



Vitamin D Supplementation May Not Reduce Cholesterol-Related Heart Disease Risk, New Study Finds

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Analysis published in *Circulation* by researchers at Quest Diagnostics and Rockefeller University contradicts prior research suggesting optimal vitamin D levels may have a beneficial impact on heart health

MADISON, N.J., July 17, 2012 /PRNewswire/ -- Raising vitamin D to optimal from deficient blood levels may not improve total cholesterol and other blood lipids, key markers of cardiovascular disease risk, according to a study published today in *Circulation*, a publication of the American Heart Association. The study, by researchers at Quest Diagnostics (NYSE: DGX) and The Rockefeller University, is the first large-scale examination of the clinical impact of correcting vitamin D deficiency on lipid levels and associated cardiovascular disease risk.

"Prior studies have associated low vitamin D level with an unhealthy lipid profile, but the effect of therapeutically correcting a vitamin D deficiency by itself on lipids is unclear," said lead investigator Manish Ponda, M.D., M.S., assistant professor of Clinical Investigation for The Rockefeller University's Laboratory of Biochemical Genetics and Metabolism. "This novel study on a large U.S. population suggests that correcting a vitamin D deficiency may not translate into a clinical benefit on the lipid profile. Patients should follow their physician's advice on whether vitamin D supplements are right for them."

An accompanying editorial in *Circulation* characterizes the study as having "great importance" for demonstrating that biomarkers, such as vitamin D, that are associated with disease risks in certain types of studies may not be found to cause those risks in other types of research.

Optimal vitamin D levels associated with favorable lipids

Heart disease is the number one killer of men and women in the United States, and individuals with high total cholesterol levels have twice the risk of heart disease as people with optimal levels. Several studies show an unfavorable association between deficient levels of vitamin D and cardiovascular disease markers such as total cholesterol and other lipids. However, randomized controlled studies are pending to assess if vitamin D deficiency is a cause or merely a marker of poor heart health and the effect of therapy to correct a deficiency.

The researchers conducted two studies on patients tested for vitamin D and lipids by Quest Diagnostics in the United States. The first study involved a cross-sectional analysis of 107,811 patients to assess differences in lipid levels between those with optimal and deficient vitamin D levels. Cross-sectional studies evaluate a study population in one moment in time.

The analysis found that patients with optimal levels of vitamin D, defined as 30 ng/ml or higher, had a statistically significant lower lipid risk profile, including lower overall total cholesterol, LDL ("bad") cholesterol and triglycerides, and higher HDL ("good") cholesterol, compared to those with deficient levels measuring less than 20 ng/ml.

The Endocrine Society defines vitamin D levels of 30 ng/ml or higher as optimal and 20 ng/ml or lower as deficient. The Institutes of Medicine defines 20 ng/ml as sufficient for most adults for bone health, but does not correlate vitamin D with cardiovascular health.

"Increases in vitamin D levels were associated with step-wise improvements in lipids. Although these findings support prior association studies, they do not demonstrate if vitamin D is a causal factor in lipid health or a passive marker for it," said investigator Harvey W. Kaufman, M.D., senior medical director, Quest Diagnostics.

Supplementation to raise vitamin D levels does not improve lipids

The investigators also performed a longitudinal analysis to assess the impact of therapy to correct vitamin D deficiency on lipid levels. Longitudinal studies evaluate changes in a study population over time. Pharmacological, oral vitamin-D therapy is typically administered to raise vitamin D levels in patients with vitamin D deficiency, although over-the-counter supplements are also widely available.

The longitudinal study examined data for 8,592 patients re-tested between four and 26 weeks. It showed that raising vitamin D levels from deficient to optimal levels had no statistically significant effect on LDL cholesterol or triglycerides, and had a small, but clinically minimal impact on total and HDL cholesterol.

"The seemingly conflicting findings of the cross-sectional analysis and longitudinal analysis suggest that while vitamin D deficiency is associated with an unfavorable lipid profile, correcting a deficiency through therapeutic vitamin D supplementation may have limited value in improving lipids," said Dr. Ponda.

Data mining in lieu of large trial

Randomized clinical trials (RCT) are considered the gold standard of clinical research on therapeutic interventions, but can require years and considerable financial investment to complete. The investigators in this study employed sophisticated data mining techniques to analyze the Quest Diagnostics dataset to provide insights on the therapeutic effect of vitamin D repletion. The company maintains the largest private source of laboratory patient data and publishes Quest Diagnostics Health Trends™ reports in peer reviewed journals as a public service.

In an editorial, Drs. Rolf Jorde and Guri Grimnes write that the study is "... of great importance as it underscores that cross-sectional results are not necessarily reproduced in prospective studies, and that cross-sectional data cannot and should never be taken as evidence for causality." They also characterize it as "another approach that with its cost-effectiveness is highly attractive" and suggest similar study methods "could be used by others with access to large databases with laboratory results."

"In the absence of RCT, observational studies based on mining large, clinical databases can provide important medical insights. Our novel, inexpensive analysis fills a major gap in current medical research on vitamin D," said Jan L. Breslow, M.D., Frederick Henry Leonhardt Professor and

head of The Rockefeller University's Laboratory of Biochemical Genetics and Metabolism. "An analogous prospective, randomized, controlled trial would take years to complete and possibly be prohibitively expensive. While additional research is required to confirm our findings, our study provides clinically valuable insights to help guide patient management until these other trials are performed."

The study's strengths include its national scope and size, which allowed the investigators to control for age and gender, and to identify clinically significant relationships between vitamin D levels and lipid profiles. Data was obtained from actual patients in settings reflective of true clinical practice across the United States. Limitations include lack of access to medical records to determine reasons vitamin D testing was performed or factors that influence lipids, such as body mass index and medications. The Western Institutional Review Board reviewed the process used to perform the study.

The study, titled "Vitamin D May Not Improve Lipid Levels: A Serial Clinical Laboratory Data Study," is in the July 17 issue of Circulation, which is also available online at: <http://circ.ahajournals.org/content/early/2012/06/18/CIRCULATIONAHA.111.077875.abstract>

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