Vitamin D, Calcium, and Mammographic Breast Densities

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Abstract

Vitamin D and calcium are being evaluated as potential breast cancer prevention agents. This study reports on the relation of dietary vitamin D and calcium to mammographic breast densities, one of the strongest breast cancer risk factors. Participants were women ages 40 to 60 years who had had a screening mammogram in Rhode Island and eastern Massachusetts (1989–1990). Diet was assessed by semiquantitative food frequency questionnaire, and the percentage of the breast showing densities was estimated visually by a single observer without information on subjects. Multivariate logistic regression was used to compare dietary intakes of vitamin D and calcium between women classified as having few densities (≤30% of the breast with density, n = 287) and extensive densities (≥70% of the breast with density, n = 256). For categories of increasing vitamin D intake (<50, 50–99, 100–199, and ≥200 IU/d),

adjusted odds ratios (OR) for extensive densities were 1.00 (reference), 0.51, 0.37, and 0.24, respectively (P for trend = 0.0005). For increasing calcium intake (<500, 500–749, 750–999, and ≥1,000 mg/d), adjusted ORs were 1.00 (reference), 0.63, 0.25, and 0.24, respectively (P for trend = 0.0006). Combination of higher intakes of vitamin D and calcium (≥100 IU/d and ≥750 mg/d, respectively) were associated with a reduction of breast densities (OR, 0.28; 95% confidence interval, 0.15–0.54) compared with those consuming <100 IU/d and <750 mg/d. Increases in vitamin D and calcium intakes were associated with decreases in breast densities, suggesting that dietary vitamin D and calcium could reduce breast cancer risk possibly through influences on breast tissue morphology. (Cancer Epidemiol Biomarkers Prev 2004;13(9):1466–72)

Introduction

Vitamin D and calcium emerge as promising chemopreventive and chemotherapeutic agents for prostate, colon, and breast cancers (1, 2). For instance, the Women's Health Initiative Study Group is presently carrying out a large clinical trial to evaluate the effect of vitamin D and calcium supplementation on several diseases, including breast cancer risk (3). Besides supplements, vitamin D is also available through dietary intake (fish oil, egg yolks, liver, and vitamin D–fortified food such as milk in Canada and United States; ref. 4) and exposure to UV light after conversion of 7-dehydrocholesterol in the skin. Following absorption, vitamin D is first metabolized by the liver into its principal circulating metabolite, 25-hydroxyvitamin D and by the kidneys and other tissues into its most biologically active form, 1,25-dihydroxyvitamin D (5). Biological activities of the latter are mediated by vitamin D receptors, and this partnership is suggested to play a role in negative growth regulation of normal mammary gland and breast cancer cells (6-8). Therefore, vitamin D has the potential to influence the development of breast cancer (9).

Epidemiologic findings concerning the role of vitamin D from either sunlight exposure, diet, or supplemental sources on breast cancer risk or mortality are inconsistent. It has been observed that populations living at sunny lower latitudes (regions with higher levels of solar UV-B radiation) have higher circulating levels of 25-hydroxyvitamin D (10) and have a decreased breast cancer risk (11, 12) and mortality rates (13-16) compared with populations living at higher latitudes (regions with lower levels of UV-B radiation). These findings suggested that part of the relation between sun exposure and breast cancer risk could be explained by the vitamin D metabolic pathways. In addition, two cohort studies reported a negative association between vitamin D and breast cancer risk. Dietary vitamin D was associated with breast cancer risk reduction in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. The risk reduction was slightly greater when using combined vitamin D exposure measures (moderate to considerable sun exposure and a dietary vitamin D intake of ≥200 IU/d) compared with these exposures taken individually (17). Furthermore, recent data from the Nurses' Health Study suggest that, among premenopausal women, dietary vitamin D might protect from breast cancer independently of sun exposure and intake of milk and its constituents, including calcium (18). On the other hand, data from two case-control studies conducted in Canada (19) and Switzerland (20) showed an increasing risk of breast cancer with increasing intake of vitamin D. Statistical significance was reached in one of these studies (20).

Vitamin D also plays a major role in calcium homeostasis. Calcium is an important mineral primarily

found in dairy products. All living cells require calcium to maintain their structures and functions (21). Cellular proliferation and differentiation can be modulated by calcium, and these cell functions are also involved in carcinogenesis. Two cohort (18, 22) and nine case-control (20, 23-30) studies, with the exception of one (25), suggest that calcium intake may be associated with decreased breast cancer risk. However, statistically significant trends and/or associations have been observed in only half of them (18, 22, 28-30).

