serious adverse events was generally similar between treatment and control groups. In the 10 trials that reported incidence of kidney stones, there was only 1 case.[26,27]

## Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from September 22, 2020, to October 19, 2020. Some comments requested the USPSTF to evaluate the evidence on or make a recommendation regarding vitamin D supplementation. In response, the USPSTF wants to clarify that this recommendation focuses on screening for vitamin D deficiency. The USPSTF does have separate recommendations that address vitamin D supplementation (ie, providing vitamin D to all persons without testing, and regardless of vitamin D level) for a variety of conditions.[22-24] In response to comments, the USPSTF also wants to clarify that this recommendation applies to asymptomatic, community-dwelling adults. It does not apply to persons in institutional or hospital settings, who may have underlying or intercurrent conditions that warrant vitamin D testing or treatment. The USPSTF also wants to clarify that it did not review the emerging evidence on COVID-19, the disease caused by the new coronavirus SARS-CoV-2, and vitamin D.

# Research Needs and Gaps

More studies are needed that address the following areas:

- More research is needed to determine whether total serum 25 (OH)D levels are the best measure of vitamin D deficiency and whether the best measure of vitamin D deficiency varies by sub-groups defined by race, ethnicity, or sex.
- More research is needed to determine the cutoff that defines vitamin D deficiency and whether that cutoff varies by specific clinical outcome or by subgroups defined by race, ethnicity, or sex.
- When vitamin D deficiency is better defined, studies on the benefits and harms of screening for vitamin D deficiency will be helpful.

## Recommendations of Others

No organization recommends population-based screening for vitamin D deficiency, and the American Society for Clinical Pathology recommends against it.[47] The American Academy of Family Physicians supports the USPSTF 2014 recommendation, which states that there is insufficient evidence to recommend screening the general population for vitamin D deficiency.[48] The Endocrine Society[49] and the American Association of Clinical Endocrinologists[50] recommend screening for vitamin D deficiency in individuals at risk. The Endocrine Society does not recommend population screening for vitamin D deficiency in individuals not at risk.[49]

Table. Summary of USPSTF Rationale

| Rationale | Assessment |
|---|---|
| Detection | • Vitamin D requirements may vary by individual, and there is no one 25(OH)D level that defines deficiency for all individuals.<br>• Total 25(OH)D levels are currently considered the best marker of vitamin D status; however, levels are difficult to measure accurately.<br>• Evidence suggests that results vary by testing method and between laboratories using the same testing methods. |
| Benefits of early detection and intervention and treatment | • No direct evidence on the benefits of screening for vitamin D deficiency.<br>• Adequate evidence that treatment of asymptomatic vitamin D deficiency has no benefit on mortality, risk for fractures in persons selected solely on the basis of low vitamin D levels (as opposed to clinical risks such as low bone density), or incidence of type 2 diabetes mellitus.<br>• Inadequate evidence on the benefit of treatment of asymptomatic vitamin D deficiency on other outcomes, including falls, cancer, cardiovascular events, depression, infection, or physical functioning.<br>• Despite adequate evidence to conclude no benefit for a few health outcomes, evidence on the benefits of treatment of asymptomatic vitamin D deficiency in adults for other health outcomes remains inadequate. The overall evidence on the benefits of treatment of asymptomatic vitamin D deficiency in adults is inadequate. |
| Harms of early detection and intervention and treatment | • No direct evidence on the harms of screening for vitamin D deficiency.<br>• Adequate evidence that the harms of treatment of vitamin D deficiency are small to none. |
| USPSTF assessment | The overall evidence on the benefits of screening for vitamin D deficiency is lacking. Therefore, the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic adults cannot be determined. |

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; USPSTF, US Preventive Services Task Force.

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

| | |
|---|---|
| **What does the USPSTF recommend?** | **For asymptomatic, community-dwelling, nonpregnant adults:**<br>The USPSTF found that the **evidence is insufficient** to assess the balance of benefits and harms of screening for vitamin D 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 for which vitamin D treatment is recommended.<br>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 statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others. |

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

USPSTF indicates US Preventive Services Task Force.

# *summary*

**IMPORTANCE** Vitamin D is a fat-soluble vitamin that performs an important role in calcium homeostasis and bone metabolism and also affects many other cellular regulatory functions outside the skeletal system. Vitamin D requirements may vary by individual; thus, no one serum vitamin D level cutpoint defines deficiency, and no consensus exists regarding the precise serum levels of vitamin D that represent optimal health or sufficiency.

