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Effect of Vitamin D on Chronic Obstructive Pulmonary Disease: A Systematic Review of Randomized Controlled Trials

Efecto de la vitamina D en la enfermedad pulmonar obstructiva crónica: una revisión sistemática de ensayos controlados aleatorios

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SUMMARY

Objective: *To evaluate the clinical and biological effects of vitamin D supplementation in patients with chronic obstructive pulmonary disease, based on evidence from randomized controlled trials*. **Materials and Methods:** *A systematic review was conducted in accordance with the PRISMA guidelines. Three databases (PubMed/MEDLINE, Scopus, and Web of Science) were searched for randomized controlled trials published until June 2025. Studies were included if they assessed the effects of vitamin D supplementation in patients with chronic obstructive pulmonary disease and reported clinical or biological outcomes*. **Results:** *Twelve randomized controlled trials involving 6626 participants from diverse regions, with wide variability in sample sizes (36 to 5 110 participants). Most studies targeted patients with baseline vitamin D deficiency and evaluated varied dosing strategies (daily, weekly, monthly, or single high-dose regimens). Supplementation significantly increased serum 25(OH) D levels in all trials. Symptom burden and exacerbation frequency were reduced in most studies, particularly among patients with vitamin D deficiency. Consistent reductions in inflammatory markers, including IL-6, IL-8, and CRP, were observed. However, findings on pulmonary function (e.g., FEV_1) and quality of life were*

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mixed and often not statistically significant. Eleven studies (91.7 %) were classified as high methodological quality, and six (50 %) met high reporting standards. **Conclusions:** *Vitamin D supplementation appears to offer clinical and biological benefits in COPD, particularly in patients with documented deficiency. Consistent findings across high-quality trials support its role in reducing symptoms and inflammation. However, its impact on lung function and long-term outcomes remains uncertain.*

Keywords: *Vitamin D, Chronic Obstructive Pulmonary Disease, Randomized Controlled Trials as Topic, Health Care Outcome Assessment.*

RESUMEN

Objetivo: *Evaluar los efectos clínicos y biológicos de la suplementación con vitamina D en pacientes con enfermedad pulmonar obstructiva crónica (EPOC), según ensayos aleatorizados y controlados.* **Materiales y métodos:** *Revisión sistemática que siguió la guía PRISMA. Se realizó una búsqueda en tres bases de datos para identificar ensayos aleatorizados y controlados publicados hasta junio de 2025.* **Resultados:** *Se identificaron 12 ensayos clínicos aleatorizados con un total de 6 626 participantes, y una amplia variabilidad en el tamaño muestral (de 36 a 5 110 participantes). La mayoría de los estudios incluyó pacientes con deficiencia basal de vitamina D y evaluó diferentes estrategias de dosificación (diarias, semanales, mensuales o esquemas de dosis única alta). La suplementación aumentó significativamente los niveles séricos de 25(OH)D en todos los ensayos. En la mayoría de los estudios se observó una reducción de la carga de síntomas y de la frecuencia de exacerbaciones, especialmente en pacientes con deficiencia de vitamina D. Asimismo, se identificaron reducciones consistentes en marcadores inflamatorios como IL-6, IL-8 y PCR. Sin embargo, los hallazgos sobre la función pulmonar (p. ej., VEF_1) y la calidad de vida fueron heterogéneos y, en muchos casos, no alcanzaron significación estadística. Once estudios (91,7 %) se clasificaron como de alta calidad metodológica y seis (50 %) cumplieron con altos estándares de reporte.* **Conclusiones:** *La suplementación con vitamina D parece ofrecer beneficios clínicos y biológicos en pacientes con EPOC, especialmente en quienes presentan deficiencia documentada. No obstante, su impacto sobre la función pulmonar y los desenlaces a largo plazo permanece incierto.*

Palabras clave: *Vitamina D, enfermedad pulmonar obstructiva crónica, ensayos clínicos aleatorizados como tema, evaluación de resultados en la atención en salud.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide (1), affecting an estimated 390 million individuals and accounting for over three million deaths annually (1). Characterized by persistent airflow limitation, chronic inflammation, and progressive functional decline, COPD imposes a substantial burden on patients, caregivers, and healthcare systems (2). In addition to pharmacological management, there is a growing imperative to explore adjunctive strategies that can mitigate exacerbations, reduce systemic inflammation, and improve patients' quality of life (3).

Recent attention has focused on the potential role of micronutrients, particularly vitamin D, as modulators of inflammatory and immune pathways in chronic respiratory conditions (4). Vitamin D deficiency is highly prevalent among individuals with COPD and has been associated with increased disease severity, greater frequency of exacerbations, and impaired pulmonary function (5). Mechanistically, vitamin D is thought to exert anti-inflammatory, immunomodulatory, and epithelial-protective effects, which may confer therapeutic benefits in patients with COPD (6).

Despite growing interest, the clinical evidence on vitamin D supplementation in COPD remains fragmented. Individual randomized controlled trials (RCTs) have yielded inconsistent results, with substantial variation in study design, dosing regimens, populations, and outcome measures (7-9). Consequently, the utility of vitamin D as evidence-based adjunctive treatment in COPD has yet to be clearly defined (10).

In this context, synthesizing the existing body of RCTs using a rigorous, transparent approach is essential (11-13). Systematic reviews of RCTs, when conducted according to established methodological standards, provide the highest level of evidence to guide clinical decision-making (14,15). Furthermore, integrating principles of meta-science, such as assessing methodological and reporting quality, enhances the credibility, interpretability, and applicability of evidence in real-world settings (16-19).

This systematic review aims to evaluate the effects of vitamin D supplementation on clinical and biological outcomes in patients with COPD, based exclusively on evidence from RCTs. By appraising both the effectiveness and quality of the available studies, this review seeks to inform evidence-based recommendations and identify priority areas for future research.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (20).

Eligibility criteria

Studies were included if they met the following criteria: 1) original peer-reviewed articles; 2) RCTs; 3) focused on assessing the effect of vitamin D supplementation on any clinical or biological outcome in patients with COPD; 4) full-text available in English; and 5) explicitly reported methodological design and outcome measures.

Exclusion criteria comprised the following: non-randomized trials, reviews, editorials, commentaries, conference abstracts, letters to the editor, and studies with unclear methodology or outcome assessment.

Four electronic databases were systematically searched: PubMed/MEDLINE, Scopus, and Web of Science Core Collection. No language filters were applied during the initial search. The last search was performed on June 15, 2025.

