

## Research Article

# Vitamin D deficiency testing and supplementation in adult medical practice

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**Abstract:** Vitamin D testing and supplementation are common in adult medical practice, but their clinical use has become uneven. Severe vitamin D deficiency causes osteomalacia, secondary hyperparathyroidism, bone pain, proximal muscle weakness, and increased skeletal fragility. In selected high-risk adults, testing and treatment are clearly justified. In contrast, routine screening of asymptomatic adults and broad supplementation for non-skeletal disease prevention are not well supported by trial evidence. This review evaluates vitamin D deficiency testing and supplementation in adult practice, with attention to bone health, falls, fatigue, immune claims, overtesting, toxicity, and high-risk groups. PubMed-indexed guidelines, systematic reviews, randomized trials, meta-analyses, and toxicity reviews were examined. Current evidence supports targeted testing in adults with clinical suspicion of deficiency, osteoporosis or fragility fracture, osteomalacia features, malabsorption, chronic kidney or liver disease, bariatric surgery, medicines affecting vitamin D metabolism, persistent hypocalcaemia, or other clear risk factors. The 2021 US Preventive Services Task Force found insufficient evidence to assess the balance of benefits and harms of screening asymptomatic community-dwelling nonpregnant adults. The 2024 Endocrine Society guideline also advised against routine 25-hydroxyvitamin D testing in generally healthy populations without established indications. Supplementation remains important for deficient patients and for maintaining recommended intake in those with low dietary or sunlight exposure. However, large trials in generally healthy adults do not support vitamin D supplementation as a stand-alone strategy for preventing fractures, falls, cardiovascular disease, cancer, or most immune outcomes. High intermittent doses may increase fall risk in some older adults. Toxicity is uncommon but clinically important and usually results from excessive supplementation, prescription error, or unmonitored high-dose use. Adult practice should therefore shift from reflex testing and non-specific supplementation toward risk-based assessment, safer dosing, and outcome-focused follow-up.

**Keywords:** Vitamin D deficiency, 25-hydroxyvitamin D, supplementation, bone health, falls, fatigue, immune function, overtesting, toxicity, osteoporosis, adult medicine

## Introduction

Vitamin D used to be a simple deficiency story. Low sunlight exposure, poor intake, malabsorption, kidney or liver disease, and certain medicines could lead to inadequate vitamin D activity. In severe cases, adults developed osteomalacia, bone pain, muscle weakness, hypocalcaemia, secondary hyperparathyroidism, and fractures. Testing had a purpose. Treatment had a target.

Modern adult practice is more complicated. Vitamin D is now requested for tiredness, muscle aches, low mood, hair loss, “immunity,” recurrent infections, vague body pain, weight gain, metabolic risk, cardiovascular prevention, cancer prevention, and general wellness. Many patients arrive already taking over-the-counter vitamin D. Some take modest doses. Others take repeated high doses without baseline calcium, renal function, or 25-hydroxyvitamin D assessment.

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The clinical challenge is therefore not whether vitamin D matters. It does. The question is where vitamin D testing and supplementation improve outcomes, and where they mainly add cost, confusion, false reassurance, or avoidable risk.

The recent direction of evidence is more restrained than earlier clinical enthusiasm. The 2024 Endocrine Society guideline on vitamin D for prevention of disease does not endorse routine 25-hydroxyvitamin D testing in generally healthy adults without established indications and no longer supports a universal serum target such as 30 ng/mL for disease prevention (1). The 2021 US Preventive Services Task Force concluded that evidence was insufficient to determine the balance of benefits and harms of screening asymptomatic, community-dwelling, nonpregnant adults for vitamin D deficiency (3). These positions do not deny true deficiency. They separate true clinical need from indiscriminate testing.

A useful adult medicine approach must hold two ideas at the same time. First, vitamin D deficiency is real and can be clinically important. Second, low or borderline 25-hydroxyvitamin D values in otherwise healthy adults do not automatically explain non-specific symptoms or justify repeated testing and high-dose therapy.

## **2. How the evidence was reviewed**

This narrative review used PubMed-indexed sources on adult vitamin D testing, 25-hydroxyvitamin D thresholds, supplementation, bone health, falls, fractures, fatigue, immune outcomes, respiratory infection, cardiovascular and cancer outcomes, overtesting, toxicity, and high-risk populations. The evidence base included clinical practice guidelines, evidence reports, systematic reviews, meta-analyses, randomized controlled trials, and clinical reviews.

Particular attention was given to large randomized trials and recent guideline documents because vitamin D has a long history of observational associations that were not consistently confirmed in intervention trials. Older trials and reviews were included when they shaped clinical practice or showed why conclusions changed over time.

The review focuses on adult medical practice rather than paediatrics, pregnancy-specific management, or dialysis protocols. Pregnancy is mentioned only as a high-risk state because the article's main question is adult general medical use.

## **3. Vitamin D physiology in one clinical paragraph**

Vitamin D is obtained from skin synthesis after ultraviolet B exposure and from dietary or supplemental sources. It is converted in the liver to 25-hydroxyvitamin D, the main circulating marker used for assessment. It is then converted, mainly in the kidney, to 1,25-dihydroxyvitamin D, the active hormonal form. Vitamin D supports calcium and phosphate homeostasis, intestinal calcium absorption, bone mineralisation, and muscle function. Severe deficiency reduces calcium absorption, raises parathyroid hormone, increases bone turnover, and can produce osteomalacia in adults. Because 1,25-dihydroxyvitamin D may remain normal or rise in early deficiency, it is not the routine test for nutritional vitamin D status. The practical test is total serum 25-hydroxyvitamin D, interpreted with clinical context, calcium, renal function, phosphate, alkaline phosphatase, and parathyroid hormone when indicated.

## **4. The threshold problem**

Vitamin D testing looks precise because the laboratory result is numerical. The interpretation is less precise.