**OBJECTIVE** To update its 2014 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a systematic review on screening for vitamin D deficiency, including the benefits and harms of screening and early treatment.

**POPULATION** Community-dwelling, nonpregnant adults who have no signs or symptoms of vitamin D deficiency or conditions for which vitamin D treatment is recommended.

**EVIDENCE ASSESSMENT** The USPSTF concludes that the overall evidence on the benefits of screening for vitamin D deficiency is lacking. Therefore, the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic adults cannot be determined.

**RECOMMENDATION** The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic adults. (I statement)


Salmon
Fortified cereal
Milk
Vitamin
D
Cheese
Tuna
Eggs
Sunlight

# Vitamin D Overview

It is a fat soluble vitamin.

Not just a vitamin it is a prehormone

Found in some food and made in the body after exposure to UV rays

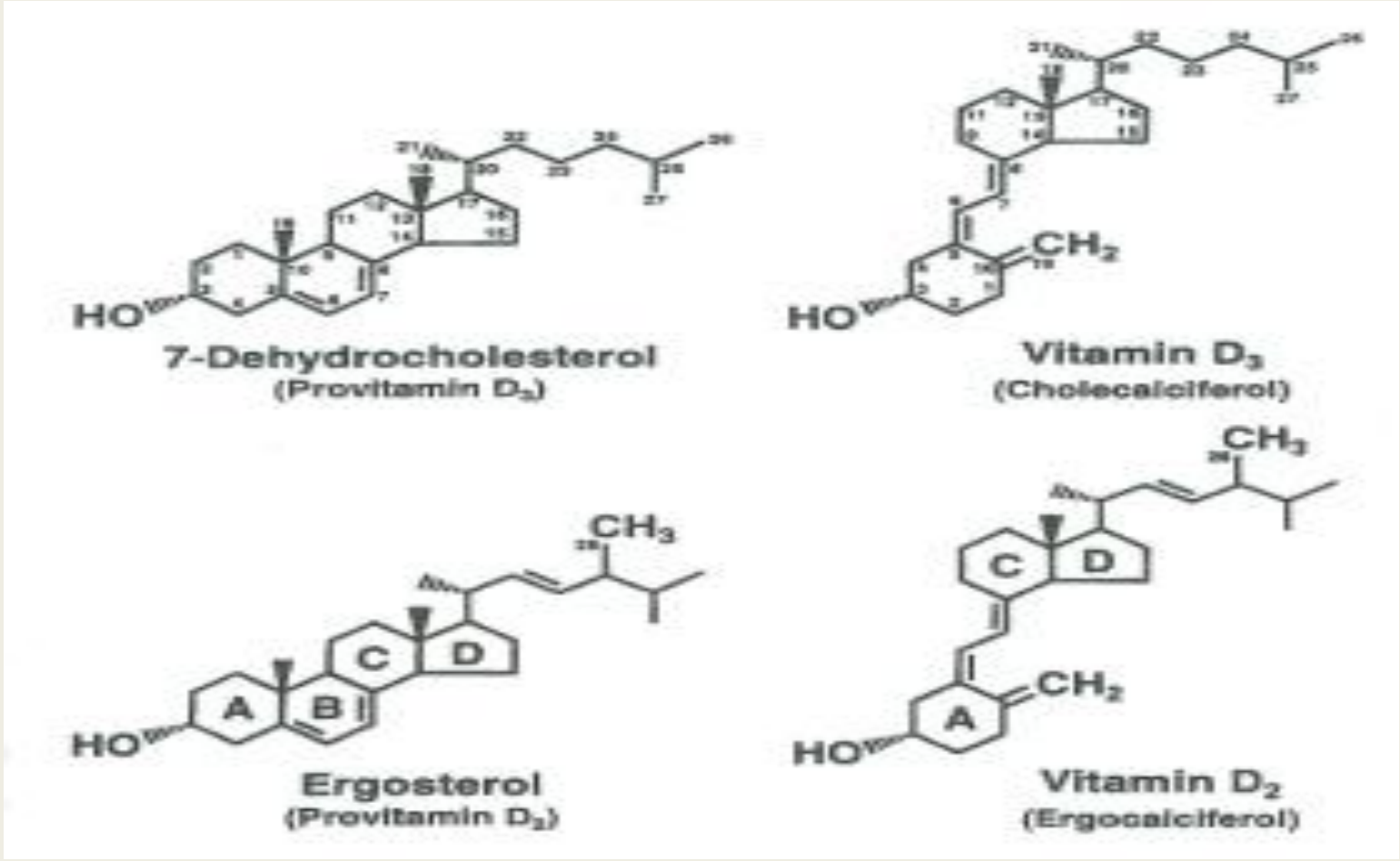
Major biological function is to maintain normal blood levels of Ca and Po4

