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The Impact of Vitamin D Deficiency on Population Health: Assessment, Monitoring, and Intervention Strategies

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Abstract

Background: Vitamin D is an essential fat-soluble hormone involved in calcium and phosphate homeostasis, bone mineralization, and multiple extra-skeletal physiological processes. Despite advances in nutrition and food fortification, vitamin D deficiency remains a major global public health problem, affecting diverse populations and contributing to significant morbidity.

Aim: This review aims to assess the global burden of vitamin D deficiency, examine its etiology, pathophysiology, clinical manifestations, and evaluate current strategies for assessment, monitoring, prevention, and management.

Methods: A narrative synthesis of epidemiological data, clinical outcomes, diagnostic criteria, and therapeutic approaches to vitamin D deficiency was conducted, incorporating evidence from observational studies, clinical trials, and international guidelines discussed in the literature.

Results: Vitamin D deficiency affects approximately one billion individuals worldwide, particularly older adults, obese individuals, hospitalized patients, and those with limited sun exposure. Deficiency is linked to skeletal disorders such as rickets and osteomalacia, increased fracture risk, muscle weakness, and potential non-skeletal complications. Vitamin D3 supplementation is superior to vitamin D2 in correcting deficiency and maintaining adequate serum levels.

Conclusion: Targeted screening, individualized supplementation, and interprofessional healthcare strategies are essential to reduce the burden of vitamin D deficiency and its complications.

Key Words: Vitamin D deficiency; 25-hydroxyvitamin D; Osteomalacia; Rickets; Supplementation; Public health.

Introduction

Vitamin D plays a critical role in maintaining skeletal integrity by regulating calcium and phosphate metabolism. Its deficiency impairs bone mineralization, leading to rickets in children, characterized by skeletal deformities, growth retardation, and delayed motor development, and osteomalacia in adults, which manifests as bone pain, muscular weakness, and increased fracture risk.[1] The discovery of vitamin D and its relationship to rickets in the early 20th century prompted public health initiatives, including the fortification of milk in North America during the 1930s, which significantly reduced the incidence of childhood rickets.[2] Despite these efforts, vitamin D deficiency remains widespread, particularly in populations with limited sun exposure, darker skin pigmentation, or diets low in vitamin D-rich foods.[4] Dietary intake recommendations vary based on age, sex, and physiological status. Adults are generally advised to consume 400 to 800 international units (IU) daily to maintain adequate serum levels and support bone health.[3] However, many individuals fail to meet these recommendations due to dietary insufficiency, limited outdoor activity, or underlying medical conditions that affect absorption or metabolism. Observational studies have expanded the significance of vitamin D beyond musculoskeletal health, suggesting associations with cardiovascular disease, diabetes, cancer, autoimmune disorders, and mood

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disorders, though causal relationships remain under investigation.[5] The assessment of vitamin D status relies on measuring serum total 25-hydroxyvitamin D. Current guidelines by the Endocrine Society define sufficiency as levels above 30 ng/mL (50 nmol/L), insufficiency as 12–30 ng/mL (30–77 nmol/L), and deficiency as levels below 12 ng/mL (30 nmol/L). The optimal concentration for broader health outcomes continues to be debated, highlighting the need for population-specific strategies for prevention, screening, and supplementation. Monitoring vitamin D levels and addressing deficiencies represent important components of public health nutrition, laboratory evaluation, and clinical management.

Etiology:

Vitamin D, a fat-soluble secosteroid, is obtained primarily through dermal synthesis, as natural dietary sources are limited. Cholecalciferol (vitamin D3), synthesized in the skin under ultraviolet B (UVB) radiation, and ergocalciferol (vitamin D2), obtained from dietary sources such as fortified foods and plant-based products, undergo sequential hydroxylation to become biologically active. The first hydroxylation occurs in the liver, where both D2 and D3 forms are converted to 25-hydroxyvitamin D by hepatic 25-hydroxylase. This circulating form serves as the primary indicator of vitamin D status. The second hydroxylation occurs in the kidneys, where 1α-hydroxylase converts 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D, the most active metabolite. This active form increases intestinal calcium absorption, promotes bone resorption, and reduces renal excretion of calcium and phosphate, thereby maintaining calcium homeostasis and skeletal integrity. All hydroxylation steps are mediated by cytochrome P450 mixed-function oxidases, highlighting the complex enzymatic regulation of vitamin D metabolism.[6][7] Vitamin D deficiency may arise from multiple mechanisms that disrupt synthesis, metabolism, or action. Dietary insufficiency or malabsorption is a leading cause, particularly in conditions such as celiac disease, short bowel syndrome, gastric bypass, inflammatory bowel disease, chronic pancreatic insufficiency, and cystic fibrosis. Older adults are at higher risk due to decreased dietary intake and reduced nutrient absorption efficiency.[8] Insufficient sun exposure contributes significantly to deficiency. Daily exposure of approximately 20 minutes with over 40% skin surface exposed is necessary for adequate dermal synthesis. Cutaneous production declines with age, and individuals with darker skin pigmentation have reduced efficiency of UVB-mediated synthesis. Institutionalized individuals, those with prolonged hospitalizations, or individuals who regularly use sunscreen are at increased risk of vitamin D deficiency due to limited sun exposure.[9][10]

Defects in endogenous synthesis also contribute to deficiency. Chronic liver disease, such as cirrhosis, impairs 25-hydroxylation, while renal failure and hypoparathyroidism reduce 1α-hydroxylation, limiting production of the active metabolite.[11][12][13] Certain medications, including phenobarbital, carbamazepine, dexamethasone, rifampin, and others, induce hepatic cytochrome P450 enzymes, accelerating the catabolism of vitamin D into inactive metabolites.[14] Finally, hereditary disorders, such as vitamin D-resistant rickets, cause end-organ resistance, whereby normal circulating levels of vitamin D fail to elicit an adequate biological response.[15] Collectively, these etiological factors illustrate the multifactorial nature of vitamin D deficiency, emphasizing the interplay between environmental exposure, nutritional intake, metabolic capacity, pharmacologic influences, and genetic predispositions. Recognition of these diverse causes is essential for targeted prevention, early diagnosis, and appropriate management to reduce the risk of skeletal and non-skeletal complications associated with inadequate vitamin D status.