Increased mammographic breast densities are strongly associated with increased breast cancer risk (31-37). Moreover, extent of mammographic densities have been repeatedly associated with breast epithelial hyperplasia (without atypia), atypia, and carcinoma *in situ* (38-44), histologic changes known to be related with breast cancer risk (45). Thus, it has been suggested that mammographic breast densities might serve as an intermediate marker for breast cancer risk in studies of potential approaches for prevention of the disease (46-50).

To our knowledge, only two studies have examined vitamin D and/or calcium intakes with breast densities and found inconsistent results (51, 52). The first study failed to show any trend in means of breast densities with increasing quartiles of vitamin D intake (*P* for trend = 0.68; ref. 51). This study reported on the intake of vitamin D from food and supplements. Calcium intake was not examined by the authors. In contrast, Holmes et al. (52) found that vitamin D and calcium from foods were both negatively associated with mammographic density among premenopausal women (*P* for trend = 0.02 and 0.01, respectively). The present study reports on the relation of independent and combined dietary intakes of vitamin D and calcium to mammographic breast densities.

Methods

Eligibility. The study subjects were recruited among women ages 40 to 60 years who resided in Rhode Island or eastern Massachusetts and received a screening mammogram between December 1988 and December 1990. Three of the nine participating sites were hospital radiology departments, four were freestanding mammography centers, and two were facilities of a health maintenance organization (Harvard Community Health Plan of New England). All sites used film screen mammography and were accredited by the American College of Radiology.

The eligibility criteria for inclusion in the study were (*1*) no mammogram within the previous 12 months; (*2*) radiologist's findings of no suspicion of malignancy and no significant abnormalities on the current mammogram and a recommendation for a repeat screen in ≥12 months; (*3*) no history of breast lumps, thickening of breast or nipple, nipple irritation, or nipple discharge; (*4*) no history of benign breast disease; and (*5*) no history of breast operation, including breast biopsy, aspiration, implant (prosthesis), or reduction. Eligibility for the study was determined by review of questionnaires completed by the women at the time of mammogram and review of reports provided by the radiologists. Routine paperwork completed by the women at the time of the

mammogram included a consent form granting permission to be contacted for research studies. Women who satisfied the eligibility criteria were sent a letter explaining the study and were contacted by telephone to confirm participation and schedule a face-to-face interview. Women without a work or home telephone number were considered to be ineligible for the study. To remain eligible, a woman needed to be interviewed within 4 months after her mammogram.

A total of 1,688 women were identified as potentially eligible for the study. Among these women, 196 women were excluded due to language barriers (*n* = 37), reduced mental ability (*n* = 4), maintenance on a liquid diet (*n* = 1), or excessive delay (*n* = 154) between the mammogram and the interview. One woman was inadvertently not contacted. Of the 1,491 remaining potentially eligible women, 362 (24.3%) declined to participate. Of those who agreed to participate, 24 women were found to be ineligible during the interview; the eligibility of two could not be confirmed, and film mammograms were not available for 11 women. Women who were inadvertently interviewed 4 months and 1 day (*n* = 2) and 4 months and 1 week (*n* = 2) after the date of the mammogram were retained in the study. Therefore, a total of 1,092 eligible women were available for the present analysis.

Interviews. The interviews were standardized and conducted by trained interviewers. Most interviews took place at home; several took place at another more convenient place for the woman such as her workplace.

The interview focused mainly on assessment of food intake using a semiquantitative food frequency questionnaire, which was based on those developed by Willett et al. (53) and the National Cancer Institute of Canada (54). Information was collected on the average diet over the previous 12-month period. Questions were asked regarding average portion size and frequency of intake of foods consumed ≥12 times in the last year. Measuring guides were used to help subjects estimate average portion size. The questionnaire, covering the consumption of 232 food items, was designed to measure total calories and intakes of nutrients including vitamin D and calcium. In addition, women were asked to report their intake of alcoholic beverages such as light or regular beer, wine, wine coolers, hard liquor, or cordials, including mixed drinks. During the interview, information was collected on past and current smoking status; sociodemographic, menstrual, and reproductive characteristics; and family history of breast cancer.

