Clinician Reviews®

# Can Vitamin D Prevent Acute Respiratory Infections?

A systematic review and meta-analysis say "Yes"—but the dosages used may not be what you'd expect.

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## PRACTICE CHANGER

Reduce acute respiratory tract infections (ARTIs) in those with significant vitamin D deficiency (circulating 25-hydroxyvitamin D levels < 10 ng/mL) with daily or weekly vitamin D supplementation—not bolus vitamin D treatment.[1]

## STRENGTH OF RECOMMENDATION

**A:** Based on a systematic review and meta-analysis of 25 trials.

Ms. M, a generally healthy 55-year-old woman, was diagnosed recently with severe vitamin D deficiency (serum 25-hydroxyvitamin D [25(OH)D] level of 8 ng/mL). She presents with her second episode of acute viral bronchitis in the past 6 months. She has no history of significant smoking or exposure or history of asthma and does not take respiratory medications. Standard treatment for her level of vitamin D deficiency is 50,000 IU/wk in bolus dosing—but is that your best option for the patient?

ARTIs include nonspecific upper respiratory illnesses, otitis media, sinusitis (~70% viral), pharyngitis, acute bronchitis (also ~70% viral), influenza, respiratory syncytial virus, and pneumonia.[1,2] In the United States, ARTIs strain the health care system and are the most common reason for ambulatory care visits, accounting for almost 120 million (about 10% of all) visits per year.[3] In addition, ARTIs account for almost 50% of antibiotic prescriptions for adults and almost 75% of antibiotic prescriptions for children—many of which are unnecessary.[2,4]

While patient and parent education, antibiotic stewardship programs, and demand management may reduce inappropriate antibiotic use and the overall burden of ARTIs on the health care system, prevention of infections is a powerful tool within the overall approach to managing ARTIs.

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## STUDY SUMMARY

### Vitamin D is protective in smaller doses

This 2017 systematic review and meta-analysis of 25 trials (N = 10,933) evaluated vitamin D supplementation for the prevention of ARTIs in the primary care setting. Individual participant data were reevaluated to reduce risk for bias. The Cochrane risk-for-bias tool was used to address threats to validity.

The study included institutional review board–approved, randomized, double-blind, placebo-controlled trials of vitamin $D_3$ or $D_2$ supplementation of any duration and in any language. The incidence of ARTI was a prespecified efficacy outcome. Duration of the included randomized controlled trials (RCTs) ranged from 7 weeks to 1.5 years.

***Outcomes.*** The primary outcome was an incidence of at least 1 ARTI. Secondary outcomes included incidence of upper and lower ARTIs; incidence of adverse reactions to vitamin D; incidence of emergency department visits or hospital admission or both for ARTI; use of antimicrobials for ARTI; absence from work or school due to ARTI; and mortality (ARTI-related and all-cause).

***Findings.*** Daily or weekly vitamin D supplementation (in doses ranging from < 20 to ≥ 50 μg/d) reduced the risk for ARTI (adjusted odds ratio [AOR], 0.88; number needed to treat [NNT], 33). In subgroup analysis, daily or weekly vitamin D was protective (AOR, 0.81), but bolus dosing (≥ 30,000 IU) was not (AOR, 0.97).

In 2-step analysis, patients benefited if they had baseline circulating 25(OH)D concentrations < 10 ng/mL (AOR, 0.30; NNT, 4); had baseline circulating 25(OH)D levels of 10 to 28 ng/mL (AOR, 0.75; NNT, 15); were ages 1.1 to 15.9 (AOR, 0.59); were ages 16 to 65 (AOR, 0.79); or had a BMI < 25 (AOR, 0.82).

***Higher D levels are a different story.*** Vitamin D supplementation in people with circulating levels of 25(OH)D ≥ 30 ng/mL did not appear to provide benefit (AOR, 0.96). Supplementation in this population did not influence any of the secondary outcomes, including risk for all-cause serious adverse events (AOR, 0.98).

## WHAT'S NEW

### A more accurate snapshot

Previous studies of vitamin D and respiratory tract infections were mostly observational in nature. Those that were RCTs used variable doses of vitamin D, had variable baseline 25(OH)D levels, and employed various methods to monitor ARTI symptoms/incidence.[5-8] This is the first systematic review and meta-analysis of randomized, double-blind, placebo-controlled trials with supplementation using vitamin $D_3$ or $D_2$ that used individual participant-level data, which gives a more accurate estimate of outcomes when compared with traditional meta-analyses.

## CAVEATS

### Only the most deficient benefit?

Vitamin D supplementation was safe and protected against ARTIs overall, but the greatest effect was noted in those who were most severely vitamin D deficient (those with circulating 25(OH)D levels < 10 ng/mL [NNT, 4] and those with circulating 25(OH)D levels 10-28 ng/mL [NNT, 15]). There was no demonstrable effect once circulating 25(OH)D levels reached 30 ng/mL.

## CHALLENGES TO IMPLEMENTATION

### Breaking tradition

The study found that both daily and weekly doses of vitamin D were effective in reducing the incidence of ARTIs. However, the doses studied were much lower than those commonly used (10,000 to 50,000 IU bolus), which were ineffective in reducing ARTIs in this meta-analysis. Changing from bolus dosing may prove challenging, as it is an ingrained practice for many providers.

In addition, the authors of the study suggest that one way to provide this level of vitamin D is through food fortification. But this method is often complicated by emotional and/or political issues that could thwart implementation. **CR**

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## REFERENCES

1. Martineau AR, Jolliffe DA, Hooper RL, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ*. 2017;356:i6583.
2. Renati S, Linder JA. Necessity of office visits for acute respiratory infections in primary care. *Fam Pract.* 2016,33:312-317.
3. CDC National Center for Health Statistics. National Health Care Surveys. www.cdc.gov/nchs/dhcs.htm. Accessed September 5, 2019.
4. Grijalva CG, Nuorti JP, Griffin MR. Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *JAMA*. 2009;302:758-766.
5. Rees JR, Hendricks K, Barry EL, et al. Vitamin D3 supplementation and upper respiratory tract infections in a randomized, controlled trial. *Clin Infect Dis*. 2013;57:1384-1392.
6. Murdoch DR, Slow S, Chambers ST, et al. Effect of vitamin D3 supplementation on upper respiratory tract infections in healthy adults: the VIDARIS randomized controlled trial. *JAMA*. 2012;308:1333-1339.
7. Laaksi I, Ruohola J-P, Mattila V, et al. Vitamin D supplementation for the prevention of acute respiratory tract infection: a randomized, double-blinded trial among young Finnish men. *Infect Dis*. 2010;202:809-814.
8. Bergman P, Norlin A-C, Hansen S, et al. Vitamin D3 supplementation in patients with frequent respiratory tract infections: a randomised and double-blind intervention study. *BMJ Open*. 2012;2:e001663.