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ORIGINAL ARTICLE

Vitamin D supplementation and lower urinary tract symptoms: a systematic review and meta-analysis

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Popular scientific summary

- This meta-analysis evaluates, for the first time, both the preventive and therapeutic effects of vitamin D supplementation on lower urinary tract symptoms (LUTS).
- Serum vitamin D levels show a significant association with LUTS.
- Vitamin D supplementation may help alleviate LUTS symptoms in individuals with low serum vitamin D levels.
- Vitamin D supplementation does not reduce the incidence of LUTS in the general population.

Abstract

***Background*:** Lower urinary tract symptoms (LUTS) are highly prevalent and impact quality of life. While vitamin D insufficiency is a major public health concern. This study systematically investigated the relationship between serum vitamin D levels and LUTS, and the effects of supplementation on outcomes.

***Methods*:** We conducted a systematic review and meta-analysis of studies from Web of Science, PubMed, Embase, and Cochrane Library up to September 2025. Pooled Weighted mean difference (WMD) and Odds Ratios (ORs), along with their 95% confidence intervals (CI) were calculated using the random-effects model. Sensitivity analysis was conducted to examine the robustness of the results.

***Results*:** A total of 48 studies (221,735 participants) were included. Vitamin D levels were significantly lower in individuals with LUTS than in controls (WMD: −3.15, 95% CI: −4.65, −1.66). Low vitamin D levels were associated with a 67% increased risk of LUTS (95% CI: 1.31, 2.12). Subgroup analyses confirmed these associations among men and children but not among women. Vitamin D supplementation significantly promoted LUTS remission, particularly among individuals with low baseline serum vitamin D concentrations (OR: 9.02, 95% CI: 2.94, 27.62), but did not reduce LUTS incidence in the general population (OR: 0.98, 95% CI: 0.91, 1.05).

***Conclusions*:** Serum vitamin D levels are significantly associated with LUTS, particularly among men and children. Vitamin D supplementation may alleviate LUTS symptoms in individuals with low vitamin D levels, but it is not currently supported as a preventive measure for LUTS in the general population due to insufficient evidence.

Registration: Prospero registration no. CRD42025630727.

Keywords: *Vitamin D*; *supplementation*; *lower urinary tract symptoms*; *meta-analysis*

To access the supplementary material, please visit the article landing page

Received: 21 January 2026; Revised: 23 February 2026; Accepted: 10 March 2026; Published: 11 August 2026

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Lower urinary tract symptoms (LUTS) encompass a range of voiding, storage, and post-micturition manifestations, commonly including urinary frequency, urgency, incontinence, and nocturia (1). LUTS are highly prevalent among adults in both Western countries and China, with an estimated prevalence ranging from 55 to 76% (2, 3). Notably, approximately 15% of children aged 5–6 years continue to experience nocturnal enuresis (4). LUTS may result from organic or neurological abnormalities of the bladder, prostate, or urethra. Although not life-threatening, these conditions are often challenging to manage (5). Importantly, LUTS can lead to a series of health problems such as attention deficit disorder, sleep disorders, anxiety, depression, cardiovascular and metabolic disorders, sexual dysfunction, reduced quality of life, and an increased risk of mortality (6–10). Therefore, effective treatment and prevention of LUTS are clinically significant.

Vitamin D, a fat-soluble secosteroid, plays essential roles in numerous physiological processes. However, its deficiency remains a major global public health concern. A comprehensive meta-analysis including data from approximately eight million participants across 81 countries reported that 47.9% of the global population exhibited vitamin D insufficiency (11). Increasing evidence demonstrates a strong link between vitamin D deficiency and immune dysregulation, increased infection risk, and urological disorders (12). Studies have identified the vitamin D receptor (VDR) in bladder tissue and in the striated muscles of the pelvic floor (13), suggesting that vitamin D deficiency may influence LUTS by altering muscle strength or activity.

Recently, growing evidence has linked serum vitamin D levels to LUTS. Although meta-analysis has been conducted (1), the current evidence remains inconclusive. Therefore, this study updated prior analyses to further evaluate the association between serum vitamin D levels and LUTS across diverse populations. In addition, we sought to clarify whether vitamin D supplementation could alleviate or prevent LUTS, and whether its effectiveness extends to the general population.

Methods

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and was registered with the International Prospective Register of Systematic Reviews (PROSPERO; no. CRD42025630727).

Search strategy

PubMed, Embase, Web of Science, and the Cochrane Library were searched for studies published up to September 2, 2025. Search strategy combined MeSH terms and their free-text equivalents related to LUTS and vitamin D. Synonymous terms within each concept were combined using the Boolean operator 'OR', and the two concepts were linked using 'AND'. The detailed search strategy for each database is provided in Supplementary Appendix 1.

Eligibility criteria

The inclusion criteria were defined according to the PICOS framework: population (P), human participants with or without LUTS; intervention/exposure (I), vitamin D supplementation or serum vitamin D levels; comparison (C), placebo (in intervention studies) or comparison across different levels of serum vitamin D (e.g. high vs. low) or between individuals with and without LUTS (in observational studies); outcome (O), presence or severity of LUTS; and study design (S), randomized controlled trials (RCTs), cohort, case–control, or cross-sectional designs.

LUTS was defined in each study based on urodynamic testing, validated questionnaires, or clinical assessments. The exclusion criteria were non-English publications and studies addressing urinary conditions without reference to LUTS.

Screening and data extraction

Two authors independently screened the literature and extracted relevant data. Any disagreements were resolved by discussion with a third author. The following variables were collected from the included studies: first author; publication year; study design; research location; sample size; participants' age; vitamin D status; laboratory methods for assessing serum vitamin D levels; definition of LUTS; follow-up duration; variables used for matching or statistical adjustment; mean ± standard deviation (SD) of serum vitamin D concentrations in participants with and without LUTS; LUTS scores and frequency; adjusted odds ratios (ORs) for LUTS in participants with low vitamin D levels relative to those with higher concentrations; and changes in LUTS scores, frequency, and adjusted ORs in participants receiving vitamin D supplementation versus controls.

Quality assessment

The quality of the case-control and cohort studies was evaluated using the Newcastle–Ottawa Scale (NOS). For cross-sectional research, we used the Joanna Briggs Institute (JBI) Critical Appraisal Checklist, which comprises eight questions, with one point awarded for each criterion. The risk of bias in RCTs was assessed with the Cochrane Collaboration tool.

