

A low-fat dietary pattern intervention did not reduce incidence of breast cancer, colorectal cancer, or CVD in postmenopausal women

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Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Endocrinology ★★★★★☆☆ Oncology ★★★★★☆☆ GIM/FP/GP ★★★★★☆☆
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QUESTION

Does a dietary modification intervention promoting a low-fat dietary pattern reduce risk for breast cancer, colorectal cancer, or cardiovascular disease (CVD) in postmenopausal women?

METHODS

Design: 3 reports of different outcome measures of a randomized controlled trial (Women's Health Initiative).

Allocation: {Concealed}†.*

Blinding: Blinded (physician adjudicators verifying outcomes, {data collectors, data analysts, and monitoring committee}†).*

Follow-up period: Mean 8.1 years.

Setting: 40 clinical centers in the United States.

Patients: 48 835 postmenopausal women 50 to 79 years of age (mean age 62 y) with baseline fat intake \geq 32% of total calories. Exclusion criteria were previous cancer except for nonmelanoma skin cancer in the past 10 years, medical conditions with predicted survival $<$ 3 years, type 1 diabetes, such adherence concerns as alcoholism or dementia, or frequent consumption of meals prepared away from home.

Intervention: Low-fat dietary pattern intervention ($n = 19\ 541$) or no dietary intervention ($n = 29\ 294$). The dietary modification intervention promoted dietary change with the goals of reducing total fat to 20% of energy intake and increasing fruits and vegetables to \geq 5 servings per day and grains to \geq 6 servings per day. A specially trained nutritionist led 18 group sessions in the first year and quarterly sessions thereafter. Each par-

ticipant received her own fat-gram goal according to height. Participants self-monitored fat, fruit, and vegetable intake and engaged in individual interview sessions that used reflective listening techniques, targeted message campaigns, and personalized feedback on fat intake. Control-group participants received *Dietary Guidelines for Americans* and other health-related materials, but were not asked to make dietary changes.

Outcomes: Invasive breast cancer; invasive colorectal cancer; coronary heart disease (CHD) (myocardial infarction [MI] or CHD death); and a composite endpoint of CHD and revascularization, stroke, and total CVD (MI, CHD death, revascularization, and stroke). A global index endpoint was also measured that consisted of the first occurrence of invasive breast cancer, invasive colorectal cancer, CHD, or death from other causes.

Patient follow-up: 44 351 women (91%) were alive with outcomes data submitted at study end; all patients were included in the intention-to-treat analysis. {As implemented, the study had 60% power to detect a 14% reduction in breast cancer, 40% power to detect a 14% reduction in colorectal cancer, and 40% power to detect a 14% reduction in CHD with dietary modification intervention compared with control.}†

MAIN RESULTS

The dietary modification intervention and control groups did not differ for development of invasive breast cancer, invasive colorectal cancer, or any CVD outcomes

(Table). Secondary analyses showed that the intervention led to a greater reduction in breast cancer among women with higher baseline percentage of energy from fat (hazard ratio [HR] 0.78, 95% CI 0.64 to 0.95) and a greater reduction in CHD risk among women who achieved the lowest intake of saturated fat (HR 0.81, CI 0.69 to 0.96). The intervention had no adverse effect on levels of triglycerides, high-density lipoprotein cholesterol, or insulin. The mean reductions in percentage of energy from fat were lower in the intervention group than in the control group (mean difference between groups at 6 y -8.2 , CI -8.3 to -8.0), but only 14% of women met the dietary target of 20% energy from fat.

CONCLUSION

A dietary modification intervention promoting a low-fat dietary pattern did not reduce risk for breast cancer, colorectal cancer, or cardiovascular disease in postmenopausal women.

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For correspondence: Dr. R.L. Prentice, Fred Hutchinson Cancer Research Center, Seattle, WA, USA. E-mail rprentice@whi.org. Dr. S.A. Beresford, University of Washington, Seattle, WA, USA. E-mail beresfrd@u.washington.edu. Dr. B.V. Howard, MedStar Research Institute, Hyattsville, MD, USA. E-mail barbara.v.howard@medstar.net. ■

*See Glossary.

†Information provided by authors.