Epidemiology

Vitamin D deficiency represents a significant global public health concern, with estimates suggesting that approximately one billion individuals worldwide are affected. Epidemiological data indicate that nearly half of certain populations experience suboptimal vitamin D status, defined as insufficiency or deficiency. The condition is particularly prevalent among older adults, individuals with obesity, residents of long-term care facilities, and hospitalized patients. Obesity confers a substantially increased risk, with affected individuals demonstrating a 35% higher prevalence of vitamin D deficiency irrespective of geographic latitude or chronological age [16]. In the United States, epidemiological studies report that between 50% and 60% of nursing home residents and hospitalized patients exhibit deficient vitamin D levels [17][18]. Ethnic and cultural factors further influence deficiency prevalence. Individuals with higher melanin pigmentation or those practicing extensive skin coverage are at heightened risk due to reduced cutaneous synthesis of vitamin D. In the U.S., 47% of African American infants and 56% of Caucasian infants present with vitamin D deficiency. The prevalence is markedly higher in regions such as the Middle East and South Asia, with more than 90% of infants in Iran, Turkey, and India affected. Among adults, 35% of the U.S. population demonstrates deficiency, whereas the rates exceed 80% in Pakistan, India, and Bangladesh. Older adults exhibit even greater susceptibility, with 61% of older Americans deficient, compared to 90% in Turkey, 96% in India, 72% in Pakistan, and 67% in Iran [19]. Vitamin D deficiency is also highly prevalent among patients with chronic kidney disease. Hemodialysis, concomitant hepatic dysfunction, or a history of liver transplantation significantly exacerbate this risk, with 85% to 99% of these patients affected [20]. Critically ill individuals admitted to intensive care units frequently exhibit deficiency, which is associated with more severe disease manifestations, increased morbidity, and higher mortality rates [21]. These data underscore the widespread and multifactorial nature of vitamin D deficiency, highlighting its disproportionate burden among high-risk populations and the need for targeted public health strategies to mitigate adverse health outcomes.

Pathophysiology

Vitamin D plays a central role in maintaining calcium homeostasis and supporting normal bone metabolism. Its active form, 1,25-dihydroxyvitamin D, facilitates intestinal absorption of calcium and phosphorus, ensuring adequate mineral availability for bone formation and remodeling. In conditions of chronic or severe vitamin D deficiency, intestinal calcium and phosphorus absorption is impaired, resulting in hypocalcemia. The reduction in circulating calcium levels triggers a compensatory increase in parathyroid hormone (PTH) secretion, leading to secondary hyperparathyroidism [22]. Elevated PTH levels stimulate osteoclastic bone resorption, mobilizing calcium from the skeleton to maintain serum calcium concentrations. This process accelerates bone turnover, promotes urinary phosphate excretion, and contributes to cortical bone thinning and increased porosity [23]. These alterations in mineral metabolism can have profound skeletal consequences. In adults, chronic vitamin D deficiency often manifests as osteomalacia, characterized by impaired bone mineralization and bone softening, and may progress to osteoporosis, marked by reduced bone mass and structural deterioration. In children, insufficient vitamin D leads to rickets, a disorder of growing bones that results in skeletal deformities, growth retardation, and increased fracture susceptibility. The skeletal complications of vitamin D deficiency are therefore a direct consequence of the interplay between impaired mineral absorption, compensatory hormonal responses, and heightened bone resorption, which together compromise bone strength and structural integrity. Beyond the skeletal system, vitamin D deficiency can also affect neuromuscular function, immune regulation, and cardiovascular health, illustrating the broad systemic impact of this nutrient deficiency on overall health.

History and Physical

Most individuals with vitamin D deficiency remain asymptomatic, particularly in mild or subclinical cases. Nevertheless, even modest chronic deficiency can result in hypocalcemia and secondary hyperparathyroidism, increasing the risk of osteoporosis, falls, and fragility fractures, especially among older adults [24]. As the deficiency progresses, patients may develop symptoms attributable to elevated PTH levels and impaired mineralization, including diffuse bone pain, arthralgia, generalized myalgia, muscle weakness, fatigue, and fasciculations [25]. These manifestations reflect both the skeletal and neuromuscular effects of prolonged hypocalcemia. In adults, chronic vitamin D deficiency contributes to structural bone changes that predispose to fragility fractures, often occurring in the vertebrae, hip, and distal radius. Osteomalacia presents clinically with diffuse skeletal pain, gait disturbances, and tenderness over weight-bearing bones. Children are particularly vulnerable to the consequences of deficiency due to active bone growth. Clinical features of pediatric vitamin D deficiency include irritability, lethargy, delayed developmental milestones, skeletal deformities such as bowed legs or rachitic rosary, and increased fracture susceptibility [26]. A careful history should explore dietary intake, sun exposure, chronic illnesses affecting absorption or metabolism, and family history of metabolic bone disorders. Physical examination may reveal bone tenderness, muscular hypotonia, and skeletal deformities in severe cases. Early recognition of deficiency through clinical evaluation is crucial for initiating timely interventions that prevent irreversible skeletal damage and neuromuscular complications.

