The VITamin D and OmegA-3 TriaL (VITAL)

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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*

* 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.

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Intervention Tested (factorial design vs placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicians' Health Study I</td>
<td>Aspirin, beta-carotene</td>
</tr>
<tr>
<td>Physicians' Health Study II</td>
<td>Multivitamins, vitamin E, vitamin C</td>
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<tr>
<td>Women's Health Study</td>
<td>Aspirin, vitamin E</td>
</tr>
<tr>
<td>Women’s Antioxidant and Folic Acid Study</td>
<td>Beta carotene, vitamin C, vitamin E, folic acid/B6/B12</td>
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</tbody>
</table>
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.
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 Omeg*A*-3 Tria*L* (*VITAL*): Design

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

- **Vitamin D₃** (2000 IU/d); N=10,000
  - EPA+DHA (1 gm/d); N=5000
  - Placebo N=5000
- **Placebo** N=10,000
  - 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

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

- 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.
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