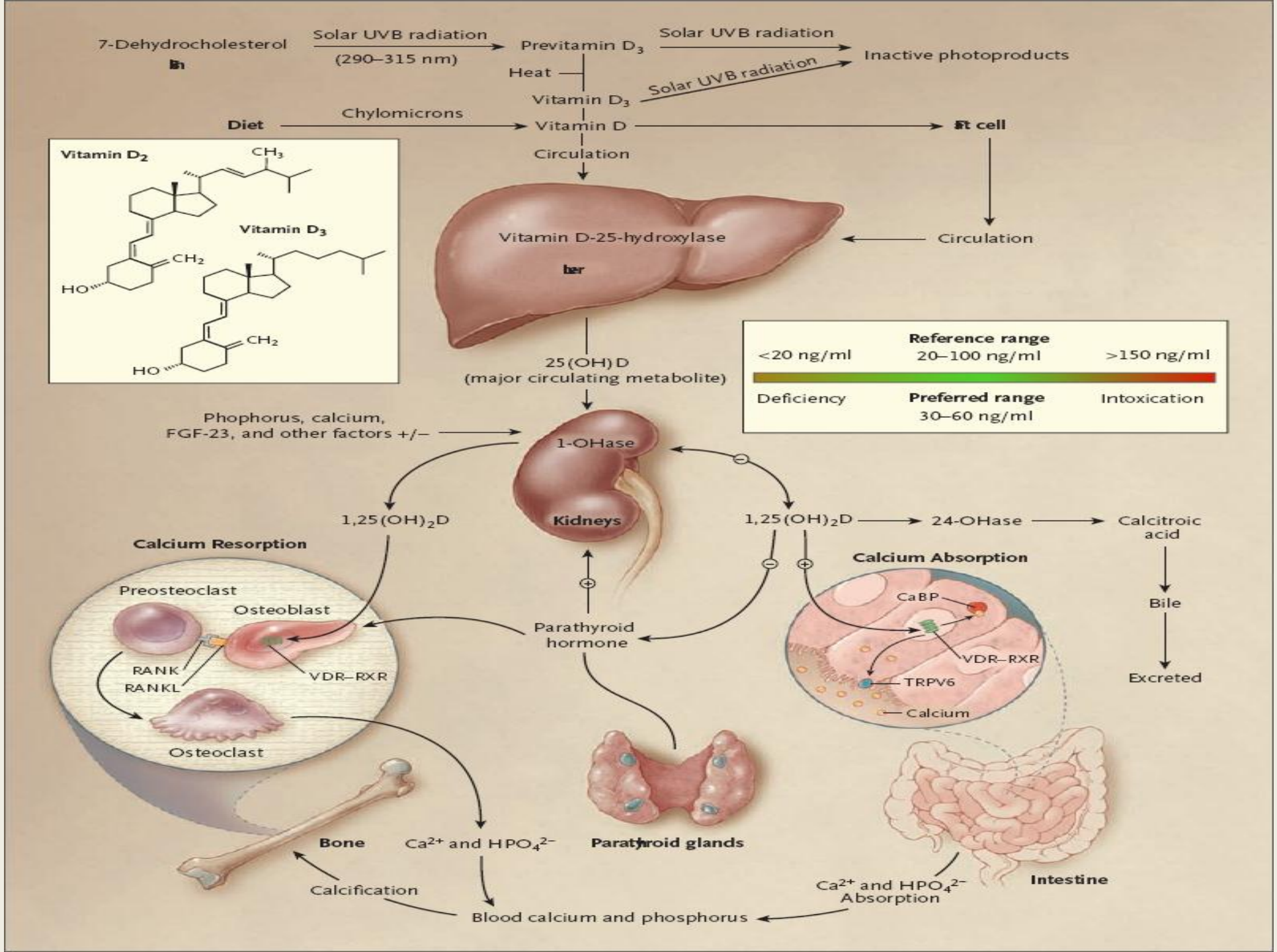
Other tissues like macrophages, prostrate tissue also have vit D receptor

# History of Vitamin D

- Existed over 500 million years
- Industrial revolution : rickets
- Cod liver oil: common folklore medicine
- Discovery of Vit D as the antirachitic factor in cod liver oil(1920)
- Discovery of conversion of 7-dehydrocholesterol in the skin to vit D (1937)
- Antirachitic property in food
- Fortification of food with vitamin D was patented
- Complete eradication of rickets in US
- US public service issuing warnings about sun-induced health risk
- Over next 30 yrs skin cancer hazard of excessive sun exposure became well established