Evaluation

Evaluation of vitamin D status is indicated in individuals at high risk for deficiency, including older adults, individuals with limited sun exposure, malabsorption syndromes, obesity, chronic kidney or liver disease, and those on medications affecting vitamin D metabolism. Measurement of total serum 25-hydroxyvitamin D remains the standard diagnostic test, as it reflects both dietary intake and endogenous synthesis [27]. Optimal serum levels of 25-hydroxyvitamin D remain a subject of debate, but the International Society for Clinical Densitometry and the International Osteoporosis Foundation recommend maintaining concentrations above 30 ng/mL to reduce the risk of falls and fractures in older adults [28].

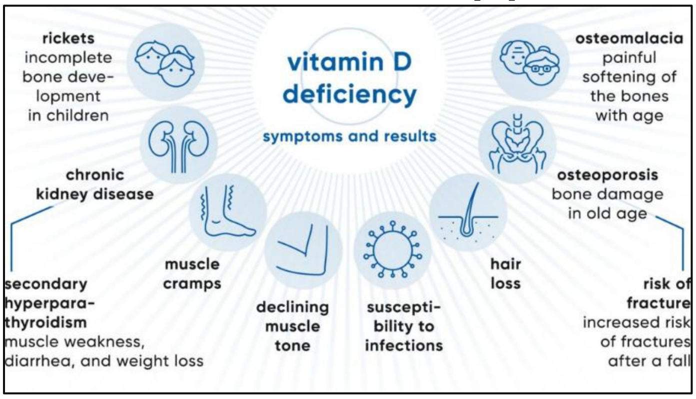

Fig. 1: Vitamin D Deficiency.

Assessment should also consider racial and ethnic variations in bone mineral density and fracture risk. African Americans, for example, often have higher bone density and lower fracture incidence despite lower 25-hydroxyvitamin D levels compared to other populations. The response to calcium and vitamin D supplementation may differ across racial groups, highlighting the need for individualized evaluation and treatment planning. When deficiency is detected, clinicians should evaluate secondary hyperparathyroidism by measuring serum PTH and calcium levels. Elevated PTH in the context of low vitamin D confirms the presence of secondary hyperparathyroidism and guides therapeutic interventions. While the upper safe limit of 25-hydroxyvitamin D is not precisely defined, concentrations above 100 ng/mL may increase the risk of hypercalcemia, and levels exceeding 150 ng/mL are considered toxic, necessitating careful monitoring in patients receiving supplementation [29]. Comprehensive evaluation ensures accurate diagnosis, guides appropriate management, and mitigates the risk of long-term skeletal and systemic complications associated with vitamin D deficiency.

Treatment / Management

Vitamin D supplementation is the cornerstone in preventing and managing deficiency, and its formulation significantly influences efficacy. Among available options, vitamin D3 (cholecalciferol) demonstrates superior potency compared to vitamin D2 (ergocalciferol) in elevating serum 25-hydroxyvitamin D levels, making it the preferred choice for correcting deficiencies [30]. The pharmacokinetic superiority of vitamin D3, including greater stability and longer half-life, translates into more consistent biochemical repletion and sustained maintenance of adequate vitamin D status. Prevention strategies for vitamin D deficiency emphasize age-specific supplementation and lifestyle modifications. Adults younger than 65 who do not receive sufficient sun exposure year-round are advised to consume 400 to 800 IU of vitamin D3 daily to maintain optimal serum levels. Older adults, particularly those aged 65 years and above, require higher daily intake, ranging from 800 to 1,000 IU of vitamin D3, to reduce the risk of fractures, falls, and bone demineralization [31]. Caution is warranted with higher doses, as supplementation exceeding 4,000 IU daily is not recommended in adults with adequate vitamin D stores due to the potential for toxicity. Lifestyle modifications, including safe sun exposure and dietary intake of fortified foods, complement pharmacologic prevention. Management of established vitamin D deficiency is guided by baseline serum 25-hydroxyvitamin D concentrations and patient-specific risk factors. Vitamin D3 remains the agent of choice due to its higher efficacy in raising serum levels compared with vitamin D2 [32]. For patients with severe deficiency, defined as serum 25-hydroxyvitamin D levels below 12 ng/mL, an intensive repletion regimen is recommended for approximately eight weeks. Oral supplementation may involve daily doses of 6,000 IU (150 mcg) or weekly doses ranging from 25,000 to 50,000 IU (625–1,250 mcg). Following normalization, typically defined by serum levels exceeding 30 ng/mL, a maintenance dose of 1,000 to 2,000 IU daily is advised. Patients with high-risk profiles, including individuals with obesity, malabsorption syndromes, African American or Hispanic descent, or those on medications accelerating vitamin D catabolism, may require higher initial doses up to 10,000 IU daily, with maintenance doses of 3,000 to 6,000 IU daily [32].

