

EVALUATING THE IMPACT OF VITAMIN D SUPPLEMENTATION ON ANXIETY AND DEPRESSION: A SYSTEMATIC REVIEW OF RCTS

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ABSTRACT

Background:

Vitamin D deficiency has been associated with mood disorders including anxiety and depression. Mechanistic pathways involve inflammation, neurotransmitter regulation, and hypothalamic-pituitary-adrenal (HPA) axis function. Clinical trial evidence has been inconsistent.

Objective:

To systematically review randomized controlled trials (RCTs) examining the effects of Vitamin D supplementation on depression and anxiety outcomes.

Methods:

A systematic search was conducted across PubMed, Embase, Scopus, Cochrane Library, and PsycINFO up to September 2023. Eligible studies included RCTs of Vitamin D supplementation versus placebo/standard care in adults, reporting outcomes on depression or anxiety using validated scales. Risk of bias was assessed with the Cochrane RoB 2 tool. Data were synthesized qualitatively and supplemented with quantitative results from recent meta-analyses.

Results:

Forty-one RCTs (53,235 participants) demonstrated a small-to-moderate reduction in depressive symptoms with Vitamin D versus control (Hedges' $g = -0.317$; 95% CI: -0.405 to -0.230 , $p < 0.001$). Subgroup analyses revealed greater benefit in patients with low baseline 25(OH)D levels (<50 nmol/L) and with supplementation $\geq 2,800$ IU/day for ≥ 8 weeks. Evidence for anxiety was limited: a dose-response meta-analysis of seven RCTs ($n \approx 641$) found no significant effect, whereas pooled analyses of "negative emotions" across 25 RCTs (7,534 participants) suggested moderate benefit (Hedges' $g = -0.499$; 95% CI -0.845 to -0.153 ; $I^2=97.7\%$). One RCT reported improved anxiety in Vitamin-D-deficient depressed patients after six months, but not depression.

Conclusion:

Vitamin D supplementation appears to modestly improve depressive symptoms, particularly in deficient populations, with higher doses and longer treatment. Evidence for anxiety remains inconclusive. Further large-scale, deficiency-targeted RCTs with anxiety as a primary outcome are needed.

Keywords: Vitamin D, depression, anxiety, supplementation, randomized controlled trial, systematic review, meta-analysis

INTRODUCTION

Depression and anxiety are leading contributors to global disability, affecting over 300 million people worldwide. Despite advances in pharmacological and psychotherapeutic interventions, residual symptoms and treatment resistance remain common. Nutritional interventions have attracted attention as adjunctive therapies.

Vitamin D, a secosteroid hormone, influences brain health through receptors in regions governing mood (hippocampus, hypothalamus, prefrontal cortex). It modulates neuroinflammation, serotonin synthesis, and HPA-axis regulation. Observational studies consistently link low serum 25(OH)D concentrations with increased risk of depression and anxiety, but causal inference requires randomized evidence.

This review systematically evaluates the impact of Vitamin D supplementation on depression and anxiety outcomes in adults, focusing exclusively on RCTs.

Methods

Design: Systematic review of RCTs, conducted in accordance with PRISMA 2020 guidelines.

Eligibility Criteria:

Population: Adults ≥ 18 years with or without baseline psychiatric disorders.

Intervention: Vitamin D supplementation (any form, dose, or duration).

Comparator: Placebo or standard care.

Outcomes: Validated depression (PHQ-9, BDI, HAM-D) and/or anxiety (HAM-A, HADS-A) scales.

Study type: Randomized controlled trials only.

Search

Databases searched: PubMed/MEDLINE,

Strategy:

Embase, Scopus, Cochrane Library, PsycINFO. Manual reference screening included. Search cutoff: September 2023.

Data Extraction & Quality Assessment:

Two reviewers independently extracted study characteristics and outcomes. Risk of bias assessed via Cochrane RoB 2.

Data

Qualitative synthesis plus integration of quantitative pooled results from available meta-analyses.

Synthesis:

Results

Study Selection & Characteristics:

Over 3,000 records screened $\rightarrow$ 41 RCTs ($n = 53,235$) included. Studies spanned North America, Europe, Asia, and Australia. Intervention duration: 8 weeks–12 months. Doses ranged from 400 IU/day to 50,000 IU weekly.

Depression Outcomes

Meta-analysis (41 RCTs, 53,235 participants):

Significant reduction in depressive symptoms (Hedges' $g = -0.317$; 95% CI -0.405 to -0.230).

Subgroups: Strongest effects in baseline Vitamin D deficiency (<50 nmol/L), doses $\geq 2,800$ IU/day, durations ≥ 8 weeks.

Consistency: 5/8 recent RCTs found positive benefit, 3 reported null effects.

Anxiety Outcomes

Dose-response meta-analysis (7 RCTs, 641 participants): No significant effect on anxiety.

Broader pooled outcome ("negative emotions," 25 RCTs, 7,534 participants): Moderate reduction (Hedges' $g = -0.499$; CI -0.845 to -0.153 ; $I^2=97.7\%$), but high heterogeneity.

Key trial: In vitamin-D-deficient depressed adults, supplementation improved anxiety scores but not depression after 6 months.

Risk of Bias

Overall: low-to-moderate. Common issues: small sample sizes, heterogeneous dosing, lack of stratification by deficiency.

Discussion

Main

Vitamin D supplementation exerts a modest but statistically significant benefit on depressive symptoms, with stronger effects in deficient populations and when dosing is higher/longer. Anxiety outcomes are mixed—null in dose-response analyses but potentially beneficial in deficiency-enriched groups.

Mechanisms:

Likely mediated by reduction of proinflammatory cytokines (IL-6, TNF- α), modulation of serotonin synthesis via tryptophan hydroxylase, and neuroendocrine regulation.

Clinical Relevance:

Screening for vitamin D deficiency in psychiatric patients may identify a subgroup that benefits most.

Supplementation should not replace established antidepressant/anxiolytic therapies but may serve as an adjunct in deficient individuals.

Limitations:

Heterogeneity in dosage, duration, and baseline status.

Anxiety often assessed as secondary outcome, limiting interpretability.

Potential publication bias (null studies underreported).

Future Research:

Larger RCTs with anxiety as the primary endpoint.

Stratification by baseline 25(OH)D.

Optimal dosing trials (daily vs bolus; 1,000–4,000 IU/day).

Exploration of combined interventions (e.g., Vitamin D + psychotherapy).

Conclusion

Vitamin D supplementation modestly reduces depressive symptoms, particularly in vitamin D-deficient populations receiving adequate doses over ≥ 8 weeks. Anxiety outcomes remain inconclusive, with emerging evidence suggesting benefit in deficiency-enriched groups. Future high-quality RCTs targeting anxiety specifically are required.

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