Search strategies were developed using Medical Subject Headings (MeSH) and synonyms related to vitamin D and COPD. The strategy was adapted for each database using appropriate tags (e.g., TITLE-ABS). Filters for "Randomized Controlled Trial" or equivalent expressions were applied where supported. An example of the search string used in Scopus was: (TITLE-ABS("Vitamin D" OR "Calcitriol Receptors" OR Cholecalciferol* OR Hydroxycholecalciferol* OR Ergocalciferol* OR "25-Hydroxyvitamin D2" OR Dihydrotachysterol* OR "Vitamin D3" OR Calciol OR "Hydroxyvitamins D" OR Dihydroxycholecalciferol* OR Calcifediol OR "25-Hydroxycholecalciferol" OR "25 Hydroxycholecalciferol" OR "25-Hydroxyvitamin D3" OR "25 Hydroxyvitamin D3" OR Calcidiol OR "25-Hydroxycholecalciferol Monohydrate" OR "25 Hydroxycholecalciferol Monohydrate" OR Dedrogyl OR Calderol OR Hidroferol OR "Calcifediol Anhydrous" OR Calciferols OR "Vitamin D2" OR Ercalcidiol OR "25 Hydroxyvitamin D2" OR "25-Hydroxycalciferol" OR "25 Hydroxycalciferol" OR "25-Hydroxyergocalciferol" OR "25 Hydroxyergocalciferol" OR Dihydrotachysterin OR Tachystin OR "AT 10" OR "AT-10" OR AT10 OR Calcamine)) AND (TITLE-ABS("Chronic Obstructive Pulmonary Disease*" OR COPD OR "Chronic Obstructive Lung Disease*" OR COAD OR "Chronic Obstructive Airway Disease*" OR "Chronic Airflow Obstruction*" OR "Asthma Chronic Obstructive Pulmonary Disease Overlap Syndrome*" OR "Asthma-Chronic Obstructive Pulmonary Disease Overlap Syndrome*" OR "Asthma-COPD Overlap Syndrome*" OR "Asthma COPD Overlap Syndrome*" OR "Chronic Bronchitis" OR "Pulmonary Emphysema*" OR "Centriacinar Emphysema*" OR "Centrilobular Emphysema*" OR "Panacinar Emphysema*" OR "Panlobular Emphysema*" OR "Focal Emphysema*")).

All records were imported into Rayyan (21) for initial screening. Two reviewers independently assessed titles and abstracts to determine eligibility. Full texts were retrieved for potentially eligible studies. Disagreements were resolved through discussion or consultation with a third reviewer.

Data extraction was independently conducted by two reviewers using a standardized template. Extracted information included publication details, study design, population characteristics, intervention and comparator description, outcomes, effect sizes, and conclusions. A third reviewer resolved discrepancies. No automation tools were used during data collection.

Outcomes related to both disease and people were considered. When multiple time points or measures were reported, the most clinically relevant and final values were prioritized.

Effect measures extracted included mean differences (MD), odds ratios (OR), incidence rate ratios (IRR), and hazard ratios (HR), with their corresponding 95 % confidence intervals (CI) and p-values, when available. Within-group changes and between-group comparisons were documented for relevant outcomes.

The risk of bias in each included RCT was independently assessed by two reviewers using the Cochrane Risk of Bias 2.0 (RoB 2.0) tool (22). This instrument evaluates bias across five domains: 1) the randomization process, 2) deviations from intended interventions, 3) missing outcome data, 4) measurement of the outcome, and 5) selection of the reported result. Each domain was rated as "low risk," "some concerns," or "high risk," and an overall risk of bias judgment was assigned accordingly. Disagreements were resolved through discussion with a third reviewer.

The methodological quality of each RCT was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Randomized Controlled Trials (23). Two reviewers independently applied this 13-item tool. Responses were scored as 1 point for "Yes," 0.5 points for "Unclear," and 0 for "No." Based on the total score, studies were categorized as: A) High quality (≥ 70 % compliance; ≥ 9 points); B) Moderate quality (50 %-69 % compliance; 6.5–9 points); and C) Low quality (< 50 % compliance; < 6.5 points) (24,25). Discrepancies were resolved through consensus or by a third reviewer. The reporting quality of each trial was assessed using the CONSORT checklist (26). This tool includes 30 main items (up to 37 subitems depending on the study design). Each item was scored as follows: 1 point for full compliance ("Yes"), and 0 points for non-compliance ("No"). Based on the total score, reporting quality was classified as: 1) High (≥ 75 % compliance; ≥ 22.5 points); 2) Moderate (50–74 % compliance; 15–22 points); and 3) Low (< 50 % compliance; < 15 points) (24,25). Two reviewers independently assessed each study, and a third reviewer resolved disagreements.

Synthesis methods

All included studies were tabulated by their intervention and outcome domains. Studies were grouped for synthesis based on the comparability of interventions (e.g., vitamin D3 supplementation) and outcomes.

Data was extracted in a standardized format. Where necessary, units were harmonized (e.g., converting serum vitamin D from nmol/L to ng/mL). No imputation methods were applied for missing data.

Study characteristics and outcome results were summarized in structured tables. Visualizations included a PRISMA flow diagram, bar plots, and other plots to display reporting and methodological quality.

Given the heterogeneity in interventions, populations, and outcome measurements, no meta-analysis was performed. A narrative synthesis was conducted for each outcome domain, highlighting consistency and discrepancies across studies.

Potential sources of heterogeneity were explored qualitatively based on differences in baseline vitamin D status, dosing regimens, study populations, and follow-up duration. No formal sensitivity analyses were conducted, as no pooled effect estimates were generated.

No statistical assessments of reporting bias (e.g., funnel plot asymmetry) were conducted because no meta-analysis was carried out. Potential selective reporting was addressed narratively by comparing outcomes reported in the methods with those reported in the results for each study.

The certainty of evidence for each outcome was not formally graded using GRADE or similar frameworks, but limitations in methodological and reporting quality were considered in the interpretation of results

Since this study did not involve human participants, animals, or medical records, no ethics committee approval was required.

RESULTS

Study selection

A total of 2 194 records were retrieved through electronic searches in PubMed/MEDLINE (n = 749), Scopus (n = 824), and Web of Science Core Collection (n = 621). After

removing duplicates, non-randomized studies, and publications unrelated to RCTs, and after screening titles and abstracts for relevance, a total of 17 studies were selected for full-text retrieval and assessment.

Ultimately, twelve randomized controlled trials met all inclusion criteria and were included in the final analysis. A visual summary of the study selection process is provided in Figure 1.

Study characteristics

Twelve RCTs published between 2012 and 2025 were included in this review (7-9,27,30-35), encompassing a total of 6 626 participants across diverse geographical regions. The studies were conducted in Asia (Iran, India), Europe (the Netherlands, Belgium, the UK), Oceania (New Zealand), and North America (the USA), with sample sizes ranging from 36 to 5110 participants (Table 1).

All trials evaluated the effect of vitamin D supplementation in adult patients with COPD, although participant characteristics varied. Most trials enrolled patients with documented vitamin D deficiency at baseline, and the severity of COPD ranged from moderate to very severe across studies.

Interventions included diverse dosing strategies: A) Daily doses ranging from 1200 IU to 2000 IU; B) Weekly or monthly regimens such as 50 000 IU weekly or 100 000 IU monthly; C) Single high-dose protocols, such as intramuscular injections of 300 000 IU. The control groups uniformly received placebos. The duration of follow-up ranged from 6 weeks to more than 3 years.

