

## Effect of High-Dose vs Standard-Dose Wintertime Vitamin D Supplementation on Viral Upper Respiratory Tract Infections in Young Healthy Children

### BACKGROUND

- A variety of trials have examined the correlation between vitamin D supplementation and risk of respiratory tract infections; however, their focus has not been exclusively on children.
- Vitamin D levels can decrease in children during the winter months, so supplementation may be necessary.

### OBJECTIVE

- To determine whether high-dose vs standard-dose vitamin D supplementation reduces the incidence of wintertime upper respiratory tract infections in young children.

### METHODS

- **Design:** multisite blinded, randomized, parallel controlled clinical superiority trial; Duration: 4 to 8 months
- **Inclusion criteria:** healthy children by parental report; 1 to 5 years of age; present to a TARGet Kids! practice for routine primary health care prior to the viral season (September through November); enrolled in TARGet Kids!; parents provide informed consent
- **Exclusion criteria:** children with gestation age <32 weeks; children with chronic illness (except for asthma) on parental report; children with a sibling participating in the study
- **Primary outcome measure:** the number of laboratory-confirmed viral upper respiratory tract infections based on parent-collected nasal swabs over the winter months
- **Secondary outcome measures:** the number of influenza infections, noninfluenza infections; parent-reported upper respiratory tract illnesses; time to first upper respiratory tract infection; serum 25-hydroxyvitamin D levels at study termination
- 703 participants randomized
  - 354 received standard-dose vitamin D (400IU/day)
  - 349 received high-dose vitamin D (2000IU/day)
- 90% power with an alpha level of 0.05 to detect a reduction of one upper respiratory tract infection in each child per winter. This was calculated using 300 participants in each group.
- Data handling method was intent-to-treat

### RESULTS

- 699 participants included in the primary analysis
  - 350 in the standard-dose group
  - 349 in the high-dose group
- **Primary outcome measure:** mean number of laboratory-confirmed upper respiratory tract infections was 1.05 infections per child in the high-dose group (95% CI, 0.91-1.19) and 1.03 infections per child in the standard-dose group

(95% CI, 0.90-1.16). There was no statistically significant difference in the rate of all-cause upper respiratory tract infections between groups (incidence RR < 0.97; 95% CI, 0.08-1.16); p=0.71

- **Secondary outcome measures:** no clinically significant reduction in influenza infections between groups (95% CI, 0.28-0.89, p=0.02); no statistically significant reduction in noninfluenza infections between groups (95% CI, 0.83-1.23, p=0.91); no statistically significant difference in the incidence of parent-reported upper respiratory tract illnesses between groups (incidence RR, 1.01; 95% CI, 0.88-1.16; p=0.89); no statistically significant difference in the groups with respect to time to first laboratory-confirmed infection, p=0.23; statistically significant difference in serum 25-hydroxyvitamin D levels between groups at termination with a 12.3ng/mL (95% CI, 10.3-14.3ng/mL, p<0.001) increase in the high-dose group compared to the standard dose-group
- **Author's conclusions:** The study results do not support the use of vitamin D 2000IU daily to prevent upper respiratory tract infections in children.

#### STRENGTHS

- Large sample size constructed from multiple sites
- Lack of bias
- Correct interpretation and use of statistical tests for primary and secondary outcomes

#### LIMITATIONS

- Conflicting inclusion and exclusion criteria
- Omission of several secondary measures from the article
- Long study duration with minimal effort to ensure compliance
- Lack of contact with participants and parents
- Increased room for error by assigning many of the procedural roles to the participants' parents
- Addition of a placebo, "no treatment" group, would have provided a better comparison

#### CONCLUSION

- High-dose vitamin D supplementation did not show superiority over standard-dose vitamin D for prevention of upper respiratory tract infections. The study had a variety of weaknesses, starting with the methods used. Future research should examine children who are vitamin D deficient or who have chronic disease that predispose them to infection.

**Reference:** Aglipay M, Birken CS, Parkin PC, et al. Effect of High-Dose vs Standard-Dose Wintertime Vitamin D Supplementation on Viral Upper Respiratory Tract Infections in Young Healthy Children. JAMA. 2017; 318(3):245-254.

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