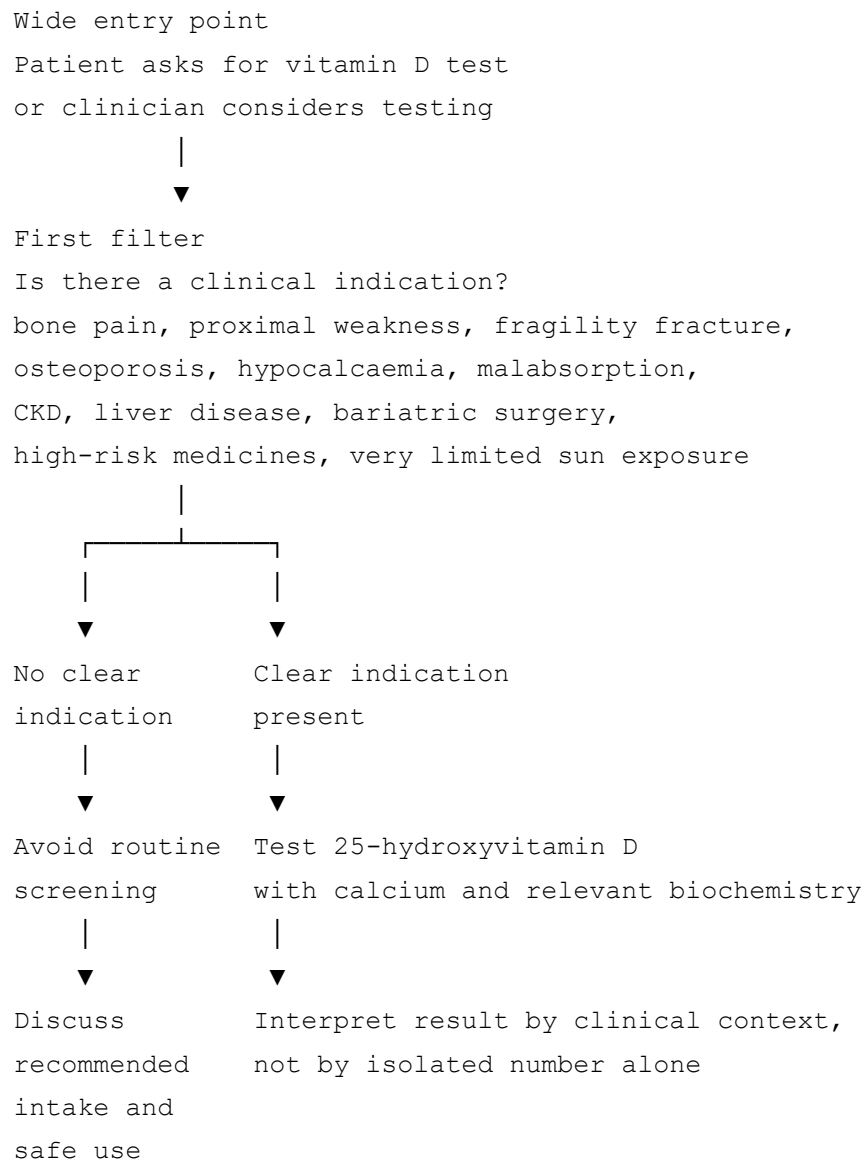
Different organizations have used different thresholds. Some older clinical frameworks defined deficiency as 25-hydroxyvitamin D below 20 ng/mL, insufficiency as 21-29 ng/mL, and sufficiency as 30 ng/mL or higher (7,8). The Institute of Medicine dietary reference intake report took a more conservative position, using skeletal outcomes as the strongest basis for intake recommendations and concluding that a 25-hydroxyvitamin D level of 20 ng/mL met the needs of most of the population (5,6). The 2024 Endocrine Society guideline moved further away from universal thresholds for disease prevention, stating that trial evidence did not

establish outcome-specific 25-hydroxyvitamin D thresholds for the populations considered (1).

This creates a practical tension. A clinician may receive a laboratory report marking 22 ng/mL as insufficient, while a guideline may not support testing or treating that level in an otherwise healthy adult for disease prevention. Conversely, a frail adult with bone pain, low calcium, high alkaline phosphatase, low phosphate, secondary hyperparathyroidism, malabsorption, and a 25-hydroxyvitamin D of 14 ng/mL needs treatment regardless of debates over the exact definition.

The right question is not “what number is abnormal for everyone?” The better question is “does this result explain a clinical problem or change management in this patient?”

**Figure 1 Vitamin D testing as a clinical decision funnel**



## 5. When testing is useful

Vitamin D testing is most useful when the result changes care. Common indications include suspected osteomalacia, osteoporosis, fragility fracture, low-trauma fracture risk assessment, unexplained hypocalcaemia, secondary hyperparathyroidism, chronic kidney disease, chronic liver disease, malabsorption, inflammatory bowel disease with poor absorption, coeliac disease, pancreatic insufficiency, bariatric surgery, long-term anticonvulsant therapy,

long-term glucocorticoid therapy, very limited sunlight exposure, full skin-covering clothing, institutional living, and recurrent falls or proximal muscle weakness when deficiency is plausible.

Testing may also be reasonable before high-dose replacement, in patients with previous toxicity or hypercalcaemia, granulomatous disease, lymphoma, nephrolithiasis risk, sarcoidosis, advanced kidney disease, or when adherence and absorption are uncertain.

Testing is less useful as a general wellness investigation in asymptomatic adults. The USPSTF found no direct evidence that screening asymptomatic adults improves health outcomes, and the updated evidence review found that vitamin D treatment in screen-detected or low-level populations did not clearly improve mortality, fractures, falls, depression, diabetes, cardiovascular disease, cancer, or physical functioning (3,4). This does not mean no patient benefits. It means the population screening pathway is unproven.

