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VITAMIN D AND THE HUMAN GUT MICROBIOTA: A NARRATIVE REVIEW

Review Article

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Abstract

Background: Vitamin D is an endocrine secosteroid with recognized extra-skeletal functions, including modulation of immune responses, epithelial barrier integrity, antimicrobial peptide expression, and inflammatory signaling. In parallel, the intestinal microbiota is increasingly recognized as a metabolic and immunological interface relevant to obesity, diabetes, inflammatory bowel disease, and systemic health. This review evaluates the evidence linking vitamin D status or supplementation to the composition and diversity of the human gut microbiota. Methods: A systematic narrative review was conducted using PubMed, ScienceDirect, and Google Scholar for studies published from 2010 to 2025. Human interventional and observational studies, systematic reviews, and mechanistic reports addressing vitamin D status or supplementation and gut microbiota outcomes were considered. The search and selection process was summarized using a PRISMA-style flow diagram. Findings were synthesized qualitatively because of substantial heterogeneity in populations, vitamin D regimens, microbiome sequencing methods, and reported endpoints. Results: Seventy-four records were identified; after duplicate removal and screening, 25 full-text reports were assessed and 11 evidence sources were retained for detailed synthesis. Higher serum 25-hydroxyvitamin D was generally associated with a more favorable microbiota profile, including greater microbial diversity and enrichment of taxa such as Bifidobacterium, Lactobacillus, Akkermansia, Bacteroides, and butyrate-associated organisms. Randomized supplementation studies showed biologically plausible but inconsistent effects on alpha diversity, beta diversity, and phylum-level changes, particularly the Bacteroidetes/Firmicutes balance. Conclusions: Current evidence supports a plausible vitamin D-gut microbiota axis, but causality remains unproven. Vitamin D supplementation should not yet be considered a targeted microbiota-modifying therapy outside correction of deficiency. Larger standardized randomized trials with integrated metabolomic, endocrine, and clinical endpoints are required.

Word count: 262 words.

Keywords

Vitamin D; Gut microbiota; Vitamin D receptor; Dysbiosis; Endocrine metabolism;

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List of abbreviations

- 25(OH)D: 25-hydroxyvitamin D
- 1,25(OH)2D: 1,25-dihydroxyvitamin D
- AOEDS: Advances in Obesity, Endocrinology and Diabetes
- BMI: Body mass index
- IBD: Inflammatory bowel disease
- PICO: Population, intervention/exposure, comparator, outcome
- PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
- RCT: Randomized controlled trial
- SCFA: Short-chain fatty acid
- VDR: Vitamin D receptor

Introduction

Vitamin D is a fat-soluble secosteroid hormone classically involved in calcium and phosphate homeostasis and skeletal health. Over the last two decades, however, vitamin D has also been implicated in immune regulation, epithelial barrier maintenance, antimicrobial peptide production, and inflammatory control [1,12-14]. These extra-skeletal activities are clinically relevant to endocrinology and metabolism because vitamin D insufficiency is frequently observed in populations with obesity, insulin resistance, diabetes, inflammatory bowel disease, and chronic systemic inflammation [6,16,17,20].

The human gut microbiota is a complex ecological community that contributes to digestion, microbial defense, immune maturation, short-chain fatty-acid production, bile acid metabolism, and endocrine-metabolic homeostasis [2-5]. Alterations in microbial richness, evenness, community structure, or metabolic output are commonly referred to as dysbiosis and have been associated with intestinal, metabolic, autoimmune, and cardiometabolic disorders [2-5].

A bidirectional relationship between vitamin D and the gut microbiota has therefore become a biologically plausible research question. On one side, vitamin D may influence the intestinal niche through the vitamin D receptor (VDR), tight-junction regulation, antimicrobial peptides such as cathelicidin, and modulation of innate and adaptive immune responses [12-14]. On the other side, gut microorganisms may influence vitamin D metabolism, including the availability of vitamin D metabolites and the host inflammatory milieu in which VDR signaling takes place [17].

This review asks three clinically oriented questions: (1) to what extent is vitamin D status associated with gut microbiota composition and diversity in humans? (2) does vitamin D supplementation reproducibly modulate the gut microbiota? and (3) what are the potential implications for endocrine, metabolic, and intestinal health?

