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Supplemental Material

Serum Vitamin D and Risk of Breast Cancer within Five Years

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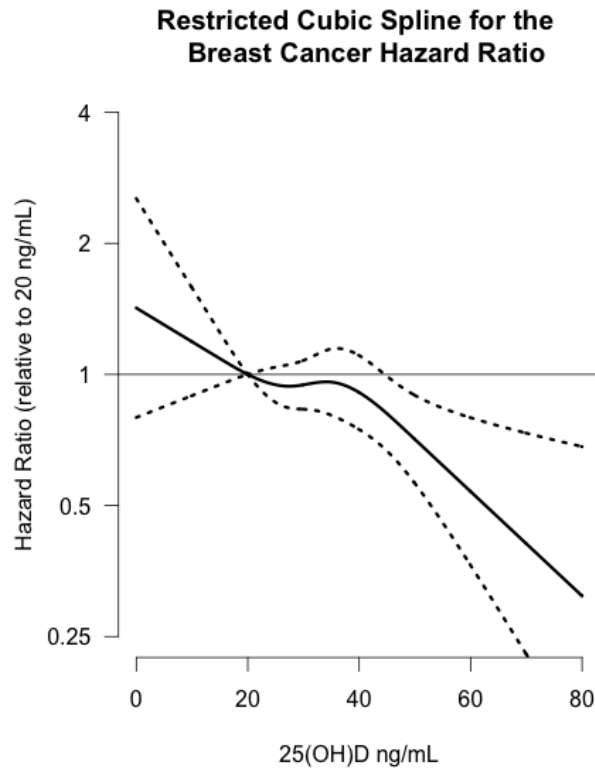


Figure 1: A restricted cubic spline modeling hazard ratios for the association between total 25(OH)D and breast cancer within 5 years, relative to the breast cancer hazard at 20 ng/mL. The dashed lines indicate 95% confidence intervals. Knots were placed at the 5th, 35th, 65th, and 95th percentiles.

Table 1. Time since blood draw, 25(OH)D and breast cancer in the Sister Study.

Description of Analysis	Sample Size ^a		Categories of 25(OH)D (in ng/mL)	Hazard Ratio (95% Confidence Interval)
	Cases	Sub-cohort		
Exclude first two years of follow-up time	1003	1770	1 st Quartile (0-24.6)	1.00
			2 nd Quartile (>24.6-31.4)	1.08 (0.86-1.36)
			3 rd Quartile (>31.6-38.0)	1.00 (0.79-1.26)
			4 th Quartile (>38.0)	0.77 (0.60-0.99)
Exclude last two years of follow-up time	977	1822	1 st Quartile (0-24.6)	1.00
			2 nd Quartile (>24.6-31.4)	1.05 (0.84-1.31)
			3 rd Quartile (>31.4-38.0)	1.00 (0.79-1.26)
			4 th Quartile (>38.0)	0.72 (0.56-0.93)

All models are adjusted for batch, seasonal trends, race, education level, current hormonal birth control use, current hormone therapy type, menopausal status, physical activity, BMI, osteoporosis, parity, alcohol consumption, and a BMI by menopausal status interaction term.

^aSample size with complete covariate information.

Table 2. Hazard ratios (HR) and 95% confidence intervals (CI) for the association between vitamin-D related exposures and breast cancer within 5 years (370 premenopausal cases, 1,329 post-menopausal cases, 49,044 non-cases)

