

#### Thriving and Breast Cancer: What We've Learned from the Pathways Study Webinar

# Vitamin D May Make A Difference After A Breast Cancer Diagnosis

Song Yao, PhD // Professor of Oncology

**Roswell Park Comprehensive Cancer Center** 

02.06.2023



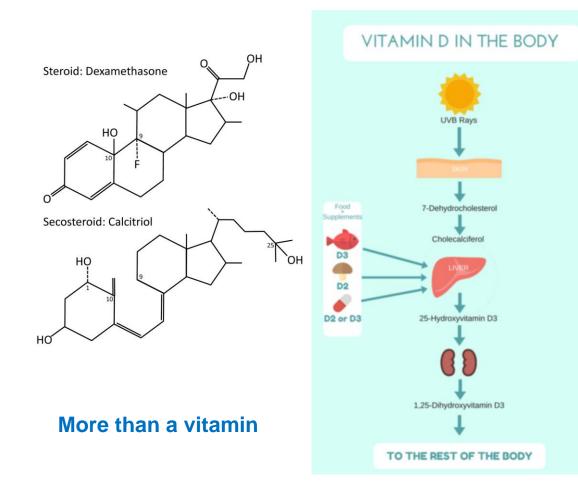








### What is Special about Vitamin D?



#### Sunshine and skin color Jablonski showed that humans' skin is darker where ultraviolet light is strongest-in the Scandinavians have pale skin tropics, at high altitude, and by the oceans, to absorb vitamin D in the as shown by the map shading. muted light of the far north. Tibetans living on the high-altitude Tibetan Plateau have relatively dark skin. Native North Americans show a gradient in skin tone, from dim northern The Bougainville islanders have very latitudes to the sunny tropics. dark skin because they live under cloudless skies near the equator and near water. Bolivian highlanders have dark skin from the intense UV light in the Andes mountains. The Chopi of Mozambique have dark skin because they live near the equator and the coast.

SCIENCE 21 Nov 2014 Vol 346, Issue 6212 pp. 934-936





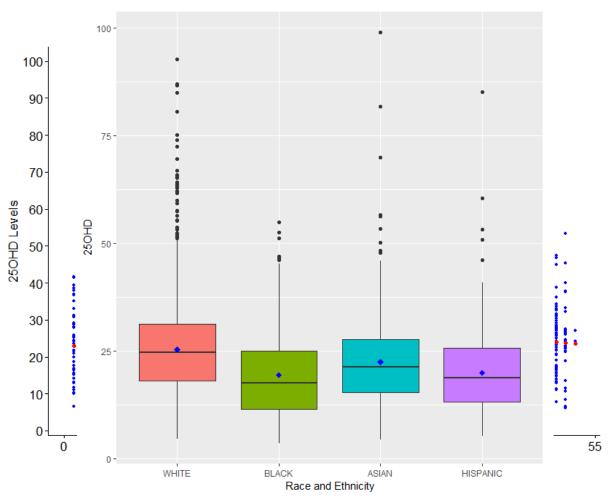






## Where Do We Get Vitamin D?

Variables	R^2 (%)
Vitamin D supplement use	8.95
Body mass index	6.96
Race and ethnicity	3.38
Age at diagnosis	1.18
AJCC stage	0.84
Physical activity	0.59
Employment status	0.49
Season of blood collection	0.41
Polygenic score	0.31
Dietary vitamin D intake	0.25
Menopausal status at diagnosis	0.08
TOTAL	22.8