Materials and Methods

Review design

This work was designed as a systematic narrative review. It was not planned as a quantitative meta-analysis because the included studies differed substantially in population characteristics, baseline vitamin D status, intervention regimens, microbiome sequencing platforms, bioinformatic pipelines, and outcome reporting. The review was organized according to a PRISMA-style screening process, and the flow of records is presented in Figure 1.

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Search strategy

PubMed, ScienceDirect, and Google Scholar were searched for publications from January 2010 to December 2025. Search terms combined vitamin D concepts with microbiome concepts using Boolean operators, including: vitamin D, cholecalciferol, vitamin D3, 25-hydroxyvitamin D, 25(OH)D, calcifediol, calcitriol, 1,25-dihydroxyvitamin D, gut microbiota, intestinal microbiome, dysbiosis, VDR, supplementation, randomized controlled trial, and observational study.

Eligibility criteria

Eligible publications included human observational studies, randomized or controlled interventional studies, systematic reviews, and selected mechanistic studies providing biological plausibility. Studies were considered when they reported vitamin D status, vitamin D intake, or vitamin D supplementation together with gut microbiota composition, diversity, sequencing, microbial metabolites, or closely related intestinal immunological endpoints. Studies unrelated to intestinal microbiota, lacking vitamin D exposure or outcome data, duplicate reports, and publications with insufficient methodological relevance were excluded.

Study selection and PRISMA reconstruction

The initial search identified 74 records. Eighteen duplicates were removed, leaving 56 records for title and abstract screening. Thirty-one records were excluded at screening, and 25 full-text reports were assessed. Fourteen full-text reports were excluded because they were not directly focused on intestinal microbiota, lacked a vitamin D exposure or microbiota outcome, were animal or in vitro only without clinical relevance, were narrative/opinion articles with insufficient extractable data, or overlapped with already included evidence. Eleven evidence sources were retained for qualitative synthesis.

Data extraction and synthesis

For each retained article, the following data were extracted: article title, authors and year, study design, sample size and population, vitamin D exposure or intervention, microbiome method when available, key findings, and relevance to the present review. The evidence was summarized qualitatively in the text and in Table 1.

Ethical considerations

This manuscript is based exclusively on published literature and does not involve individual patient data, human subject recruitment, biological sampling, or access to confidential medical records. Formal ethics committee approval and informed consent were therefore not required.

Results

Study selection

The literature search and selection process is summarized in Figure 1. In brief, 74 records were identified through electronic database searching. After removal of duplicates, 56 records were screened, 25 reports were assessed in full text, and 11 evidence sources were included in the qualitative synthesis. The reasons for exclusion at the full-text stage were mainly lack of direct microbiota outcomes, absence of a vitamin D exposure or status measure, insufficient methodological relevance, or overlap with broader reviews.

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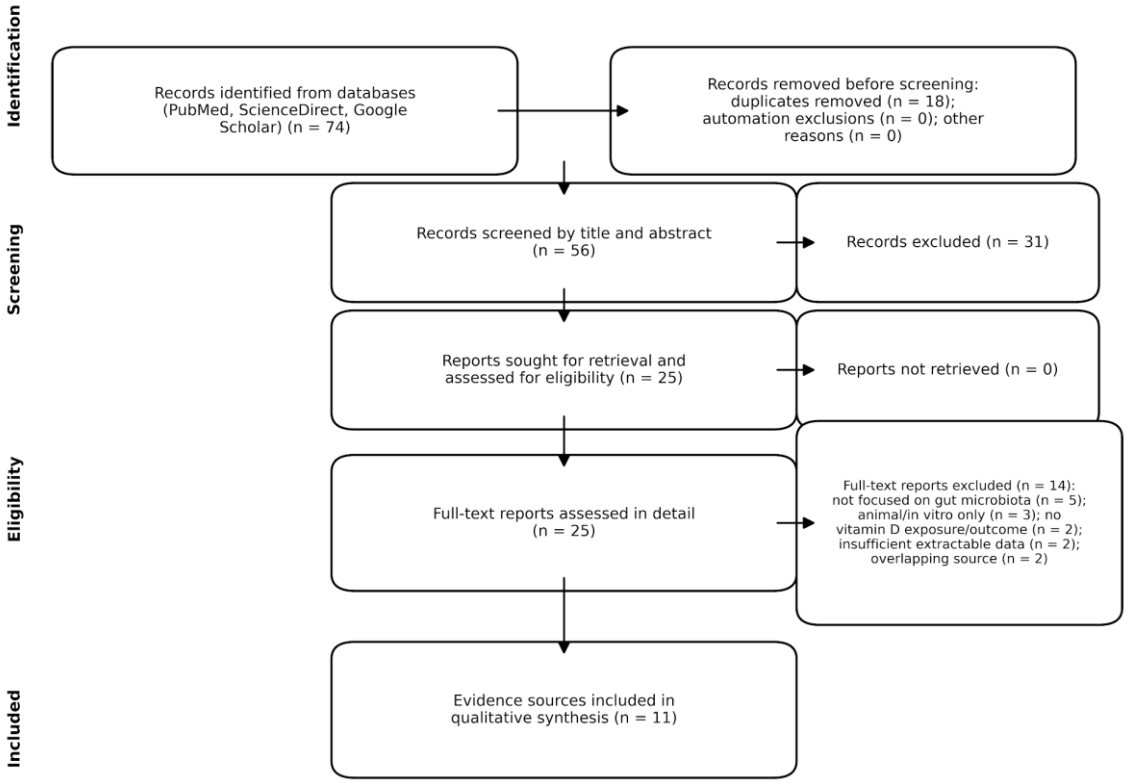
Figure 1. PRISMA-style flow diagram of the literature search and study selection process.