For moderate deficiency, with serum levels between 12 and 20 ng/mL, supplementation with 800 to 1,000 IU daily is sufficient, with serum reassessment after three months to ensure correction. Individuals with mild deficiency or insufficiency, defined as serum levels between 20 and 30 ng/mL, typically achieve optimal status with 600 to 800 IU daily. Pediatric populations require tailored dosing strategies. Children with deficiency receive 2,000 IU daily or 50,000 IU weekly for six weeks, followed by a maintenance dose of 1,000 IU daily after achieving sufficient serum levels. Breastfed infants or children consuming less than one liter of fortified milk daily should receive 400 IU of vitamin D daily in accordance with American Academy of Pediatrics guidelines [33]. In individuals with persistent deficiency despite conventional therapy, calcitriol may be indicated. As the active form of vitamin D, calcitriol bypasses renal 1α-hydroxylation, making it particularly suitable for patients with advanced kidney disease or hypoparathyroidism. Careful monitoring of serum calcium is essential due to the increased risk of hypercalcemia [34]. Similarly, calcidiol, the major circulating metabolite of cholecalciferol, may be employed in patients with significant hepatic dysfunction because it does not require hepatic 25-hydroxylation for activation. Therapeutic dosing ranges from 30 to 200 μg daily, tailored to the degree of deficiency and hepatic impairment [35]. Treatment and management strategies emphasize individualized therapy, taking into account the severity of deficiency, comorbidities, age, baseline vitamin D status, and risk factors for impaired metabolism or absorption. Regular monitoring of serum 25-hydroxyvitamin D, calcium, and PTH levels is essential to guide therapy, assess efficacy, and avoid complications. When applied systematically, these interventions effectively restore and maintain optimal vitamin D status, thereby reducing the risk of skeletal complications, improving musculoskeletal function, and contributing to overall metabolic and systemic health. The integration of preventive supplementation with targeted therapeutic interventions ensures that both deficiency and insufficiency are addressed across diverse populations, supporting long-term clinical outcomes and public health objectives.

Differential Diagnosis

Vitamin D deficiency often presents insidiously, making a comprehensive differential diagnosis essential for accurate identification and management. Several conditions can mimic or contribute to insufficient vitamin D status, either by impairing absorption, metabolism, or endogenous synthesis. Celiac sprue, a gluten-induced enteropathy, disrupts intestinal villous architecture, thereby reducing the absorption of fat-soluble vitamins, including vitamin D. Patients with cystic fibrosis experience malabsorption due to pancreatic enzyme insufficiency, resulting in chronic deficiencies of fat-soluble vitamins, including vitamin D. End-stage liver disease also contributes to deficiency by impairing 25-hydroxylation, a critical hepatic step in vitamin D activation. In addition to these disease-related causes, lifestyle and environmental factors must be considered. Insufficient sunlight exposure remains a major contributor, particularly in individuals living at high latitudes, those with limited outdoor activity, or those who consistently employ sun-protective measures such as clothing or sunscreen. Dietary inadequacy is another key factor, particularly in populations with low intake of fortified foods or naturally rich sources such as fatty fish, cod liver oil, or fortified dairy products. The use of certain medications, including antiepileptic drugs like phenytoin, carbamazepine, and phenobarbital, accelerates hepatic metabolism of vitamin D, increasing the risk of deficiency over time. Chronic corticosteroid therapy similarly impairs vitamin D-mediated calcium absorption and bone metabolism. A systematic approach that incorporates these potential contributors allows clinicians to differentiate primary vitamin D deficiency from secondary forms arising from malabsorption, metabolic derangements, or medication-induced alterations. Comprehensive assessment should include a detailed dietary history, medication review, lifestyle evaluation, and screening for gastrointestinal or hepatic disorders. Laboratory evaluation, including measurement of serum 25-hydroxyvitamin D, parathyroid hormone, calcium, and phosphate, helps corroborate clinical suspicion and guide individualized treatment strategies. Recognizing these differential factors ensures early intervention, prevents skeletal complications, and addresses underlying etiologies to maintain long-term bone health and systemic physiological function. Properly identifying the etiology also informs public health strategies, especially in high-risk populations where deficiency is prevalent due to environmental or dietary limitations.

Pertinent Studies and Ongoing Trials

Evidence from large-scale clinical trials and meta-analyses has consistently highlighted the potential benefits of vitamin D supplementation beyond bone health, with implications for mortality, cancer prevention, and chronic disease management. A comprehensive meta-analysis of eighteen randomized controlled trials encompassing over 57,000 participants demonstrated that daily supplementation with vitamin D significantly reduced total mortality rates, supporting its role in overall population health [36]. This finding underscores the importance of maintaining adequate serum 25-hydroxyvitamin D levels, particularly among older adults and individuals with chronic health conditions, as a preventive strategy. Further evidence emerges from the Women's Health Initiative, which evaluated the combined supplementation of calcium and vitamin D. The study revealed that supplementation was associated with a reduced risk of total cancer, as well as site-specific reductions in breast and colorectal cancers, although overall mortality was not significantly altered [37]. These findings suggest that vitamin D, in combination with calcium, may play a protective role in neoplastic processes, potentially through mechanisms involving cellular differentiation, apoptosis, and immune modulation. Additional research specifically targeting postmenopausal women found that calcium plus vitamin D supplementation significantly decreased the risk of all cancers, highlighting a population that may derive particular benefit from repletion strategies [38].

Beyond cancer prevention, vitamin D supplementation has demonstrated benefits in chronic pulmonary conditions. A meta-analysis of three randomized trials revealed that patients with chronic obstructive pulmonary disease (COPD) and baseline serum 25-hydroxyvitamin D levels below 25 nmol/L experienced fewer exacerbations following supplementation [39]. This effect may relate to vitamin D's immunomodulatory properties, including regulation of innate and adaptive immune responses, which reduce susceptibility to respiratory infections and inflammatory triggers. Ongoing trials continue to investigate the broader systemic effects of vitamin D, including cardiovascular outcomes, metabolic regulation, and neurocognitive function. Many studies aim to define optimal dosing strategies, particularly in high-risk populations, including individuals with obesity, malabsorption syndromes, chronic kidney or liver disease, and ethnic groups with higher melanin content that reduces cutaneous synthesis. Collectively, these studies provide a growing evidence base supporting the role of vitamin D as a critical micronutrient with both skeletal and extra-skeletal benefits, guiding clinical recommendations and public health policies.