Statistical analysis

The weighted mean difference (WMD) with 95% confidence interval (CIs) was used to compare serum

Citation: Food & Nutrition Research 2026, **70**: 13933 - http://dx.doi.org/10.29219/fnr.v70.13933

vitamin D concentrations between patients with LUTS and controls. Vitamin D values reported in nmol/L were converted to ng/mL (1 ng/mL = 2.5 nmol/L).

To examine the association between serum vitamin D levels and LUTS, the standardized mean difference (SMD) was applied to compare LUTS scores between the low and high vitamin D groups, accounting for differences in scoring scales across studies. ORs and adjusted ORs (95% CIs) were employed to assess the risk of LUTS associated with low vitamin D levels across studies. Due to the varying definitions of low and high serum vitamin D levels across the included studies, we grouped the studies based on their vitamin D thresholds. When multiple estimates were reported within a single study (e.g. different LUTS subtypes or vitamin D categories), they were pooled into an overall effect size using the inverse variance method. In addition, the dose–response relationship between serum vitamin D levels and LUTS risk was evaluated using the robust error meta-regression (REMR) model (14, 15).

For intervention studies, the SMD was used to assess changes in LUTS scores before and after vitamin D supplementation, whereas ORs or adjusted ORs were used to evaluate the effects of vitamin D supplementation on LUTS symptoms or risk.

A random-effects model was applied to all analyses. Heterogeneity was evaluated using the chi-square test and the I^2 statistics, with $I^2 \geq 50\%$ indicating substantial heterogeneity. Publication bias was evaluated using Egger's test and funnel plots. The trim-and-fill method was used to examine the robustness of the results. Sensitivity analyses were conducted using the leave-one-out approach. Subgroup analyses were performed according to the study population, LUTS subtype, and study design. All meta-analyses were performed using Stata version 15.1. $P < 0.05$ was considered statistically significant.

Results

Study characteristics

The study selection process is summarized in Fig. 1. A total of 2,003 studies were identified, of which 48 studies involving 221,735 participants were ultimately included (13, 16–62). Overall, the included studies comprised eight RCTs, eight cohort studies, 12 case-control studies, and 20 cross-sectional studies. Among these, 20 studies (11 cross-sectional, seven case-control, and two cohort) with 22,400 participants reported serum vitamin D concentrations in individuals with and without LUTS. In addition, 28 studies (two cohort, 10 case-control, and 16 cross-sectional) with 27,320 participants evaluated the relationship between low serum vitamin D levels and LUTS risk. Furthermore, 17 studies (eight RCTs, six cohorts, two case-control, and one cross-sectional) with 186,546 participants investigated the effect of vitamin D supplementation on LUTS. The key characteristics of the included studies are shown in Table 1.

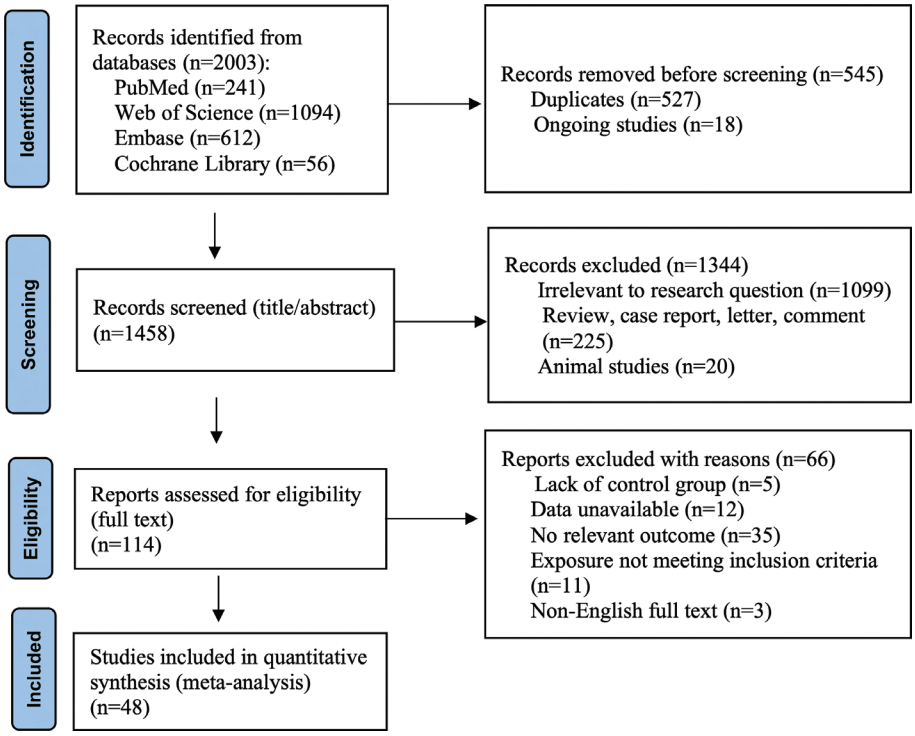

Fig. 1. PRISMA flowchart depicting study search and selection for meta-analysis.