Mean daily intakes of nutrients were computed primarily by use of the Canadian Nutrient File. Although much of the data in the Canadian Nutrient File have been derived from the U.S. Department of Agriculture Nutrient Database for Standard Reference, this matrix was reviewed by a U.S. registered dietician and modified as needed to ensure that the nutrient composition of each food was representative of foods consumed in the United States at the time data were collected. The nutrient information for foods with compositions that differed from those in Canada and for foods not included in the Canadian file were derived from other sources (55-57) and from the manufacturer, as a last resort.

Mammogram Review. The mammograms were reviewed by one of the authors (J.B.) at the participating

sites without reference to other patient data. This reviewer is experienced in classifying mammographic features (31, 37, 58, 59). The review was based on the mammograms of one breast, chosen at random, for each subject. Mammographic features that were assessed included the percentage of the breast showing densities.

Statistical Analysis. Among the 1,092 women who were recruited, a subset of women was selected based on whether they had few densities ($\leq$30% of the breast with density, n = 287) or extensive densities ($\geq$70% of the breast with density, n = 256). Restricting our analysis to these women was aimed at better discriminating between women at low and high breast cancer risk (37).

Main explanatory variables were the mean daily dietary vitamin D and calcium intakes, both expressed as four categories (0–49, 50–99, 100–199, and $\geq$200 IU/d for vitamin D and 0–499, 500–749, 750–999, and $\geq$1,000 mg/d for calcium) for descriptive and analytic purposes.

Covariates included in models were age (years) at time of screening mammography, body mass index (<27.0, 27.0–30.0, >30.0 kg/m^2), age at menarche (<12, 12, 13, or >13 years), number of births and age at first birth combined (nullipares, 1–2 children and first birth <25 years, >2 children and first birth <25 years, 1–2 children and first birth $\geq$25 years, or >2 children and first birth $\geq$25 years), use of oral contraceptives (nonuser, user <5 years, or user $\geq$5 years), menopausal status and use of hormone replacement therapy (premenopausal, perimenopausal, or postmenopausal nonusers; postmenopausal users for <48 months; or postmenopausal users for $\geq$48 months), family history of breast cancer (yes or no), education expressed in women's age when leaving full-time school (<17, 17–18, or $\geq$19 years), alcohol consumption (0, <0.5, $\geq$0.5 and <1.0, $\geq$1.0 and <2.0, $\geq$2.0 drinks per day), total caloric intake (kcal/d), and smoking status (current, former, or nonsmokers). Menopausal status was defined using similar criteria as the Nurses' Health Study (60). Women were considered premenopausal if they had at least one natural menstrual cycle in the previous 12 months or were <48 years (if a nonsmoker) or 46 years (if a smoker) after hysterectomy without bilateral oophorectomy. Women were considered as postmenopausal if they reported complete cessation of menses for $\geq$12 months and previous bilateral oophorectomy and were ages $\geq$56 years (if a nonsmoker) or 54 years (if a current smoker) after hysterectomy without bilateral oophorectomy or uninterrupted menses following continuous use of hormonal derivatives. Women ages between 48 and 55 years (if nonsmokers) or between 46 and 53 years (if current smokers) who had hysterectomy without bilateral oophorectomy or uninterrupted menses following continuous use of hormonal derivatives were considered as perimenopausal. Family history of breast cancer was defined as having at least one relative (mother, sister, daughter, maternal or paternal grandmother, or aunt) with breast cancer.

Unconditional logistic regressions were carried out to examine whether vitamin D or calcium intake were related to the presence of extensive densities. Categories of the explanatory variables as described above were first used in the multivariate models. In Table 2, models 1 and 2 take simultaneously into account the same covariates, except that models are mutually adjusted for dietary calcium or vitamin D intake, respectively. P for trend in

odds ratios (OR) were calculated with the Wald statistics using a single variable, taking as values the median for each of the four categories of intake in women with few densities. Combined effect of dietary vitamin D and calcium intakes on mammographic densities were done using dichotomized vitamin D (0–99 or $\geq$100 IU/d) and calcium (0–749 or $\geq$750 mg/d) intakes. All statistical analyses were carried out using the Statistical Analysis System software (SAS Institute, Inc., Cary, NC).

