

Plenary 5: Long-term Influence of the WHI Dietary Modification Trial Intervention on Chronic Disease Incidence and Mortality

Opening Remarks/ Introductions

Linda Van Horn, PhD, RDN, Northwestern

Mortality from and mortality after cancer diagnoses in the Dietary Modification Trial with long-term follow-up

Rowan Chlebowski, MD, UCLA

Cardiovascular disease and total mortality in the Dietary Modification Trial with long-term follow-up

Ross Prentice, PhD, Fred Hutchinson
Cancer Research Center

Long-term effects of the Dietary Modification Trial intervention on diabetes incidence and severity

Barbara Howard, PhD, Medstar



WHI is:

1 Observational Study
3 Controlled Trials

27,347

Hormone Therapy Trials:
Coronary Heart Disease & Fractures.
Adverse effect for Breast Cancer?

36,282

Calcium/Vitamin D Trial:
Fractures & Colorectal Cancer

48,835

**Dietary Modification Trial of Low-fat diet
compared to usual diet:
Breast & Colorectal Cancers & Coronary Heart
Disease**

93,676

Observational Study

161,808 postmenopausal women

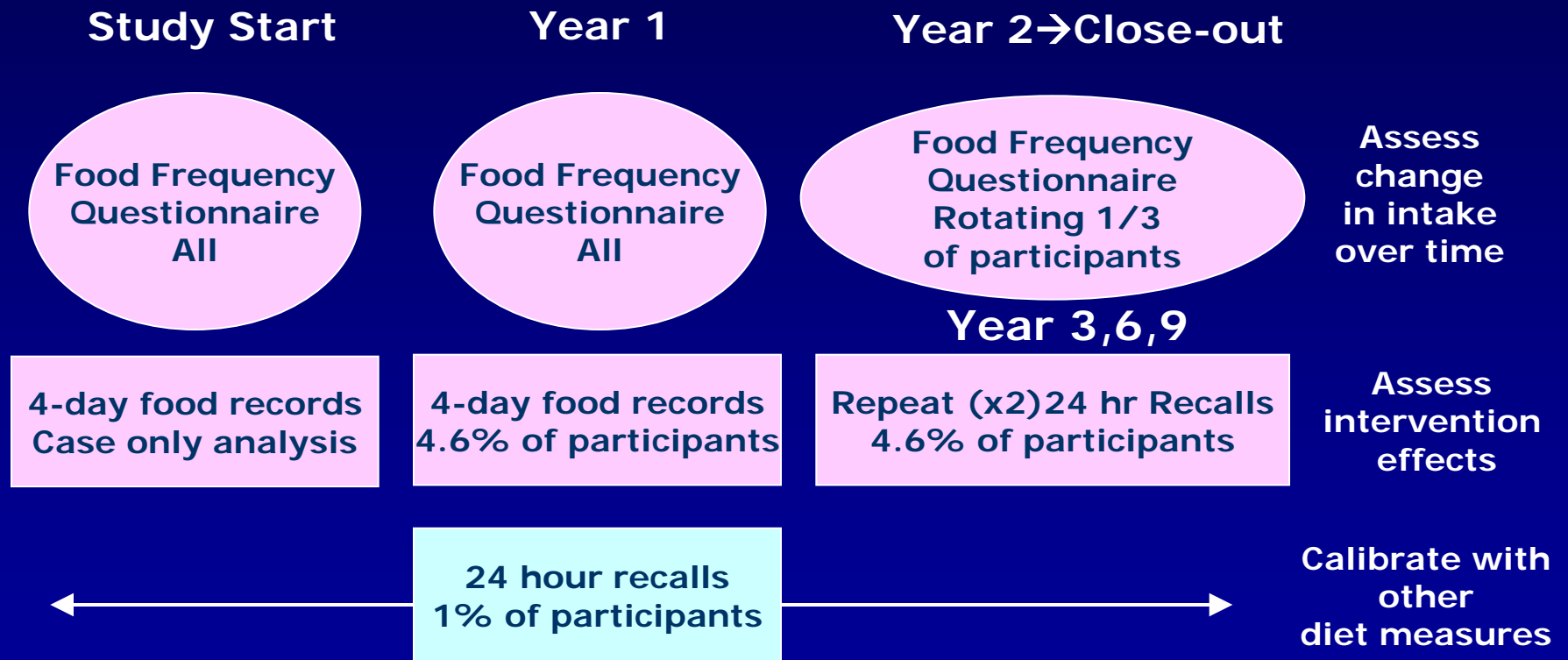
1993-2005

2005-2010: n = 115,407

2010-2015: n = 93,558



How Was Diet Measured?