Table 1. Characteristics of included studies

Study	Design	Vitamin D status	Vitamin D Measurement	Region	Case definition of LUTS	Population	Age	Follow up	Matched or adjusted variables
Gülyüz 2025	Case-control	Deficiency	Chemiluminescence immunoassay	Egypt	Medical history	307 cases and 254 controls from children	5–18 years	-	Age, gender, BMI, serum iron, parental education level, family history of enuresis
Li 2024	Cross-sectional	Insufficiency/ Deficiency	Radioimmunoassay/ LC-MS/MS	USA	Validated questionnaire	4,565 cases from 9,525 women	> 45 years	-	Age, race, education, income and BMI, drink, smoke, diabetes, hypertension, hyperlipidemia, pregnant and vaginal deliveries history
Mostafa 2024	Case-control	Deficiency	Elisa	Egypt	Medical history and estimated bladder capacity	60 cases and 60 controls from children	5–15 years	-	Age, sex
Alshogran 2023	Cross-sectional	Insufficiency/ Deficiency	Chemiluminescent assay	Jordan	Validated questionnaire	34 cases from 96 adults	≥ 18 years	-	-
Arjmand 2023	RCT	Supplementation (50,000 IU/week)	-	Iran	Validated questionnaire	45 cases and 45 controls from women	50–80 years	8 weeks	Age, BMI, vitamin D levels, urinary incontinence severity, nocturia frequency, impact of daily life
Gul 2023	Cross-sectional	Deficiency	Elisa	Turkey	Validated questionnaire	210 cases from 250 women	≥ 18 years	-	-
Liu 2023	Cross-sectional	Insufficiency/ Deficiency	LC-MS/MS	USA	Validated questionnaire	1,698 cases from 4,663 men	≥ 50 years	-	Age, race, BMI, alcohol use, diabetes, hypertension, family poverty rate, depression, and smoking
Markland 2023	RCT	Supplementation (2,000 IU/day)	LC-MS/MS	USA	Validated questionnaire	5,256 cases and 5,218 controls from men	≥ 50 years	5 years	Age, race, education, attainment, geographic region, behavioral and life-style characteristics, dietary vitamin D intake, BMI, Health History
Siroosbakht 2023	Case-control	Insufficiency/ Deficiency	Elisa	Iran	Medical history	267 cases and 267 controls from children	6–15 years	-	Gender, age, height, BMI, constipation, level of education of parents, parents' enuresis history
Tangpricha 2023	Case-control	Insufficiency	Electrochemiluminescence immunoassay	USA	Validated questionnaire	398 cases and 398 controls from women	Average 50 years		Age, BMI, physical activity, cigarette smoking, menopausal status, hypertension, type 2 diabetes
Yeo 2023	Cohort	Supplementation (25,000 IU/2 weeks)	-	Korea	Validated questionnaire	29 cases from 57 men	> 40 years	9 months	Age, weight, BMI, prostate volume, PSA, hemoglobin, hematocrit, total cholesterol, glucose, vitamin D, testosterone, Qmax, postvoid urine volume, IPSS, AMS, comorbidities
Abbaspoor 2022	Cross-sectional	Insufficiency/ Deficiency	HPLC	Iran	Validated questionnaire	233 cases from 437 women	15–49 years	-	-
Kim 2022	Cross-sectional	Deficiency	Chemiluminescent protein binding assay	Korea	Validated questionnaire	420 cases from 534 men	average 60 years	-	-
Markland 2022	RCT	Supplementation (2,000 IU/day)	LC-MS/MS	USA	Validated questionnaire	5,232 cases and 5,295 controls from women	≥ 55 years	5 years	Age, race, education, attainment, geographic region, behavioral and life-style characteristics, dietary vitamin D intake, health history, obstetric/ gynecologic, pregnancies
Shahraki 2022	RCT	Supplementation (5,000 IU/week)	Chemiluminescent immunoassay	Iran	Validated questionnaire	30 cases and 30 controls from women	40–49 years	3 months	Age, type of delivery, weight, height, BMI, serum levels of vitamin D

Table 1. (Continued)

Study	Design	Vitamin D status	Vitamin D Measurement	Region	Case definition of LUTS	Population	Age	Follow up	Matched or adjusted variables
Vaughan 2022	Cross-sectional	Supplementation	-	USA	Validated questionnaire	19,691 cases from 75,316 women	55–98 years	-	Age, BMI, history of hypertension, history of high cholesterol, history of type 2 diabetes, and reported limitations in moderate or vigorous physical activities
Özçift 2022	Case-control	Deficiency	-	Turkey	Validated questionnaire and urodynamic test	52 cases and 41 controls from children	5–16 years	-	Age, sex
El-Baz 2021	Case-control	Deficiency	Elisa	Egypt	Medical history	50 cases and 50 controls from children	5–16 years	-	Age, weight, height, gender, birth order, parents' education, parents' work, per-capita income, crowding index
Kim 2021	Cross-sectional	-	-	Korea	Validated questionnaire	432 cases from 4,390 women	> 19 years	-	Age, BMI, HOMA-IR, current medication for hypertension, diabetes, BEPSI-K score
Markland 2020	Cohort	Supplementation	-	USA	Validated questionnaire	38,101 Cases from cohort 1 and 35,190 cases from cohort 2	25–55 years	10 years	Age, BMI, history of type 2 diabetes, history of vascular disease, cigarette smoking, parity, use of postmenopausal hormone therapy, physical activity
Stafne 2020	Cross-sectional	Insufficiency/ Deficiency	Electrochemiluminescence immunoassay	Europe	Validated questionnaire	351 cases from 851 women	average 30 years	-	Age, PTH, BMI, Parity
Swenson 2020	Cross-sectional	Insufficiency/ Deficiency	Chemiluminescent immunoassay	USA	Validated questionnaire	113 cases from 154 women	≥ 18 years	-	Age, BMI, parity
Zendehdel 2020	RCT	Supplementation (50,000 IU/2 weeks)	Elisa	Iran	Validated questionnaire	54 cases and 54 controls from men	> 50 years	6 months	Age, BMI, education, marital status, employment status, diabetes
Abdul-Razzak 2019	Case-control	Insufficiency/ Deficiency	Chemiluminescent assay	Jordan	Urodynamic test and validated questionnaire	55 cases and 129 controls from adults	18–56 years	4 weeks	Age, BMI, dietary Ca intake, HADS, depression, HADS, anxiety
Markland 2019	RCT	Supplementation (50,000 IU/week)	IDS-iSYS analyzer	USA	Validated questionnaire	28 Cases and 28 controls from postmenopausal women	≥ 55 years	12 weeks	Age, race, insurance, BMI, waist circumference, current tobacco usage, UI, functional comorbidity index, hysterectomy, parity
Aydogmus 2018	Case-control	Deficiency	Elisa	Turkey	Validated questionnaire	101 Cases and 49 controls from women	25–81 years	-	Age, gravity, parity, BMI, birth weight, pelvic organ prolapse, menopause
Rahmani 2018	RCT	Supplementation (1,000 IU/day)	Elisa	Iran	Interview with each child's mother	36 Cases and 34 controls from children	7–15 years	2 months	Age, sex, bowel habits, baseline nocturnal enuresis/week, urination/day, family history of enuresis, weight, height, waist-to-hip ratio, mid-upper-arm circumference of the participants
Yoo 2018	Cross-sectional	Insufficiency/ Deficiency	Chemiluminescent protein binding assay	Korea	Validated questionnaire	61 cases from 115 men	Average 56–61 years	-	Age, BMI, serum PSA, serum testosterone, serum hemoglobin A1c, prostate volume

