Supplemental Online Content

Albert CM, Cook NR, Pester J, et al. Effect of marine omega-3 fatty acid and vitamin D supplementation on incident atrial fibrillation: a randomized clinical trial. *JAMA*. Published March 16, 2021. doi:10.1001/jama.2021.1489

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. CMS Linkage Methods Used in the VITAL Study

To supplement the yearly ascertainment of AF from follow-up questionnaires, we have ascertained inpatient and outpatient AF diagnoses (ICD-9 diagnosis code 427.31 and ICD-10 diagnosis code I48.91) and atrial flutter (ICD-9 diagnosis code 427.32 and ICD-10 diagnosis code I48.92) by linking claims data from the Centers for Medicare and Medicaid Services (CMS). Medicare is a US federal health insurance program that reimburses medical costs for most citizens and permanent residents aged ≥65 years, as well as some younger people with disabilities. Annual CMS data becomes available 11-12 months after the end of a calendar year, and this analysis includes CMS data from 2011-2017.

On an annual basis, the VITAL trial obtained Identifiable (Medicare) Data Files through ResDAC (www.resdac.unm.edu/Index.asp), which is a Centers for Medicare and Medicaid Services (CMS) contractor that provides free assistance to academic and non-profit researchers interested in using Medicare or Medicaid data. VITAL participants were informed of our intention to use this methodology to ascertain their claims data from CMS through a study newsletter and were given the option to opt out. The data use agreement (DUA) delineates the confidentiality requirements of the Privacy Act and data release policies and procedures.

The CMS linkage was performed by social security number (SSN). A finder file with complete, 9-digit SSNs was sent to CMS, and CMS matched SSN to their data sets and provided us with a crosswalk file SSN - BENE_ID (beneficiary ID uniquely created for the VITAL linkage). Data obtained included Medicare Provider and Analysis Review (MedPar) files with inpatient hospital and skilled nursing facility stay records, and Standard Analytical Files (SAFs) for outpatient and non-institutional claims. Emergency room visits are included in the MedPAR files and the outpatient SAFs.

All requested data sets (Medpar/inpatient claims, outpatient, carrier/non-institutional claims) were identified by BENE_ID, while the SSN is only included in the crosswalk. Data was provided on a DVD as a text file, then converted to a SAS data set, which was then linked back to the participant's study record. AF diagnosis reports and treatment dates were cross-checked with self-reports to identify any potential AF case/recurrence not already ascertained. We then used the same follow-up procedures as outlined in the manuscript to obtain medical records and adjudicate events.

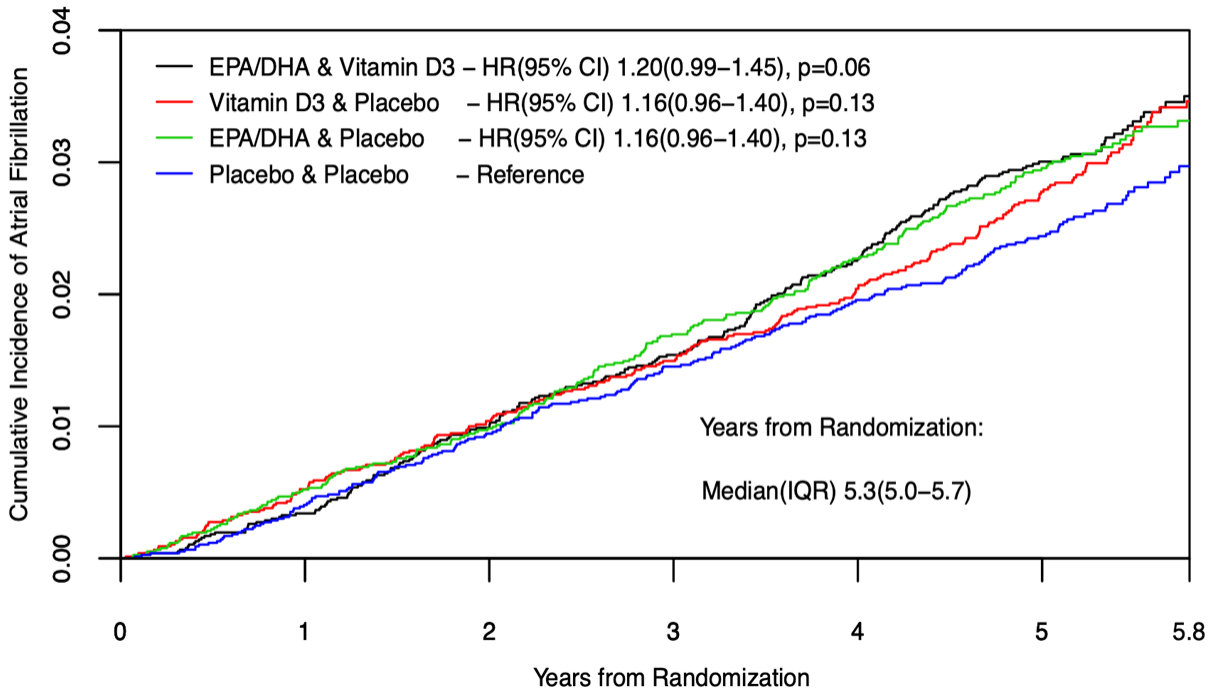
eTable. Characteristics of Incident Atrial Fibrillation