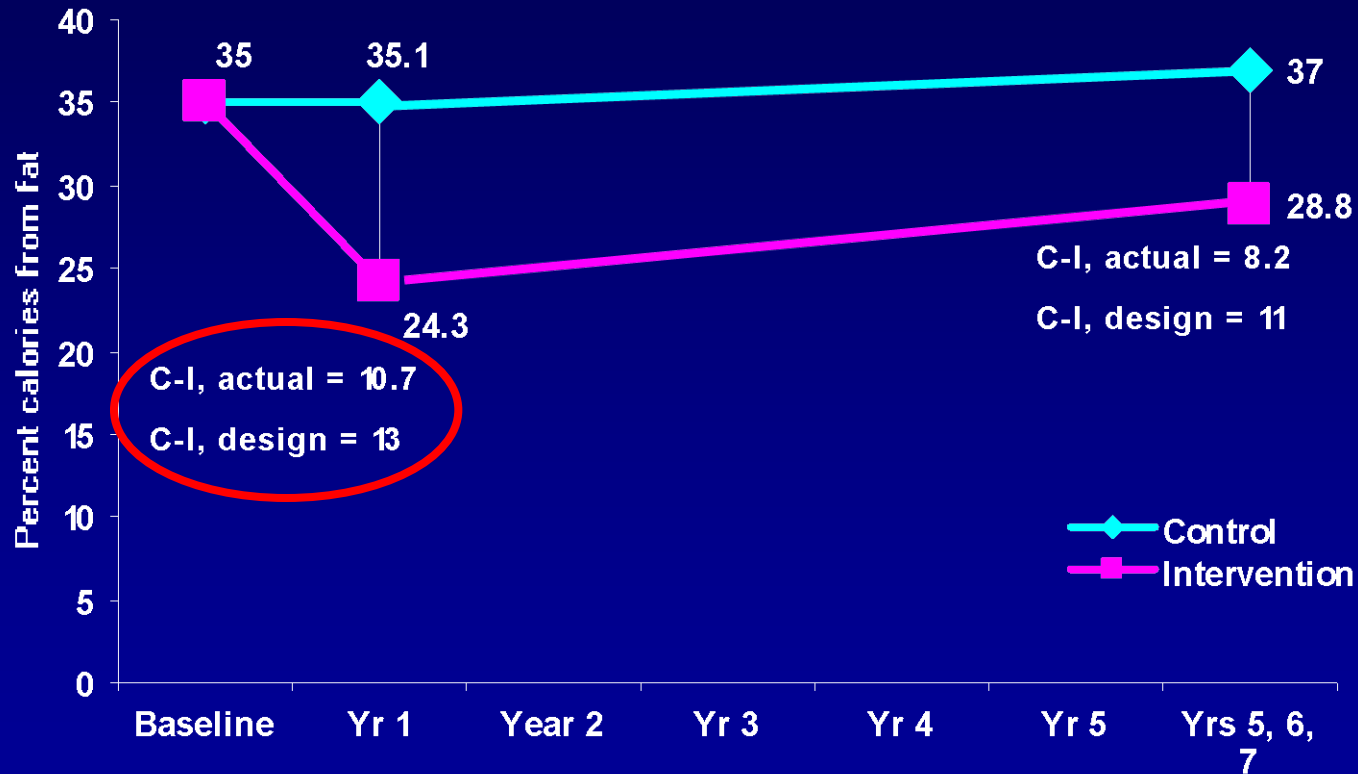


The Women's Health Initiative: Scholarly Productivity

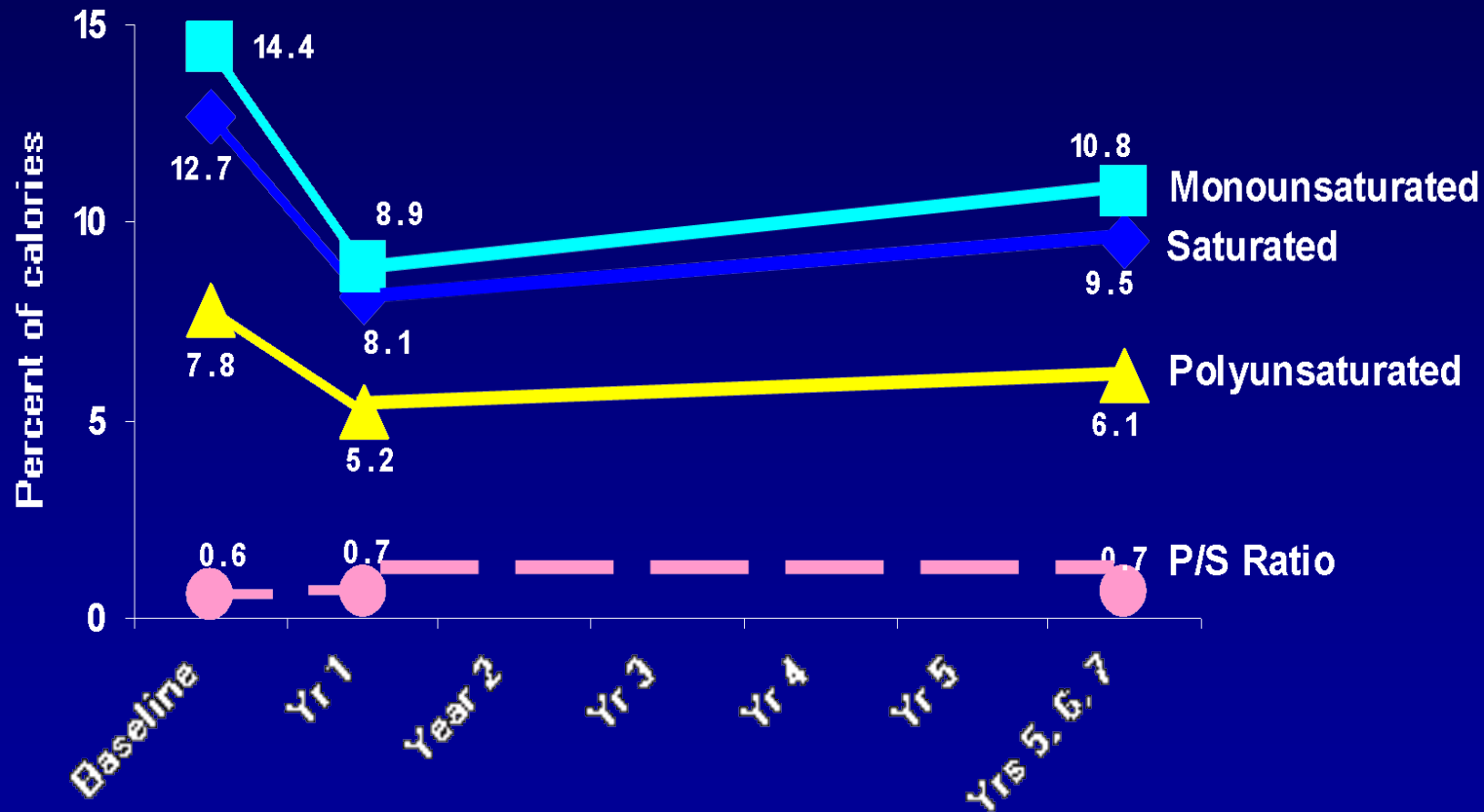
Publications/Studies	Total Number to Date
WHI Publications	1,498
Diet/Nutrition Publications (1996-2017; 16% of total)	243
Cancer	56 (23%)
Cardiovascular	43 (18%)
Ca/D Bone/Osteoporosis	22 (9%)
Diet Assessment/Methods	26 (11%)