Legend: The diagram shows records identified, duplicates removed, records screened, records excluded, full-text reports assessed, full-text reports excluded, and evidence sources included in the qualitative synthesis.

General characteristics of included evidence

The included literature comprised randomized controlled trials, controlled supplementation studies, observational analyses, systematic reviews of human studies, and clinically relevant mechanistic reviews. Most studies assessed serum 25(OH)D or administered cholecalciferol and measured microbial diversity or relative abundance using 16S rRNA gene sequencing or related high-throughput approaches. The evidence base covered healthy adults, vitamin D-deficient or overweight adults, older men, older Australians, women with normal weight or obesity, and pediatric populations (Table 1).

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Table 1. Summary of reviewed articles and findings

Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
The Association between Vitamin D and Gut Microbiota: A Systematic Review of Human Studies	Bellerba et al., 2021	Systematic review of human studies	25 studies; human observational and interventional evidence	Vitamin D status and supplementation were associated with changes in microbial diversity and composition, but results differed by population, sampling site, and methodology.	Provides the main human evidence framework and supports the distinction between vitamin D status and supplementation.
Effect of Vitamin D Supplementation on Human Gut Microbiota: A Systematic Review of Randomized Controlled Trials	Zeb et al., 2025	Systematic review of RCTs	14 RCTs; 1,458 participants	Supplementation was associated with increases in taxa such as Bifidobacterium and Lactobacillus and changes in the Bacteroidetes/Firmicutes ratio; heterogeneity limited causal interpretation.	Directly relevant to the supplementation question and supports the need for standardized RCTs.
Effect of Vitamin D Supplementation on Faecal Microbiota: A Randomised Clinical Trial	Naderpoor et al., 2019	Randomized clinical trial	26 vitamin D-deficient overweight or obese adults	Supplementation produced taxon-specific effects, including changes in Lachnospira, Blautia, Coprococcus, and Ruminococcus, without uniform diversity changes.	Important obesity/endocrine population demonstrating that supplementation effects may be context-dependent.
The Effect of Various Doses of Oral Vitamin D3 Supplementation on Gut Microbiota in Healthy Adults	Charoenngam et al., 2020	Randomized, double-blind, dose-response study	20 adults with vitamin D insufficiency/deficiency	Higher vitamin D exposure was associated with dose-dependent changes in Bacteroides and Parabacteroides and with taxa considered beneficial for gut homeostasis.	Shows dose-response biological plausibility in humans.