Outcomes assessed included: 1) Pulmonary function parameters (Forced Expiratory Volume in 1 second[FEV_1], Forced Vital Capacity [FVC], FEV_1/FVC); 2) Frequency of COPD exacerbations; 3) Symptom burden (COPD Assessment Test score [CAT], Modified Medical

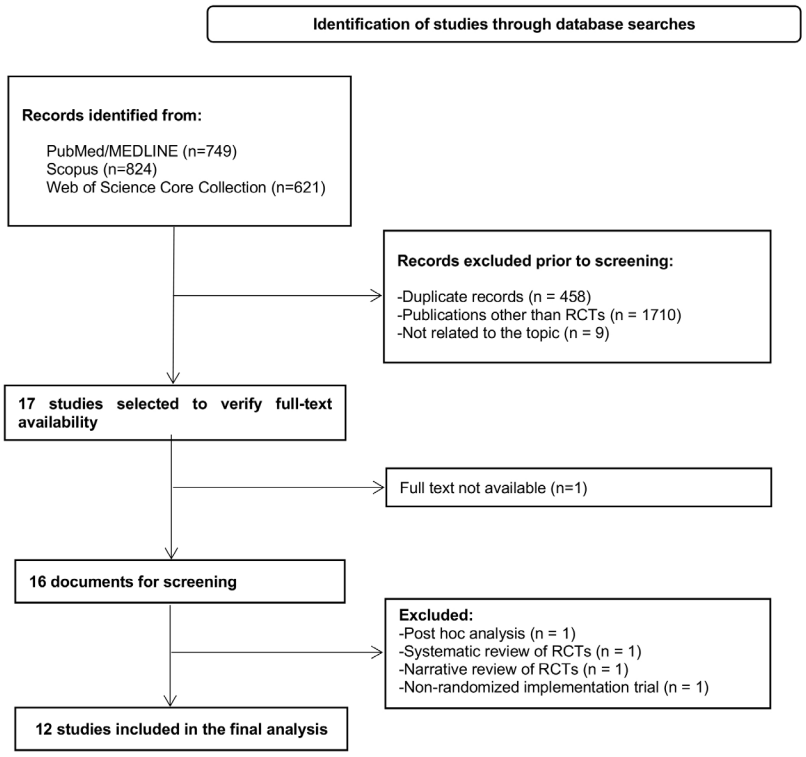

Figure 1. PRISMA Flow Diagram.

Table 1. Characteristics of Included Studies.

Author, year	Country	Study Design	Sample Size	Participant	Intervention
Lakra et al., 2025 (8)	India	Randomized controlled trial	98	Stable COPD patients with vitamin D deficiency (<30 ng/mL)	Vitamin D3 supplementation to achieve normal levels (45.6 ng/mL after 3 months)
Rafiq et al., 2022 (7)	Netherlands	Randomized controlled trial	126	COPD patients receiving maintenance treatment with inhaled corticosteroids	Vitamin D3 supplementation 1680 IU/day for 6 months
Dastan et al., 2019 (9)	Iran	Randomized controlled trial	70	Patients with AECOPD and vitamin D deficiency	Single dose of 300,000 IU intramuscular vitamin D
Foumani et al., 2019 (27)	Iran	Randomized double-blind placebo-controlled trial	63	Patients with COPD	Vitamin D3 50,000 IU weekly for 8 weeks, then monthly for 4 months
Ghodrati et al., 2019 (28)	Iran	Randomized controlled trial	40	COPD patients with vitamin D deficiency	Vitamin D (dose not specified)
Rafiq et al., 2017 (29)	Netherlands	Randomized double-blind placebo-controlled pilot trial	50	COPD patients with vitamin D deficiency	Vitamin D3 1,200 IU/day for 6 months
Sluyter et al., 2017 (30)	New Zealand	Randomized double-blind placebo-controlled trial	5110	Older adults ≥50 years	Monthly oral vitamin D3 (100,000 IU) for median 3.3 years
Sanjari et al., 2016 (33)	Iran	Randomized double-blind placebo-controlled trial	88	COPD patients with vitamin D deficiency	100,000 IU oral vitamin D per month for 3 months
Martineau et al., 2015 (32)	UK	Multicentre randomized double-blind placebo-controlled trial	240	Patients with COPD, community and hospital recruited	3 mg vitamin D3 every 2 months for 1 year
Zendedel et al., 2015 (31)	Iran	Randomized double-blind placebo-controlled trial	88	Patients with severe and very severe COPD	Oral vitamin D 100,000 IU/month for 6 months
Bjerk et al., 2013 (34)	USA	Randomized controlled trial	36	Patients with severe COPD	Cholecalciferol 2000 IU/day for 6 weeks
Lehouck et al., 2012 (35)	Belgium	Randomized double-blind placebo-controlled trial	182	Patients with moderate to very severe COPD and recent exacerbations	Vitamin D 100,000 IU monthly for 1 year

6MWT: 6 Minute Walk Test; AECOPD: Acute Exacerbation of Chronic Obstructive Pulmonary Disease; COPD: Chronic Obstructive Pulmonary Disease; CRP: C-Reactive Protein; FEV1: Forced Expiratory Volume in one second; FVC: Forced Vital Capacity; IL-6: Interleukin-6; IL-8: Interleukin-8; Hs-CRP: High-Sensitivity C-Reactive Protein; mMRC: Modified Medical Research Council Dyspnea Scale; QoL: Quality of Life; TNF: Tumor Necrosis Factor

Research Council dyspnea [mMRC]); 4) Physical performance (6-minute walk test, handgrip strength); 5) Serum vitamin D concentrations; 6) Systemic inflammatory markers (IL-6, IL-8, hs-CRP); and 7) Health-related quality of life.

Risk of bias in included studies

The risk of bias across the included studies was variable, with several methodological concerns identified. The distribution of risk across the five domains and overall judgments is visually summarized in Figure 2.

Reporting quality of included studies

According to the scoring criteria, the studies were evenly distributed between high and moderate reporting quality. Six studies (50 %) demonstrated high reporting quality, achieving scores of 22.5 or

Figure 2. RoB 2.0 for bias assessment.

higher (≥75 % item compliance). These studies provided comprehensive descriptions of trial design, randomization methods, participant flow, outcomes, and statistical analysis. Several also reported trial registration and protocol access, reinforcing their transparency and reproducibility.

The remaining six studies (50 %) were classified as having moderate reporting quality, with scores ranging from 15 to 22 points (51 %-74 % compliance). These studies typically reported primary outcomes and interventions adequately but lacked detail on specific methodological aspects, such as blinding procedures, handling of missing data, and reporting of adverse events. Registration information was inconsistently provided. No study met the criteria for low reporting quality (score < 15 points, compliance rate < 50 %). The distribution of scores is shown in Figure 3.

Methodological quality of included studies

Based on the predefined scoring criteria (JBI checklist), 11 studies (91.7 %) demonstrated high methodological quality, achieving ≥9 points (≥70 % compliance). These trials consistently reported on key domains, including appropriate randomization, allocation concealment, and valid outcome measurement procedures. Only one study (8.3 %) fell into the moderate quality category (6.5–9 points, 50 %-69 % compliance), primarily due to unclear descriptions of participant blinding and potential baseline imbalances. No study was classified as having low methodological quality (<6.5 points, <50 % compliance). These findings indicate a high level of methodological rigor across most included trials, strengthening the overall credibility of the synthesized evidence. The full distribution is illustrated in Figure 4.