WHI Dietary Modification Trial: Percent Calories from Fat



Dietary Changes in the Intervention Group: Types of Fat



Nutrient Intakes & Blood Biomarkers

	Baseline	Baseline-Year 3, Inter-Cont
Daily Nutrient Intakes		
Folate (dietary), μg	259	+ 62 (+24.5% **)
Fiber, g	15.4	+ 3.1* (+20.0%)
Red meats, servings	0.9	- 0.2 (-22.0% **)
Biomarkers in Blood		
Total cholesterol, mg/dL	224	- 3.3 *
LDL-cholesterol, mg/dL	133	- 3.6 *
HDL-cholesterol, mg/dL	60.1	- 0.4
Total carotenoids, $\mu\text{g}/\text{dL}$	0.88	+ 0.04 (+ 5%)
Gamma tocopherol, $\mu\text{g}/\text{dL}$	2.3	- 0.21*

* $p < .05$

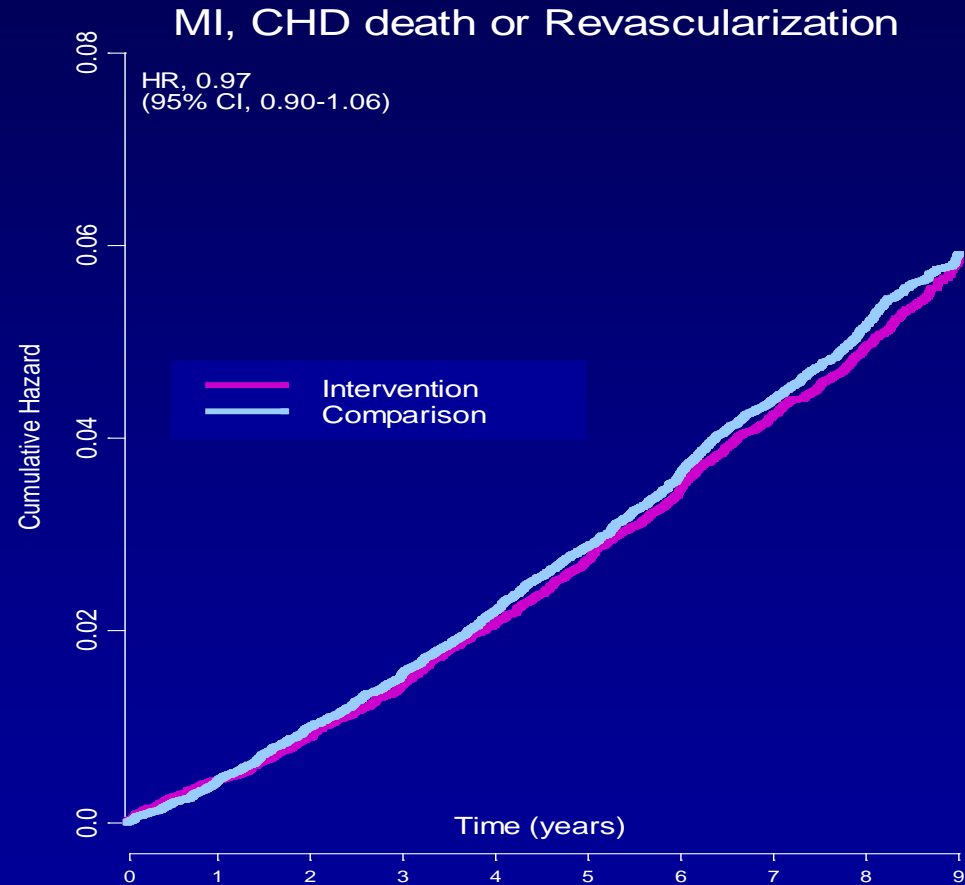
** $p < .001$

JAMA 2006; 295; 629-642; JAMA 2006; 295; 642-654;

JAMA 2006; 295; 655-666



Coronary Heart Disease: Cumulative Hazard Ratios



2,549 total diagnoses
(5% of all DM
participants)

Hazard ratio = 0.97
(95% CI = 0.90-1.06)

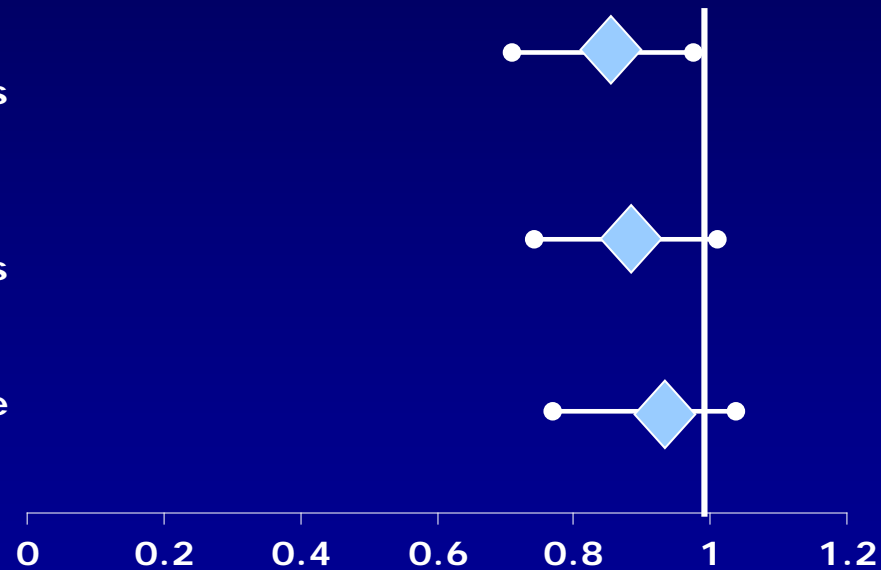
Additional Analyses: Heart Disease Risk

Intake at Year 1

Saturated fat