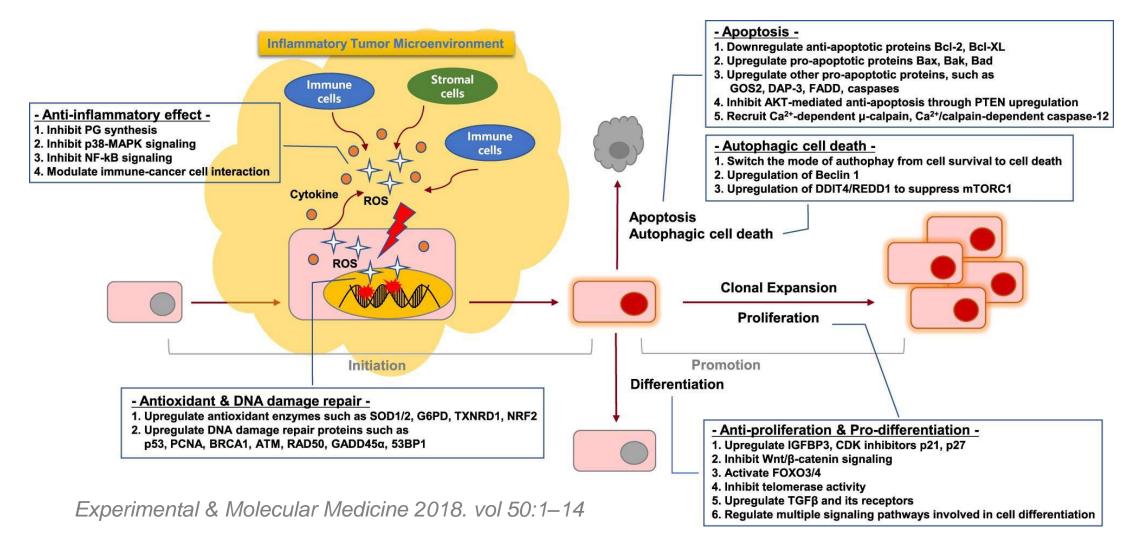








## What is the Relevance of Vitamin D and Breast Cancer?









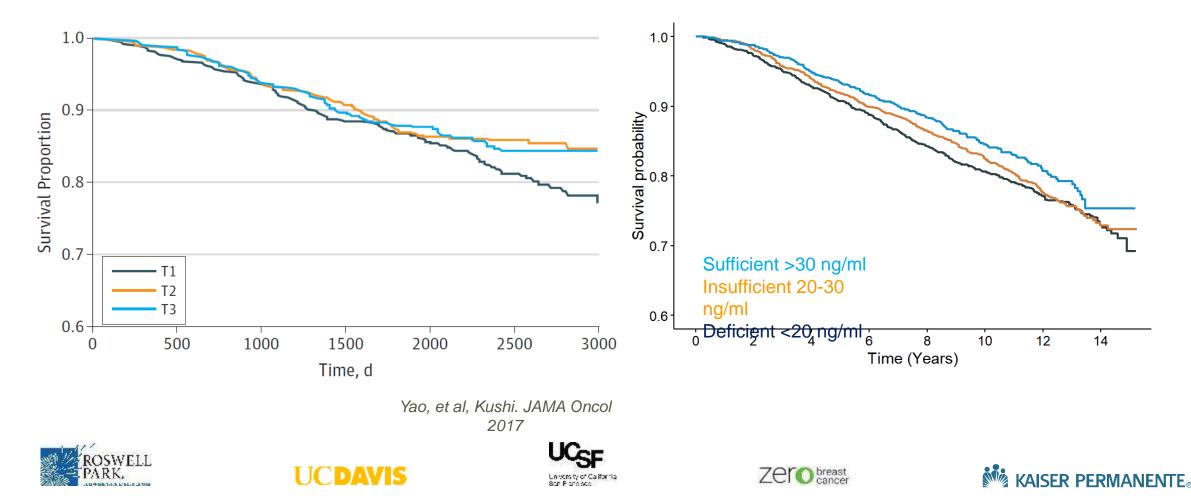




#### What Do Data from Pathways Study Tell Us?

2013: 1,666 patients median f/u 84 months





## What Do Data from Pathways Study Tell Us?

Hazard Ratios (and 95 CI) for Overall Survival by Serum Vitamin D Levels						
Vitamin D N events / Total	M1: non-clinical factors	M2: M1+ clinical factors	M3: M2 + treatment factors			
levels		HR (95% CI)	HR (95% CI)	HR (95% CI)		
Deficient	360 / 1,518	1.00	1.00	1.00		
Insufficient	326 / 1,487	0.89 (0.76-1.04)	1.00 (0.85-1.19)	1.02 (0.88-1.21)		
Sufficient	178 / 990	0.68 (0.56-0.82)	0.78 (0.63-0.95)	0.78 (0.64-0.96)		
P for trend		6.5e-06	0.008	0.01		
M4 non aligical factores and at diagraphic reactions to the second of black callestics, where is a stirity conclusion status						