Table 1. (Continued)

Study	Design	Vitamin D status	Vitamin D Measurement	Region	Case definition of LUTS	Population	Age	Follow up	Matched or adjusted variables
Kaur 2017	Case-control	Supplementation (60,000 IU/week)	Elisa	India	Validated questionnaire and clinical examination	23 cases and 100 controls from women	65–78 years	6 months	Age, BMI
Lee 2017	Cross-sectional	Insufficiency/ Deficiency	RIA	Korea	Validated questionnaire	558 cases from 1,674 women	> 20 years	-	Menopause, number of pregnancies, hypertension, diabetes, BMI, age, stroke, asthma, COPD
Li 2017	Cross-sectional	Deficiency	RIA	USA	Validated questionnaire	370 cases from 1,293 men	≥ 40 years	-	Age, race, education, poverty income ratio, veteran/military status, smoking, drinker, physical
Oberg 2017	RCT	Supplementation (20,000 IU/2 weeks)	LC-MS/MS	Norway	Validated questionnaire	134 cases and 139 controls from postmenopausal women	50–80 years	1 year	Age, serum 25(OH)D, current smoking, prior hysterectomy, BMI, IPAQ category
Parker-Autry 2017	Cohort	-	RIA	USA	Validated questionnaire	223 cases from 673 postmenopausal women	70–79 years	4 years	Age, race, current estrogen use, anticholinergic use, smoking
Elshazly 2016	Case-control	Deficiency	RIA	Egypt	Validated questionnaire	70 cases and 80 controls from men	> 50 years	8 weeks	Age, PSA
Kilic 2016	Cross-sectional	-	-	Turkey	Validated questionnaire	295 cases and 410 controls from adults	average 72 years	-	Age, BMI, osteoporosis, coronary artery disease, blood pressure, nutritional assessment, instrumental activities of daily living, basic activities of daily living
Liu 2016	Cohort	-	RIA	China	Validated questionnaire	820 cases from 1,998 men	≥ 65 years	4 years	BMI, marriage, smoking, calcium supplement, multivitamin use, medical history,VDR, serum hormones
Vaughan 2016	Cohort	Insufficiency/ Deficiency	IDS-iSYS analyzer	USA	Validated questionnaire and clinical examination	65 cases from 175 adults	≥ 65 years	42 months	age, gender, race/ethnicity
Zhang 2016	Case-control	Deficiency	E601 modular	China	Urodynamic test, validated questionnaire	231 Cases and 91 controls from men	60–75 years	-	Age, IPSS, urination time, urinary volume, abdominal obesity, aldosterone, glucose, insulin, parathyroid hormone, C- reactive protein
Aydogmus 2015	Cross-sectional	Deficiency	Elisa	Turkey	Validated questionnaire	66 cases from 148 women	18–40 years	-	Age, gestational, age
Caretta 2015	Cross-sectional	Insufficiency/ Deficiency	Chemiluminescent immunoassay	Italy	Validated questionnaire	50 cases from 67 men	18–80 years	-	-
Foti 2014	Cross-sectional	Insufficiency/ Deficiency	RIA	Italy	Validated questionnaire	129 cases from 233 women	average 59 years	-	-
Li 2014	Cross-sectional	Deficiency	LC-MS/MS	China	Validated questionnaire	61 cases from 247 children	5–7 years	-	Gender, age, gestational age, birth weight, maternal education, paternal education, and family income

Citation: Food & Nutrition Research 2026, **70**: 13933 - http://dx.doi.org/10.29219/fnr.v70.13933

Table 1. (Continued)

Study	Design	Vitamin D status	Vitamin D Measurement	Region	Case definition of LUTS	Population	Age	Follow up	Matched or adjusted variables
Parker-Autry 2012	Case-control	Insufficiency/ Deficiency	Liquid chromatography	USA	Validated questionnaire	138 cases and 130 controls from women	> 19 years	-	GFR, significant smoking history, medical problems, medications
Vaughan 2011	Cross-sectional	Insufficiency/ Deficiency	RIA	USA	Validated questionnaire	666 cases from 1,432 men	≥ 40 years	-	Age, racial/ethnic differences, education, poverty-to-income ratio, self-rated health status, depression, GFR, categories of comorbid conditions, prostatic enlargement and prostate cancer
Badalian 2010	Cross-sectional	Insufficiency/ Deficiency	RIA	USA	Validated questionnaire	331 cases from 1,950 women	> 19 years	-	Age, BMI, parity, education, race or ethnicity.
Kristal 2008	Cohort	Supplementation	-	USA	Validated questionnaire	876 Cases from 4,770 men	≥ 55 years	7 years	Age, race/ethnicity, waist-to-hip ratio, total energy
Dallosso 2004	Cohort	Supplementation	-	UK	Validated questionnaire	429 Cases from 5,816 women	≥ 40 years	1 years	Age, energy intake, stress urinary incontinence
Dallosso 2004-1	Cohort	Supplementation	-	UK	Validated questionnaire	380 Cases from 5,816 women	≥ 40 years	1 years	Age, energy intake, OAB

Quality assessment

For cohort and case-control studies, NOS scores ranged from 5 to 7 (Supplementary Table 1). Among the cross-sectional studies, 10 were judged to be high quality and another 10 to be of moderate quality (Supplementary Table 2). The quality assessments of RCTs are presented in Supplementary Fig. 1 and 2.

Meta-analysis

Serum vitamin D levels between LUTS and controls

A total of 20 studies comprising 22,400 participants (9,236 with LUTS; 13,164 controls) reported mean ± SD serum vitamin D concentrations. The pooled analysis showed that serum vitamin D levels were 3.15 ng/mL lower in individuals with LUTS compared with controls (95% CI: − 4.65, − 1.66). Substantial heterogeneity was detected across the included studies (I^2 = 94.9%) (Fig. 2).