**Table 1 Adult vitamin D testing according to clinical yield**

| Testing category       | Examples                                                                                                                                                                           | Practical interpretation                                                  |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| High-yield testing     | Osteomalacia features, fragility fracture, osteoporosis, hypocalcaemia, secondary hyperparathyroidism, malabsorption, bariatric surgery, CKD, chronic liver disease                | Testing is likely to influence diagnosis, dosing, monitoring, or referral |
| Moderate-yield testing | Recurrent falls with muscle weakness, severe dietary restriction, institutional living, long-term anticonvulsants, long-term glucocorticoids, very low sunlight exposure           | Testing is reasonable when deficiency is plausible and action will follow |
| Low-yield testing      | Asymptomatic healthy adult requesting routine annual vitamin D check                                                                                                               | Evidence does not support routine screening                               |
| Misleading testing     | Non-specific fatigue alone without risk factors, repeated short-interval tests after small dose changes, testing while taking unknown high-dose supplements without calcium review | May create diagnostic noise unless interpreted carefully                  |
| Safety testing         | High-dose therapy, history of hypercalcaemia, sarcoidosis, lymphoma, granulomatous disease, nephrolithiasis risk                                                                   | Include calcium and renal function, not only 25-hydroxyvitamin D          |

## 6. Bone health remains the strongest indication

Bone is still the strongest biological and clinical basis for vitamin D use. Vitamin D deficiency impairs calcium and phosphate metabolism and can cause osteomalacia in adults. Symptoms may include diffuse bone pain, proximal muscle weakness, difficulty rising from a chair, waddling gait, low calcium or phosphate, raised alkaline phosphatase, and secondary hyperparathyroidism. These presentations justify testing and treatment.

The more difficult question is whether routine vitamin D supplementation prevents fractures in generally healthy adults. Large modern trials have not supported that assumption. In the VITAL ancillary fracture study, vitamin D3 supplementation did not significantly reduce total, nonvertebral, or hip fractures in generally healthy midlife and older adults who were not selected for vitamin D deficiency, low bone mass, or osteoporosis (11). A recent systematic review and meta-analysis in community-dwelling adults found little to no effect of calcium, vitamin D, or combined supplementation on most fracture and fall outcomes (20). Earlier meta-analyses were more favourable in some settings, particularly when calcium and vitamin

D were combined or when institutionalized populations were included, but later evidence shows that population, baseline risk, co-intervention, and dosing pattern matter (15,17,18).

This distinction is central for adult practice. Vitamin D is necessary for bone health, but giving vitamin D to unselected, generally healthy adults is not the same as treating deficiency, osteomalacia, osteoporosis, or malabsorption. In osteoporosis care, vitamin D sufficiency is usually part of safe antiresorptive or anabolic treatment planning, especially to reduce hypocalcaemia risk and support calcium handling. That is different from using vitamin D alone as fracture prevention.

## 7. Falls and the high-dose reversal

Vitamin D was once promoted for fall prevention. Older meta-analyses suggested benefit, especially at moderate daily doses in older adults (16,17). Newer trials complicated this view. Annual high-dose cholecalciferol in older community-dwelling women increased falls and fractures (14). Monthly high-dose vitamin D in older adults did not improve lower-extremity function and was associated with increased fall risk compared with a lower monthly dose (13). The D-Health fall analysis found that monthly high-dose vitamin D did not reduce falling and suggested possible increased falling risk in some analyses (12).

The biological reasons remain debated. Large intermittent doses may produce non-physiological fluctuations in vitamin D metabolites, alter muscle function, affect calcium handling, or identify other behavioural or biological mechanisms not yet fully understood. Whatever the mechanism, the clinical message is straightforward: high intermittent dosing should not be used casually to prevent falls in generally healthy older adults.

Falls are multifactorial. Vision, footwear, sedatives, antihypertensives, neuropathy, sarcopenia, Parkinson disease, arthritis, postural hypotension, home hazards, alcohol, cognition, and previous falls often matter more than vitamin D. Vitamin D replacement is appropriate when deficiency is documented or strongly suspected, but fall prevention should not be reduced to a supplement prescription.

### Chart 1 Fall and fracture evidence shift across clinical contexts

#### Context A

Deficiency, osteomalacia, osteoporosis care, malabsorption

Clinical direction

Test when indicated, replace deficiency, maintain safe intake

#### Context B

Institutionalized or frail adults with low intake

Clinical direction

Potential benefit is more plausible, especially with calcium adequacy,

but patient selection matters

#### Context C

Generally healthy community-dwelling adults not selected for deficiency

Clinical direction

Large trials do not show meaningful fracture prevention

#### Context D

High intermittent dose regimens

Clinical direction

Avoid routine use for fall prevention because some trials show increased falls or no functional benefit

This chart is intended as a context map rather than a pooled estimate. The same supplement can be appropriate in one clinical context and low-value or risky in another.

## 8. Fatigue and non-specific symptoms

Fatigue is one of the most common reasons adults request vitamin D testing. Severe deficiency can cause muscle weakness and generalized symptoms, but fatigue is non-specific. Anaemia, sleep disorders, depression, hypothyroidism, chronic infection, inflammatory disease, medication adverse effects, chronic pain, menopause, overwork, and cardiopulmonary disease may all present with tiredness.

Trial evidence for fatigue exists but is limited. Nowak et al. reported that vitamin D3 improved self-perceived fatigue in otherwise healthy adults with vitamin D deficiency in a randomized placebo-controlled trial (23). A narrative review on fatigue mechanisms described plausible biological pathways involving muscle function, mitochondrial activity, inflammation, and neuroimmune effects, but also emphasized that fatigue is multifactorial (25).

In practice, vitamin D testing for fatigue is most defensible when fatigue is accompanied by risk factors or compatible musculoskeletal features: low sunlight exposure, dietary restriction, malabsorption, bone pain, proximal weakness, recurrent falls, pregnancy or postpartum risk, chronic kidney or liver disease, or medicines affecting vitamin D metabolism. Testing every patient with fatigue is less defensible.

If vitamin D deficiency is found and treated, response should be judged clinically. Improvement in fatigue after replacement supports but does not prove causality. Lack of improvement despite biochemical correction should prompt reassessment rather than indefinite dose escalation.

## 9. Immune claims and respiratory infection

Vitamin D has important immunological effects in laboratory and mechanistic studies. It influences innate immunity, antimicrobial peptide expression, barrier function, macrophage activity, T-cell responses, and inflammatory signalling. This biology made vitamin D attractive as a respiratory infection and immune-support supplement.