Toxicity and Adverse Effect Management

Vitamin D is a fat-soluble nutrient, which inherently increases the risk of accumulation and toxicity when administered in excessive doses. Hypervitaminosis D, though uncommon, typically results from prolonged or extreme oral supplementation rather than ultraviolet-mediated synthesis. Toxicity is generally reported when serum 25-hydroxyvitamin D levels exceed 88 ng/mL, and acute manifestations of excessive vitamin D intake are primarily related to hypercalcemia. Clinical presentations may include neurocognitive disturbances such as confusion, gastrointestinal symptoms including anorexia and vomiting, excessive urination (polyuria), excessive thirst (polydipsia), and generalized muscle weakness. Chronic toxicity may result in nephrocalcinosis, renal impairment, and diffuse bone pain due to dysregulated calcium-phosphate metabolism. Management of vitamin D toxicity requires prompt discontinuation of vitamin D supplements, restriction of dietary calcium intake, and careful monitoring of serum calcium and renal function. In cases of severe hypercalcemia, acute interventions may include intravenous hydration with isotonic saline, loop diuretics to enhance calcium excretion, and bisphosphonates to inhibit osteoclastic bone resorption. Glucocorticoids may be indicated in specific cases, particularly where there is concomitant granulomatous disease causing endogenous vitamin D overproduction. Clinicians must remain vigilant in monitoring high-risk populations, including those receiving high-dose supplementation for deficiency correction or individuals with impaired renal or hepatic function, as they are particularly susceptible to adverse effects. Preventive strategies include adherence to recommended upper intake levels, individualized dosing based on baseline serum 25-hydroxyvitamin D, and periodic biochemical monitoring during long-term supplementation. Proper patient education on the risks of excessive vitamin D intake is also essential to mitigate inadvertent toxicity and ensure safe correction of deficiency [38].

Prognosis

The prognosis of vitamin D deficiency is generally favorable with timely and appropriate intervention. Restoration of adequate vitamin D status through supplementation or lifestyle modifications allows for normalization of calcium homeostasis, reduction of secondary hyperparathyroidism, and reversal of early skeletal demineralization. When deficiency is identified and treated before the development of irreversible bone disease, patients typically recover without long-term complications. Outcomes are particularly positive in populations adhering to recommended supplementation regimens, with documented improvements in bone mineral density and reduced incidence of fractures, falls, and related morbidity. However, prolonged or severe vitamin D deficiency can have deleterious effects on musculoskeletal and systemic health. Chronic insufficiency may contribute to osteomalacia in adults, rickets in children, and osteoporosis across all age groups. These conditions increase susceptibility to fragility fractures, impaired mobility, and diminished quality of life, particularly in elderly individuals. Furthermore, emerging evidence suggests that chronic deficiency may exacerbate susceptibility to infections, influence immune regulation, and potentially contribute to metabolic and cardiovascular disorders. Prognostic outcomes depend on the severity and duration of deficiency, the presence of comorbidities, and the timeliness of intervention. Early recognition, assessment of underlying etiologies, and individualized supplementation are critical for optimizing long-term health and preventing irreversible skeletal and systemic complications associated with vitamin D deficiency [38].

Complications

Vitamin D deficiency is associated with a spectrum of complications that affect skeletal, muscular, and systemic health. Skeletal complications are among the most pronounced, with chronic deficiency predisposing individuals to osteomalacia in adults and rickets in children. Insufficient vitamin D disrupts calcium and phosphorus homeostasis, resulting in defective bone mineralization, cortical thinning, and increased bone fragility. Consequently, patients are at higher risk of low-impact fractures and long-term skeletal deformities, particularly when deficiency is prolonged or severe. In older adults, the combination of bone demineralization and muscle weakness heightens the risk of falls, contributing further to fracture incidence and associated morbidity. Muscular complications include proximal muscle weakness, reduced muscle mass, and impaired function, which collectively compromise postural stability and physical performance. Deficient individuals frequently present fatigue, myalgia, and diminished exercise tolerance. Beyond the musculoskeletal system, long-term vitamin D deficiency is increasingly recognized as a contributor to systemic complications, including heightened susceptibility to infections, increased risk of autoimmune disorders, and potential exacerbation of cardiovascular disease. Chronic insufficiency may also influence metabolic processes, insulin sensitivity, and inflammatory pathways, amplifying overall morbidity. The compounded effects of these complications underscore the importance of early detection and timely intervention. Preventive supplementation, lifestyle modification, and correction of underlying causes, such as malabsorption or inadequate sunlight exposure, are essential to mitigate these risks. Monitoring high-risk populations, including the elderly, institutionalized individuals, and those with chronic illnesses, allows for proactive management and reduces the burden of vitamin D deficiency-related complications on individual and public health outcomes [38][39].