Subgroup analysis by study population showed significant differences in serum vitamin D levels among children (WMD: −6.38, 95% CI: −10.59, −2.16) and men (WMD: −4.14, 95% CI: −7.48, −0.80), whereas levels in women were comparable to those in controls (WMD: 0.35, 95% CI: −0.51, 1.22). When stratified by LUTS subtype, serum vitamin D levels were similar in individuals with UI and controls (WMD: −0.45, 95% CI: −1.68, 0.78), whereas a significant difference was found among participants with other LUTS subtypes (WMD: −4.81, 95% CI: −7.12, −2.50). Finally, subgroup analysis by study design showed a significant difference in cohort and case-control studies (WMD: −5.94, 95% CI: −9.49, −2.39) (Table 2; Supplementary Fig. 3).

Funnel plot inspection revealed asymmetry, and Egger's test confirmed publication bias (Egger's test P = 0.002) (Supplementary Fig. 4). Nevertheless, the leave-one-out sensitivity analysis demonstrated that the pooled association remained statistically significant after sequential exclusion of each study.

Low serum vitamin D level and LUTS

From 16 studies, we derived the frequencies of LUTS and controls among participants with low serum vitamin D levels and those with higher levels. The pooled analysis indicated that low vitamin D levels were associated with a higher risk of LUTS (OR = 2.95, 95% CI: 1.82, 4.76). Considerable heterogeneity was detected across studies (I^2 = 91.3%) (Fig. 3A). Notably, when comparing individuals with serum vitamin D < 20 ng/mL versus ≥ 20 ng/mL, the association appeared stronger (OR = 3.57) than that observed between < 30 ng/mL and ≥ 30 ng/mL (OR = 2.72). No evidence of publication bias was observed according to funnel plot and Egger's test (Egger's test P = 0.240) (Supplementary Fig. 5). Sensitivity analysis confirmed that the results remained robust even after sequential exclusion of each study.

Eight studies (27 sets of data) were included to evaluate the dose–response relationship (Supplementary Fig. 6). We found no evidence of a non-linear association between serum vitamin D levels and the risk of LUTS (P non-linearity = 0.073). Instead, a significant overall inverse association was observed (P overall < 0.001), suggesting that the risk of LUTS decreases as serum vitamin D levels increase.

Table 2. Subgroup analysis of serum vitamin D levels in individuals with LUTS and controls

Subgroup	No. Studies	WMD (95% CI)	Heterogeneity test I^2 (%)	P
Study population				
Women	9	0.35 (−0.51, 1.22)	69.6	0.425
Men	5	−4.14 (−7.48, −0.80)	92.8	0.015
Children	4	−6.38 (−10.59, −2.16)	91.4	0.003
Type of LUTS				
UI	7	−0.45 (−1.68, 0.78)	69.4	0.476
Other	13	−4.81 (−7.12, −2.50)	96.6	< 0.001
Study design				
Cohort/case-control	9	−5.94 (−9.49, −2.39)	96.3	0.001
Cross-sectional	11	−0.52 (−1.57, 0.54)	82.1	0.337

Meta-analysis of adjusted OR values from 15 studies showed a significant relationship between low serum vitamin D levels and LUTS risk (adjusted OR: 1.67, 95% CI: 1.31, 2.12; I^2 = 85.3%). Similarly, when comparing individuals with serum vitamin D < 20 ng/mL versus ≥ 20 ng/mL, the association appeared stronger (OR = 1.72) than that observed between < 30 ng/mL and ≥ 30 ng/mL (OR = 1.63) (Fig. 3B). Subgroup analysis by study population demonstrated a significant relationship between low serum vitamin D and increased LUTS risk among children (adjusted OR: 2.96, 95% CI: 2.12, 4.14) and men (adjusted OR: 1.63, 95% CI: 1.18, 2.25), while no such association was found in women (adjusted OR: 1.05, 95% CI: 0.92, 1.20). When stratified by LUTS subtype, low vitamin D levels were associated with a modest increase in the risk of UI (adjusted OR: 1.29, 95% CI: 1.03, 1.61). By study design, a stronger effect was observed in cohort and case-control studies (adjusted OR: 2.70, 95% CI: 1.41, 5.17), whereas cross-sectional studies showed a weaker yet still significant association (adjusted OR: 1.30, 95% CI: 1.07, 1.57) (Table 3; Supplementary Fig. 7).

Funnel plot inspection and Egger's test indicated publication bias (Egger's test P = 0.001). However, the association remained significant after applying the trim-and-fill method (adjusted OR: 1.44, 95% CI: 1.13, 1.84) (Supplementary Fig. 8). Sensitivity analysis confirmed

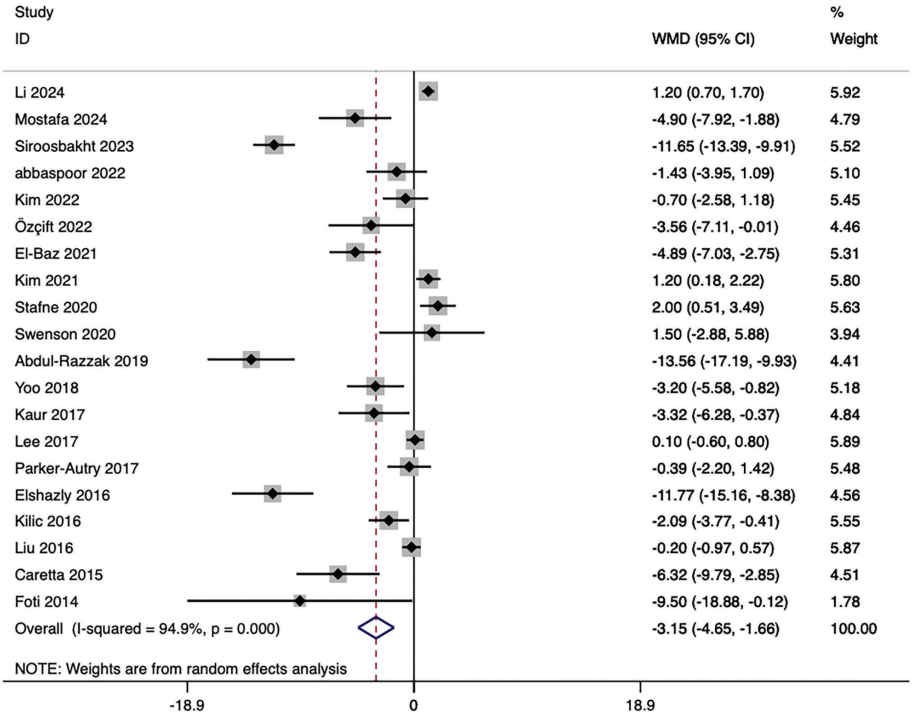

Fig. 2. Comparison of serum vitamin D levels between individuals with LUTS and controls. LUTS, lower urinary tract symptoms; WMD, weighted mean difference.