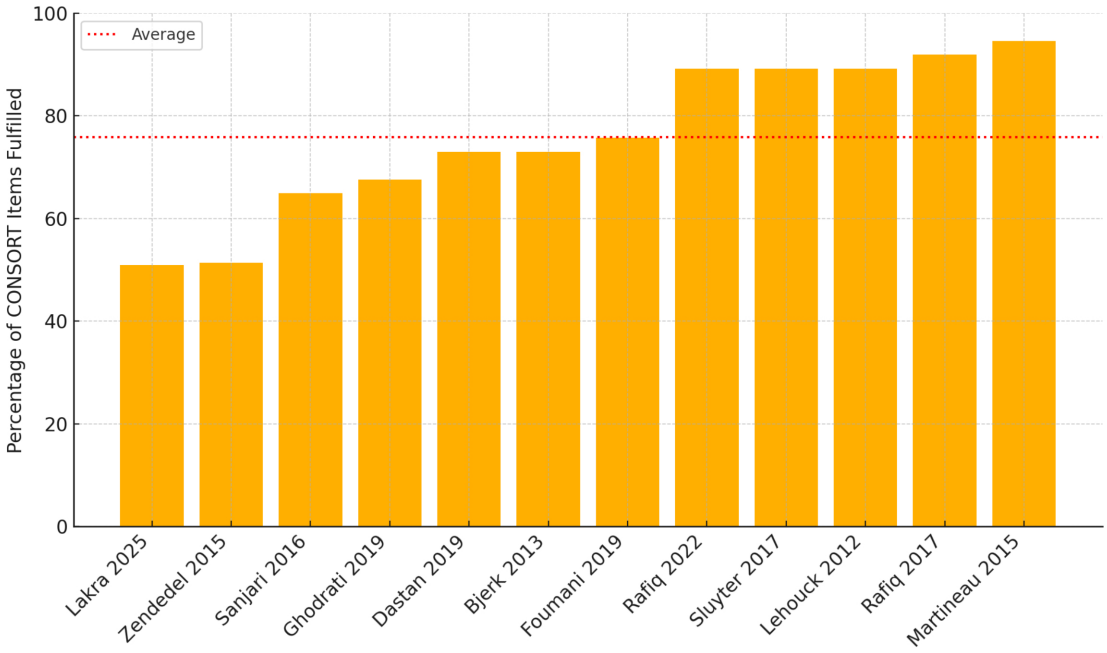

Figure 3. Reporting quality of RCTs. Percentage of total compliance according to CONSORT.

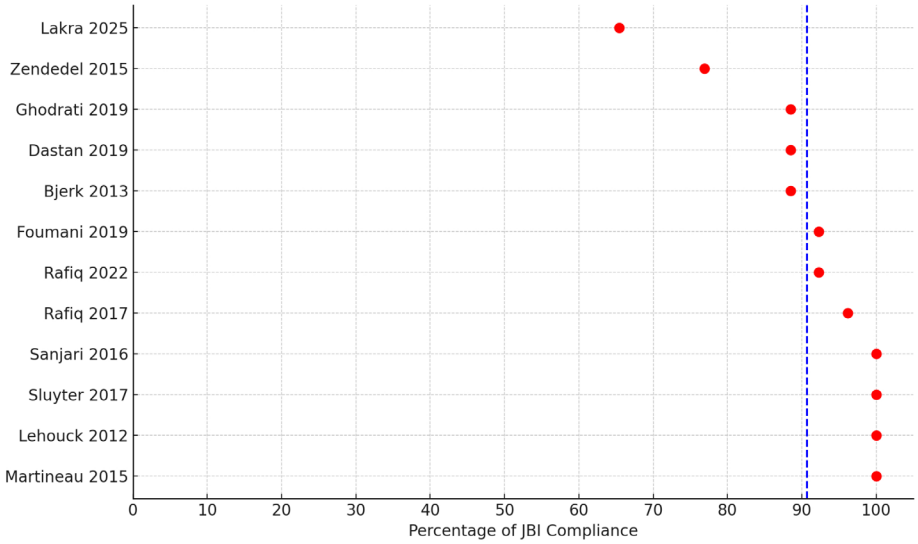

Figure 4. Methodological quality of RCTs. Percentage of total compliance according to Joanna Briggs Institute checklist for RCTs. The dotted line delimits the average score.

Results of individual studies

The twelve included RCTs reported a wide range of outcomes related to the impact of vitamin D supplementation in COPD patients. Despite the heterogeneity in dosing regimens, populations, and follow-up periods, several consistent patterns emerged.

Several trials have demonstrated a statistically significant reduction in COPD symptom scores and exacerbation frequency in patients receiving vitamin D. For instance, Lakra et al. (8) and Rafiq et al. (7) reported greater improvements in CAT scores and fewer exacerbation events in the intervention group compared to the placebo group ($p < 0.05$).

Findings on lung function were mixed. While studies such as Zendedel et al. (31) and Foumani et al. (27) demonstrated significant improvements in FEV_1 following supplementation, others (29, 35) reported no notable changes.

Trials that evaluated inflammatory biomarkers observed favorable effects. Dastan et al. (9) found significant reductions in IL-6, IL-8, and hs-CRP levels after a high-dose intramuscular vitamin D intervention ($p < 0.01$). Sanjari et al. (33) similarly reported decreases in IL-6 and CRP, along with an increase in the anti-inflammatory IL-10.

All studies that measured serum 25(OH)D confirmed substantial increases in circulating levels post-intervention ($p < 0.001$), confirming the physiological effect of supplementation.

Some studies, such as those by Bjerk et al. (34), have shown modest improvements in physical performance; however, improvements in quality of life have been inconsistently reported and are not always statistically significant. Detailed summary statistics, effect estimates, and confidence intervals for each study and outcome are provided in Table 2.

Results of syntheses

The synthesis of findings across the 12 included RCTs revealed moderate consistency in certain outcome domains. However, the overall strength of the evidence varied due to methodological and risk-of-bias considerations.

Most trials assessing symptom burden and exacerbation rates reported beneficial effects of vitamin D supplementation. These studies typically involved patients with baseline vitamin D deficiency and used moderately to high-dose regimens. Despite some variation in follow-up duration and outcome scales, the direction of effect was generally favorable. However, three of these studies were judged to have "some concerns" or "high" risk of bias, primarily due to unclear randomization methods or non-blinded outcome assessment.

Evidence regarding lung function (e.g., FEV_1, FEV_1/FVC) was less consistent. While several trials reported within-group improvements, between-group differences were frequently not statistically significant. These inconsistencies may be attributable to differences in baseline lung function, comorbidities, and intervention duration. Notably, half of these studies were at low risk of bias, lending moderate confidence to the conclusion that vitamin D may have a limited direct impact on pulmonary mechanics.

Among studies evaluating systemic inflammation, consistent reductions in IL-6, IL-8, and hs-CRP were observed post-supplementation. These findings support the proposed anti-inflammatory role of vitamin D in the pathophysiology of COPD. Most of these studies were rated as having low to moderate risk of bias, which increases confidence in the biological effects.

All trials reported significant increases in serum 25(OH)D in the intervention groups, confirming the supplement's effective absorption and systemic availability, regardless of route or frequency of administration.

Results in this domain were highly variable. Improvements in physical performance measures and quality of life were inconsistently reported and often lacked statistical significance. Most studies addressing this domain were small in sample size and subject to some methodological limitations.

Table 2. Summary of Findings.