Patient Education

Patient education on vitamin D is critical to ensure appropriate supplementation and prevent deficiency-related complications. Vitamin D’s skeletal benefits are well-documented, particularly for individuals with serum 25-hydroxyvitamin D levels below 20 ng/mL, and are most pronounced in those with severe deficiency under 12 ng/mL. Adequate vitamin D status supports calcium homeostasis, bone mineralization, and skeletal integrity. In children, sufficient vitamin D prevents rickets and promotes proper bone growth, while in adults it helps maintain bone density and reduce the risk of fractures. Older adults, especially those at risk of osteoporosis, benefit from vitamin D supplementation as part of a comprehensive strategy that includes calcium intake and physical activity [40]. Educating patients about the importance of consistent supplementation, appropriate dosing, and lifestyle factors such as sunlight exposure is essential for effective prevention and management of deficiency. Beyond skeletal health, observational studies have suggested potential links between vitamin D and extraskeletal outcomes, including cardiovascular disease, cancer, immune function, and type 2 diabetes mellitus. However, results from large randomized controlled trials, including VITAL, ViDA, and D2d, involving more than 30,000 participants collectively, indicate that supplementation in adults with sufficient baseline vitamin D levels does not reduce the risk of cardiovascular events, cancer, type 2 diabetes, or overall mortality [41][42][43][44][45]. Additionally, recent studies have not demonstrated clear benefits of supplementation in preventing falls among older adults [46][47][48]. Patients must understand that supplementation is most effective when deficiency is present and that unnecessary intake above recommended levels may not confer additional health benefits. Despite these findings, many individuals with confirmed deficiency remain unsupplemented, while some replete individuals continue supplementation unnecessarily [49]. Patient education should focus on identifying personal risk factors, understanding appropriate dosage and duration, and emphasizing periodic monitoring for high-risk groups. Counseling should also address the potential adverse effects of excessive intake, including hypercalcemia, kidney injury, and toxicity, reinforcing that individualized supplementation, guided by serum 25-hydroxyvitamin D measurement and clinical evaluation, is the safest and most effective approach.

Enhancing Healthcare Team Outcomes

Effective management of vitamin D deficiency relies on a coordinated interprofessional approach to ensure accurate screening, diagnosis, supplementation, and monitoring. Despite its prevalence, vitamin D deficiency is frequently overlooked in both outpatient and inpatient care settings. The U.S. Preventive Services Task Force does not recommend universal screening; however, targeted assessment of high-risk individuals is critical to prevent long-term complications, including bone disorders, muscle weakness, and fractures. Healthcare providers must recognize populations at heightened risk, including older adults, nursing home residents, individuals with osteoporosis, hospitalized patients, and those with chronic kidney disease, liver disease, or malabsorption syndromes. African American and Hispanic individuals are also disproportionately affected due to differences in skin melanin content, dietary intake, and potential socioeconomic barriers to healthcare access. The healthcare team should include physicians, nurse practitioners, pharmacists, dietitians, and laboratory specialists working collaboratively to provide comprehensive care. Physicians and nurse practitioners are responsible for assessing patient risk, ordering appropriate laboratory testing, interpreting results, and prescribing supplementation. Pharmacists play a crucial role in ensuring the correct formulation, dose, and duration of vitamin D therapy while monitoring for potential drug-nutrient interactions. Dietitians provide nutritional counseling, encouraging consumption of vitamin D-rich foods and fortified products, and integrating lifestyle interventions such as safe sunlight exposure. Laboratory professionals ensure accurate measurement of serum 25-hydroxyvitamin D levels, which is essential for guiding therapy and monitoring treatment response. Communication and care coordination are essential to optimize outcomes. High-risk patients should have individualized supplementation plans, periodic monitoring of serum vitamin D and calcium levels, and education regarding adherence and potential adverse effects. Incorporating electronic health records and clinical decision support systems can help flag high-risk individuals, track supplementation, and alert providers to abnormal laboratory results. Through a structured, interprofessional approach, healthcare teams can effectively identify deficiency, implement evidence-based interventions, and reduce the incidence of associated complications, ultimately improving skeletal health and overall patient well-being [40][41].

Conclusion:

Vitamin D deficiency remains a prevalent and recognized global health concern with significant skeletal and systemic consequences. Although many affected individuals are asymptomatic, chronic insufficiency contributes to secondary hyperparathyroidism, bone demineralization, muscle weakness, and increased fracture risk, particularly among elderly and high-risk populations. Early identification through targeted screening and accurate laboratory assessment of serum 25-hydroxyvitamin D is critical for timely intervention. Vitamin D3 supplementation represents the most effective strategy for both prevention and treatment, with dosing tailored to baseline levels, age, comorbidities, and risk factors affecting absorption or metabolism. Evidence indicates that supplementation offers the greatest benefit in individuals with confirmed deficiency, while excessive or unnecessary intake may increase toxicity risk. An interprofessional healthcare approach—integrating physicians, pharmacists, dietitians, and laboratory professionals—is essential to optimize patient outcomes. Public health efforts focusing on education, prevention, and individualized management are vital to reducing the long-term burden of vitamin D deficiency and improving overall population health.

References:

1. Chang SW, Lee HC. Vitamin D and health - The missing vitamin in humans. Pediatr Neonatol. 2019 Jun;60(3):237-244.
2. Rajakumar K. Vitamin D, cod-liver oil, sunlight, and rickets: a historical

perspective. Pediatrics. 2003 Aug;112(2):e132-5.