	Premenopausal HR (95% CI)	Post-menopausal HR (95% CI)
Total vitamin D intake (supplement + diet)^a		
<200 IUs	1.00	1.00
200-399 IUs	1.10 (0.82, 1.47)	0.97 (0.82, 1.15)
400-599 IUs	1.28 (0.99, 1.67)	0.91 (0.80, 1.05)
≥600 IUs	1.20 (0.84, 1.70)	0.83 (0.71, 0.98)
per 100 IUs	1.06 (1.01, 1.10) ^b	0.98 (0.96, 1.00) ^b
Regular vitamin D supplementation^{c,d}		
No	1.00	1.00
Yes	1.13 (0.92, 1.39) ^b	0.83 (0.74, 0.93) ^b
Hours per week doing any sports/exercise (including walking)^e		
0-2 hours/week	1.00	1.00
>2-5 hours/week	0.88 (0.59, 1.32)	0.87 (0.70, 1.07)
>5-10 hours/week	0.95 (0.66, 1.37)	0.92 (0.76, 1.12)
>10 hours/week	0.93 (0.64, 1.35)	0.89 (0.73, 1.08)
per hour/week	1.00 (0.98, 1.02)	1.00 (0.99, 1.01)
Latitude, current residence^f		
≤34°	1.00	1.00
35-39°	0.99 (0.73, 1.35)	1.07 (0.92, 1.24)
40-42°	1.11 (0.83, 1.49)	1.01 (0.87, 1.18)
>42°	1.30 (0.94, 1.81)	0.99 (0.84, 1.18)
Per degree	1.02 (1.00, 1.04)	1.00 (0.99, 1.01)
Hours spent outdoors per year^g		
0-320	1.00	1.00
321-530	1.05 (0.79, 1.39)	1.01 (0.86, 1.17)
531-850	0.98 (0.73, 1.30)	0.93 (0.80, 1.08)
>850	0.94 (0.70, 1.27)	0.93 (0.80, 1.08)
Per 200 hours/year	1.00 (0.95, 1.05)	0.99 (0.97, 1.01)

All covariates in the table were assessed during the baseline interview, unless otherwise specified.

^aAdjusted for age, race, education, physical activity, BMI, current birth control use, current hormone therapy type, current alcohol use, total energy intake, osteoporosis, and parity. Women with energy intake <400 or >4,000 were excluded from the analysis.

^bP for heterogeneity by menopausal status <0.05

^cAdjusted for age, race, education, physical activity, BMI, current birth control use, current hormone therapy type, current alcohol use, osteoporosis, and parity

^dWomen who took a multivitamin or separate vitamin D supplement at least 4 times per week were considered regular users.

^eAdjusted for age, race, education, BMI, current birth control use, current hormone therapy type, current alcohol use, osteoporosis, and parity.

^fAdjusted for age, race, education

^gAdjusted for age, race, education, physical activity, hours walked per week, BMI, current birth control use, current hormone therapy type, current alcohol use, osteoporosis and parity.

Table 3. Means (standard deviation) of measured total 25(OH)D by covariates of interest in all sub-cohort members (n= 1,843).