The clinical evidence is more modest. An individual participant data meta-analysis published in 2017 found that vitamin D supplementation reduced acute respiratory infection risk overall, with stronger protection in those receiving daily or weekly dosing and in participants with very low baseline vitamin D levels (26). A later 2021 meta-analysis reported a small protective effect against acute respiratory infections, although heterogeneity was present and the effect size was modest (27). An updated 2025 systematic review and meta-analysis incorporating newer trials no longer found a statistically significant protective effect for acute respiratory infection prevention (28).

The immune message should therefore be careful. Vitamin D deficiency should be corrected for established health reasons. A patient with low vitamin D and recurrent infections may reasonably be treated if deficiency is present. But vitamin D should not be marketed or prescribed as a reliable general immune shield for adults with adequate status. Vaccination, smoking cessation, respiratory disease control, nutrition, sleep, hand hygiene, and exposure reduction remain more evidence-based infection prevention strategies.

There is also emerging evidence in autoimmune disease prevention. In the VITAL autoimmune disease analysis, vitamin D supplementation for five years reduced incident autoimmune disease by 22% in the primary analysis (29). Follow-up two years after the intervention suggested that the benefit was attenuated after stopping supplementation (30). These

findings are interesting, but they do not justify routine vitamin D testing of all adults or high-dose prescribing without a clear indication. They support further research and may influence prevention discussions in selected populations.

## 10. Cardiovascular disease, cancer, and diabetes claims

Vitamin D has been linked observationally with cardiovascular disease, cancer, diabetes, depression, dementia, and mortality. Observational associations are difficult to interpret because low vitamin D status can reflect older age, obesity, low outdoor activity, chronic illness, poor diet, inflammation, frailty, institutional living, socioeconomic factors, and darker winter seasons. Low vitamin D may be a marker of ill health rather than the cause.

The VITAL trial found that vitamin D supplementation did not significantly reduce invasive cancer or major cardiovascular events in generally healthy adults (31). The Finnish Vitamin D trial similarly found no reduction in major cardiovascular events or invasive cancer among older adults, possibly in a population with largely sufficient vitamin D status (32). A D-Health cardiovascular analysis suggested a possible small reduction in major cardiovascular events with monthly vitamin D in older adults, but the absolute risk difference was small and uncertainty remains (33). Meta-analyses have generally not supported vitamin D supplementation as a routine cardiovascular prevention strategy in the general population (34).

Diabetes prevention is a more nuanced field. In the D2d trial, vitamin D3 4000 IU daily did not significantly reduce diabetes incidence compared with placebo in adults at high risk (35). An individual participant data meta-analysis later found a 15% relative risk reduction in diabetes among adults with prediabetes, with an absolute 3-year risk reduction of 3.3% (36). This partly explains why the 2024 Endocrine Society guideline suggests empiric vitamin D supplementation in adults with high-risk prediabetes (1). Still, vitamin D should not displace weight loss, physical activity, dietary change, metformin where indicated, or cardiometabolic risk management.

**Table 2 Claims commonly attached to vitamin D and what current adult evidence supports**

| Claim                                                                             | Evidence-based position in adult practice                                                           |
|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| Prevents osteomalacia when deficiency is corrected                                | Supported                                                                                           |
| Supports osteoporosis treatment planning when deficiency or low intake is present | Supported                                                                                           |
| Prevents fractures in generally healthy adults not selected for deficiency        | Not supported by large modern trials                                                                |
| Prevents falls in community-dwelling older adults                                 | Not supported as a stand-alone strategy; high intermittent doses may increase risk                  |
| Treats fatigue in all adults                                                      | Not supported; may help selected deficient patients                                                 |
| Prevents acute respiratory infections in the general adult population             | Evidence has weakened with newer meta-analysis; benefit, if present, is small and context-dependent |
| Prevents cardiovascular disease                                                   | Not supported for routine general adult prevention                                                  |
| Prevents cancer incidence                                                         | Not supported by major trials                                                                       |
| Reduces diabetes progression in high-risk prediabetes                             | Possible modest benefit in selected high-risk adults                                                |

## Claim

## Evidence-based position in adult practice

Improves general wellness in replete adults

Not established

## 11. Overtesting and the diagnostic cascade

Vitamin D overtesting has become a recognizable problem. Reviews and practice audits describe large increases in 25-hydroxyvitamin D testing, often outside clear indications (21,22). Electronic ordering, patient demand, media attention, supplement marketing, and broad non-specific symptom lists all contribute.

Overtesting has several harms. It increases cost. It labels many people with borderline abnormal results of uncertain significance. It may distract from better explanations for symptoms. It encourages repeated monitoring after minor dose changes. It may lead to high-dose treatment in low-risk adults, especially if the clinician or patient treats the laboratory threshold as a disease diagnosis.

