



The VITamin D and OmegaA-3 Trial (VITAL)

JoAnn E. Manson, MD, DrPH
Principal Investigator, VITAL
Brigham and Women's Hospital
Professor of Medicine and the
Michael and Lee Bell Professor of Women's Health
Harvard Medical School

Clinical Trials Transformation Initiative

Rockville, Maryland

May 13, 2013

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.**
-

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.**
-

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.**
-

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)
-

Ancillary Studies in VITAL

Funded

- Cognitive Function
- Diabetes/Glucose Tolerance
- Hypertension
- Autoimmune Disorders
- Asthma/Respiratory Diseases
- Fractures
- DXA/Bone Microarchitecture
- Mood Disorders/Depression
- Infections
- 2D Echocardiogram
- Macular Degeneration
- Anemia
- Atrial Fibrillation

Pending

Vitamin D Genomics
Telomere Biology
Heart Failure

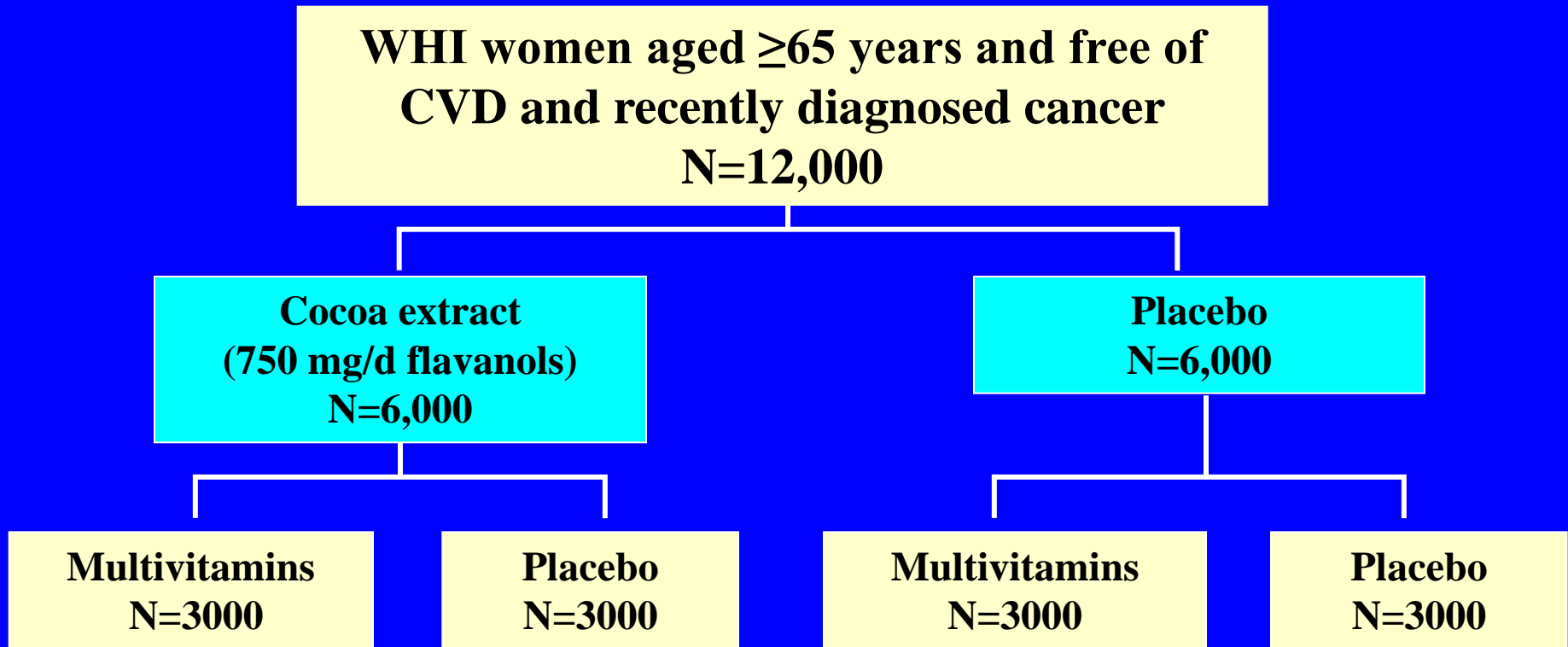
Hybrid Design In-Clinic Visits: Protocol (N=1000 at Baseline and 2 Yrs)

- **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**
-

Current Status of Recruitment

- **24,018 currently randomized: total will be ~25,000.**
 - **~16,000 have provided baseline blood collection (EMSI assistance for some).**
 - **Expect to achieve demographic recruitment goals (greatest challenge).**
 - **Follow-up (12 and 18 months) 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.**
-

Proposed Trial Design



Mean Treatment Period = 4 years

Primary Outcomes: CVD (MI, stroke, CVD death and coronary revascularization); cancer.

Baseline Blood collection in $\sim 1,500$, follow-up bloods in 1,000.

Conclusions

- Vitamin D and omega-3s 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