Citation: Food & Nutrition Research 2026, **70**: 13933 - http://dx.doi.org/10.29219/fnr.v70.13933

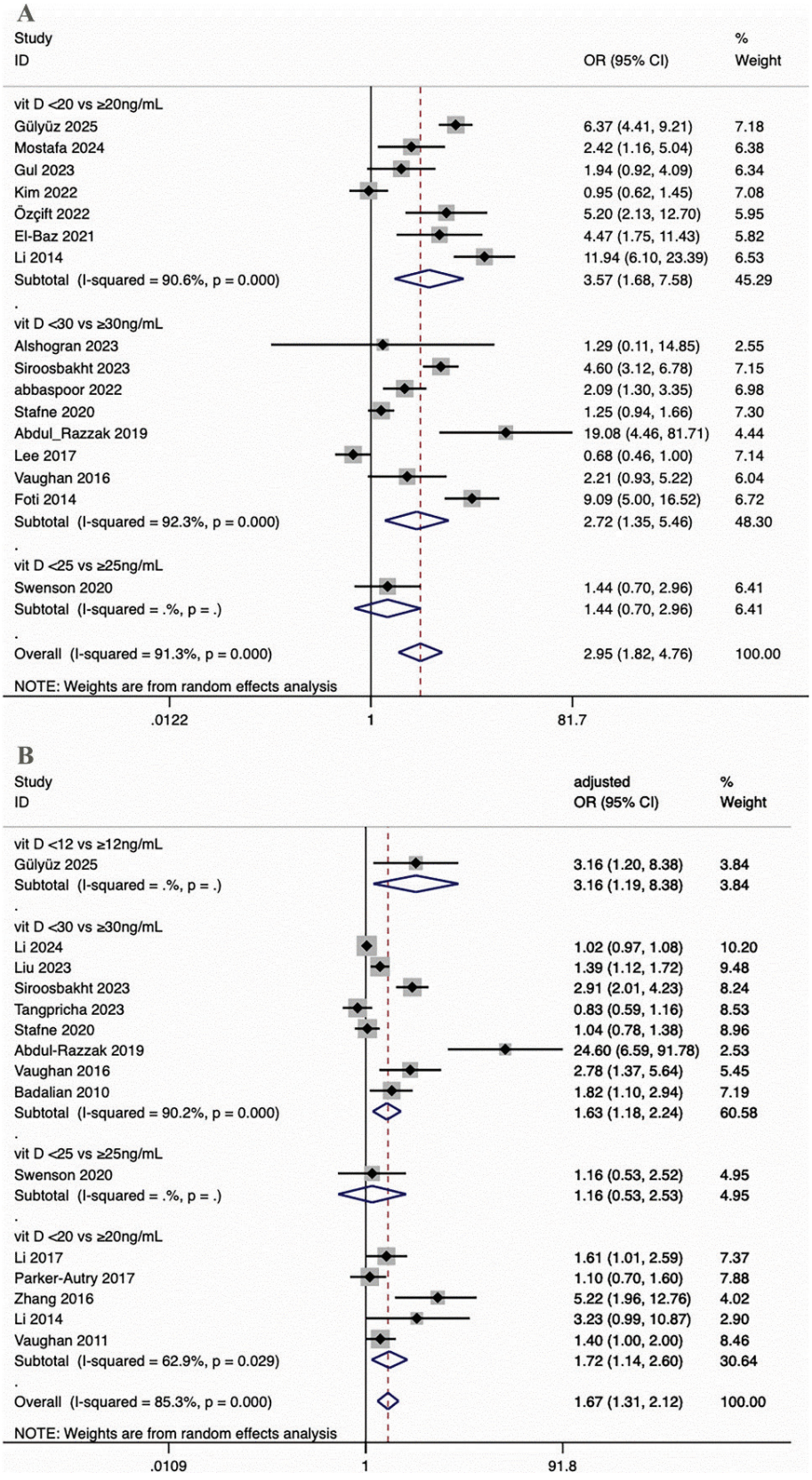

Fig. 3. Association between low serum vitamin D levels and the risk of LUTS. (A) ORs were calculated from the frequency of LUTS among participants with low versus high serum vitamin D levels. (B) Adjusted ORs extracted from included studies. LUTS, lower urinary tract symptoms; OR, odds ratio.

Table 3. Subgroup analysis of the association between low serum vitamin D levels and the risk of LUTS

Subgroup	No. of Studies	Adjusted OR (95% CI)	Heterogeneity test I^2 (%)	*P*
Study population				
Women	6	1.05 (0.92, 1.20)	28.0	0.483
Men	4	1.63 (1.18, 2.25)	60.0	0.003
Children	3	2.96 (2.12, 4.14)	0.0	< 0.001
Type of LUTS				
UI	8	1.29 (1.03, 1.61)	58.4	0.024
Other	7	2.84 (1.58, 5.13)	91.8	0.001
Study design				
Cohort/case-control	7	2.70 (1.41, 5.17)	88.9	0.003
Cross-sectional	8	1.30 (1.07, 1.57)	67.2	0.008

that the results remained stable when each study was sequentially removed.

Seven studies assessed the differences in LUTS scores between groups with low and high serum vitamin D levels. The meta-analysis demonstrated that the low vitamin D group had higher LUTS scores, indicating more severe symptoms (SMD: 0.57, 95% CI: 0.18, 0.96; I^2 = 91.0%) (Supplementary Fig. 9). Sensitivity analyses supported the stability of the finding.

Vitamin D supplementation and LUTS

Three RCTs, two case-control studies, and one cohort study investigated the effects of vitamin D supplementation on LUTS scores. Due to data limitations, we compared only the LUTS scores of the intervention group before and after supplementation. The pooled result revealed that vitamin D supplementation was linked to a greater reduction in LUTS scores (SMD: −1.23, 95% CI: −2.01, −0.46; I^2 = 91.1%). Sensitivity analyses confirmed the robustness of these results (Supplementary Fig. 10A).