M1 non-clinical factors: age at diagnosis, race/ethnicity, season of blood collection, physical activity, smoking status M2 clinical factors: covariates in M1, plus tumor stage, grade, and IHC subtype M3 treatment factors: covariates in M2, plus surgery, radiation therapy, chemotherapy, endocrine therapy.





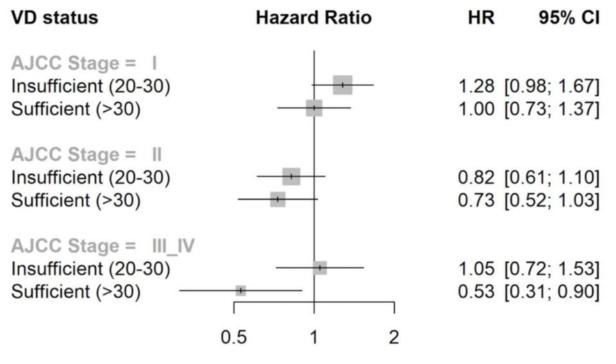






#### **The Impact of Breast Cancer Stage**

Stage	No. (%)	Mean $\pm$ SD	P-value
Stage I	2,157 (54.7)	22.5 (21.6-23.4)	7.0e-20
Stage II	1,360 (34.4)	20.9 (20.0-21.8)	
Stage III/IV	429 (10.9)	19.8 (18.6-21.0)	



<u>*P* for interaction = 0.006</u>











#### Put the Results in the Context

	No of events/total				
Study	Vitamin D	Control	Risk ratio (95% CI)	Weight (%)	Risk ratio (95% CI)
Cancer mortality					
Trivedi 2003	63/1345	72/1341		14.1	0.87 (0.63 to 1.21
Lappe 2007	13/446	17/445		3.3	0.76 (0.38 to 1.55
Prince 2008	1/151	5/151		1.0	0.20 (0.02 to 1.69
Zhu 2008	2/39	5/40	· · · · · · · · · · · · · · · · · · ·	1.0	0.41 (0.08 to 1.99
Sanders 2010	7/1131	10/1127		2.0	0.70 (0.27 to 1.83
Lehouck 2012	0/91	2/92	4	0.5	0.20 (0.01 to 4.15
RECORD 2012	151/2649	178/2643	-	34.8	0.85 (0.69 to 1.04
Baron 2015	8/1130	2/1129		0.4	4.00 (0.85 to 18.7
Martineau 2015	1/122	1/118	*	→ 0.2	0.97 (0.06 to 15.2
Uusi-Risi 2015	0/204	2/205	•	0.5	0.20 (0.01 to 4.16
ViDA 2017	28/2558	30/2550		5.9	0.93 (0.56 to 1.55
VITAL 2018	154/12 927	187/12 944		36.5	0.82 (0.67 to 1.02
Total (95% CI)	428/22 793	511/22 785	+	100.0	0.84 (0.74 to 0.95
Test for heterogeneity	/: χ <sup>2</sup> =8.60, df=11,	P=0.66; I <sup>2</sup> =0%			
Test for overall effect:	Z=2.77, P=0.006				
Cardiovascular mort	ality				
Brohult 1973	1/25	0/25	4	→ 0.1	3.00 (0.13 to 70.3
Inkovaara 1983	5/45	3/42		→ 0.5	1.56 (0.40 to 6.1
Trivedi 2003	101/1345	117/1341		17.3	0.86 (0.67 to 1.1
Sanders 2010	17/1131	13/1127		- 1.9	1.30 (0.64 to 2.67
Lips 2010	1/114	0/112		> 0.1	2.95 (0.12 to 71.6
Cherniack 2011	1/23	0/23		→ 0.1	3.00 (0.13 to 70.0
Punthakee 2012	0/607	1/614	< · · · · · · · · · · · · · · · · · · ·	→ 0.2	0.34 (0.01 to 8.20
RECORD 2012	350/2649	376/2643		55.7	0.93 (0.81 to 1.00
Massart 2014	0/29	1/32	< · · · · · · · · · · · · · · · · · · ·	→ 0.2	0.37 (0.02 to 8.60
EVITA 2017	12/199	9/201		- 1.3	1.35 (0.58 to 3.12
ViDA 2017	18/2558	15/2550		2.2	1.20 (0.60 to 2.3
VITAL 2018	152/12 927	138/12 944		20.4	1.10 (0.88 to 1.39
Total (95% CI)	658/21 652	673/21 654	+	100.0	0.98 (0.88 to 1.08
Test for heterogeneity	/: χ <sup>2</sup> =6.74, df=11,	P=0.82; I2=0%		51 * S (2) * (3) (3) (3)	
Test for overall effect:					
Non-cancer, non-car	diac mortality				
Inkovaara 1983	2/45	2/42	4	→ 0.4	0.93 (0.14 to 6.33
RECORD 2012	335/2558	327/2550	•	64.2	1.02 (0.89 to 1.18
ViDA 2017	19/2558	13/2550		2.6	1.46 (0.72 to 2.94
VITAL 2018	179/12 927	168/12 944	-	32.9	1.07 (0.87 to 1.32
Total (95% CI)	535/18 088	510/18 086	+	100.0	1.05 (0.93 to 1.18
Test for heterogeneity	/: χ <sup>2</sup> =1.01, df=3, P	=0.80; 12=0%	0.2 0.5 1 2	5	
Test for overall effect:	Z=0.78, P=0.44		Favours vitamin D	Favours	

