Vitamin D Supplements for Prevention of Tuberculosis Infection and Disease N Engl J Med. 2020; 383(4):359.

**Background:** Vitamin D inhibits Mycobacterium tuberculosis infection in macrophages through the induction of autophagy. Observational studies indicate that vitamin D deficient patients are more likely to be affected with tuberculosis. In populations where vitamin D deficiency is prevalent, its supplementation has been suggested as an intervention to reduce the risk of acquiring latent tuberculosis infection. However, the clinical trials on the role of vitamin D in tuberculosis have variable results. Here in this study, the investigators hypothesized that vitamin D supplementation would reduce the risk of tuberculosis infection and tuberculosis disease in populations in which both vitamin D deficiency and tuberculosis are prevalent.

# **ACADEMIC P.E.A.R.L.S**

Pediatric Evidence And Research Learning Snippet



## Vit D Supplementation in TB Prevention

**Methods:** This was a phase 3, double-blind, randomized, placebo-controlled trial of vitamin D supplementation in schoolchildren living in Mongolia. Children who had negative results for M. tuberculosis infection according to the QuantiFERON-TB Gold In-Tube assay (QFT) were randomly assigned to receive a weekly oral dose of either 14,000 IU (0.35 mg) of vitamin D3 or placebo for 3 years.

- \* The primary outcome was development of M. tuberculosis infection as a positive QFT result at the 3-year follow-up expressed as a proportion of children.
- \* Secondary outcomes included the serum 25-hydroxyvitamin D (25[OH] D) level at the end of the trial and the incidence of tuberculosis disease, acute respiratory infection and adverse events.

**Results:** A total of 8851 children were randomized: 4418 were assigned to the vitamin D group and 4433 to the placebo group. 95.6% of children had a baseline serum 25(OH) D level of less than 20 ng per millilitre. The mean 25(OH) D level at the end of the trial was 31.0 ng per millilitre in the vitamin D group and 10.7 ng per millilitre in the placebo group (mean between-group difference, 20.3 ng per millilitre; 95% CI, 19.9 to 20.6). Tuberculosis disease was diagnosed in 21 children in the vitamin D group and in 25 children in the placebo group (adjusted risk ratio, 0.87; 95% CI, 0.49 to 1.55). A total of 29 children in the vitamin D group and 34 in the placebo group were hospitalized for treatment of acute respiratory infection (adjusted risk ratio, 0.86; 95% CI, 0.52 to 1.40). The incidence of adverse events did not differ significantly between the two groups.

**Conclusion:** Vitamin D supplementation did not result in a lower risk of tuberculosis infection, tuberculosis disease or acute respiratory infection than placebo among vitamin D deficient school children in Mongolia.

## **EXPERT COMMENT**



"This study by D. Ganmaa and colleagues is a well designed study assessing the effect of vitamin D3 supplementation in children with low serum 25-hydroxyvitamin D concentrations. This trial result negates the utility of vitamin D supplementation in prevention of Tuberculosis infection and disease in Mongolian school going children."

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Ganmaa D, Uyanga B, Zhou X, Gantsetseg G et al. Vitamin D Supplements for Prevention of Tuberculosis Infection and Disease. N Engl J Med. 2020 Jul 23;383(4):359–368. doi: 10.1056/NEJMoa1915176.