Results

Study Population. Among the 1,092 participants, the overall mean $\pm$ SD and median of the percentage of the breast showing densities were 48.2 $\pm$ 22.5% and 50.0%, respectively. The present analysis is restricted to women classified as having few densities ($\leq$30% of the breast with density, n = 287) or extensive densities ($\geq$70% of the breast with density, n = 256). These women account for 26.3% and 23.4% of the cohort, respectively. Characteristics of these two groups are presented in Table 1. As compared with women having few densities, those with extensive densities were younger and leaner. Women with extensive densities had lower mean parity and higher mean age at first birth than women with few densities. They were also more likely to have ever taken

Table 1. Characteristics of women according to whether they had $\leq$30% or $\geq$70% of the breast showing mammographic densities

	Mammographic densities*	
	$\leq$30% (n = 287)	$\geq$70% (n = 256)
Age, y (mean $\pm$ SD)	51.4 $\pm$ 5.7	46.1 $\pm$ 4.5
Body mass index, kg/m^2 (mean $\pm$ SD)	28.9 $\pm$ 6.0	23.3 $\pm$ 3.1
Age at menarche, y (mean $\pm$ SD)	12.5 $\pm$ 1.6	12.7 $\pm$ 1.5
Parity (mean $\pm$ SD)	3.0 $\pm$ 1.7	2.1 $\pm$ 1.4
Age at first birth,[†] y (mean $\pm$ SD)	23.2 $\pm$ 3.9	24.7 $\pm$ 4.8
Oral contraceptive use (%)	55.4	70.1
Menopausal status (%)		
Premenopausal	31.4	75.3
Perimenopausal	7.0	4.7
Postmenopausal	61.7	20.0
Hormone replacement therapy use (%)[‡]	41.3	49.0
Family history of breast cancer[§] (%)	23.2	32.0
Age when leaving full time school, y (mean $\pm$ SD)	18.3 $\pm$ 2.3	19.3 $\pm$ 2.7
Daily average alcohol intake, drinks (mean $\pm$ SD)	0.30 $\pm$ 0.57	0.55 $\pm$ 0.89
Daily average caloric intake, kcal (mean $\pm$ SD)	1,964 $\pm$ 730	1,994 $\pm$ 760
Smoking status (%)		
Nonsmoker	43.6	45.7
Former smoker	37.3	27.7
Current smoker	19.2	26.6

*Percentage of the breast showing mammographic densities.
[†]In parous women.
[‡]In postmenopausal women.
[§]Mother, sister, daughter, maternal or paternal grandmother, or aunt.

oral contraceptives (70.1% as compared with 55.4%), to be premenopausal (75.3% as compared with 31.4%), and, if postmenopausal, to have ever used hormone replacement therapy (49.0% as compared with 41.3%). Women with extensive densities more frequently reported a family history of breast cancer. Mean alcohol intake was higher in women with extensive densities, these women being also more likely to report current smoking at time of screening mammography. The two groups of women were quite similar with respect to age at menarche, education, and daily caloric intake. Women with few densities and women with extensive densities had similar mean daily intakes of proteins (82 and 80 g, respectively), carbohydrates (235 and 242 g, respectively), and lipids (74 and 72 g, respectively).

Dietary Vitamin D and Calcium Intakes and Mammographic Densities. After adjusting for known and suspected breast cancer risk factors, vitamin D and calcium intakes were both associated with mammographic densities (Table 2). Using women consuming <50 IU/d of vitamin D as reference, we observed a progressive decrease in the OR [95% confidence interval (95% CI)] of extensive versus few densities to 0.51 (0.23–1.11), 0.37 (0.18–0.76), and 0.24 (0.11–0.53) for those consuming 50–99, 100–199, and ≥200 IU/d, respectively. Similarly, using women consuming <500 mg/d of calcium as reference, we observed a progressive decrease in the OR (95% CI) of extensive versus few densities to 0.63 (0.30–1.32), 0.25 (0.11–0.54), and 0.24 (0.10–0.57) for those consuming 500–749, 750–999, and ≥1,000 mg/d, respectively. Both trends in decreasing ORs with increasing vitamin D or calcium intake were statistically significant (model 1; $P = 0.0005$ and 0.0006, respectively). Trends in decreasing ORs with increasing intakes of vitamin D and calcium were observed in premenopausal and postmenopausal women. For categories of increasing vitamin D intake (<50, 50–99, 100–199, and ≥200 IU/d), adjusted ORs for extensive densities were 1.00 (reference), 0.24, 0.25, and 0.13 (P for trend = 0.003), respectively, in premenopausal women and 1.00 (refer-

ence), 1.04, 0.33, and 0.30 (P for trend = 0.05), respectively, in postmenopausal women. For increasing calcium intake (<500, 500–749, 750–999, and ≥1,000 mg/d), adjusted ORs were 1.00 (reference), 0.33, 0.09, and 0.13 (P for trend = 0.003), respectively, in premenopausal women and 1.00 (reference), 1.21, 0.55, and 0.27 (P for trend = 0.06), respectively, in postmenopausal women.