# Structure of Vitamin D




7-Dehydrocholesterol
Solar UVB radiation
(290–315 nm)
Previtamin D3
Solar UVB radiation
Inactive photoproducts
Heat
Vitamin D3
Solar UVB radiation
Diet
Chylomicrons
Vitamin D
Circulation
Vitamin D2
Vitamin D3
Vitamin D-25-hydroxylase
Circulation
25(OH)D
(major circulating metabolite)
Reference range
<20 ng/ml
20–100 ng/ml
>150 ng/ml
Deficiency
Preferred range
30–60 ng/ml
Intoxication
Phophorus, calcium,
FGF-23, and other factors +/–
1-OHase
Kidneys
1,25(OH)2D
1,25(OH)2D
24-OHase
Calcitroic acid
Bile
Excreted
Calcium Resorption
Preosteoclast
Osteoblast
RANK
RANKL
VDR–RXR
Osteoclast
Parathyroid hormone
Calcium Absorption
CaBP
VDR–RXR
TRPV6
Calcium
Bone
Ca2+ and HPO42–
Parathyroid glands
Intestine
Calcification
Ca2+ and HPO42–
Absorption
Blood calcium and phosphorus

# Endocrine, paracrine and intracrine functions of Vitamin D

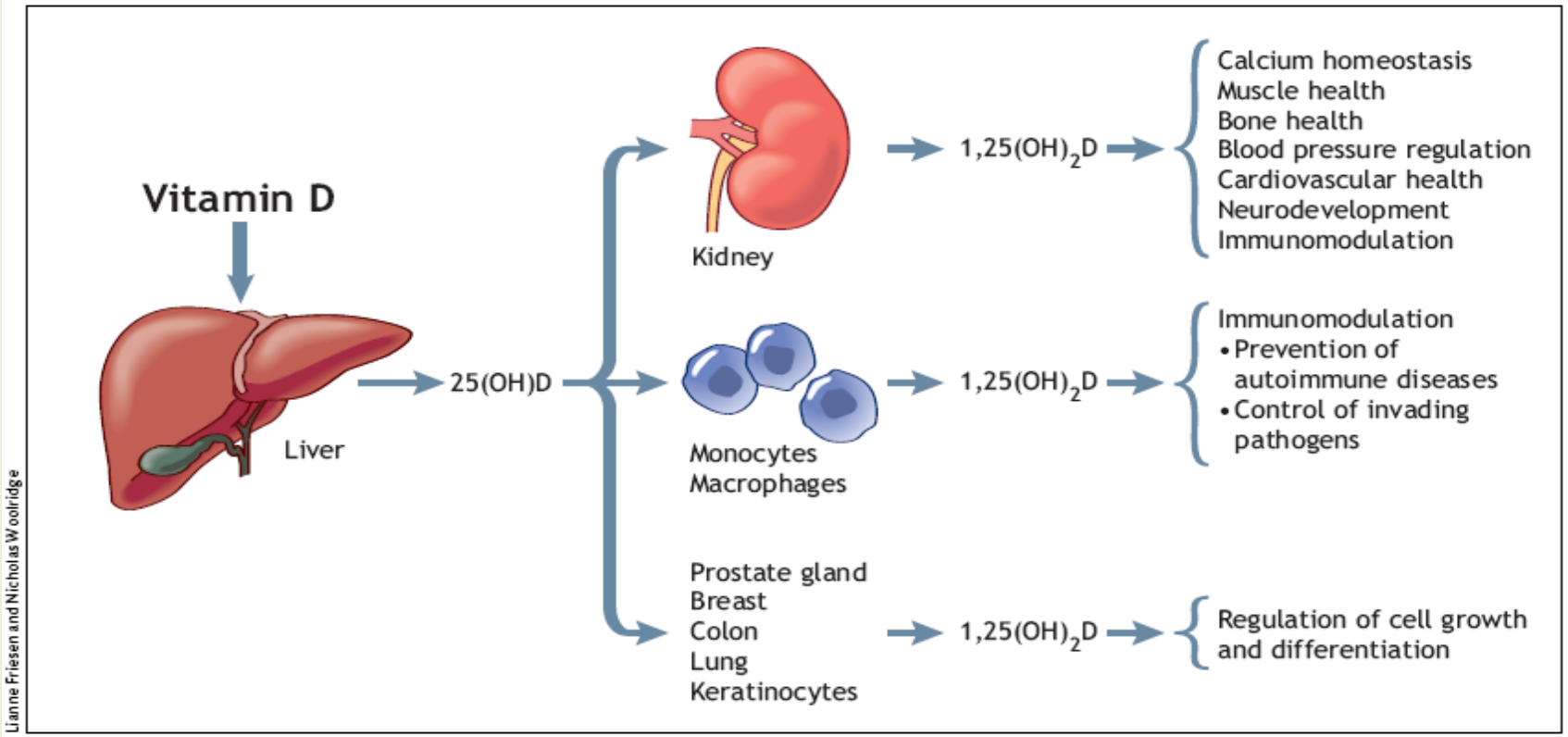



**Fig. 2:** The endocrine, paracrine and intracrine functions of vitamin D. Vitamin D is converted in the liver to 25(OH)D, which enters the systemic circulation and is converted to 1,25(OH)2D in a variety of end-organ tissues. As shown, 1,25(OH)2D is involved in the regulation of numerous systems.

# Food Sources of Vitamin D

| | |
|---|---|
| Cod liver oil – 1 TBS | 1,360 IU |
| Salmon 3.5 oz. | 360 |
| Mackerel 3.5 oz. | 345 |
| Tuna, canned, in oil, 3 oz. | 200 |
| Sardines 3.5 oz. | 250 |
| Milk (fortified) 8 oz. | 98 |
| Ready to eat cereal (fortified) ¾ - 1 cup | 40 |
| Egg 1 whole | 20 |
| Liver, 3.5 oz. | 15 |
| Cheese, swiss 1 oz. | 12 |

# How much sun?

Depends on:

- *Age*
- *Amount of vitamin D obtained from diet*
- *Skin darkness*
- *Sunshine intensity*

# How much sun?

- Significant skin exposure
  - *Face, neck, arms, hands*
  - *Arms, legs*
- Adequate sun strength
- Time
  - *25% of the time it would take to cause pinkness of the skin (Caucasians)*
  - *People with dark skin require significantly more sun exposure*

# Vitamin D Across the Lifespan

Factors influencing accumulation of bone minerals:

- *Heredity*
- *Gender*
- *Diet*
- *Physical activity*
- *Endocrine status*
- *Maternal vitamin D status*

- Association of low intake of milk and vit D during pregnancy with decreased birth weight.
- Maternal vitamin D status during pregnancy and childhood bone mass at age 9yrs.
- Vitamin D deficiency in breastfed infants in Iowa.
- Prevalence of vitamin D deficiency among healthy adolescents.GIRL\BOY,....
- Vitamin D Deficiency in Hospitalized Patients (Renal Transplant Patients/ GI cancer, prostate and breast cancers, lymphomas, endometrial and lung cancers/malignant melanoma cells and myeloid leukemia cells/Pancreatic cancer/Type 2 -1 Diabetes/Metabolic Syndrome/Congestive Heart Failure/ Hypertension/Stroke/Chronic Kidney Disease/Multiple Sclerosis/RA /

# Vitamin D Assessment

- Lab assays are available to measure both 25(OH)D and 1,25-D.
- 25(OH)D closely reflects total amount of vit D produced in the skin and from diet
- D2 and D3: have similar biological activity
- Both D2 and D3 should be measured
- DO NOT USE - 1,25-D. This can often be normal with vit D deficiency

# Recommendations

- Annual testing of 25(OH)D
- Consider time of year in testing
  - *Lowest levels generally towards end of winter, early spring*

# Goals in Maintaining Vitamin D Levels

١. Prevent disease of deficiency – rickets, osteomalacia

٢. Prevent complications of insufficiency – impaired calcium absorption and increased bone resorption

٣. Minimize risks of future disease – cancer, cardiopulmonary diseases, diabetes, other immune-related diseases

# 25(OH)D concentration

- To prevent deficiency disease – *> 25 nmol / L*
- To prevent complications of insufficiency – *≥ 50 nmol/L*
- For maximum bone health and prevention of chronic disease – *75 – 100 nmol/L*

# IRAN ( vit D supplementation)

| Age | dose |
|---|---|
| Pregnancy | 1000 IU/ Daily |
| 3-5 day- 2 yrs | 400 IU/ Daily |
| 6-17 yrs | 50000 IU/ Monthly (9 PEARL) |
| 18-29 yrs | 50000 IU/ Monthly |
| 30-59 Yrs | 50000 IU/ Monthly |
| ≥60 | 50000 IU/ Monthly |


Thank you