Author, year	Outcome	Participants (n)	Effect Size	95 % CI	p-value	Interpretation
Lakra et al., 2025 (8)	-COPD Assessment Test score	96	-Mean reduction = –2.3 pts -6 (Vit D) vs 13 (Control)	NR	0.018	-Statistically significant reduction in symptoms
	-Exacerbations		-7 (Vit D) vs 14 (Control)		0.021	-Vitamin D reduced the number of exacerbations significantly
	-Emergency visits				0.031	-Fewer emergency visits in vitamin D group, statistically significant
	-Serum 25(OH)D		-Increase from 17.2 ± 5.8 to 45.6 ± 8.1 ng/mL		<0.001	-Vitamin D levels increased significantly after supplementation
Rafiq et al., 2022 (7)	-COPD Assessment Test score	155	-Mean change: –2.9 (Vit D) vs –1.1 (Placebo)	NR	0.02	Statistically significant greater symptom improvement in Vit D group
	-Exacerbations		-Events: 18 (Vit D) vs 27 (Placebo)		0.04	Statistically fewer exacerbations in vitamin D group
	-FEV1 (% predicted)		-No significant difference		>0.05	No effect on lung function
	-Serum 25(OH)D		-Increase from 30.1 to 72.4 nmol/L (Vit D group)		<0.001	Serum vitamin D significantly increased post-supplementation
Dastan et al., 2019 (9)	-IL-6	67	-MD = –1.85 pg/mL (within-group)	–2.91 to –0.79		-Significant reduction in IL-6 after vitamin D treatment
	-IL-8		-MD = –3.13 pg/mL (within-group)	–4.54 to –1.72	0.001	-Significant reduction in IL-8 levels
	-hs-CRP		-MD = –1.92 mg/L (within-group)	–3.26 to –0.58	<0.001	-Statistically significant decrease in systemic inflammation marker
	-mMRC dyspnea scale			–1.08 to –0.02	0.006	
	-30-day mortality		-MD = –0.55 (within-group)	NR	0.041	-Improvement in perceived breathlessness
Foumani et al., 2019 (27)	-	63	-4 deaths (Vit D) vs 5 (placebo)	NR	0.72	-No significant difference in short-term mortality
	FEV1		+8.9 % (within-group, Vit D)			
	-FEV1/FVC		+3.2 % (within-group, Vit D)		0.013	-Significant improvement in FEV1 in intervention group
	-Exacerbations		-4 vs 8 events (Vit D vs placebo)		0.023	-Statistically significant increase in FEV1/FVC
	-Quality of life				0.048	-Fewer exacerbations in intervention group, significant difference
	-		-MD = –2.4 pts		0.090	-Not statistically significant Quality of life improvement
Ghodrati et al., 2019 (28)	Dyspnea severity (mMRC scale)	40	-Between-group comparison not quantified (but significant)	NR	0.03	-Vitamin D supplementation significantly improved dyspnea (vs. placebo)
	-FEV1 (% predicted)		-Within-group diff. (Vit D): +1.66 %		0.50	-No significant change in spirometry in intervention group
			-1.25 (Vit D) vs 1.26 (Placebo) events			

Continued in page 182…

…contiuation Table 2. Summary of Findings.

Author, year	Outcome	Participants (n)	Effect Size	95 % CI	p-value	Interpretation
Rafiq et al., 2017 (29)	-Exacerbation rate	43	-No significant change reported	NR		-No significant difference in exacerbation rate
	-FEV1% predicted		-Mean change –0.3 (Vit D) vs –0.4 (Placebo)		0.97	-No effect of vitamin D on lung function
	-COPD Assessment Test score				>0.05	-No improvement in COPD symptoms
	-Serum 25(OH)D levels		-Increase from 29.7 to 67.0 nmol/L (Vit D group)		0.90	
					<0.001	-Significant increase in serum vitamin D levels post-supplementation
Sluyter et al., 2017 (30)	-Exacerbations (≥1 in past year)	442	-OR = 0.90 (Vit D vs placebo)	0.62 – 1.32	0.60	-No statistically significant reduction in exacerbation risk with Vit D
	-FEV1 (% predicted)		-Mean difference: –0.3%	–2.5% to 1.8%	0.78	-No significant difference in lung function
	-Serum 25(OH)D		-Increase from 67 to 114 nmol/L (Vit D group)	NR	<0.001	-Serum levels increased significantly post-intervention
Sanjari et al., 2016 (33)	-COPD Assessment Test score	120	-Mean reduction = –5.5 (Vit D) vs –2.2 (Placebo)	NR	0.002	-Vitamin D significantly improved COPD symptom burden
	-hs-CRP		-Decrease from 5.88 ± 2.1 to 3.11 ± 1.3 mg/L (Vit D)		0.001	-Significant reduction in systemic inflammation marker
	-IL-6		-Decrease from 8.21 ± 1.9 to 5.24 ± 1.7 pg/mL (Vit D)		0.003	-Statistically significant reduction in IL-6
	-IL-10		-Increase from 1.53 ± 0.7 to 2.37 ± 0.6 pg/mL (Vit D)		0.005	-Anti-inflammatory IL-10 increased significantly
	-FEV1 (% predicted)		-No significant difference		>0.05	-Lung function remained unchanged
Martineau et al., 2015 (32)	-Time to first moderate/ severe exacerbation	240	-HR = 1.04	0.73 – 1.49	0.83	-No significant difference in time to first exacerbation
	-Rate of moderate/severe exacerbations	240	-IRR = 0.88	0.67 – 1.15	0.34	-No overall effect of vitamin D on exacerbation rate
	-Rate of exacerbations (baseline 25[OH]D <25 nmol/L)	86	-IRR = 0.57	0.35 – 0.92	0.02	-Significant reduction in exacerbations in deficient subgroup
	-Serum 25(OH)D concentration	240	-Increase from median 38 to 66 nmol/L	NR	<0.001	-Significant increase in vitamin D levels in intervention group
Zendedel et al., 2015 (31)	-FEV1 (%)	88	-Increase from 42.9 ± 14.4 to 60 ± 14.9 (Vit D)		<0.001	-Statistically significant increase in FEV1 after vitamin D supplementation
	-COPD exacerbations		-27 events (Vit D) vs 50 (Placebo)	NR	<0.001	-Fewer exacerbations in vitamin D group, statistically significant
Bjerk et al., 2013 (34)	-Physical performance	36	-MD = +0.9 pts	0.2 – 1.6	0.01	-Vitamin D improved physical performance modestly
	-Quality of life		-MD = –2.1 pts	-11.3 to 7.1	0.40	-No significant difference in quality of life
	-Serum 25(OH)D		-MD = +17.2 ng/mL -HR = 1.07	11.6 – 22.6	<0.001	-Serum vitamin D levels

Continued in page 183…

…contiuation Table 2. Summary of Findings.

Author, year	Outcome	Participants (n)	Effect Size	95 % CI	p-value	Interpretation
Lehouck et al., 2012 (35)	-	182				increased significantly with supplementation
	-Time to first exacerbation		-Rate Ratio = 0.86		0.66	-No significant difference in time to exacerbation
	-Exacerbation rate (per patient-year)		-Between-group diff: –0.6 ± 2.1%	0.79 – 1.46	0.41	-Non-significant reduction in exacerbation rate
	-FEV1 change		-Between-group diff: –8.5 ± 17 m	0.60 – 1.23	0.78	-No significant difference in lung function
	-6-minute walk distance				0.63	-No improvement in physical capacity
	-St George's Respiratory Questionnaire		-Between-group diff: –0.8 ± 2.9	NR	0.79	-No improvement in quality of life
	-Mortality		-10 deaths (Vit D) vs 7 (Placebo)		0.49	-No statistically significant difference in mortality

DISCUSSION

This systematic review synthesized evidence from twelve randomized controlled trials evaluating the effects of vitamin D supplementation in patients with COPD. Overall, the findings suggest that vitamin D may reduce symptom burden and exacerbation frequency in selected populations, particularly those with baseline vitamin D deficiency. Additionally, favorable effects on inflammatory biomarkers were observed, supporting the proposed immunomodulatory role of vitamin D in chronic pulmonary inflammation (36-39). However, the evidence regarding improvements in lung function parameters and quality of life remains inconsistent. Several trials demonstrated within-group improvements in FEV_1 or dyspnea scores; however, these effects were not consistently superior to those of the placebo in between-group comparisons. Similarly, gains in functional performance and quality of life were variable and, in many cases, not statistically significant.