Characteristic	No. (%)
How AF confirmed	
ECG	656 (72.9)
Medical record report	244 (27.1)
Pattern of AF[a]	
Paroxysmal[b]	526 (58.4)
Persistent[c]	262 (29.1)
Long-standing persistent[d]	84 (9.3)
Unable to be classified	28 (3.1)
Symptoms present at diagnosis	
Yes	557 (61.9)
No	247 (27.4)
Unclear	96 (10.7)
Symptoms may have preceded randomization[e]	58 (6.4)
AF post-cardiac surgery	66 (7.3)
Atrial flutter only	52 (5.8)
LVEF on echo available	775 (86.1)
LVEF percentage, mean (SD)[f]	57.2 (10.9)

Abbreviations: AF, atrial fibrillation; ECG, electrocardiogram, LVEF, left ventricular ejection fraction

a. Pattern of AF at the time of diagnosis was classified in accordance with ACC/AHA/HRS and ESC guidelines.[19,20]
b. Self terminating episode(s) of AF lasting 7 days or less which may be recurrent
c. Duration of AF lasting for more than 7 days
d. Duration of AF estimated to have been greater than 1 year.
e. participant experienced symptoms which could have been secondary to AF or palpitations prior to randomization, but was not officially diagnosed until after randomization.
f. LVEF closest to time of presentation, with consideration of the possibility of tachycardic myopathy at presentation. If two EF measurements are available within 3 months of the AF presentation and the EF has improved in the interim, the higher EF was chosen.

eFigure. Cumulative Incidence of Atrial Fibrillation According to Four Treatment Groups



Cumulative incidence of the primary endpoint according to four group randomized treatment assignment to EPA/DHA, Vitamin D_3, and respective placebo derived from Cox regression models that were controlled for age, sex, and randomization group.

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Data and Safety Monitoring Board

Voting members of the data and safety monitoring board for VITAL and the ancillary studies, including the VITAL Rhythm Study, included: Lawrence S. Cohen, MD, Theodore Colton, ScD, Mark A. Espeland, PhD, I. Craig Henderson, MD, Alice H. Lichtenstein, DSc, Rebecca A. Silliman, MD, PhD, and Nanette Wenger, MD (chair). The ex-officio members included: Josephine Boyington, PhD, MPH, Rebecca B. Costello, PhD, Cindy D. Davis, PhD, Lawrence Fine, MD, DrPH, Lori Minasian, MD, Peter Greenwald, MD, Gabriela Riscuta, MD, CNS, and Harold Seifried, MS, PhD.