<6.1% calories

Trans fat
<1.1 % calories

Fruit/vegetable
≥6.5 servings



Decreased Risk

Subsequent Diet Publications Including OS (mostly)/DM/CaD/HT

Examples:

- Dietary Patterns and Adherence: HEI, AHEI, DASH, Mediterranean, Inflammatory Index (Belin, 2011, Van Horn, 2012; Tabung, 2016; Orchard, 2016)
- Diet and Heart Failure (Belin, 2011; Levitan, 2013)
- Diet and Cancer (DM–Post Stop) (Thomson, 2014)
- Ancillary NBS/NPAAS Diet Assessment Methodology Calibration Studies (Prentice, 2013, 2016, 2017)
- Other diet/lifestyle studies (Mossavar-Rahmani, 2013; Bertoia, 2014)

Mediterranean and Dietary Approaches to Stop Hypertension dietary patterns and risk of sudden cardiac death (SCD) in postmenopausal women

Bertoia ML, Triche EW, Michaud DS, Baylin A, Hogan JW, Neuhaus ML, Tinker LF, Van Horn L, Waring ME, Li W, Shikany JM, Eaton CB.

Hypothesis: Mediterranean and DASH diets, foods and nutrients affect cholesterol, inflammation, the development of atherosclerosis, and risk SCD.