Additionally, two RCTs and one case-control study provided data on the number of participants who experienced remission before and after vitamin D supplementation. Pooled analysis showed a significantly improved remission rate following supplementation (OR = 10.56, 95% CI: 3.75, 29.75; I^2 = 0.0%) (Supplementary Fig. 10B). Furthermore, vitamin D supplementation resulted in a significantly greater remission rate than the control group (OR = 4.79, 95% CI: 1.40, 16.42; I^2 = 73.9%). However, sensitivity analysis showed unstable results. Further investigation revealed that two studies restricted inclusion to participants with low (< 30 ng/mL) baseline vitamin D. In this subgroup, supplementation alleviated LUTS (OR = 9.02, 95% CI: 2.94, 27.62; I^2 = 0.0%). By contrast, no significant effect was observed in studies without baseline serum vitamin D restrictions (OR = 2.95, 95% CI: 0.47, 18.60; I^2 = 82.8%) (Fig. 4A).

The association between vitamin D supplementation and LUTS risk was reported in eight studies (two RCTs, five cohort studies, and one cross-sectional study) using adjusted ORs. Pooled analysis revealed no significant reduction in LUTS risk with supplementation (OR = 0.98, 95% CI: 0.91, 1.05; I^2 = 39.4%) (Fig. 4B). Subgroup analyses consistently demonstrated no substantial effect modification by population, LUTS subtype, or study design (Table 4; Supplementary Fig. 11). These findings remained stable in sensitivity analyses, and no significant publication bias was observed (Egger's test P = 0.150) (Supplementary Fig. 12).

Discussion

This study demonstrated that patients with LUTS had significantly lower serum vitamin D levels compared with controls. These lower levels were associated with higher LUTS severity scores and a 1.67-fold increased likelihood of having the condition, particularly among men and children. Although vitamin D supplementation appeared to alleviate LUTS symptoms, it did not significantly reduce the overall incidence of LUTS in the general population.

Consistent with our findings, a prior systematic review and meta-analysis of 23 studies involving 86,332 participants demonstrated a significant association between vitamin D status and LUTS.[1] However, our review synthesized evidence from 48 studies comprising 221,735 participants, thereby offering a more comprehensive and up-to-date evaluation of this relationship. Consistent with prior results, substantial heterogeneity was observed among the included studies. Participants with LUTS had lower serum vitamin D concentrations, which was associated with a higher risk of the condition. However, these associations were not significant among women. Moreover, the potential benefits of vitamin D supplementation may be limited to specific populations or LUTS subtypes.

In subgroup analyses among women, serum vitamin D levels were neither significantly different between the LUTS and control groups nor associated with LUTS risk. Moreover, vitamin D supplementation did not reduce the risk of LUTS in women. The VDR plays a crucial role in regulating estrogen balance and maintaining pelvic floor muscle function (63, 64). Therefore, vitamin D may influence LUTS through VDR-mediated modulation of hormonal activity and muscle strength. However, factors such as parity, aging, and obesity can weaken pelvic floor function, while menopausal estrogen decline and inconsistent use of hormone therapy may disrupt hormonal balance (65, 66), thereby diminishing the potential protective effects of vitamin D on LUTS. Previous studies have reported inconsistent results, suggesting that the effect of vitamin D

Citation: Food & Nutrition Research 2026, **70**: 13933 - http://dx.doi.org/10.29219/fnr.v70.13933

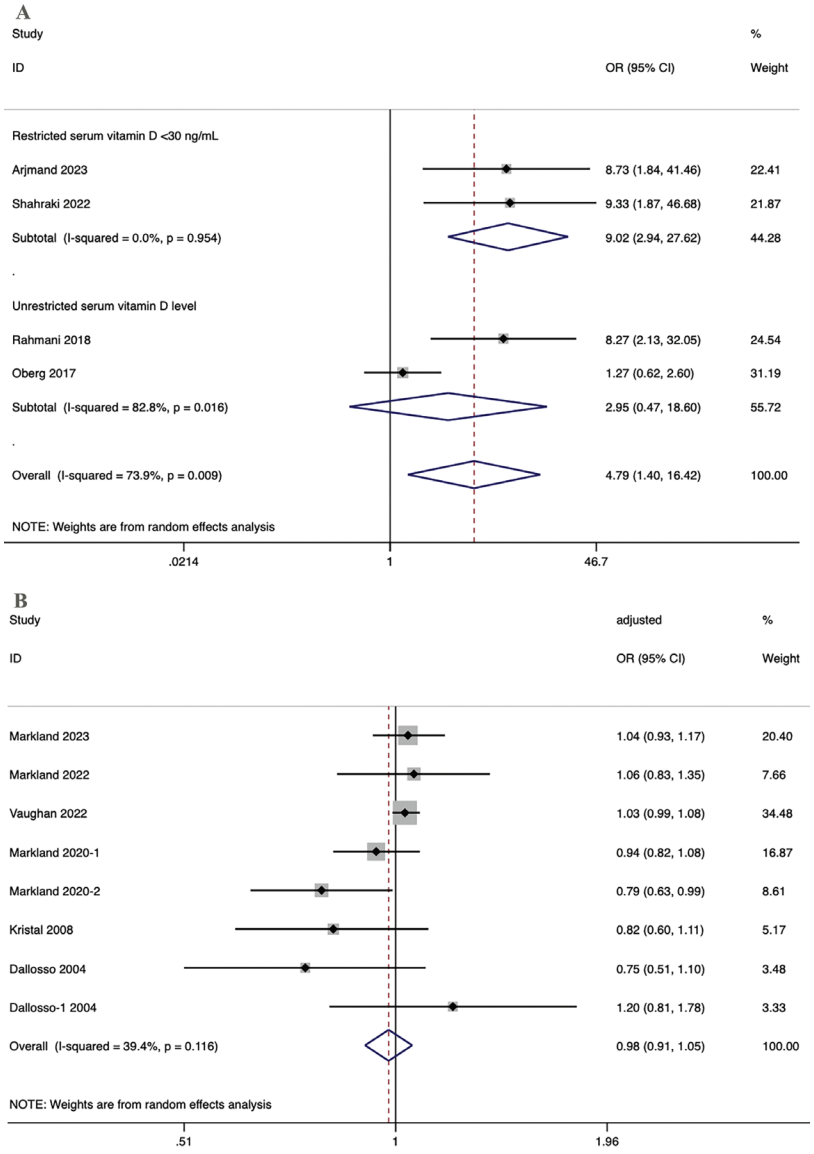

Fig. 4. Forest plots showing the effect of vitamin D supplementation on LUTS. (A) Effect on the remission rate of LUTS, with subgroup analyses according to baseline serum vitamin D levels. (B) Effect on the risk of LUTS, expressed as adjusted ORs. LUTS, lower urinary tract symptoms; OR, odds ratio.