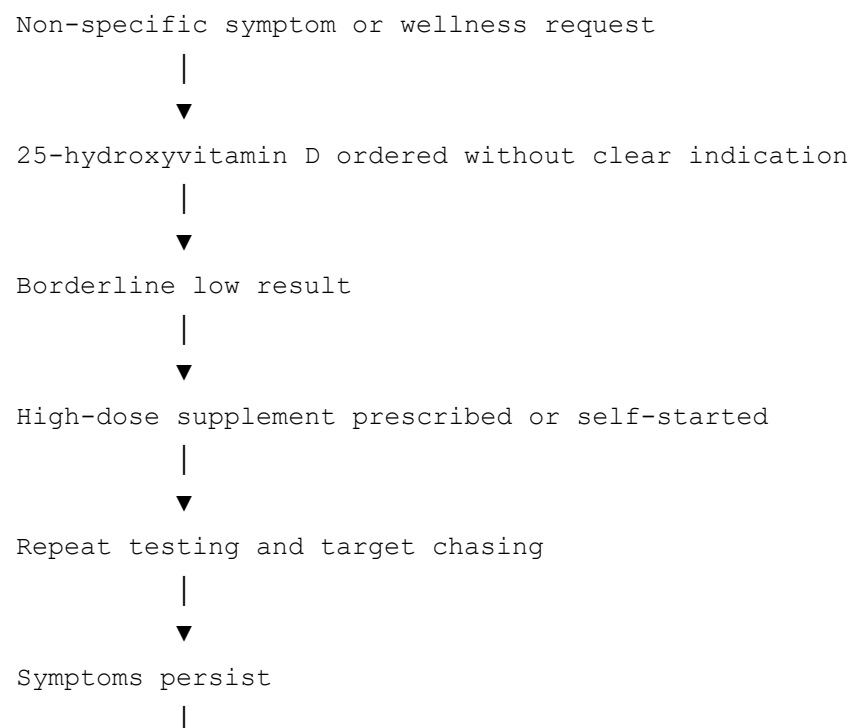
There is also assay variation. The same patient may receive different results depending on method, laboratory, standardization, season, and supplement timing. A small change in value may not represent a meaningful biological change. The USPSTF evidence report specifically noted difficulty in defining deficiency thresholds and variability of assays as part of the screening challenge (4).

A better testing culture would ask three questions before ordering:

Will this result change management?  
Is the patient in a high-risk group or symptomatic in a compatible way?  
Will I know what to do with a borderline result?

If the answer is no, supplementation to meet recommended dietary intake, dietary advice, safe sun exposure counselling, and attention to broader health may be more appropriate than laboratory screening.

**Figure 2 The overtesting cascade**





More supplements, missed diagnosis, or patient anxiety

The cascade can be interrupted at the first step by risk-based testing and at the second step by interpreting results in clinical context.

## 12. High-risk groups

High-risk patients are the group in whom vitamin D practice should become more careful, not less. These patients may be harmed by under-recognition of deficiency or by careless high-dose treatment.

High-risk groups include adults with osteoporosis, fragility fracture, osteomalacia symptoms, older adults in residential or institutional care, adults with little sunlight exposure, people wearing full skin-covering clothing, individuals with malabsorption, inflammatory bowel disease, coeliac disease, pancreatic disease, bariatric surgery, chronic liver disease, chronic kidney disease, nephrotic syndrome, long-term anticonvulsant use, glucocorticoid therapy, and medicines that alter vitamin D metabolism. Adults with obesity may have lower measured 25-hydroxyvitamin D concentrations, although the 2024 Endocrine Society guideline advises against routine screening in generally healthy adults with obesity unless another indication exists (1).

Dark skin pigmentation is associated with lower cutaneous vitamin D synthesis under the same ultraviolet exposure conditions. However, the 2024 Endocrine Society guideline also advises against routine screening based on dark complexion alone in generally healthy individuals, because trial evidence has not established screening thresholds linked to outcome benefit (1). This is an important distinction. Population-level risk does not automatically mean every individual needs testing in the absence of clinical indication.

A practical approach is to combine risk factors. A healthy adult with darker skin and no symptoms may not need testing. An older adult with darker skin, limited sun exposure, proximal muscle weakness, low calcium intake, and a fall history is different. Context changes yield.

**Table 3**

### Risk-based adult groups and practical vitamin D approach

| Patient group                                      | Test or supplement strategy                                                                                 |
|----------------------------------------------------|-------------------------------------------------------------------------------------------------------------|
| Osteomalacia symptoms or unexplained hypocalcaemia | Test 25-hydroxyvitamin D, calcium, phosphate, alkaline phosphatase, renal function, and parathyroid hormone |
| Osteoporosis or fragility fracture                 | Test and correct deficiency as part of bone-health management                                               |
| Institutionalized or housebound older adults       | Consider empiric intake support and testing when clinical risk is high                                      |
| Malabsorption or bariatric surgery                 | Testing and long-term monitoring are usually appropriate                                                    |
| Chronic kidney disease                             | Interpret with calcium, phosphate, parathyroid hormone, and kidney disease context                          |
| Long-term anticonvulsants or glucocorticoids       | Consider testing and bone-risk assessment                                                                   |

| Patient group                                                                   | Test or supplement strategy                                                                                                                              |
|---------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Generally healthy adult under 75 with no indication                             | Routine testing and high-dose supplementation are not supported                                                                                          |
| Adult over 75                                                                   | Ensure recommended intake; 2024 Endocrine Society supports empiric supplementation above DRI for mortality prevention but optimal dose remains uncertain |
| High-risk prediabetes                                                           | Empiric supplementation may be considered, but lifestyle intervention remains primary                                                                    |
| History of stones, hypercalcaemia, sarcoidosis, lymphoma, granulomatous disease | Avoid unsupervised supplementation; monitor calcium and renal function                                                                                   |

### 13. Supplementation strategy

Vitamin D supplementation should match the clinical question. There are three broad aims: maintaining recommended intake, correcting deficiency, and preventing disease in selected populations.

For maintenance, adults can use diet, fortified foods, safe sunlight exposure where appropriate, and standard-dose supplements. The Institute of Medicine report set recommended dietary allowance values of 600 IU daily for adults up to 70 years and 800 IU daily for those older than 70 years, based mainly on skeletal outcomes (5,6). The 2024 Endocrine Society guideline advises that healthy adults under 75 are unlikely to benefit from supplementation above current dietary reference intake solely for disease prevention (1).

For deficiency correction, dosing depends on baseline level, severity, symptoms, cause, absorption, body size, adherence, and comorbidity. Common regimens use daily or weekly cholecalciferol followed by maintenance dosing. The exact regimen should follow local guidance and patient context. Severe deficiency with hypocalcaemia, osteomalacia, malabsorption, bariatric surgery, chronic kidney disease, or granulomatous disease should not be managed as casual over-the-counter supplementation.

For adults over 50 who have an indication for vitamin D treatment, the 2024 Endocrine Society guideline suggests daily lower-dose supplementation rather than intermittent high-dose supplementation (1). This is consistent with fall evidence showing possible harm from large intermittent doses (12-14).