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Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
Effects of High Doses of Vitamin D3 on Mucosa-Associated Gut Microbiome Vary between Regions of the Human Gastrointestinal Tract	Bashir et al., 2016	Interventional pilot study / clinical trial	16 healthy volunteers; mucosal and stool samples from 7 GI sites	High-dose vitamin D3 changed mucosa-associated microbiota differently across gastrointestinal regions, with shifts in taxa including Bifidobacterium and Lactobacillus.	Highlights that fecal samples may not capture the whole intestinal microbiome response.
Gut Microbiota Interactions with the Immunomodulatory Role of Vitamin D in Normal Individuals	Luthold et al., 2017	Observational study	Adults without major disease; vitamin D intake/status and microbiota measures	Vitamin D status was associated with microbiota patterns and inflammatory markers, supporting an immunometabolic link.	Supports observational association between vitamin D status, inflammation, and microbial ecology.
The Potential Role of Vitamin D Supplementation as a Gut Microbiota Modifier in Healthy Individuals	Singh et al., 2020	Prospective supplementation study	80 vitamin D-deficient healthy women	Vitamin D supplementation increased microbial diversity, increased the Bacteroidetes/Firmicutes ratio, and enriched Akkermansia and Bifidobacterium.	Provides strong human interventional support for microbiota modulation in deficient subjects.
The Effect of Vitamin D Supplementation on the Gut Microbiome in Older Australians: Results from Analyses of the D-Health Trial	Pham et al., 2023	Randomized trial analysis	21,315 randomized older Australians; stool microbiome subset n = 835	Large trial-based analysis found limited or heterogeneous effects of supplementation on gut microbiome outcomes.	Important for balancing positive smaller studies with evidence from older adults.
Vitamin D Metabolites and the Gut Microbiome in Older Men	Thomas et al., 2020	Cross-sectional analysis	567 older men	Active vitamin D metabolites and activation ratios were associated with alpha and beta diversity and with butyrate-producing bacteria.	Shows that vitamin D metabolite biology may be more informative than total 25(OH)D alone.

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Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
Serum Vitamin D Level and Gut Microbiota in Women	Al-Khaldy et al., 2023	Case-control study	92 Saudi women aged 18-25 years; 48 normal weight and 44 with obesity	Vitamin D deficiency and obesity were inversely associated with alpha diversity; serum vitamin D correlated with Bacteroides thetaiotaomicron and Bifidobacterium adolescentis in subgroups.	Highly relevant to obesity and endocrine-metabolic framing.
Immunomodulatory Role of Vitamin D on Gut Microbiome in Children	Tabassum et al., 2023	Systematic review	10 pediatric studies	Most studies reported vitamin D-related alterations in Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria, with links to immune pathways.	Extends the review to pediatric immune development and highlights mechanisms.

Legend: This table summarizes the principal evidence sources retained for qualitative synthesis. It includes systematic reviews, randomized or interventional studies, and observational studies relevant to vitamin D status, vitamin D supplementation, gut microbiota composition, microbial diversity, and endocrine-metabolic interpretation.

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Vitamin D status and microbial diversity

Several observational studies reported that higher vitamin D status is associated with greater microbial diversity or more favorable community structure [6,11,15,17]. In older men, active vitamin D metabolites and activation ratios, rather than total 25(OH)D alone, were linked to alpha and beta diversity and to butyrate-associated taxa [17]. In young Saudi women, vitamin D deficiency combined with obesity was associated with lower alpha diversity and distinct beta diversity, suggesting that vitamin D status and adiposity may interact in shaping microbial ecology [6].

Supplementation studies

Interventional data remain more heterogeneous. Some studies suggest that vitamin D supplementation can alter microbial composition, increase taxa considered beneficial, or modify fecal metabolite networks [7-10,15,18]. For example, supplementation trials have reported increases in Bifidobacterium, Lactobacillus, Bacteroides, Parabacteroides, or Bifidobacteriaceae, although the direction and magnitude of effects vary by dose, baseline deficiency, anatomical sampling site, duration, and sequencing pipeline [7-10,18]. Naderpoor et al. found taxon-specific changes without a uniform diversity signal, highlighting that microbiome effects may be subtle and context-dependent [8].

Taxonomic and functional patterns

Across studies, taxa most frequently discussed in relation to vitamin D include Bifidobacterium, Lactobacillus, Akkermansia, Bacteroides, Parabacteroides, Coprococcus, Ruminococcus, Lachnospira, and Blautia [6-11,15-18]. These organisms are clinically interesting because several are involved in mucosal barrier maintenance, short-chain fatty-acid production, or immunological tolerance. However, the same bacterial genus may have different implications according to species, strain, host context, diet, and analytical method; therefore, taxonomic findings should not be overinterpreted as direct clinical benefit.