3. Pludowski P, Holick MF, Grant WB, Konstantynowicz J, Mascarenhas MR, Haq A, Povoroznyuk V, Balatska N, Barbosa AP, Karonova T, Rudenka E, Misiorowski W, Zakharova I, Rudenka A, Łukaszkiewicz J, Marcinowska-Suchowierska E, Łaszcz N, Abramowicz P, Bhattoa HP, Wimalawansa SJ. Vitamin D supplementation guidelines. J Steroid Biochem Mol Biol. 2018 Jan;175:125-135.
4. Nair R, Maseeh A. Vitamin D: The "sunshine" vitamin. J Pharmacol Pharmacother. 2012 Apr;3(2):118-26.
5. Holick MF. Vitamin D: important for prevention of osteoporosis, cardiovascular heart disease, type 1 diabetes, autoimmune diseases, and some cancers. South Med J. 2005 Oct;98(10):1024-7.
6. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. Chem Biol. 2014 Mar 20;21(3):319-29.
7. Sugimoto H, Shiro Y. Diversity and substrate specificity in the structures of steroidogenic cytochrome P450 enzymes. Biol Pharm Bull. 2012;35(6):818-23.
8. Czernichow S, Fan T, Nocea G, Sen SS. Calcium and vitamin D intake by postmenopausal women with osteoporosis in France. Curr Med Res Opin. 2010 Jul;26(7):1667-74
9. Naeem Z. Vitamin d deficiency- an ignored epidemic. Int J Health Sci (Qassim). 2010 Jan;4(1):V-VI.
10. Thomas MK, Lloyd-Jones DM, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, Vamvakas EC, Dick IM, Prince RL, Finkelstein JS. Hypovitaminosis D in medical inpatients. N Engl J Med. 1998 Mar 19;338(12):777-83.
11. Elangovan H, Chahal S, Gunton JE. Vitamin D in liver disease: Current evidence and potential directions. Biochim Biophys Acta Mol Basis Dis. 2017 Apr;1863(4):907-916.
12. Yeung WG, Toussaint ND, Badve SV. Vitamin D therapy in chronic kidney disease: a critical appraisal of clinical trial evidence. Clin Kidney J. 2024 Aug;17(8):sfae227.
13. Cipriani C, Cianferotti L. Vitamin D in hypoparathyroidism: insight into pathophysiology and perspectives in clinical practice. Endocrine. 2023 Aug;81(2):216-222.
14. Gröber U, Kisters K. Influence of drugs on vitamin D and calcium metabolism. Dermatoendocrinol. 2012 Apr 01;4(2):158-66.
15. Levine MA. Diagnosis and Management of Vitamin D Dependent Rickets. Front Pediatr. 2020;8:315.
16. Pereira-Santos M, Costa PR, Assis AM, Santos CA, Santos DB. Obesity and vitamin D deficiency: a systematic review and meta-analysis. Obes Rev. 2015 Apr;16(4):341-9.
17. Elliott ME, Binkley NC, Carnes M, Zimmerman DR, Petersen K, Knapp K, Behlke JM, Ahmann N, Kieser MA. Fracture risks for women in long-term care: high prevalence of calcaneal osteoporosis and hypovitaminosis D. Pharmacotherapy. 2003 Jun;23(6):702-10.
18. Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: when to test and how to treat. Mayo Clin Proc. 2010 Aug;85(8):752-7; quiz 757-8.
19. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? J Steroid Biochem Mol Biol. 2014 Oct;144 Pt A:138-45.
20. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Tmava Berisha A, Martucci G, Pilz S, Malle O. Vitamin D deficiency 2.0: an update on the current status worldwide. Eur J Clin Nutr. 2020 Nov;74(11):1498-1513. [
21. Cariolou M, Cupp MA, Evangelou E, Tzoulaki I, Berlanga-Taylor AJ. Importance of vitamin D in acute and critically ill children with subgroup analyses of sepsis and respiratory tract infections: a systematic review and meta-analysis. BMJ Open. 2019 May 22;9(5):e027666.
22. Veldurthy V, Wei R, Oz L, Dhawan P, Jeon YH, Christakos S. Vitamin D, calcium homeostasis and aging. Bone Res. 2016;4:16041.
23. Rejnmark L, Ejlsmark-Svensson H. Effects of PTH and PTH Hypersecretion on Bone: a Clinical Perspective. Curr Osteoporos Rep. 2020 Jun;18(3):103-114.
24. Bouillon R, Marcocci C, Carmeliet G, Bikle D, White JH, Dawson-Hughes B, Lips P, Munns CF, Lazaretti-Castro M, Giustina A, Bilezikian J. Skeletal and Extraskeletal Actions of Vitamin D: Current Evidence and Outstanding Questions. Endocr Rev. 2019 Aug 01;40(4):1109-1151.
25. Jones AN, Hansen KE. Recognizing the musculoskeletal manifestations of vitamin D deficiency. J Musculoskelet Med. 2009 Oct;26(10):389-396.
26. Zhang X, Liu Z, Xia L, Gao J, Xu F, Chen H, Du Y, Wang W. Clinical features of vitamin D deficiency in children: A retrospective analysis. J Steroid Biochem Mol Biol. 2020 Feb;196:105491.
27. Giustina A, Adler RA, Binkley N, Bouillon R, Ebeling PR, Lazaretti-Castro M, Marcocci C, Rizzoli R, Sempos CT, Bilezikian JP. Controversies in Vitamin D: Summary Statement From an International Conference. J Clin Endocrinol Metab. 2019 Feb 01;104(2):234-240.
28. Dawson-Hughes B, Mithal A, Bonjour JP, Boonen S, Burckhardt P, Fuleihan GE, Josse RG, Lips P, Morales-Torres J, Yoshimura N. IOF position statement: vitamin D recommendations for older adults. Osteoporos Int. 2010 Jul;21(7):1151-4.