Calcium should not be forgotten. Vitamin D cannot correct inadequate calcium intake by itself. At the same time, unnecessary calcium supplementation can increase pill burden and may increase kidney stone risk in some contexts. Dietary calcium is often preferable when feasible. Calcium supplementation should be individualized, especially in adults with nephrolithiasis risk, chronic kidney disease, cardiovascular concerns, or high dietary calcium intake.

### 14. Toxicity

Vitamin D toxicity is uncommon but important. It is usually caused by excessive supplementation, prescription error, manufacturing error, or prolonged high-dose use. Sun exposure does not cause vitamin D toxicity because cutaneous production is self-limited.

The main clinical problem is hypercalcaemia. Symptoms may include nausea, vomiting, constipation, thirst, polyuria, dehydration, confusion, weakness, nephrolithiasis, acute kidney injury, arrhythmia, and in severe cases renal failure or soft-tissue calcification. Toxicity risk is

higher when high-dose vitamin D is combined with calcium, when patients use several products containing vitamin D, or when medical conditions increase sensitivity to vitamin D.

Marcinowska-Suchowierska et al. described vitamin D toxicity as a clinical state related to excessive long-term vitamin D intake or altered vitamin D metabolism, with severe hypercalcaemia as the major manifestation (37). Jones noted that toxicity usually requires very high 25-hydroxyvitamin D concentrations, although susceptibility varies (38). Tebben et al. reviewed vitamin D-mediated hypercalcaemia and highlighted multiple mechanisms, including excessive intake and extrarenal production of active vitamin D in granulomatous disease and lymphoma (39).

The safety message is not to frighten patients away from appropriate supplementation. It is to avoid unsupervised megadoses, repeated loading doses without indication, and treatment plans that monitor only 25-hydroxyvitamin D while ignoring calcium and renal function.

**Table 4 Toxicity warning points for adult practice**

| Situation                                                                          | Why it matters                                                                  |
|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| Multiple supplements containing vitamin D                                          | Patients may not realise their total dose                                       |
| Repeated high-dose prescriptions                                                   | Accumulation can occur, especially without monitoring                           |
| Hypercalcaemia or kidney stones                                                    | Vitamin D may worsen calcium-related risk                                       |
| Sarcoidosis, tuberculosis, fungal granulomatous disease, lymphoma                  | Extrarenal 1-alpha hydroxylase activity can increase active vitamin D           |
| Chronic kidney disease                                                             | Calcium, phosphate, parathyroid hormone, and active vitamin D physiology differ |
| High calcium intake plus vitamin D                                                 | Hypercalcaemia or stones may occur in susceptible patients                      |
| Persistent nausea, constipation, thirst, confusion, polyuria after supplementation | Check calcium, creatinine, and vitamin D exposure history                       |

## 15. A practical adult medicine pathway

Vitamin D care should begin with patient classification.

The first group is symptomatic or high risk. These patients deserve testing and targeted treatment. Examples include osteomalacia features, osteoporosis, fragility fracture, hypocalcaemia, malabsorption, bariatric surgery, chronic kidney disease, long-term anticonvulsants, and strong clinical suspicion.

The second group is generally healthy but likely to have low intake or low sunlight exposure. Testing may not be required. Intake advice and standard-dose supplementation may be enough, especially when the patient is not symptomatic and has no safety risk.

The third group is the worried well. These patients often request testing because of media claims or non-specific symptoms. The best response is not dismissal. It is explanation: vitamin D is important, but routine screening has not been shown to improve outcomes in asymptomatic adults, and normal intake can be maintained without repeated blood tests.

The fourth group is the self-supplementing high-dose user. These patients need a medication and supplement history, including dose, frequency, brand, calcium intake, and

duration. If high-dose use is present, check calcium and renal function, and consider 25-hydroxyvitamin D measurement.

**Figure 3 Four adult vitamin D pathways**

|                             |
|-----------------------------|
| 1. High-risk or symptomatic |
| Test, interpret fully,      |
| replace and monitor         |

|                            |
|----------------------------|
| 2. Low intake or low sun   |
| Standard intake support,   |
| testing only if risk rises |

|                           |
|---------------------------|
| 3. Asymptomatic wellness  |
| Avoid routine screening,  |
| discuss diet and safe use |

|                             |
|-----------------------------|
| 4. High-dose self-use       |
| Review total dose, calcium, |
| renal function, toxicity    |

## Discussion

Vitamin D is a good example of a nutrient that became both under-recognized in some patients and overmedicalised in others. Severe deficiency is clinically important. It can cause osteomalacia, muscle weakness, hypocalcaemia, secondary hyperparathyroidism, and skeletal fragility. In high-risk adults, failure to test and treat can cause harm.

At the same time, modern trial evidence has narrowed the claims that should be made for supplementation. Generally healthy adults not selected for deficiency do not appear to gain meaningful fracture protection from vitamin D alone. Fall prevention is not supported as a stand-alone reason for supplementation in community-dwelling older adults, and large intermittent doses may increase fall risk. Cardiovascular and cancer prevention claims are not supported by major trials as general adult indications. Immune claims have also weakened as newer respiratory infection meta-analysis evidence has become more neutral.

This does not make vitamin D unimportant. It makes patient selection more important.

Overtesting persists partly because vitamin D sits at the intersection of real biology and vague symptoms. Fatigue, pain, low mood, poor sleep, weight gain, and recurrent minor illness are common. A low or borderline vitamin D result can feel like an answer. Sometimes it is part of the answer. Often it is not. The clinician's job is to avoid both extremes: dismissing deficiency where it matters and treating a laboratory number as the whole diagnosis.

The 2024 Endocrine Society guideline is especially important because it separates disease-prevention supplementation from treatment of established indications. It does not provide a full manual for every patient with malabsorption, osteomalacia, chronic kidney disease, or osteoporosis. Rather, it says that in populations without established indications, evidence does not support routine 25-hydroxyvitamin D testing or universal high-dose supplementation for prevention. That distinction should be preserved in clinical interpretation.