Status versus supplementation

A major finding of this review is the distinction between vitamin D status and vitamin D supplementation. Observational associations between adequate vitamin D levels and favorable microbiota profiles appear more consistent than supplementation effects [1,6,7,15,17]. This may reflect confounding by diet, adiposity, sunlight exposure, physical activity, ethnicity, geography, baseline microbiota composition, or host genetics. Conversely, supplementation trials may be limited by small sample size, short duration, variable dosing, and limited adjustment for dietary or medication exposures.

Clinical populations

The relationship between vitamin D and gut microbiota may be particularly relevant in obesity, diabetes, inflammatory bowel disease, and ageing, where vitamin D deficiency and dysbiosis frequently coexist [6,16,20,21,23]. Nevertheless, current data do not justify using vitamin D supplementation as a specific microbiota-directed treatment. Correction of documented deficiency remains clinically appropriate for established endocrine and skeletal indications, while any microbiome-directed benefit should be considered investigational.

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Discussions

Principal interpretation

This review supports the existence of a biologically plausible vitamin D-gut microbiota axis. The most consistent signal is that adequate vitamin D status is associated with healthier microbial patterns, whereas the effect of supplementation is variable. The evidence is therefore hypothesis-generating rather than definitive.

Biological plausibility

Several mechanisms may explain the association. VDR signaling contributes to epithelial tight-junction integrity, regulation of intestinal permeability, antimicrobial peptide expression, and immune tolerance [12-14]. Vitamin D may also influence the intestinal inflammatory environment, indirectly selecting for or against particular microbial communities. Conversely, microbial metabolites such as short-chain fatty acids may influence systemic inflammation, endocrine metabolism, and the host response to vitamin D metabolites [17,23,24].

Relevance to obesity, endocrinology, and diabetes

The topic is relevant to obesity and endocrine-metabolic disease because vitamin D deficiency is common in obesity, while dysbiosis has been linked to insulin resistance, chronic low-grade inflammation, metabolic syndrome, and altered energy homeostasis [6,20]. However, the presence of parallel associations does not establish that vitamin D supplementation will improve metabolic outcomes through microbiota modulation. Future studies in obesity and diabetes should integrate vitamin D metabolites, body composition, diet, glycemic endpoints, microbiome taxonomy, microbial function, and metabolomics.

Clinical caution

At present, the evidence should not be translated into claims that vitamin D supplementation is a probiotic-like or microbiome-targeted therapy. In clinical practice, vitamin D supplementation should follow established indications, such as correction of deficiency and bone-health management. Microbiota modulation may represent an additional area of research, but it is not yet an evidence-based therapeutic indication.

Strengths

This manuscript synthesizes observational, interventional, and mechanistic evidence; distinguishes vitamin D status from supplementation; summarizes the review process using a PRISMA-style diagram; and provides a structured table to facilitate comparison across studies.

Limitations

The main limitations are the heterogeneity of included populations and interventions, the absence of quantitative meta-analysis, reliance on published summary data, variable sequencing methods, and limited ability to address confounding factors such as diet, ethnicity, geography, medications, antibiotic exposure, obesity, inflammation, and baseline microbiome composition. Some included evidence sources are reviews rather than primary studies, and causality cannot be inferred from observational associations.

Future research

Future trials should recruit sufficiently powered populations with documented baseline vitamin D insufficiency or deficiency, standardize dosing and duration, control diet and medication exposure, measure multiple vitamin D metabolites, use harmonized microbiome sequencing and functional analyses, and evaluate clinically meaningful endpoints such as glycemic control, inflammatory markers, intestinal symptoms, and metabolic health.

Conclusions

Current literature suggests a meaningful association between vitamin D and the gut microbiota, especially when serum vitamin D status is considered. Adequate vitamin D levels are often linked to greater microbial diversity and enrichment of taxa involved in intestinal homeostasis, immune regulation, and metabolic balance. Nevertheless, supplementation studies remain inconsistent, and existing data do not prove causality. Vitamin D supplementation should therefore be viewed as a treatment for deficiency rather than a validated strategy for targeted microbiota modulation. Standardized, adequately powered randomized trials are needed to determine whether modifying vitamin D status can reproducibly influence the microbiome and improve endocrine, metabolic, or intestinal outcomes.

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Data availability: This review used only data from published articles; no new dataset was generated.

Author contributions: Conceptualization, [Author initials]; literature search, [Author initials]; data extraction, [Author initials]; writing-original draft, [Author initials]; writing-review and editing, all authors. All authors approved the final version of the manuscript.

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