

## Cancer Meta-Analyses Shine on Vitamin D

SAN DIEGO, Feb. 8 -- High levels of vitamin D can significantly reduce the relative risks of breast and colorectal cancer, according to two meta-analyses reported separately by the same group of researchers here.

One of the meta-analyses of published literature shows that a daily dose of 2,000 IUs of vitamin D3 would reduce the relative risk of both forms of cancer by at least 50%, according to a team headed by Edward Gorham, Ph.D., of the Moores Cancer Center at the University of California at San Diego.

Currently, the recommended daily intake is 400 IUs, which leaves serum levels of the main circulating form of the vitamin -- 25-hydroxyvitamin D (25[OH]D) -- too low to have an effect on cancer, Dr. Gorham and colleagues said.

A serum level of about 34 nanograms per milliliter of 25[OH]D was associated with a 50% reduction in relative risk of colorectal cancer, Dr. Gorham and colleagues reported in the *American Journal of Preventive Medicine*.

A daily dose of 2,000 IUs would raise the serum level to about 46 ng/mL, Dr. Gorham said, which would lead to a two-thirds reduction in colorectal cancer relative risk if the entire population reached that level.

That level, he said, could be achieved through "a combination of diet, supplements, and 10 to 15 minutes per day in the sun."

For breast cancer, 2,000 IUs a day of vitamin D3 -- plus a few minutes a day in the sun when the weather is good -- would reduce the relative risk by half, the researchers reported in the *Journal of Steroid Biochemistry and Molecular Biology*.

"The data were very clear," said Cedric Garland, Dr.P.H., also of UCSD, the lead author of the other meta-analysis. "Individuals in the group with the lowest blood levels had the highest rates of breast cancer, and the breast cancer rates dropped as the blood levels of 25-hydroxyvitamin D increased," he said.

The findings from both meta-analyses "add to a growing body of evidence that vitamin D is important for cancer prevention," commented Marji McCullough, Sc.D., a nutritional epidemiologist for the American Cancer Society.

The colorectal cancer analysis pooled five nested case-control studies that reported 25[OH]D serum levels and cancer incidence. Follow-up ranged from two to 25 years.

The researchers divided serum levels of 25[OH]D were divided into quintiles -- with median values of six, 16, 22, 27, and 37 ng/mL -- and looked at cancer occurrence rates with the lowest quintile as a reference.

The analysis found:

Odds ratios for cancer from lowest to highest were 1.00, 0.82, 0.66, 0.59, and 0.46, with a *P*-value for the trend of  $P < 0.0001$ .

The odds ratio for the highest quintile versus the lowest was 0.49, with a 95% confidence interval from 0.35 to 0.68, a difference that was significant at  $P < 0.0001$ .

A 50% lower risk of colorectal cancer was associated with a serum 25[OH]D level of at least 33 ng/mL, compared with 12 or less.

For the breast cancer study, the researcher found two trials that reported 25[OH]D serum levels and cancer incidence. Again, they divided 25[OH]D levels into quintiles, with median values of six, 18, 29, 37, and 48 ng/mL, and used the lowest as a reference.

The analysis found:

The odds ratios for breast cancer from lowest to highest quintile were 1.00, 0.90, 0.70, 0.70 and 0.50. The trend was significant at  $P < 0.001$ .

People with serum 25[OH]D of approximately 52 ng/mL had a 50% lower relative risk of breast cancer than those with less than 13.

A serum level of 52 ng/mL corresponds to intake of 4,000 IUs of vitamin D3 a day, far above the National Academy of Science upper limit of 2,000 IU, the researcher noted.

On the other hand, they said, the level could be maintained by 2,000 units a day, coupled with about 12 minutes a day in the sun.

The researchers noted that no vitamin D toxicity has been seen below serum levels of about 100 ng/mL.

"We need to look closely at the intake levels necessary for risk reduction," the cancer society's Dr. McCullough added, since earlier prospective studies have suggested that low doses do not have a benefit.

"These sorts of data (from meta-analyses) add pieces to the puzzle," Dr. McCullough said, adding that since prospective, randomized trials are likely to be difficult to organize, such analyses may be among the best available data.

The two studies are "intriguing and worth following up," she said.

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