



# The Role of Vitamin D in Multiple Sclerosis Prevention: A Research Review

Current scientific evidence strongly suggests that vitamin D plays a significant role in preventing multiple sclerosis (MS), with both observational studies and genetic analyses supporting a causal relationship between vitamin D deficiency and increased MS risk. While research into treatment effects continues, the preventive benefits appear substantial.

## Evidence for Vitamin D's Preventive Effect on MS

### Observational Studies Show Reduced Risk

Numerous observational studies have found associations between higher vitamin D levels and reduced MS risk. In a large prospective cohort study, vitamin D supplementation was associated with a 40% reduction in the risk of developing MS<sup>[1]</sup>. This finding was reinforced by data from the Nurses' Health Study, which followed over 185,000 women and found that those who consumed at least 400 IU of vitamin D daily through supplements had a 40% lower risk of developing MS compared to women who didn't take supplements<sup>[2] [3] [4]</sup>.

Interestingly, these studies noted that the protective effect was primarily observed with vitamin D from supplements rather than from dietary sources alone<sup>[2]</sup>. Individuals with vitamin D deficiency showed a 54% higher risk of MS compared to those with sufficient vitamin D status, further supporting this relationship<sup>[5]</sup>.

### Mendelian Randomization Studies Establish Causality

While observational studies demonstrate associations, Mendelian randomization (MR) studies provide stronger evidence for causation by using genetic variants as natural experiments. Several MR studies have demonstrated that genetically determined lower vitamin D levels causally increase MS risk:

"A genetically lowered 25OHD level is strongly associated with increased susceptibility to MS," with each genetically determined one-standard-deviation decrease in vitamin D level conferring a 2.0-fold increase in MS odds<sup>[6]</sup>. This finding persisted in multiple sensitivity analyses, reducing the possibility that other factors might explain the relationship<sup>[6]</sup>.

Additional MR studies have consistently confirmed that "low 25(OH)D is causally associated with MS susceptibility"<sup>[7]</sup>, and identified vitamin D as one of the "causal factors for multiple sclerosis"<sup>[8]</sup>. A 2024 study provided further evidence by examining vitamin D receptor binding mechanisms, finding that "variation in VDR binding at a locus contributes to MS risk"<sup>[9]</sup>.

## Maternal Vitamin D and Offspring MS Risk

The protective effect of vitamin D may begin even before birth. Research shows that maternal vitamin D status during pregnancy affects children's later MS risk:

1. Children of vitamin D-deficient mothers had a 90% greater risk of developing MS than children whose mothers had higher vitamin D levels<sup>[10]</sup>.
2. Higher maternal vitamin D intake during pregnancy was associated with lower MS risk in offspring, with an adjusted rate ratio of 0.57 (43% risk reduction) when comparing mothers in the highest versus lowest quintiles of vitamin D intake<sup>[11]</sup>.

## Geographic and Environmental Evidence

The geographic distribution of MS cases provides additional supporting evidence for vitamin D's role. MS prevalence increases with distance from the equator, where sun exposure (and thus vitamin D production) is lower<sup>[4]</sup>. Living south of 35° latitude during the first 10 years of life is associated with a 50% lower risk of developing MS compared to those living at higher latitudes<sup>[12]</sup>, supporting the connection between environmental factors, vitamin D synthesis, and MS risk.

## Potential Mechanisms

The protective effect of vitamin D against MS likely involves its immunomodulatory functions. Vitamin D helps regulate immune responses by:

1. Decreasing production of inflammatory cytokines
2. Reducing Th1 and Th17 cell differentiation
3. Increasing regulatory T cells<sup>[7]</sup>

Additionally, vitamin D influences genes that play important roles in MS development, particularly through interaction with the HLA-DRB1 gene region, a known genetic risk factor for MS<sup>[7]</sup>.

## Limitations and Ongoing Research

Despite substantial evidence supporting vitamin D's preventive role, researchers acknowledge the need for larger controlled clinical trials to establish vitamin D supplementation as a standard preventive measure<sup>[13] [14]</sup>. While the evidence for prevention is strong, the impact of vitamin D supplementation on disease progression in established MS remains less clear and is still being investigated<sup>[15]</sup>.

## Conclusion

The accumulated evidence from observational studies, Mendelian randomization analyses, and geographic distribution patterns strongly supports a causal relationship between vitamin D deficiency and increased MS risk. This suggests that maintaining adequate vitamin D levels, particularly through supplementation, may be an effective strategy for MS prevention. The protective effect appears to begin even before birth, highlighting the importance of maternal vitamin D status. While more clinical trials are needed to establish optimal supplementation

protocols, the current evidence provides compelling support for vitamin D's role in MS prevention.

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2. <https://pubmed.ncbi.nlm.nih.gov/14718698/>
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