There are unresolved areas. Optimal thresholds remain debated for specific diseases. Assay variability still complicates interpretation. The effect of supplementation may differ by baseline status, body weight, calcium intake, dosing pattern, genetics, adherence, sun exposure, and comorbidity. Trials often include many participants who are not severely deficient, which may dilute benefit in those who are. More research is needed in malabsorptive states, frailty, institutional care, severe deficiency, and diverse populations with different baseline risk.

The most defensible direction for adult practice is risk-based use. Test when the pre-test probability is meaningful. Supplement to meet recommended intake when diet and sunlight are inadequate. Treat deficiency when it is clinically relevant. Avoid high intermittent doses for convenience unless there is a clear reason. Monitor calcium and renal function when dose or patient risk makes toxicity plausible. Do not promise benefits that trials have not shown.

## Conclusion

Vitamin D deficiency testing and supplementation should be used with clinical intention rather than habit. In adult practice, testing is appropriate when deficiency is suspected, when skeletal disease is present, when calcium or phosphate abnormalities suggest disordered mineral metabolism, or when malabsorption, bariatric surgery, chronic kidney disease, liver disease, high-risk medicines, or marked sunlight limitation make deficiency likely.

Routine screening of asymptomatic adults is not supported by current evidence. The USPSTF found insufficient evidence to determine whether screening asymptomatic community-dwelling adults improves outcomes, and the 2024 Endocrine Society guideline advises against routine 25-hydroxyvitamin D testing in generally healthy populations without established indications. These recommendations should reduce low-value testing but should not prevent testing in clinically appropriate high-risk patients.

Supplementation remains important for correcting deficiency and maintaining adequate intake. It is also part of osteoporosis and osteomalacia care when deficiency or inadequate intake is present. However, vitamin D should not be promoted as a general solution for falls, fatigue, immunity, cardiovascular prevention, cancer prevention, or wellness in adults who have no clear indication. The best evidence shows little benefit for many of these broad uses, and high intermittent doses may cause harm in older adults.

A safe approach is simple: identify high-risk patients, test when results will change management, use reasonable daily dosing where supplementation is indicated, avoid unnecessary megadoses, check calcium and renal function when toxicity risk exists, and reassess symptoms rather than chasing a number. Vitamin D practice should return to clinical medicine: the right patient, the right dose, the right reason, and the right follow-up.

## References

1. Demay MB, Pittas AG, Bikle DD, Diab DL, Kiely M, Lazaretti-Castro M, et al. Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2024;109(8):1907-1947. PMID: 38828931.
2. Shah VP, Nayfeh T, Alsawas M, et al. A Systematic Review Supporting the Endocrine Society Clinical Practice Guidelines on Vitamin D. *J Clin Endocrinol Metab.* 2024;109(8):1961-1974. PMID: 38828942.
3. Krist AH, Davidson KW, Mangione CM, Cabana M, Caughey AB, Davis EM, et al. Screening for Vitamin D Deficiency in Adults: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2021;325(14):1436-1442. PMID: 33847711.

4. Kahwati LC, LeBlanc E, Palmieri Weber R, 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):1443-1463. PMID: 33847712.
5. 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):53-58. PMID: 21118827.
6. Ross AC. The 2011 Dietary Reference Intakes for Calcium and Vitamin D. *Public Health Nutr*. 2011;14(5):938-939. PMID: 21443983.
7. Holick MF. Vitamin D Status: Measurement, Interpretation, and Clinical Application. *Ann Epidemiol*. 2009;19(2):73-78. PMID: 18329892.
8. 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):1911-1930. PMID: 21646368.
9. Herrick KA, Storandt RJ, Afful J, Pfeiffer CM, Schleicher RL, Gahche JJ, et al. Vitamin D Status in the United States, 2011-2014. *Am J Clin Nutr*. 2019;110(1):150-157. PMID: 31076739.
10. Cui A, Zhang T, Xiao P, Fan Z, Wang H, Zhuang Y. Prevalence, Trend, and Predictor Analyses of Vitamin D Deficiency in the US Population, 2001-2018. *Front Nutr*. 2022;9:965376. PMID: 36263304.
11. LeBoff MS, Chou SH, Ratliff KA, Cook NR, Khurana B, Kim E, et al. Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults. *N Engl J Med*. 2022;387(4):299-309. PMID: 35939577.
12. Waterhouse M, Sanguineti E, Baxter C, Duarte Romero B, McLeod DSA, English DR, et al. Vitamin D Supplementation and Risk of Falling: Outcomes from the Randomized, Placebo-Controlled D-Health Trial. *J Cachexia Sarcopenia Muscle*. 2021;12(6):1428-1439. PMID: 34337905.
13. Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ, Stachelin HB, Meyer OW, Theiler R, et al. Monthly High-Dose Vitamin D Treatment for the Prevention of Functional Decline: A Randomized Clinical Trial. *JAMA Intern Med*. 2016;176(2):175-183. PMID: 26747333.
14. Sanders KM, Stuart AL, Williamson EJ, Simpson JA, Kotowicz MA, Young D, et al. Annual High-Dose Oral Vitamin D and Falls and Fractures in Older Women: A Randomized Controlled Trial. *JAMA*. 2010;303(18):1815-1822. PMID: 20460620.
15. Chakhtoura M, Bacha DS, Gharos C, Ajjour S, Assaad M, Jabbour Y, et al. Vitamin D Supplementation and Fractures in Adults: A Systematic Umbrella Review of Meta-Analyses of Controlled Trials. *J Clin Endocrinol Metab*. 2022;107(3):882-898. PMID: 34687206.
16. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, Stachelin HB, Bazemore MG, Zee RY, et al. Effect of Vitamin D on Falls: A Meta-Analysis. *JAMA*. 2004;291(16):1999-2006. PMID: 15113819.
17. Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture Prevention with Vitamin D Supplementation: A Meta-Analysis of Randomized Controlled Trials. *JAMA*. 2005;293(18):2257-2264. PMID: 15886381.
18. Weaver CM, Alexander DD, Boushey CJ, Dawson-Hughes B, Lappe JM, LeBoff MS, et al. Calcium Plus Vitamin D Supplementation and Risk of Fractures: An Updated Meta-Analysis from the National Osteoporosis Foundation. *Osteoporos Int*. 2016;27(1):367-376. PMID: 26510847.
19. Zhao JG, Zeng XT, Wang J, Liu L. Association Between Calcium or Vitamin D Supplementation and Fracture Incidence in Community-Dwelling Older Adults: A Systematic Review and Meta-Analysis. *JAMA*. 2017;318(24):2466-2482. PMID: 29279934.
20. Massé O, Boutron I, Baron G, et al. Calcium, Vitamin D, or Combined Supplementation to Prevent Falls and Fractures in Community-Dwelling Adults: Systematic Review and Meta-Analysis. *BMJ*. 2026;393:e088050. PMID: 42161415.
21. Woodford HJ, Barrett S, Pattman S. Vitamin D: Too Much Testing and Treating? *Clin Med (Lond)*. 2018;18(3):196-199. PMID: 29858427.
22. Basatemur E, Horsfall L, Marston L, Rait G, Sutcliffe A. Trends in the Diagnosis of Vitamin D Deficiency. *Pediatrics*. 2017;139(3):e20162748. PMID: 28209721.