The negative associations between dietary vitamin D and calcium and mammographic densities were still apparent after further adjustment for each other, but the strength of associations for each category of intake was reduced and the trends were no longer statistically significant (model 2).

Combination of higher intakes of vitamin D and calcium were negatively associated with mammographic densities (Table 3). The OR (95% CI) of extensive versus few densities for women consuming ≥100 IU/d of vitamin D and ≥750 mg/d calcium was 0.28 (0.15–0.54) when compared with those consuming <100 IU/d of vitamin D and <750 mg/d of calcium. In addition, mean daily moderate dietary intakes of vitamin D (≥100 IU/d) and calcium (≥750 mg/d) were independently associated with a reduction of mammographic densities (ORs, 0.79 and 0.52, respectively), although these reductions were not statistically significant.

Discussion

Our data suggest that increases in vitamin D and calcium intakes are associated with decreases in mammographic breast densities, which have been associated with decreased risk of breast cancer in other studies. Thus, our results support the idea that dietary vitamin D and calcium may be helpful for the prevention of breast cancer.

A diet rich in calcium and vitamin D might reduce breast densities and the risk of breast cancer via the antiproliferative action of these nutrients. There is growing evidence that the hormone 1,25-dihydroxyvitamin D, the biologically active form of vitamin D, might

Table 2. Relation of dietary vitamin D or calcium intake to mammographic densities

	Median	Mammographic densities*		Model 1[†] [OR (95% CI)]	Model 2[‡] [OR (95% CI)]
		≤30% ($n = 287$)	≥70% ($n = 256$)		
Dietary vitamin D, IU/d					
0–49[§]	24	51	64	1.0	1.0
50–99	74	57	55	0.51 (0.23–1.11)	0.58 (0.25–1.35)
100–199	134	91	72	0.37 (0.18–0.76)	0.55 (0.23–1.31)
≥200	263	88	65	0.24 (0.11–0.53)	0.40 (0.14–1.13)
P for trend				0.0005	0.1283
Dietary calcium, mg/d					
0–499[§]	428	54	62	1.0	1.0
500–749	623	78	68	0.63 (0.30–1.32)	0.85 (0.37–1.95)
750–999	849	81	54	0.25 (0.11–0.54)	0.39 (0.15–1.00)
≥1,000	1,201	74	72	0.24 (0.10–0.57)	0.47 (0.14–1.53)
P for trend				0.0006	0.1760

*Percentage of the breast showing mammographic densities.
[†]Model 1: these adjusted models take simultaneously into account the following factors: age, body mass index, age at menarche, number of birth and age at first birth combined, use of oral contraceptive, menopausal status and use of hormone replacement, family history of breast cancer, education, alcohol, total caloric intakes, and smoking status.
[‡]Model 2: these adjusted models take simultaneously into account the same covariates as in model 1 and are mutually adjusted for dietary calcium (0–499, 500–749, 750–999, and ≥1,000 mg/d) or vitamin D (0–49, 50–99, 100–199, and ≥200 IU/d) intake, respectively.
[§]Reference category.

Table 3. Relation of combined dietary intakes of vitamin D and calcium to mammographic densities

Dietary calcium, mg/d	Dietary vitamin D, IU/d	
	<100	≥100
<750	1.0 [95/86]	0.79 (0.36–1.74) [35/46]
≥750	0.52 (0.18–1.49) [24/22]	0.28 (0.15–0.54) [102/133]

NOTE: The odds in brackets represent the number of women with extensive versus the number of those with few densities. ORs (95% CIs) were adjusted for age, body mass index, age at menarche, age at first birth and number of birth combined, use of oral contraceptive, menopausal status and use of hormone replacement, family history of breast cancer, education, smoking status, alcohol, and total caloric intakes. The reference category corresponds to women with daily dietary intakes of vitamin D <100 IU/d and calcium <750 mg/d.