	N (%)	Season and batch-adjusted total 25(OH)D in ng/mL
Overall	1843 (100)	31.8 (10.5)
Age at blood draw		
35-49	538 (29)	29.7 (10.6)
50-59	727 (39)	31.5 (10.3)
60-74	578 (31)	34.0 (10.3)
Season of blood draw^a		
Spring (weeks 9-21)	507 (28)	30.3 (10.9)
Summer (weeks 22-34)	530 (29)	34.1 (10.7)
Fall (weeks 35-47)	396 (21)	32.2 (9.8)
Winter (weeks 47-53 and 1-8)	410 (22)	29.8 (10.6)
Latitude		
<34°	495 (27)	31.5 (10.1)
35-39°	467 (25)	30.8 (10.7)
40-42°	539 (29)	31.8 (10.6)
>42°	337 (18)	33.4 (10.7)
Race/Ethnicity		
Non-Hispanic White	1,589 (86)	32.8 (10.2)
Non-Hispanic Black	134 (7)	21.0 (9.7)
Hispanic	82 (4)	28.8 (8.6)
Other	38 (2)	33.2 (9.8)
Education level at baseline		
High school or less	294 (16)	32.7 (12.1)
Some college	645 (35)	31.4 (10.3)
Bachelor's degree	471 (26)	31.4 (10.1)
Graduate degree	433 (23)	32.0 (10.3)
Menopausal status at baseline		
Premenopausal	616 (33)	29.9 (10.8)
Postmenopausal	1226 (67)	32.7 (10.3)
Baseline body mass index		
<25.0 kg/m ²	705 (38)	35.1 (10.6)
25-29.9 kg/m ²	586 (32)	31.6 (9.8)
≥30 kg/m ²	549 (30)	27.6 (9.7)
Parity		
0 births	343 (19)	30.8 (10.5)
1 birth	277 (15)	30.9 (10.7)
2 births	669 (36)	31.9 (10.4)
≥3 births	553 (30)	32.6 (10.6)
Hormonal birth control use		
Current user	75 (4)	36.0 (13.7)
Former user	1,495 (81)	31.6 (10.4)
Never user	265 (14)	31.5 (9.9)
Hormone therapy use		
Current user	192 (10)	33.8 (10.2)
Former user	626 (34)	32.7 (9.8)
Never user	1,019 (55)	30.8 (10.9)
Physical activity (last year)		
0 – 1 hours/week	640 (35)	28.2 (10.3)
1.1 – 3 hours/week	563 (31)	32.1 (9.6)
>3 hours/week	640 (35)	34.9 (10.5)
Walking		
0-2 hours/week	426 (23)	30.3 (10.9)

2.1-6 hours/week	842 (46)	31.8 (10.1)
6.1-10 hours/week	273 (15)	33.0 (10.8)
>10 hours/week	299 (16)	32.6 (10.8)
Alcohol consumption in last year		
Never/Former drinker	342 (19)	29.8 (10.8)
Current drinker, <1 drink/day	1,241 (68)	31.6 (10.3)
Current drinker, \geq 1 drink/day	255 (14)	35.0 (10.4)
Regular vitamin D supplement use (\geq4x/wk)		
None	847 (47)	28.7 (10.5)
Multivitamin, no extra vitamin D	736 (41)	33.9 (9.4)
Multivitamin and vitamin D	134 (7)	38.4 (10.7)
Vitamin D and calcium	76 (4)	34.7 (10.7)
Vitamin D, no multivitamin or calcium	10 (1)	32.1 (7.2)
Regular vitamin D use		
No	847 (47)	28.7 (10.5)
Yes	956 (53)	34.5 (9.8)
Daily vitamin D use		
No	1,044 (58)	29.3 (10.3)
Yes	759 (42)	35.1 (9.8)
Osteoporosis		
No	1,408 (76)	30.8 (10.5)
Yes	434 (24)	35.0 (10.1)
Family history of breast cancer		
1 affected sister	1,368 (74)	32.0 (10.6)
>1 first degree relative	475 (26)	31.2 (10.5)
Minimum diagnosis age of affected sister		
18-40	388 (21)	29.8 (10.3)
41-50	719 (39)	31.2 (10.4)
51-60	551 (30)	32.5 (10.3)
>60	183 (10)	35.4 (10.9)
Time spent outdoors (hours/year)		
0-320	466 (25)	30.3 (10.9)
321-530	431 (24)	31.5 (9.4)
531-850	453 (25)	32.2 (10.5)
>850	483 (26)	32.9 (11.1)
Dietary vitamin D intake (IUs)		
0-75	493 (27)	30.1 (11.3)
76-125	435 (24)	31.7 (10.3)
126-200	438 (24)	32.2 (10.5)
>200	437 (24)	33.4 (9.5)
Prophylactic mastectomy		
No	1,834 (100)	31.8 (10.5)
Yes	9 (0)	31.3 (13.3)
History of tamoxifen use		
No	1,803 (98)	31.7 (10.6)
Yes	37 (2)	32.4 (9.7)
History of raloxifene use		
No	1,688 (92)	31.6 (10.6)
Yes	152 (8)	34.0 (8.9)

^aTotal 25(OH)D values adjusted for batch only