ROSWELL PARK. Yang et al. BMJ 2019



 Table 2. Hazard Ratios and 95% Confidence Intervals for the Primary, Secondary, and Other End Points,

 According to Randomized Assignment to Vitamin D or Placebo, in Intention-To-Treat Analyses.<sup>‡</sup>

End Point	Vitamin D Group (N=12,927)	Placebo Group (N = 12,944)	Hazard Ratio (95% CI)
End Point	no. of participa	(95% CI)	
Cancer	no. oj parucipa	nis with event	
	793	824	0.96 (0.88-1.06)
Primary end point: invasive cancer of any type Breast cancer	124	122	
	124		1.02 (0.79-1.31)
Prostate cancer		219	0.88 (0.72-1.07)
Colorectal cancer	51	47	1.09 (0.73-1.62)
Death from cancer Cardiovascular disease	154	187	0.83 (0.67–1.02)
	396	409	0.97 (0.85-1.12)
Primary end point: major cardiovascular event			
Cardiovascular event in expanded composite end point:	536	558	0.96 (0.86-1.08)
Myocardial infarction	169	176	0.96 (0.78–1.19)
Stroke	141	149	0.95 (0.76-1.20)
Death from cardiovascular causes	152	138	1.11 (0.88-1.40)
Other cardiovascular end point§			
PCI	182	188	0.97 (0.79–1.19)
CABG	73	98	0.75 (0.55-1.01)
Death from myocardial infarction	24	15	1.60 (0.84-3.06)
Death from stroke	19	23	0.84 (0.46-1.54)
Death from any cause	485	493	0.99 (0.87-1.12)
Analyses excluding the first 2 yr of follow-up			
Invasive cancer of any type	490	522	0.94 (0.83-1.06)
Death from cancer	112	149	0.75 (0.59-0.96)
Major cardiovascular event	274	296	0.93 (0.79-1.09)
Death from any cause	368	384	0.96 (0.84-1.11)