23. Nowak A, Boesch L, Andres E, Battegay E, Hornemann T, Schmid C, et al. Effect of Vitamin D3 on Self-Perceived Fatigue: A Double-Blind Randomized Placebo-Controlled Trial. *Medicine (Baltimore)*. 2016;95(52):e5353. PMID: 28033244.
24. Roy S, Sherman A, Monari-Sparks MJ, Schweiker O, Hunter K. Correction of Low Vitamin D Improves Fatigue: Effect of Correction of Low Vitamin D in Fatigue Study. *N Am J Med Sci*. 2014;6(8):396-402. PMID: 25210666.
25. Di Molfetta IV, Bordoni L, Gabbianelli R. Vitamin D and Its Role on the Fatigue Mitigation: A Narrative Review. *Nutrients*. 2024;16(2):221. PMID: 38257114.
26. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D Supplementation to Prevent Acute Respiratory Tract Infections: Systematic Review and Meta-Analysis of Individual Participant Data. *BMJ*. 2017;356:i6583. PMID: 28202713.
27. Jolliffe DA, Camargo CA Jr, Sluyter JD, Aglipay M, Aloia JF, Ganmaa D, et al. Vitamin D Supplementation to Prevent Acute Respiratory Infections: A Systematic Review and Meta-Analysis of Aggregate Data from Randomised Controlled Trials. *Lancet Diabetes Endocrinol*. 2021;9(5):276-292. PMID: 33798465.
28. Jolliffe DA, Ganmaa D, Wejse C, et al. Vitamin D Supplementation for the Prevention of Acute Respiratory Infections: Systematic Review and Meta-Analysis of Stratified Aggregate Data. *Lancet Diabetes Endocrinol*. 2025. PMID: 39993397.
29. Hahn J, Cook NR, Alexander EK, Friedman S, Walter J, Bubes V, et al. Vitamin D and Marine Omega 3 Fatty Acid Supplementation and Incident Autoimmune Disease: VITAL Randomized Controlled Trial. *BMJ*. 2022;376:e066452. PMID: 35082139.
30. Costenbader KH, Hahn J, Cook NR, Wang M, Lee IM, Buring JE, et al. Vitamin D and Marine n-3 Fatty Acids for Autoimmune Disease Prevention: Outcomes Two Years After Completion of a Double-Blind, Placebo-Controlled Trial. *Arthritis Rheumatol*. 2024;76(4):615-621. PMID: 38272846.
31. Manson JE, Cook NR, Lee IM, Christen W, Bassuk SS, Mora S, et al. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. *N Engl J Med*. 2019;380(1):33-44. PMID: 30415629.
32. Virtanen JK, Nurmi T, Aro A, Mursu J, Tuomainen TP, Voutilainen S. Vitamin D Supplementation and Prevention of Cardiovascular Disease and Cancer in the Finnish Vitamin D Trial. *Am J Clin Nutr*. 2022;115(5):1300-1310. PMID: 34982819.
33. Thompson B, Waterhouse M, English DR, McLeod DSA, Armstrong BK, Baxter C, et al. Vitamin D Supplementation and Major Cardiovascular Events: D-Health Randomised Controlled Trial. *BMJ*. 2023;381:e075230. PMID: 37380191.
34. Barbarawi M, Kheiri B, Zayed Y, Barbarawi O, Dhillon H, Swaid B, et al. Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83,000 Individuals in 21 Randomized Clinical Trials: A Meta-Analysis. *JAMA Cardiol*. 2019;4(8):765-776. PMID: 31215980.
35. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, et al. Vitamin D Supplementation and Prevention of Type 2 Diabetes. *N Engl J Med*. 2019;381(6):520-530. PMID: 31173679.
36. Pittas AG, Kawahara T, Jorde R, Dawson-Hughes B, Vickery EM, Angellotti E, et al. Vitamin D and Risk for Type 2 Diabetes in People With Prediabetes: A Systematic Review and Meta-Analysis of Individual Participant Data from 3 Randomized Clinical Trials. *Ann Intern Med*. 2023;176(3):355-363. PMID: 36745886.
37. Marcinowska-Suchowierska E, Kupisz-Urbańska M, Łukaszkiwicz J, Pludowski P, Jones G. Vitamin D Toxicity: A Clinical Perspective. *Front Endocrinol (Lausanne)*. 2018;9:550. PMID: 30294301.
38. Jones G. Pharmacokinetics of Vitamin D Toxicity. *Am J Clin Nutr*. 2008;88(2):582S-586S. PMID: 18689406.
39. Tebben PJ, Singh RJ, Kumar R. Vitamin D-Mediated Hypercalcemia: Mechanisms, Diagnosis, and Treatment. *Endocr Rev*. 2016;37(5):521-547. PMID: 27588937.