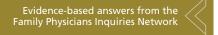
CLINICAL INQUIRIES





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Q/Does vitamin D supplementation reduce asthma exacerbations?

EVIDENCE-BASED ANSWER

YES, to some extent it does, and primarily in patients with low vitamin D levels. Supplementation reduces asthma exacerbations requiring systemic steroids by 30% overall in adults and children with mild-to-moderate asthma (number needed to treat [NNT] = 7.7). The outcome is driven by the effect in patients with vitamin D levels < 25 nmol/L (NNT = 4.3), however; supplementation doesn't decrease exacerbations in patients with higher levels. Supplementation also reduces, by a smaller amount (NNT = 26.3), the odds of exacerbations requiring emer-

gency department care or hospitalization (strength of recommendation [SOR]: **A**, meta-analysis of randomized controlled trials [RCTs]).

In children, vitamin D supplementation may also reduce exacerbations and improve symptom scores (SOR: **C**, low-quality RCTs).

Vitamin D doesn't improve forced expiratory volume in 1 second (FEV_1) or standardized asthma control test scores. Also, it isn't associated with serious adverse effects (SOR: **A**, meta-analysis of RCTs).

Evidence summary

A Cochrane systematic review of vitamin D for managing asthma performed metaanalyses on RCTs that evaluated several outcomes. The review found improvement in the primary outcome of asthma exacerbations requiring systemic steroids, mainly in adult patients, and in the secondary outcomes of emergency department visits or hospitalization, in a mix of adults and children (TABLE¹⁻⁶).

Most participants had mild-to-moderate asthma; trials lasted 4 to 12 months. Vitamin D dosage regimens varied, with a median daily dose of 900 IU/d (range, 400-4000 IU/d). Six RCTs were rated high-quality, and 1 had unclear risk of bias.

Supplementation reduced exacerbations in patients with low vitamin D levels

A subsequent (2017) systematic review and meta-analysis evaluating the primary outcome of exacerbations requiring steroids⁷ included another study⁸ (in addition to the 6 RCTs in the Cochrane review).

When researchers reanalyzed individual participant data from the trials in the Cochrane review, plus the additional RCT, to include baseline vitamin D levels, they found that vitamin D supplementation reduced exacerbations overall (NNT = 7.7) and in patients with low baseline vitamin D levels (25[OH] vitamin D < 25 nmol/L; 92 participants in 3 RCTs; NNT = 4.3) but not in patients with higher baseline levels (764 participants in 6 RCTs). Vitamin D supplementation reduced the asthma exacerbation rate in patients with low baseline vitamin D levels (0.19 vs 0.42 events per participant-year; P = .046).

Smaller benefit found on ED visits and hospitalizations

The Cochrane review, with 2 RCTs with

Effect of Vitamin D supplementation on frequency and severity of asthma exacerbations in patients with mild-to-moderate persistent asthma

Outcome measured	Studies	Population (mean ages)	Intervention vitamin D dose vs placebo ^a	Result (significant results in bold)	Comment
Asthma exacerbations requiring systemic steroids	658 Adults (2 RCTs¹) 22 Children (1 RCT¹)	Adults (40-48 y) Children (1-15 y)	Adults: 2000-4000 IU/d Children: 400-2000 IU/d	Overall: 0.28 vs 0.44 events/person-year	Low vitamin D = < 25 nmol/L
Asthma exacerbations requiring emergency department visit ± hospitalization	658 Adults (2 RCTs¹) 305 Children (5 RCTs²-6)	Adults (40-48 y) Children (1-18 y)	Adults: 2000-4000 IU/d Children: 400-1200 IU/d	25/1000 vs 63/1000 events in adults; NNT = 26.3	

NNT, number needed to treat.

adults (n = 658)¹ and 5 RCTs with children (n = 305),²⁻⁶ evaluated whether Vitamin D reduced the need for emergency department visits and hospitalization with asthma exacerbations; they found a smaller benefit (NNT = 26.3).

Effects on FEV₁, daily asthma symptoms, and serious adverse effects

Several RCTs included in the 2017 metaanalysis found no effect of vitamin D supplementation on FEV_1 , daily asthma symptoms (evaluated with the standardized Asthma Control Test Score), or reported serious adverse events. $^{2-6,9,10}$ No deaths occurred in any trial.

Additional findings in children from lower-quality studies

A 2015 systematic review and meta-analysis of RCTs evaluating vitamin D supplementation for children with asthma found¹¹:

- moderate-quality evidence for decreased emergency department visits
 (1 RCT from India, 100 children ages 3 to 14 years, decrease not specified; *P* = .015);
- low-quality evidence for reduced exacerbations (6 RCTs [3 RCTs also in Cochrane review], 507 children ages 3 to 17 years; risk ratio = 0.41; 95% confidence interval, 0.27-0.63); and
- low-quality evidence for reduced standardized asthma symptom scores

(6 RCTs [2 RCTs also in Cochrane review], 231 children ages 3 to 17 years; amount of reduction not listed; P = .01).

Recommendations

No published guidelines discuss using vitamin D in managing asthma. An American Academy of Family Physicians (AAFP) summary of the Cochrane systematic review recommends that family physicians await further studies and updated guidelines before recommending vitamin D for patients with asthma. ¹² The AAFP also points out that the Endocrine Society has recommended vitamin D supplementation for adults (1500-2000 IU/d) and children (at least 1000 IU/d) at risk for deficiency.

Editor's takeaway

In the meta-analyses highlighted here, researchers evaluated asthma patients with a wide range of ages, baseline vitamin D levels, and vitamin D supplementation protocols. Although vitamin D reduced asthma exacerbations requiring steroids overall, the effect was driven by 3 studies of patients with low baseline vitamin D levels. As a result, disentangling who might benefit the most remains a challenge. The conservative course for now is to manage asthma according to cur-

^aAdditional Vitamin D dosing details: 400 IU/d,² 1000 IU/wk,³ 500 IU/d,⁴ 800 IU/d,⁵ 1200 IU/d.⁶

rent guidelines and supplement vitamin D in patients at risk for, or with known, deficiency.

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