From a methodological perspective, this review offers reassuring findings (40-45). Most of the included studies demonstrated high methodological quality according to the JBI checklist, and none were classified as low quality. Furthermore, half of the studies achieved high reporting quality per the CONSORT standards. Nonetheless, residual concerns remain regarding risk of bias, particularly in domains such as blinding, outcome measurement, and reporting transparency.

In terms of clinical applicability, while the biological plausibility and safety profile of vitamin D are well established (46-47), the heterogeneity of trial designs, dosing regimens, baseline vitamin D status, and outcome measures limits the direct translation of these findings into standardized clinical practice. Current evidence supports considering vitamin D supplementation in COPD patients with proven deficiency, especially when the goal is to reduce exacerbation risk or systemic inflammation (48,49). However, the routine use of vitamin D as a therapeutic intervention for all COPD patients cannot be universally recommended based on the available data. Further high-quality, large-scale RCTs with standardized outcomes, clearly defined patient populations, and more extended follow-up periods are needed. Particular attention should be paid to subgroups with vitamin D deficiency to clarify whether they derive greater benefit and to elucidate optimal dosing strategies that balance efficacy and safety.

From the perspective of evidence-based medicine and meta-science, the findings of this review are both relevant and timely (50-57). First, they help address a persistent gap in the literature on non-pharmacological adjuncts for the management of COPD. Second, by incorporating explicit evaluations of methodological and reporting quality, this review advances the transparency and reproducibility of systematic synthesis (58-60). In doing so, it exemplifies the integration of meta-research principles into clinical evidence appraisal, an essential approach for refining the quality of evidence that underpins healthcare decisions and policy (51,53,54,57,60).

Recommendations for future research

Future RCTs investigating vitamin D supplementation in COPD should address key methodological gaps. Studies should clearly define baseline vitamin D status and stratify analyses accordingly.

Apply standardized dosing regimens and outcome measures, include more extended follow-up periods to assess sustained effects on exacerbations, lung function, and quality of life, ensure trial registration and protocol availability to enhance transparency, and adhere rigorously to CONSORT reporting standards to improve reproducibility Moreover, future research should prioritize subgroup analyses in populations with deficiencies, investigate optimal serum 25(OH) D targets for pulmonary outcomes, and explore the interaction between vitamin D and concurrent pharmacological therapies in COPD. A future clinical interest could be the relationship between respiratory axes and other systems, such as the nervous system, given the increasing prevalence of neuropsychiatric disorders (61-70).

Limitations

This review acknowledges several limitations. First, although the methodological quality of most studies was rated as high, variability in risk of bias, particularly related to blinding and outcome measurement, may have influenced effect estimates. Second, heterogeneity in dosing regimens, study durations, and outcome definitions hindered the feasibility of meta-analysis and limited the comparability of results. Third, the lack of access to protocols or registration information in some trials raises concerns about selective outcome reporting. Additionally, publication bias could not be formally assessed due to the absence of pooled data. Finally, the exclusion of grey literature may have led to the omission of potentially relevant evidence.

CONCLUSIONS

The findings suggest that vitamin D may contribute to reductions in symptom burden, exacerbation frequency, and systemic inflammation, particularly among individuals with baseline deficiency. However, evidence regarding improvements in lung function and quality of life remains inconclusive. While the majority of included RCTs demonstrated high methodological and reporting quality, variations in study design and risk of bias constrain the generalizability of findings. As such, vitamin D cannot yet be recommended as a universal adjunct therapy in COPD management. Nonetheless, its targeted use in populations with deficiencies appears promising and clinically justified. Future well-designed trials are needed to consolidate the evidence base and define the precise role of vitamin D in COPD care. Until then, clinicians should consider individual patient profiles, including vitamin D status, when evaluating supplementation as part of a personalized treatment strategy.

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REFERENCES

1. Boers E, Barrett M, Su JG, Benjafield AV, Sinha S, Kaye L, et al. Global Burden of Chronic Obstructive Pulmonary Disease Through 2050. JAMA Netw Open. 2023;6(12):e2346598.
2. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet Respir Med. 2020;8(6):585-596.
3. Pham HQ, Pham KHT, Ha GH, Pham TT, Nguyen HT, Nguyen THT, et al. Economic Burden of Chronic Obstructive Pulmonary Disease: A Systematic Review. Tuberc Respir Dis (Seoul). 2024;87(3):234-251.
4. Li M. The role of vitamin D in chronic obstructive pulmonary disease with pulmonary hypertension. Pulm Circ. 2023;13(4):e12294.
5. Lokesh KS, Chaya SK, Jayaraj BS, Praveena AS, Krishna M, Madhivanan P, et al. Vitamin D deficiency is associated with chronic obstructive pulmonary disease and exacerbation of COPD. Clin Respir J. 2021;15(4):389-399.
6. Park SY, Yoo KH. Vitamin D and Chronic Obstructive Pulmonary Disease: Biomarker Related to Outcomes. J Korean Med Sci. 2019;34(29):e196.
7. Rafiq R, Aleva FE, Schrumpf JA, Daniels JM, Bet PM, Boersma WG, et al. Vitamin D supplementation in chronic obstructive pulmonary disease patients with low serum vitamin D: A randomized controlled trial. Am J Clin Nutr. 2022;116(2):491-499.
8. Lakra A, Singh B, Janmeja AK, Sharma V, Kumar A. A study to assess the relationship between vitamin D3 levels and the risk of acute exacerbation in patients with chronic obstructive pulmonary disease. Monaldi Arch Chest Dis. 2025;95(1).
9. Dastan F, Salamzadeh J, Pourrashid MH, Edalatifard M, Eslaminejad A. Effects of High-Dose Vitamin D Replacement on the Serum Levels of Systemic Inflammatory Biomarkers in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease. COPD. 2019;16(3-4):278-283.
10. Janssens W, Lehouck A, Decramer M, Gayan-Ramirez G. Vitamin D and Chronic Obstructive Pulmonary Disease. Vitamin D and the Lung. 2012;3:239-260.
11. Lozada-Martinez ID, Lozada-Martinez LM, Fiorillo-Moreno O. Leiden manifesto and evidence-based research: Are the appropriate standards being used for the correct evaluation of pluralism, gaps and relevance in medical research? J R Coll Physicians Edinb. 2024;54(1):4-6.
12. Blanco-Teherán C, Quintana-Pájaro L, Narváez-Rojas A, Martínez-Pérez R, García-Ballestas E, Moscote Salazar L, et al. Evidence-based medicine in neurosurgery: Why and how? J Neurosurg Sci. 2022;66(1):49-53.
13. Brignardello-Petersen R, Santesso N, Guyatt GH. Systematic reviews of the literature: An introduction to current methods. Am J Epidemiol. 2025;194(2):536-542.
14. Shaheen N, Shaheen A, Ramadan A, Hefnawy MT, Ramadan A, Ibrahim IA, et al. Appraising systematic reviews: A comprehensive guide to ensuring validity and reliability. Front Res Metr Anal. 2023;8:1268045.
15. Soltani A, Larijani B. The rationale behind systematic reviews in clinical medicine: A conceptual framework. J Diabetes Metab Disord. 2021;20(1):919-929.
16. Lozada-Martinez ID, Hernandez-Paez DA, Palacios Velasco I, Martinez Guevara D, Liscano Y. Meta-Research in Geriatric Surgery: Improving the Quality of Surgical Evidence for Older Persons in a Multidimensional-Scale Research Field. J Clin Med. 2024;13(18):5441.
17. Angarita-Pacheco Y, Urbano López AD, Hernández-Páez DA, Fiorillo-Moreno O, Picón-Jaimes YA, Beltrán Venegas T, et al. Global Trends and Evidence Gaps in Medical Errors Research: A Mixed-Methods Scientometrics Study. J Multidiscip Healthc. 2025;18:2497-2508.
18. Lozada-Martinez ID, Hernandez-Paez D, Zárate YEJ, Delgado P. Scientometrics and meta-research in medical research: approaches required to ensure scientific rigor in an era of massive low-quality research. Rev Assoc Med Bras (1992). 2025;71(4):e20241612.
19. Galván-Pérez Y, Herrera-Polo M, Hernández-Páez DA, Neira Rodado D, Salas-Navarro K, Rueda-Olivella AM, et al. Six Sigma Applied to Healthcare: A Global Scientometrics Analysis of Health Services Quality Improvement Research. Health Serv Insights. 2025;18:11786329251352018.
20. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
21. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210.

22. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
23. Barker TH, Stone JC, Sears K, Klugar M, Tufanaru C, Leonardi-Bee J, et al. The revised JBI critical appraisal tool for the assessment of risk of bias for randomized controlled trials. JBI Evid Synth. 2023;21(3):494-506.
24. Lozada-Martinez ID, Fiorillo-Moreno O, Hernández-Paez DA, Bermúdez V. Clinical trials on medical errors need to strengthen geographical representation, methodological and reporting quality. QJM. 2025:hcaf068.
25. Lozada-Martínez ID, Visconti-López FJ, Rojas-Cueva AC, Ausejo F, Castrillón-Lozano J, Cañas Pedroza N, et al. Methodological and reporting quality of Latin American randomized controlled trials in surgery from 2012 to 2022: A meta-research study. Internat J Surg Open. 2025;63(1):21-27.
26. Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 statement: Updated guideline for reporting randomised trials. BMJ. 2025;389:e081123.
27. Foumani A, Mehrdad M, Jafarinezhad A, Nokani K, Jafari A. Impact of vitamin D on spirometry findings and quality of life in patients with chronic obstructive pulmonary disease: A randomized, double-blinded, placebo-controlled clinical trial. Int J Chron Obstruct Pulmon Dis. 2019;14:1495-1501.
28. Ghodrati S, Ezzatpanah A, Asadi-Khiavi M, Alian Samakkah S, Esmaeilzadeh A, Pezeshgi A. Administration of vitamin D to ameliorate dyspnea of chronic obstructive pulmonary disease patients: A randomized controlled trial. Immunopathol Persa. 2019;5(2):e22.
29. Rafiq R, Prins HJ, Boersma WG, Daniels JM, den Heijer M, Lips P, et al. Effects of daily vitamin D supplementation on respiratory muscle strength and physical performance in vitamin D-deficient COPD patients: A pilot trial. Int J Chron Obstruct Pulmon Dis. 2017;12:2583-2592.
30. Sluyter JD, Camargo CA, Waayer D, Lawes CMM, Toop L, Khaw KT, et al. Effect of Monthly, High-Dose, Long-Term Vitamin D on Lung Function: A Randomized Controlled Trial. Nutrients. 2017;9(12):1353.
31. Zendedel A, Gholami M, Anbari K, Ghanadi K, Bachari EC, Azargon A. Effects of Vitamin D Intake on FEV1 and COPD Exacerbation: A Randomized Clinical Trial Study. Glob J Health Sci. 2015;7(4):243-248.
32. Martineau AR, James WY, Hooper RL, Barnes NC, Jolliffe DA, Greiller CL, et al. Vitamin D3 supplementation in patients with chronic obstructive pulmonary disease (ViDiCO): A multicentre, double-blind, randomised controlled trial. Lancet Respir Med. 2015;3(2):120-130.
33. Sanjari M, Soltani A, Habibi Khorasani A, Zareinejad M. The effect of vitamin D on COPD exacerbation: A double-blind randomized placebo-controlled parallel clinical trial. J Diabetes Metab Disord. 2016;15(1):33.
34. Bjerk SM, Edgington BD, Rector TS, Kunisaki KM. Supplemental vitamin D and physical performance in COPD: A pilot randomized trial. Int J Chron Obstruct Pulmon Dis. 2013;8:97-104.
35. Lehouck A, Mathieu C, Carremans C, Baeke F, Verhaegen J, Van Eldere J, et al. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med. 2012;156(2):105-114.
36. Jiang Y, Li M, Yu Y, Liu H, Li Q. Correlation Between Vitamin D, Inflammatory Markers, and T Lymphocytes With the Severity of Chronic Obstructive Pulmonary Disease and Its Effect on the Risk of Acute Exacerbation: A Single Cross-sectional Study. Clin Ther. 2025;47(1):44-54.
37. Islam S, Sarkar NK, Mujahid AA, Bennoor KS, Hossain SS, Attar MM, et al. Association of Serum Vitamin D (25OHD) Level with Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Mymensingh Med J. 2019;28(2):441-448.
38. Jolliffe DA, James WY, Hooper RL, Barnes NC, Greiller CL, Islam K, et al. Prevalence, determinants and clinical correlates of vitamin D deficiency in patients with Chronic Obstructive Pulmonary Disease in London, UK. J Steroid Biochem Mol Biol. 2018;175:138-145.
39. Jolliffe DA, Kilpin K, MacLaughlin BD, Greiller CL, Hooper RL, Barnes NC, et al. Prevalence, determinants and clinical correlates of vitamin D deficiency in adults with inhaled corticosteroid-treated asthma in London, UK. J Steroid Biochem Mol Biol. 2018;175:88-96.
40. Lozada-Martinez ID, Neira-Rodado D, Martinez-Guevara D, Cruz-Soto HS, Sanchez-Echeverry MP, Liscano Y. Why is it important to implement meta-research in universities and institutes with medical research activities? Front Res Metr Anal. 2025;10:1497280.
41. Lozada-Martinez ID, Hernandez-Paz DA, Fiorillo-Moreno O, Picón-Jaimes YA, Bermúdez V. Meta-Research in Biomedical Investigation: Gaps and Opportunities Based on Meta-Research Publications and Global Indicators in Health, Science, and Human Development. Publications. 2025;13(1):7.
42. Pérez-Fontalvo NM, de Arco-Aragón MA, Jiménez-García JDC, Lozada-Martínez ID. Molecular and computational research in low- and middle-income countries: Development is close at hand. J Taibah Univ Med Sci. 2021;16(6):948-949.