play an important role in breast tissue morphogenesis. Vitamin D receptors are present in the nucleus of normal and transformed breast cells, and its signaling effects include inhibition of cellular proliferation, induction of differentiation, and/or apoptosis (6, 61, 62). Moreover, some *VDR* gene polymorphisms have been associated with breast cancer risk (63-65). In breast cancer, vitamin D has also been shown to down-regulate the levels of estrogen receptors and to suppress the actions of 17β-estradiol (E_2) as well as to modulate the activities of several other genes implicated in the regulation of growth factors and the cell cycle (6, 61). Although vitamin D is involved in the modulation of the calcium channel activity in a cell, calcium has the potential to affect the regulation of cellular proliferation and differentiation independently of the presence of vitamin D (21, 66). Russo and Russo (66) have observed a growth arrest of human breast epithelial cells when cultured in high concentration of calcium and were able to spontaneously immortalize this cell line by maintaining it in medium containing low calcium.

In Canada and the United States, dietary intakes of vitamin D and calcium are strongly associated and separation of their effects on breast density can be difficult. In both countries, milk is the predominant vehicle for vitamin D fortification (4), and dairy products are also a major source of calcium. Accordingly, vitamin D and calcium intakes were strongly correlated in our study population (Pearson $r = 0.74$; $P < 0.0001$). Although there was no overt problem of colinearity in models containing both nutrients, this high correlation might seriously impair the ability to adequately measure the individual association of each of these nutrients with densities. In our analysis, simultaneous adjustment for vitamin D and calcium intakes reduced the strength of their respective association with breast densities although each nutrient continued to be associated with a reduction in the OR of extensive densities. Among studies that examined the relation of vitamin D and calcium with breast cancer risk, only two took into account simultaneously the intakes of vitamin D and calcium (17) or dairy products (18) in their multivariate models.

In the present study, misclassification of vitamin D and calcium intakes, which were derived from semi-quantitative food frequency questionnaire, is likely. However, this type of questionnaire (based on self-report) has been found to be reliable and valid (67). In addition, differential recall bias is unlikely because women were not aware of the specific study objectives regarding vitamin D and calcium intakes at time of data collection. Thus, misclassification of dietary vitamin D and calcium intakes is likely to be random. In other respects, whether it is recent diet, as measured in the present study, or diet in a more distant past that is a key contributor to mammographic features is unknown. In addition, our analyses are based on vitamin D and calcium intakes from diet only. Intakes of these nutrients from supplements were not available. Vitamin D from diet or from supplements represents only a part of vitamin D intake, whereas sun exposure contributes to a large extent to vitamin D status, but the latter was not measured here.

Additional factors related to high-risk mammographic features are not likely to have affected our results substantially because adjustments were made for key factors associated with densities. Total caloric intake was also taken into account in multivariate analysis.

Our data clearly illustrate that, for a large proportion of women, intakes of vitamin D and calcium is by far less than that recommended. Only 28.2% of women included in the present analysis consumed ≥200 IU/d of vitamin D, which would be considered an adequate intake for participants ages ≤50 years and is only half the adequate intake for older participants (68). These results are similar to those of John et al. (17), who reported a mean daily intake of ≥200 IU/d for 26% of women ages 24 to 50 years in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study analytic cohort. Moreover, it is well known that prevalence of vitamin D insufficiency is high in Canada, the United States (4), and several other countries worldwide (69, 70), particularly during wintertime and regardless of population's age. Inadequate calcium intake is also frequent. In our analysis, most women (73.1%) consumed <1,000 mg/d of calcium, a level considered to be adequate intake for participants ages ≤50 years, whereas 1,200 mg/d is the adequate intake for older participants. Milk, which is fortified with vitamin D, and fish, especially high fat fish such as salmon, herring, and mackerel, constitute the major sources of dietary vitamin D. Milk and other dairy products are the key sources of calcium.

Our findings that increased dietary intakes of vitamin D and calcium seem to be associated with decreased mammographic densities suggest that these nutrients may ultimately affect breast cancer risk through influences of these nutrients on the morphology of breast tissue. Our findings also support the idea of potential health benefits of reaching the recommended dietary intakes of vitamin D and calcium (68, 71, 72), which are seemingly not yet being reached by a large proportion of women in North America.

Acknowledgments

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