(continued on page 7)

(continued from page 6)

Low-fat dietary pattern intervention vs no dietary intervention in postmenopausal women at mean 8.1 years†

Outcomes	Annualized incidence rates		Hazard ratio (95% CI)	RRR (CI)	NNT
	Diet	No diet			
Breast cancer	0.42%	0.45%	0.91 (0.83 to 1.01)	9.0% (–1 to 17)	Not significant
				RRI (CI)	NNH
Colorectal cancer	0.13%	0.12%	1.08 (0.90 to 1.29)	8.0% (–10 to 29)	Not significant
				RRR (CI)	NNT
CHD§	0.35%	0.36%	0.98 (0.88 to 1.09)	2.0% (–9 to 12)	Not significant
Composite CHD	0.63%	0.65%	0.97 (0.90 to 1.06)	3.0% (–6 to 10)	Not significant
				RRI (CI)	NNH
Fatal or nonfatal stroke	0.28%	0.27%	1.02 (0.90 to 1.15)	2.0% (–10 to 15)	Not significant
				RRR (CI)	NNT
Total CVD¶	0.86%	0.88%	0.98 (0.92 to 1.05)	2.0% (–5 to 8)	Not significant
Global index**	1.30%	1.35%	0.95 (0.90 to 1.01)	5.0% (–1 to 9.9)	Not significant

†CHD = coronary heart disease; CVD = cardiovascular disease. Other abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from hazard ratios in article.

§Nonfatal myocardial infarction (MI) or CHD death.

||Nonfatal MI, CHD death, or revascularization.

¶Clinical MI, silent MI, death caused by CHD, revascularization, and stroke.

**Time to the earliest invasive breast cancer, colorectal cancer, CHD, or death from any other cause.

COMMENTARY

The largest prevention trial ever conducted in women has left us with results showing that promoting a low-fat diet does not decrease the risk for breast cancer, colon cancer, or CVD in postmenopausal women 50 to 79 years of age, studied for over 8 years. Wow! It has to be noted that CVD incidence in the control group was only two thirds of the expected rate, and colorectal cancer incidence was also only 70% of the expected rate, resulting in a projected power for each outcome of only 40%.

We are left wondering if the dietary interventions were simply too little and too late. What is important to note is that most participants were well above the ideal body mass index and that the dietary modifications in the intervention group did not result in significant weight loss. Obesity has a huge influence on diabetes, CVD, and breast cancer risk. In addition, it may not solely be the percentage of dietary fat intake that is important in terms of CVD and cancer risk reduction but rather the composition and types of fats. Current guidelines (1) indicate that trans fats (partially hydrogenated oils) should be limited, but the World Health Institute (WHI) dietary modification study did not specifically target trans fats or promote heart-healthy types of fats, such as omega-3 fish oil. It is probable that we are only in the infant stage of understanding how macro- and micronutrient intake relate to disease expression and modification and in preventing and treating obesity.

Prentice and colleagues note in their conclusion about invasive breast cancer that a nonsignificant trend was observed, suggesting a reduced risk for breast cancer associated with a low-fat dietary pattern. They indicate that “a longer planned non-intervention follow-up might yield a more definitive comparison.” Rather than extending a large, expensive, randomized, controlled dietary modification trial, it may be more helpful to specifically look at individualized, targeted, and more intensive dietary changes, perhaps in younger persons, with the goal of lowering body mass index to the normal range. Patients who survived breast cancer were excluded from this trial. It is interesting to note that recently reported data from a study on lifestyle and dietary modification showed improvement in relapse-free survival of postmenopausal patients with estrogen-receptor–negative breast cancer (2).

So what should we be recommending to our patients? As we have learned from the hormone treatment group of the WHI, the timing of an intervention can be important. We should continue to stress the importance of maintaining a normal body weight and a heart-healthy diet low in trans fats and saturated fats for all women; however, telling older overweight women to reduce their total fat intake (without reducing their body weight) to lower their risk for breast or colon cancer or CHD is not supported. Tools are available to further risk-stratify women for breast cancer (3) and CVD (4), the goal of which is to facilitate more intensive targeting of those at high risk with evidence-based therapy; these therapies include the U.S. Food and Drug Administration–approved tamoxifen chemoprevention for women at very high risk for breast cancer and the known evidence-based strategies for women at moderate-to-high risk for CVD. It is clear that reducing an older woman's global fat intake without reducing her fat stores (i.e., improving or normalizing her body mass index) does not lead to any reduction in CVD or breast and colon cancer risks. Interventions to reduce obesity may have more success.

Holly L. Thacker, MD
Women's Health Center
Cleveland, Ohio, USA

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