

Study boosts vitamin D–multiple sclerosis link

A new study bolsters the evidence that low levels of vitamin D are implicated in multiple sclerosis (MS), but the Canadian authors say proving a causal link would require a large randomized controlled trial (RCT), and that's unlikely.

The study looked at the risk of MS in a huge international genetic database of patients with MS (almost 15 000 cases) and controls (more than 24 000), and found that those with genetic variations that cause low levels of vitamin D were much more likely to have MS. The results were published Aug. 25 in *PLOS Medicine*.

The study's results "further substantiate observational studies done so far," explained author Lauren Mokry. Coauthor Dr. Brent Richards added, "We feel that the evidence we have supports a causal relationship, but it does not prove it." Both are with Montréal's Jewish General Hospital and McGill University.

In light of this result, Richards said, "identifying those at risk of MS with low vitamin D levels has important public health consequences," especially in Canada. MS has been described as "Canada's disease" by the MS Society of Canada, as rates are higher here than in any other country. Canada's prevalence of MS is 291 per 100 000 population, according to a 2013 Multiple Sclerosis International Federation report, ahead of Denmark (227) and Sweden (189). As well, "there is a high rate of vitamin D insufficiency and deficiency in the Canadian population," Richards said.

Craig Moore, a neuroscience researcher at Memorial University of Newfoundland, explained that vitamin D signalling decreases inflammation directly and promotes an anti-inflammatory response as well, which he calls a "double whammy."

"Since MS is largely an inflammatory disease of the brain, vitamin D signalling would be protective of the brain," he said. "For a long time we



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Multiple sclerosis has been described "Canada's disease" because of a high prevalence of 291 per 100 000 population.

have known that vitamin D levels are decreasing in our MS populations, whether that is due to staying inside more or environmental influences, we don't know."

Richards explained that, to rule out confounding effects like these, the study used a Mendelian randomization technique that he calls "nature's randomized controlled trial."

"Nature randomized people to lower vitamin D levels genetically," explained Richards. The researchers found four genetic variations associated with low vitamin D by searching in a large database of human genomes. These variations were then tested in a second database that gathered patients' genomes and vitamin D levels, confirming that the genetic variations led to low vitamin D. A third large

international genetic database of patients with MS and controls was used to discover whether these genetic variations increased the risk of MS.

The results show how much people would need to boost their vitamin D levels to lower MS risk by 50%. The levels depend on whether a patient's current vitamin D level is "insufficient" (blood level of < 50 nmol/L) or "deficient" (< 25 nmol/L), Mokry said. The study showed the odds of MS are about doubled (odds ratio of around 2) for every decline in the vitamin D level of one standard deviation, said Mokry.

"Our data doesn't allow us to directly answer what the increased risk of MS is," explained Richards. "We would suggest that individuals who are at risk of MS, such as first-degree rela-

tives of current patients, should ensure they have sufficient vitamin D levels.” However, he said, extremely high levels of vitamin D supplementation are not warranted.

Moore is concerned that patients with genetic mutations affecting vitamin D may not benefit from supplementation. “Is their body going to do what it needs to with vitamin D? It’s

not going to exert the effects that it otherwise would.”

The study does not address whether vitamin D is useful in treating MS. “That’s something that only an RCT could look at. It’s really more toward the prevention of MS rather than the treatment of it,” said Mokry.

But an RCT is unlikely, said Richards. “Most high-quality RCTs in this

country are paid for by industry.” Since vitamin D is not a patentable drug, “there’s no industry to pay for this.” Moore agreed. “Unless there is government support or private support, there will not be a large RCT that will look at vitamin D.” — Carolyn Brown, Ottawa, Ont.

CMAJ 2015. DOI:10.1503/cmaj.109-5145