43. Galván-Barrios J, Fiorillo-Moreno O, Delgado P. Gaps and challenges of available clinical guidelines on treatment options for early hepatocellular carcinoma. Internat J Surg Open. 2025;63(1):60-61.

44. Lozada-Martínez ID, Ealo-Cardona CI, Marrugo-Ortiz AC, Picón-Jaimes YA, Cabrera-Vargas LF, Narváez-Rojas AR. Meta-research studies in surgery: a field that should be encouraged to assess and improve the quality of surgical evidence. Int J Surg. 2023;109(6):1823-1824.

45. Galván-Barrios J, Fiorillo-Moreno O, Alzate Mejía OA, Mansaray FT. Clinical trials on CAR T-cell therapy for childhood cancer need geographic representation in lower-income countries. Ann Med Surg. 2025;87(7):4676-4678.

46. Thai H, Hassanen R, Whittall T, Kirkham P. The potential role of 1,25(OH)2D3 (Active vitamin D3) in modulating macrophage function; implications for chronic obstructive pulmonary disease (COPD). J Inflamm (Lond). 2025;22(1):26.

47. Jolliffe DA, Stefanidis C, Wang Z, Kermani NZ, Dimitrov V, White JH, et al. Vitamin D Metabolism Is Dysregulated in Asthma and Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2020;202(3):371-382.

48. Williamson A, Martineau AR, Jolliffe D, Sheikh A, Janssens W, Sluyter J, et al. Vitamin D for the management of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2024;9(9):CD013284.

49. Rus LA, Popeţiu RO, Borta SM, Vîlcea A, Nica DV, Vintilă T, et al. Lower Vitamin D During Acute Exacerbation Is Associated with Very Severe Chronic Obstructive Pulmonary Disease. Medicina (Kaunas). 2025;61(6):979.

50. Lozada-Martínez ID, Bolaño-Romero MP, Picón-Jaimes YA, Moscote-Salazar LR, Narváez-Rojas AR. Quality or quantity? Questions on the growth of global scientific production. Int J Surg. 2022;105:106862.

51. Jaramillo Ordoñez JC, González Vides G, Lozada Martínez ID, García Espiñeira MC. Alteración de la función pulmonar en vendedores informales de gasolina expuestos a sus vapores en Maicao, Colombia. Rev Med Hered. 2022;33(4):245-254.

52. Lozada-Martínez ID, Lozada-Martínez LM, Cabarcas-Martínez A, Ruiz-Gutiérrez FK, Aristizábal Vanegas JG, Amorocho Lozada KJ, et al. Historical evolution of cancer genomics research in Latin America: A comprehensive visual and bibliometric analysis until 2023. Front Genet. 2024;15:1327243.

53. Lozada-Martínez ID, Visconti-López FJ, Marrugo-Ortiz AC, Ealo-Cardona CI, Camacho-Pérez D, Picón-Jaimes YA. Research and Publication Trends in Pediatric Surgery in Latin America: A Bibliometric and Visual Analysis from 2012 to 2021. J Pediatr Surg. 2023;58(10):2012-2019.

54. Lozada Martínez ID, Domínguez Alvarado G, Torres Pérez F, Cruz Rodríguez LJ, Galindo Ruiz LA, Gamboa Perdomo MC, et al. Uso y resultados del astegolimab en el manejo del asma severa: ¿qué se conoce?. Horiz Med. 2023;23(1):e1948.

55. Montoya-Quintero KF, Galván-Barrios J, Martinez-Guevara D, Dueñas D, Montenegro J, and Liscano Y. Bridging the gap: cancer scientific equity, global child health, and distribution of CAR T-cell therapy clinical trials in childhood cancer. Front Pediatr. 2025;13:1611187.

56. Miranda-Pacheco JA, De Santis-Tamara SA, Parra-Pinzón SL, González-Monterroza JJ, Lozada-Martínez ID. Medical interest groups and work policies as emerging determinants of a successful career: A student perspective - Correspondence. Int J Surg. 2021;92:106020.

57. Lozada-Martínez ID, Suárez-Causado A, Solana-Tinoco JB. Ethnicity, genetic variants, risk factors, and cholelithiasis: The need for eco-epidemiological studies and genomic analysis in Latin American surgery. Int J Surg. 2022;99:106589.

58. Bai AD, Komorowski AS, Lo CKL, Tandon P, Li XX, Mokashi V, et al. Methodological and Reporting Quality of Noninferiority Randomized Controlled Trials Comparing Antibiotic Therapies: A Systematic Review. Clin Infect Dis. 2021;73(7):e1696-e1705.

59. Dedivitis RA, Castro MAF, Boni AMD, Alvares ACB, Tresso AJP, Oliveira AD, et al. The methodological and reporting quality of randomized controlled trials of tyrosine kinase inhibitors for advanced differentiated thyroid cancer: Meta-research study. Head Neck. 2024;46(7):1683-1697.

60. Zhai X, Wang Y, Mu Q, Chen X, Huang Q, Wang Q, et al. Methodological Reporting Quality of Randomized Controlled Trials in 3 Leading Diabetes Journals From 2011 to 2013 Following CONSORT Statement: A Systematic Review. Medicine (Baltimore). 2015;94(27):e1083.

61. Román F, Calandri IL, Caridi A, Carosella MA, Palma PA, Llera JJ, et al. Long-term (6 months) neurological and psychiatric consequences in mild COVID community patients: J Appl Cogn Neurosci. 2022;3(1):e00264623.

62. Gautreaux-Betancourt RE, Antúñez-Laffita VA, Ordehi-González D. Brief history of the development of cognitive neuroscience applied to education in the Dominican Republic 2009-2022. J Appl Cogn Neurosci. 2022;3(1):e00234588.

63. Maciejewicz B. Neuroscience of consciousness: cognition, physics and philosophy of decoding the human brain. J Appl Cogn Neurosci. 2022;3(2):e00274600.

64. Muûls M, Carvajal R. Impact of Attention Deficit Hyperactivity Disorder on Entrepreneurial Behavior: A Neurobiological Approach. J Appl Cogn Neurosci. 2023;4(2):e00395858.
65. Tabernero ME, Morello-García F. Efecto de mejora de la memoria emocional en pacientes con deterioro cognitivo leve. J Appl Cogn Neurosci. 2024;5(1):e5677.
66. Aliqkaj A, Carvajal R. Cognitive Load on Leadership Decision-Making: Conscious and Unconscious Responses. J Appl Cogn Neurosci. 2024;5(1):e5253.
67. Park H, Lee CH. The Impact of Pulmonary Disorders on Neurological Health (Lung-Brain Axis). Immune Netw. 2024;24(3):e20.
68. Covetta AN, Palma A. Pathological syncretism and eating disorders. J Appl Cogn Neurosci. 2024;5(2):1-6.
69. Leis A, Monica Liliana I, Rojas G, Gatto E. Personality changes as an early marker of mild cognitive impairment. J Appl Cogn Neurosci. 2024;5(2):1-25.
70. Murillo Ramírez ML, Trujillo-Orrego N, Sánchez-Escudero JP, Trujillo Orrego SP. Social cognition interventions for adults with mood disorders and suicidality: A systematic review. J Appl Cogn Neurosci. 2024;5(2):e6228.