



The VITamin D and OmegaA-3 Trial (VITAL)

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Disclosure

Dr. JoAnn Manson has no real or apparent conflicts of interest related to this presentation.

Dr. Manson has received funding from the NIH to conduct a large-scale randomized trial of vitamin D and omega-3 fatty acids (VITAL).

Large, Simple, Mail-based Randomized Clinical Trials*

<u>Trial Name</u>	<u>Intervention Tested (factorial design vs placebo)</u>
Physicians' Health Study I	Aspirin, beta-carotene
Physicians' Health Study II	Multivitamins, vitamin E, vitamin C
Women's Health Study	Aspirin, vitamin E
Women's Antioxidant and Folic Acid Study	Beta carotene, vitamin C, vitamin E, folic acid/B6/B12

*** Health professional populations, mailed calendar packs, high compliance, baseline blood collection in ~70% of participants, follow-up bloods in sample, medical record confirmation of endpoints, NDI for mortality.**

Highly cost-effective: ~\$100-200/participant/year in direct costs.

Monthly Calendar Pack

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
<p>PHYSICIANS' HEALTH STUDY II BRIGHAM & WOMEN'S HOSPITAL/HARVARD MEDICAL SCHOOL 900 COMMONWEALTH AVENUE EAST BOSTON, MA 02215-1204 (800) 633-6907 Store in dry location. Avoid excessive heat. Caution: Limited by Federal law to investigational use only Packaging provided by Caraustar Custom Packaging Group, Pine Brook, NJ 07058</p>			29	30	31	

Rationale for *VITAL*

- **Emerging evidence that vitamin D and marine omega-3s (EPA+DHA) reduce risk of cancer and CVD.**
 - **Growing use of these supplements underscores the need for conclusive evidence on benefits and risks.**
 - **No previous large-scale randomized clinical trials of these agents in the primary prevention of cancer and CVD have been conducted.**
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***VITAL* Specific Aims**

Primary Aims

- 1) To test whether vitamin D₃ reduces risk of (a) total cancer, (b) major CVD events (composite of MI, stroke, CVD death).**
- 2) To test whether EPA+DHA reduces risk of (a) total cancer and (b) major CVD events.**

Secondary Aims

- 1) To test whether these agents lower risk of (a) colorectal cancer (b) breast cancer (c) prostate cancer (d) total cancer mortality.**
 - 2) To test whether these agents lower risk of (a) MI/stroke/CVD death/CABG/PCI and (b) individual components of CVD outcome.**
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The *VIT*amin D and Omega-3 *Tri*al (*VITAL*): Design

20,000 Initially Healthy Men and Women
(Men ≥ 50 yrs; Women ≥ 55 yrs)

Vitamin D₃
(2000 IU/d); N=10,000

Placebo
N=10,000

EPA+DHA
(1 gm/d); N=5000

Placebo
N=5000

EPA+DHA
(1 gm/d); N=5000

Placebo
N=5000

Mean Treatment Period = 5.0 years

Blood collection in ~16,000, follow-up bloods in ~6000

Primary Outcomes: Cancer (total) and CVD (MI, stroke, CVD death)

Eligibility Criteria

- **Men ≥ 50 , women ≥ 55 years of age**
 - **No history of cancer (except non-melanoma skin) or CVD (MI, stroke, CABG/PCI).**
 - **No history of renal failure or dialysis, hypercalcemia, severe liver disease (cirrhosis), or sarcoidosis, TB, or other granulomatous diseases.**
 - **No allergy to fish.**
 - **No supplements >800 IU/d vitamin D, >1200 mg/d calcium, or fish oil.**
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Targeted/Planned Enrollment by Race/Ethnicity

<u>Racial/Ethnic Category</u>	<u>Number of Subjects</u>
Black or African American	5,000
Hispanic or Latino	1,400
White/non-Hispanic	12,620
Asian	500
American Indian/Alaska Native	400
Native Hawaiian or other Pacific Islander	80
Total	20,000 (10,000 men + 10,000 women)

VITAL Recruitment Strategies

Overall

- Population-based (nationwide) and targeted mailings
- Media reports on VITAL (with mention of website and 1-800 number for sign up)
- Advertising (radio, print)
- Study-related brochures in medical clinics/health centers

Targeted Efforts to Enhance Minority Recruitment

- Targeted minority-enriched mailings, including alumni/ae of historically black colleges and universities
 - Community health centers
 - Church bulletins
 - Collaborations with investigators on recruitment in large urban areas (Chicago, Detroit)
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Ancillary Studies in VITAL

Funded

- Cognitive Function
- Diabetes/Glucose Tolerance
- Hypertension
- Autoimmune Disorders
- Asthma/Respiratory Diseases
- Diabetic Nephropathy
- Fractures/Bone Imaging
- Mood Disorders/Depression
- Infections
- 2D Echocardiogram
- Macular Degeneration
- Anemia

Pending

Vitamin D Genomics
Telomere Biology
Heart Failure
Atrial Fibrillation

Hybrid Design In-Clinic Visits: Protocol (N=1000 at Baseline and 2 Yrs)

- **Blood pressure measurements**
 - **Height, weight, waist, other anthropometrics**
 - **Urine collection**
 - **OGTT (2-hr) and fasting blood collections**
 - **Spirometry**
 - **Physical performance/strength/frailty**
 - **Cognitive function/mood/depression**
 - **2D Echocardiogram**
 - **DXA scans, bone microarchitecture imaging**
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Current Status of Recruitment

- **Will surpass recruitment goal: >18,500 currently randomized and ~4500 pending (in placebo run-in): total N~23,000.**
 - **~70% have provided baseline blood collection (EMSI assistance for some).**
 - **Expect to achieve demographic recruitment goals (greatest challenge).**
 - **1-year follow up has begun for those enrolled early (staggered recruitment).**
 - **Compliance to date is excellent.**
 - **Multiple ancillary studies have received funding.**
 - **In-clinic visits: on track to meet CTSC recruitment goals.**
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Conclusions

- Vitamin D and omega-3x are promising interventions for prevention of cancer, CVD, and other chronic diseases, but conclusive evidence for their efficacy in primary prevention is lacking.
- *VITAL* is the first large-scale randomized clinical trial of vitamin D and omega-3s in the primary prevention of cancer and CVD.

Study website:



www.vitalstudy.org