OBJECTIVE: Examine associations between the Mediterranean and DASH dietary patterns and risk of SCD (occurred within 1 h of symptom onset).

DESIGN: Prospective cohort of 93,122 WHI participants followed 10.5 y. FFQ scored based on adherence to each dietary pattern

RESULTS: Higher Mediterranean diet score associated with lower risk of SCD (HR: 0.64; 95% CI: 0.43, 0.94) comparing highest/ lowest quintiles (adjusted). Higher DASH diet score not associated with risk of SCD. (Sodium intake, a DASH focus, not well quantified by FFQ)

CONCLUSION:

Mediterranean dietary pattern may be associated with lower risk of SCD

Mediterranean and DASH Diet Scores and Mortality in Women With Heart Failure: WHI

Levitan, E; Lewis, C; Tinker, L ; Eaton, C ; Ahmed, A; Manson, J; Snetselaar, L; Martin,L;Trevisan, M; Howard, B; Shikany, J

Background: Recommended diet for prevention/treatment of heart failure (HF) are inconclusive and derived from non-HF populations; influence of dietary patterns, e.g, Mediterranean and DASH diet scores on HF mortality is limited.

Methods and Results: participants followed from HF hospitalization through date of death or last contact before August 2009. Mediterranean and DASH diet scores calculated from FFQ data. Cox proportional hazards models adjusted for demographics, health behaviors, and health status used to calculate hazard ratios and 95% CI. Over 4.6 years of follow- up, 1385 of 3215 (43.1%) of HF ptps died. Multivariable-adjusted hazard ratios were 1 (reference), 1.05 (95% CI, 0.89–1.24), 0.97 (95% CI, 0.81–1.17), and 0.85 (95% CI, 0.70–1.02) across quartiles of the Mediterranean diet score (P trend=0.08) and 1 (reference), 1.04 (95% CI, 0.89–1.21), 0.83 (95% CI, 0.70–0.98), and 0.84 (95% CI, 0.70–1.00) across quartiles of the DASH diet score (P trend=0.01).

CONCLUSIONS:

Higher DASH diet scores were associated with modestly lower mortality in women with HF, and there was a nonsignificant trend toward an inverse association with Mediterranean diet scores. Vegetables, nuts, and whole grains inversely associated with mortality.



Risk of Heart Failure Among Postmenopausal Women A Secondary Analysis of the Randomized Trial of Vitamin D Plus Calcium of the Women's Health Initiative

M. Donneyong; C Hornung; K Taylor; R Baumgartner ; J Myers; C Eaton; E Gorodeski; L Klein; L Martin; J Shikany ; Y Song; W Li; J Manson

