MANAGING YOUR HEALTH: BALANCING RISKS AND BENEFITS

WHI

Calcium and Vitamin D

Supplementation

Trial



The Women's Health Initiative

161,808; 5,298 in Arizona



CaD Study Rationale

- Osteoporosis major public health problem
- Fractures associated: 1.7 M annually
- Limited evidence (1990) from RCT calcium+ vitamin D reduce hip fracture risk
- Observational data suggested inverse association with colorectal cancer

Calcium Intake in

WHI women

WHI Women reported:

- Diet: 678 mg/day
- Recommended: 1200 mg/d
- 9.1% had total calcium intake below 400 mg/day
- 35.1% met requirements
- 27.4% of women > 70 y reported use of calcium supplements
- Supplementation was associated with meeting recommended intake

RCT: CaD or placebo Eligibility:

- no history of cancer,
- 3 y expected survival,
- calcium supplement < 800 mg/
 vitamin D supplement < 600 IU

Intervention: 1000 mg calcium carbonate, 400 IU vitamin D3; consumed in 2 doses daily

Outcomes: Bone fracture, heart disease, colorectal and breast cancer, mortality

CaD Trial Design



End Trial Findings

Intervention phase outcomes:

Jackson, NEJM, 2006: Fractures – increase in hip bone density; no reduction in hip fracture

Wactawski-Wende, NEJM, 2006: no effect on Colorectal Cancer **Figure 1.** Forest plot of hazard ratios for monitored and other important outcomes in the overall study population of women aged 50 to 79 years in the WHI Calcium and Vitamin D Trial (n = 36,282).



End Trial Findings

Nested case-control analysis showed suggestion that lower blood vitamin D levels at study enrollment was associated with greater risk for colorectal cancer

Odds Ratio for CRC by Quartile of Baseline S. 25-hydroxyvitamin D

Baseline S. 25- hydroxyvit D (nmol/L)	Main effect OR, 95% CI
> 58.4	1.00
42.4-58.3	1.96 (1.18-3.24)
31.0- 42.3	1.95 (1.18-3.23)
< 31.0	2.53 (1.49 -4.32)

Long-term (22 y) Follow-up Goals

Evaluate long-term outcomes by treatment assignment

Evaluate health outcomes by prior personal supplement use

Personal supplement use collected at WHI screening, 1,3,6 and 9 years; then median 13.5 and 16.2 years during extension studies via self-report

Personal supplements included: Single supplement calcium, single supplement vitamin D, multivitamins with or without minerals, or other supplement mixture (mixture containing \leq 10 vitamins or minerals; not including stress multi-supplements)

Subgroups of primary interest: No personal supplementation at both prerandomization visits (screening and year 1) v any personal supplementation **Figure 1.** Forest plot of hazard ratios for monitored and other important outcomes in the overall study population of women aged 50 to 79 years in the WHI Calcium and Vitamin D Trial (n = 36,282).



Benefit

versus Risk

In women with no personal use:

- Lower *colorectal and breast cancer* rates during intervention AND cumulative follow-up
- Lower **total cancers** during intervention and cumulative follow-up
- No effect on cancer mortality or other outcomes, including hip fracture

Benefit versus

Risk

In women with personal CaD supplement use:

- No influence on hip fracture, total or *colorectal and breast cancer* rates or total or CVD deaths during intervention
- During cumulative follow-up; Slight decrease in cancer mortality
- Slight increase in death related to CVD

What to do?

- Weight your own risk
- Prior health
- Family history
- Think about your current behaviors
- Need to correct nutrient deficiency? Can you do it through diet alone?
- Ability to adhere to daily supplements?
- Your health profile history of cancer versus history of renal stones