Table 4. Subgroup analysis of the effect of vitamin D supplementation on the risk of LUTS

Subgroup	No. of studies	Adjusted OR (95% CI)	Heterogeneity test I^2 (%)	*P*
Study population				
Women	6	0.97 (0.91, 1.05)	47.6	0.501
Men	2	0.97 (0.78, 1.20)	50.3	0.751
Type of LUTS				
UI	5	0.98 (0.88, 1.09)	36.3	0.684
Other	3	0.91 (0.74, 1.13)	56.4	0.399
Study design				
RCT/Cohort	7	0.95 (0.86, 1.05)	35.2	0.300
Cross-sectional	1	1.03 (0.99, 1.08)	0.00	0.183

supplementation on LUTS risk may vary according to body weight, ethnicity, concurrent medications, and LUTS subtype (29, 40). Some studies have reported an increased risk of stress urinary incontinence (SUI) and a reduced risk of overactive bladder (OAB) following vitamin D supplementation in specific populations (23, 29). Furthermore, several RCTs have demonstrated that vitamin D supplementation alleviated symptoms of certain LUTS subtypes, including urge urinary incontinence, SUI, and OAB (20, 30, 67). Similarly, in our subgroup analysis stratified by the LUTS subtype, no significant difference in vitamin D concentrations was observed between individuals with UI and controls. The association between vitamin D levels and UI risk

appeared weaker than that observed for other LUTS subtypes. These findings indicate that vitamin D may exert differential effects across various LUTS subtypes and emphasize the importance of stratified analyses in future studies. Further research is required to distinguish between the preventive and therapeutic roles of vitamin D in LUTS management.

Among men and children, participants with LUTS exhibited lower serum vitamin D levels than controls, and low vitamin D levels were significantly associated with an increased risk of LUTS. Subgroup analyses suggested that vitamin D supplementation did not reduce LUTS risk in men. However, findings from an RCT involving 11,486 older men indicated that vitamin D supplementation in individuals with low baseline vitamin D levels significantly reduced the incidence of OAB, whereas no such effect was observed for UI or in those with higher baseline vitamin D levels (23). This result underscores the substantial influence of LUTS subtype on the efficacy of vitamin D supplementation. Mechanistically, vitamin D exerts inhibitory effects on inflammation and proliferation in bladder smooth muscle and prostate tissue, which may alleviate detrusor overactivity and prostate-related obstruction. VDRs are expressed in the bladder and prostate, supporting their role in regulating detrusor muscle contractility and urinary flow (68, 69). In children, one RCT including 303 participants demonstrated that vitamin D supplementation significantly benefited patients with OAB and serum vitamin D levels of 20–35 ng/mL (70). Another RCT found that vitamin D supplementation reduced the number of wet nights among children aged 7–15 years with nocturnal enuresis (42). Currently, evidence on its preventive effects for LUTS in children remains limited.

In addition, dose–response analysis revealed a decreasing trend in LUTS risk with increasing serum vitamin D levels. Consistent with this, individuals with vitamin D deficiency (< 20 ng/mL) showed a markedly higher risk of LUTS. These findings suggest that vitamin D supplementation may confer benefits mainly in individuals with deficiency or insufficiency, whereas additional supplementation in populations with adequate baseline levels may provide limited advantages. Notably, most supplementation trials included in our analysis did not restrict enrolment by baseline vitamin D status, which may have diluted observable effects. Future studies should consider stratifying or preselecting participants by baseline serum vitamin D levels to better elucidate who is most likely to benefit.

Several limitations should be considered when interpreting the results of this study. Firstly, considerable heterogeneity was observed across studies. To explore potential sources, we conducted leave-one-out sensitivity analyses and performed subgroup analyses by population, study design, and outcomes. We found that the heterogeneity could not be explained by any single study or subgroup. Differences in LUTS assessment tools, LUTS types, vitamin D cutoff definitions, and population characteristics (e.g. age, sex, and comorbidities) may have contributed to this heterogeneity. Therefore, we utilized a random-effects model, which provides more conservative estimates when heterogeneity is high. The sensitivity analysis further supported the robustness of our results. Secondly, due to limited reporting in the original studies, LUTS scores were analyzed only within the intervention group using pre–post comparisons. Thirdly, although most included studies adjusted for key confounders such as age, education, and body mass index, residual confounding remains a concern. Although adjusted ORs were extracted, variations in the covariates included across studies precluded the ability to derive a fully consistent interpretation. Fourthly, LUTS encompasses various symptoms with distinct pathophysiologies, which may explain the heterogeneous responses to vitamin D. Due to the limitations of the included studies, our subgroup analysis focused largely on UI and did not comprehensively address other common subtypes, such as nocturnal enuresis. Available data on UI subtypes were also limited. Finally, the small number of intervention studies yielded inconsistent evidence on therapeutic efficacy. Through subgroup analysis, we found that interindividual variability in vitamin D levels may partly explain the observed instability in supplementation outcomes. Differences in baseline serum vitamin D concentrations, supplementation dosage, formulation, duration of intervention, and LUTS subtype likely contributed to the inconsistency across studies. These factors underscore the importance of standardized protocols and harmonized study designs in future research.

Conclusions

A significant inverse association was observed between serum vitamin D levels and LUTS, particularly among men and children. Vitamin D supplementation demonstrated potential therapeutic benefits in alleviating LUTS, especially in individuals with low vitamin D levels. However, due to the limited and heterogenous evidence currently available, routine vitamin D supplementation cannot be recommended for the prevention of LUTS.

Conflicts of interest and funding

The authors declare no competing interests. The authors have not received any funding or benefits from industry or elsewhere to conduct this study.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (82201905).

Citation: Food & Nutrition Research 2026, **70**: 13933 - http://dx.doi.org/10.29219/fnr.v70.13933

Data availability statement

All relevant data are within the manuscript and its supplementary files.

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