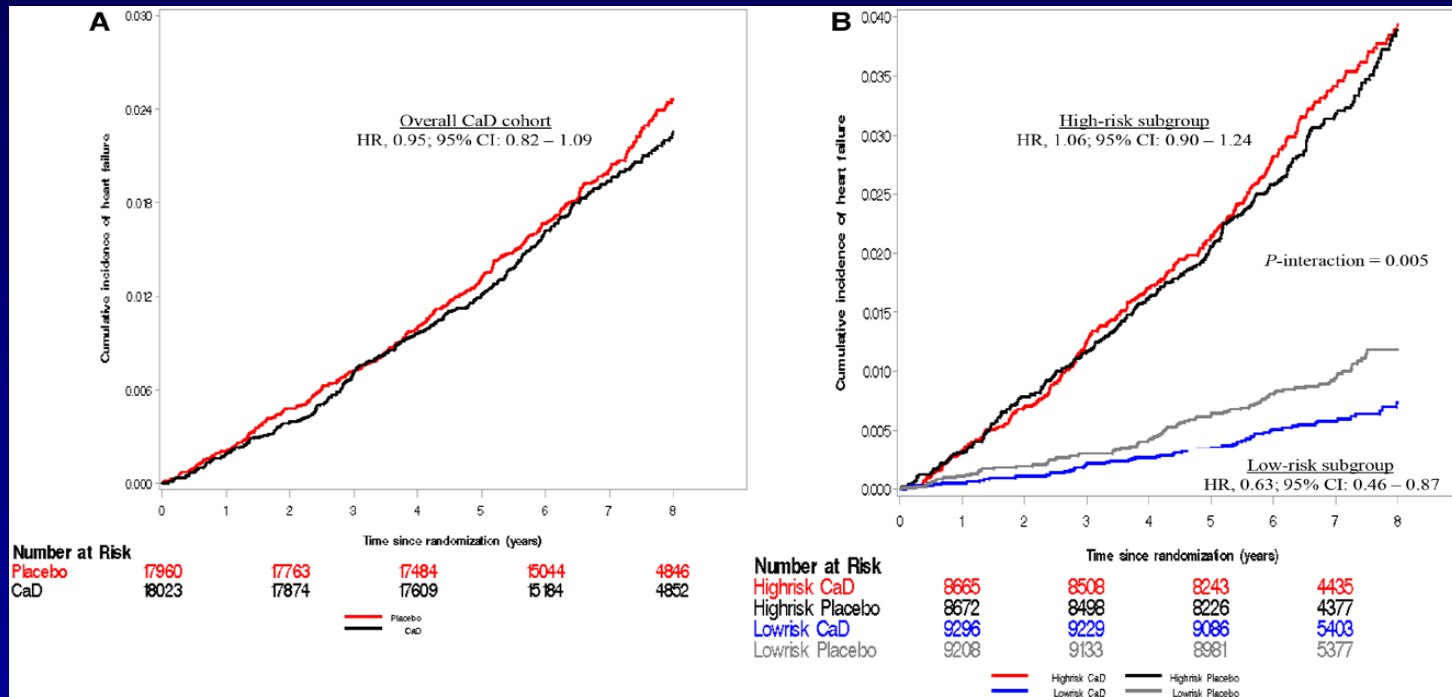


Figure 2. Kaplan–Meier curves comparing the cumulative incidence of heart failure between the vitamin D plus calcium (CaD) and placebo arms during follow-up period in the overall CaD cohort (A) and stratified baseline subgroups (B). CI indicates confidence interval; and HR, hazard ratio.

CONCLUSIONS: CaD supplementation did not significantly reduce HF incidence in the overall cohort, but was beneficial among postmenopausal women without major HF precursors and little value in high-risk subgroups.

Nutrient and Physical Activity Biomarkers in the WHI

Ross Prentice, Fred Hutch and University of Washington

Nutrient Biomarker Study: 544 women completed two-week DLW protocol with urine and blood collection and with FFQ and other questionnaire data collection (50% intervention, 50% control). A 20% reliability subsample repeated protocol separated, by about 6 months from original data collection. (NBS)

Nutrition and Physical Activity Assessment Study Biomarker study among 450 women in the WHI Observational Study for calibrating baseline FFQ, 4DFR, and PA questions, and for evaluating measurement properties of prominent dietary and physical activity assessment approaches (frequencies, records, and recalls) and their combination. (NPAAS)



Women's Health Initiative Nutrition Research Gaps

1. ↑ Basic Nutritional Science to complement diet data
 - targeted metabolomics and other “omics”
2. Validated Biomarkers of Dietary Intake, Effect (Molecular Targets) & Susceptibility at various times of life
3. Validated calibration of WHI FFQ data
4. ↑ Research on Bioactive/Engineered Food Compounds
5. ↑ Diet Intervention/Feeding Studies (Lampe, 2016)
6. Diet quality and longevity of WHI Participants



Nutrition “is the ultimate biochemical interaction – the human organism reacting with the environment, daily, in a very intimate sense. And it’s been starved for research funding.”

Bernadine Healy, 2004

Acknowledgements

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