

# Effects of Marine Omega-3 and Vitamin D Supplementation on Circulating Biomarkers of Glucose-Insulin Homeostasis and Incident Cardiovascular Disease in the VITamin D and OmegA-3 Trial (VITAL)

## Background

- Insulin resistance and imbalances in blood glucose increase the risk of cardiovascular disease (CVD).<sup>1</sup>
- However, data about the association between CVD risk and biomarkers for glucose and insulin have been inconsistent.
- **Objective:** This study examined the association between glucose-insulin biomarkers and risk of incident CVD and coronary heart disease (CHD) events. It also examined whether supplementation with vitamin D or omega-3 fatty acids (n-3 FA) modified any associations between the biomarkers and risk of incident CVD or CHD events.

## Methods

- VITAL is a randomized trial investigating whether supplemental vitamin D (cholecalciferol, 2000 IU/d) or n-3 FA (EPA+DHA, 1 g/d) influence CVD and cancer risk.<sup>2,3</sup>
- In this study, VITAL trial participants with incident CVD events (non-fatal myocardial infarction [MI], non-fatal stroke, or CV death) were matched to healthy control participants based on age and sex.
- The associations of incident CVD and CHD event risk with baseline levels of insulin, C-peptide, and HbA1c, and insulin resistance score (IRS) were assessed with conditional logistic regression.
  - The models adjusted for demographic factors, CVD risk factors, and randomized treatment (ie, vitamin D or n-3 FA supplementation).
- The association of vitamin D or n-3 FA supplementation with glucose-insulin biomarkers was also examined in control participants after 1 or 2 years of follow-up.

## Results

- The study population included 715 patients with incident CVD, including 423 who had CHD events (MI, revascularization, or CHD death), matched to 715 healthy control individuals.
  - Mean age of the matched cohorts was 71 years; ~42% were female, and 12% were African American.
- Baseline HbA1c level was associated with CVD risk (adjusted odds ratio [aOR], 1.17 per incremental standard deviation; 95% CI, 1.01-1.38). The other biomarkers and IRS were not associated with CVD risk.
- Baseline IRS was associated with CHD risk (aOR, 1.22; 95% CI, 1.01-1.46). The 3 biomarkers were not associated with CHD risk.
- Vitamin D or n-3 FA supplementation was not associated with biomarker levels and did not modify associations with CVD or CHD risk.

## Conclusions

- In this study, higher HbA1c levels were associated with increased CVD risk, and a higher IRS was associated with increased CHD risk.
- Vitamin D and n-3 FA supplementation was not associated with glucose-insulin biomarker levels and did not modify biomarker associations with risk.

## Poster presentation at the Scientific Sessions of the American Heart Association (AHA)

### Authors

Frank Qian,<sup>a,b</sup> Yanjun Guo,<sup>c</sup> Heike Luttmann-Gibson,<sup>b,c</sup> Natalya Gomelskaya,<sup>c</sup> Yanyan Liu,<sup>c</sup> Olga Demler,<sup>c</sup> Nancy Cook,<sup>b,c</sup> I-Min Lee,<sup>b,c</sup> Julie E Buring,<sup>b,c</sup> Julia Larsen,<sup>d</sup> Jennifer Boring,<sup>d</sup> Michael J McPhaul,<sup>d</sup> JoAnn E Manson,<sup>b,c</sup> Aruna Pradhan,<sup>c</sup> Samia Mora<sup>c</sup>

### Affiliations

<sup>a</sup>Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

<sup>b</sup>Harvard T.H. Chan School of Public Health, Boston, MA, USA

<sup>c</sup>Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

<sup>d</sup>Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, USA

## AHA Scientific Sessions, A Virtual Event, November 13-15, 2021

Date: November 14, 2021

Time: 3:30 PM-4:30 PM

### Webpage

[https://www.ahajournals.org/doi/10.1161/circ.144.suppl\\_1.12860](https://www.ahajournals.org/doi/10.1161/circ.144.suppl_1.12860)

### References

1. Ormazabal V, Nair S, Elfeky O, et al. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc Diabetol*. 2018;17:122. doi: 10.1186/s12933-018-0762-4
2. Manson JE, Cook NR, Lee IM, et al. Vitamin D supplements and prevention of cancer and cardiovascular disease. *N Engl J Med*. 2019;380:33-44. doi: 10.1056/NEJMoa1809944
3. Manson JE, Cook NR, Lee IM, et al. Marine n-3 fatty acids and prevention of cardiovascular disease and cancer. *N Engl J Med*. 2019;380:23-32. doi: 10.1056/NEJMoa1811403