29. Marcinowska-Suchowierska E, Kupisz-Urbańska M, Łukaszkiewicz J, Płudowski P, Jones G. Vitamin D Toxicity-A Clinical Perspective. Front Endocrinol (Lausanne). 2018;9:550.
30. Tripkovic L, Lambert H, Hart K, Smith CP, Bucca G, Penson S, Chope G, Hyppönen E, Berry J, Vieth R, Lanham-New S. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. Am J Clin Nutr. 2012 Jun;95(6):1357-64.
31. Demay MB, Pittas AG, Bikle DD, Diab DL, Kiely ME, Lazaretti-Castro M, Lips P, Mitchell DM, Murad MH, Powers S, Rao SD, Scragg R, Tayek JA, Valent AM, Walsh JME, McCartney CR. Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2024 Jul 12;109(8):1907-1947.
32. Heaney RP, Recker RR, Grote J, Horst RL, Armas LA. Vitamin D(3) is more potent than vitamin D(2) in humans. J Clin Endocrinol Metab. 2011 Mar;96(3):E447-52.
33. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M., Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008 Aug;122(2):398-417.
34. Melamed ML, Thadhani RI. Vitamin D therapy in chronic kidney disease and end stage renal disease. Clin J Am Soc Nephrol. 2012 Feb;7(2):358-65.
35. Vieth R. Vitamin D supplementation: cholecalciferol, calcifediol, and calcitriol. Eur J Clin Nutr. 2020 Nov;74(11):1493-1497.
36. Autier P, Gandini S. Vitamin D supplementation and total mortality: a meta-analysis of randomized controlled trials. Arch Intern Med. 2007 Sep 10;167(16):1730-7.
37. Bolland MJ, Grey A, Gamble GD, Reid IR. Calcium and vitamin D supplements and health outcomes: a reanalysis of the Women's Health Initiative (WHI) limited-access data set. Am J Clin Nutr. 2011 Oct;94(4):1144-9.
38. Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J Clin Nutr. 2007 Jun;85(6):1586-91.
39. Jolliffe DA, Greenberg L, Hooper RL, Mathyssen C, Rafiq R, de Jongh RT, Camargo CA, Griffiths CJ, Janssens W, Martineau AR. Vitamin D to prevent exacerbations of COPD: systematic review and meta-analysis of individual participant data from randomised controlled trials. Thorax. 2019 Apr;74(4):337-345.
40. Weaver CM, Alexander DD, Boushey CJ, Dawson-Hughes B, Lappe JM, LeBoff MS, Liu S, Looker AC, Wallace TC, Wang DD. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. Osteoporos Int. 2016 Jan;27(1):367-76.
41. Barbarawi M, Kheiri B, Zayed Y, Barbarawi O, Dhillon H, Swaid B, Yelangi A, Sundus S, Bachuwa G, Alkotob ML, Manson JE. Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83 000 Individuals in 21 Randomized Clinical Trials: A Meta-analysis. JAMA Cardiol. 2019 Aug 01;4(8):765-776.
42. Ruiz-García A, Pallarés-Carratalá V, Turégano-Yedro M, Torres F, Sapena V, Martin-Gorgojo A, Martin-Moreno JM. Vitamin D Supplementation and Its Impact on Mortality and Cardiovascular Outcomes: Systematic Review and Meta-Analysis of 80 Randomized Clinical Trials. Nutrients. 2023 Apr 07;15(8)
43. Scragg R, Khaw KT, Toop L, Sluyter J, Lawes CMM, Waayer D, Giovannucci E, Camargo CA. Monthly High-Dose Vitamin D Supplementation and Cancer Risk: A Post Hoc Analysis of the Vitamin D Assessment Randomized Clinical Trial. JAMA Oncol. 2018 Nov 01;4(11):e182178.
44. Krul-Poel YH, Westra S, Simsek S. Response to Comment on Krul-Poel et al. Effect of Vitamin D Supplementation on Glycemic Control in Patients With Type 2 Diabetes (SUNNY Trial): A Randomized Placebo-Controlled Trial. Diabetes Care 2015;38:1420-1426. Diabetes Care. 2015 Nov;38(11):e191-2.
45. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, Brodsky I, Ceglia L, Chadha C, Chatterjee R, Desouza C, Dolor R, Foreyt J, Fuss P, Ghazi A, Hsia DS, Johnson KC, Kashyap SR, Kim S, LeBlanc ES, Lewis MR, Liao E, Neff LM, Nelson J, O'Neil P, Park J, Peters A, Phillips LS, Pratley R, Raskin P, Rasouli N, Robbins D, Rosen C, Vickery EM, Staten M., D2d Research Group. Vitamin D Supplementation and Prevention of Type 2 Diabetes. N Engl J Med. 2019 Aug 08;381(6):520-530.
46. Khaw KT, Stewart AW, Waayer D, Lawes CMM, Toop L, Camargo CA, Scragg R. Effect of monthly high-dose vitamin D supplementation on falls and non-vertebral fractures: secondary and post-hoc outcomes from the randomised, double-blind, placebo-controlled ViDA trial. Lancet Diabetes Endocrinol. 2017 Jun;5(6):438-447.
47. Appel LJ, Michos ED, Mitchell CM, Blackford AL, Sternberg AL, Miller ER, Juraschek SP, Schrack JA, Szanton SL, Charleston J, Minotti M, Baksh SN, Christenson RH, Coresh J, Drye LT,

Guralnik JM, Kalyani RR, Plante TB, Shade DM, Roth DL, Tonascia J., STURDY Collaborative Research Group. The Effects of Four Doses of Vitamin D Supplements on Falls in Older Adults : A Response-Adaptive, Randomized Clinical Trial. Ann Intern Med. 2021 Feb;174(2):145-156.

48. Waterhouse M, Sanguineti E, Baxter C, Duarte Romero B, McLeod DSA, English DR, Armstrong BK, Ebeling PR, Hartel G, Kimlin MG, O'Connell RL, Pham H, van der Pols JC, Venn AJ, Webb PM, Whiteman DC, Neale RE. Vitamin D supplementation and risk of falling: outcomes from the randomized, placebo-controlled D-Health Trial. J Cachexia Sarcopenia Muscle. 2021 Dec;12(6):1428-1439.

Bouillon R, Manousaki D, Rosen C, Trajanoska K, Rivadeneira F, Richards JB. The health effects of vitamin D supplementation: evidence from human studies. Nat Rev Endocrinol. 2022 Feb;18(2):96-110.