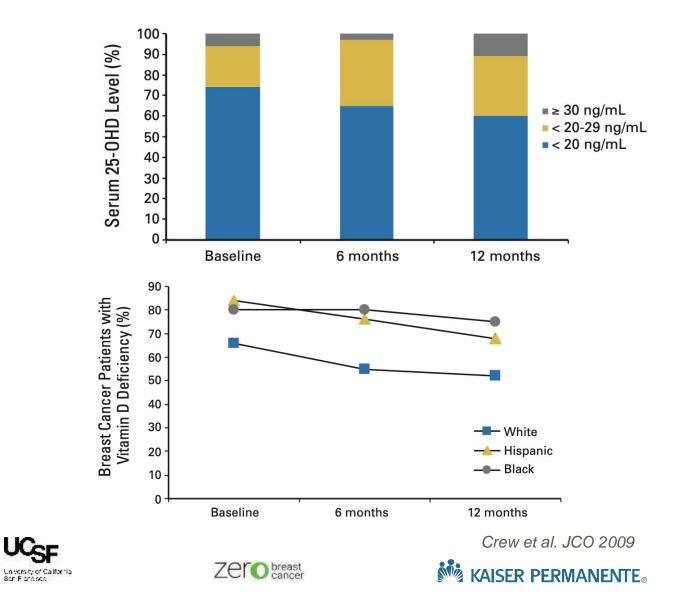




#### Put the Results in the Context

#### **Pathways Patients at Cancer Dx**

Vitamin D status	No. (%)	Mean $\pm$ SD
Deficient (<20)	1,518 (38)	$14.2 \pm 3.9$
Insufficient (20-30)	1,487 (37)	$24.9 \pm 2.8$
Sufficient (>30)	990 (25)	37.7 ± 8.5







#### Put the Results in the Context

Table 3. Multivariable-Adjusted Mean or Geometric Mean Vitamin D-Related Biomarkers at Baseline and 2 Years' Follow-up, by Randomized Treatment Assignment and BMI<sup>a</sup>

	Multivariable-adjusted mean (SEM)					
Biomarker, BMI category <sup>b</sup>	Placebo		Vitamin D		Treatment effect,	P value for treatment effect interaction
	Baseline	Year 2	Baseline	Year 2	mean (SE)	by BMI
Total 25-OHD, ng/mL						
<25.0	31.7 (0.4)	31.1 (0.5)	31.0 (0.4)	44.0 (0.5)	13.5 (0.6)	
25.0-29.9	29.9 (0.4)	28.9 (0.4)	28.7 (0.4)	41.2 (0.4)	12.7 (0.5)	- 001
30.0-34.9	29.0 (0.5)	28.7 (0.6)	28.9 (0.5)	39.4 (0.5)	10.5 (0.7)	<.001
≥35.0	28.2 (0.7)	28.3 (0.8)	26.5 (0.6)	37.9 (0.7)	10.0 (1.0)	
25-OHD3, ng/mL						
<25.0	31.2 (0.4)	30.6 (0.5)	30.8 (0.4)	43.8 (0.5)	13.5 (0.6)	
25.0-29.9	29.4 (0.4)	28.1 (0.4)	28.0 (0.4)	40.9 (0.4)	13.4 (0.5)	. 001
30.0-34.9	28.4 (0.5)	27.9 (0.6)	28.1 (0.5)	39.4 (0.6)	11.6 (0.7)	<.001
≥35.0	26.4 (0.7)	26.8 (0.8)	25.8 (0.6)	37.6 (0.7)	10.5 (1.0)	
Free vitamin D, pg/mL						
<25.0	6.13 (0.12)	6.14 (0.16)	6.39 (0.12)	10.20 (0.16)	3.84 (0.19)	
25.0-29.9	6.03 (0.10)	6.15 (0.14)	5.77 (0.10)	8.85 (0.14)	2.92 (0.17)	
30.0-34.9	5.75 (0.16)	5.79 (0.20)	5.40 (0.19)	7.79 (0.24)	2.57 (0.32)	<.001
≥35.0	5.08 (0.18)	4.96 (0.23)	5.07 (0.17)	7.04 (0.21)	2.22 (0.34)	
Bioavailable vitamin D, geo <mark>me</mark>	etric mean (95% CI), ng	ı/mL				
<25.0	2.3 (2.2-2.4)	2.3 (2.2-2.4)	2.4 (2.3-2.5)	3.8 (3.7-4.0)	1.5 (0.1)	
25.0-29.9	2.3 (2.2-2.3)	2.3 (2.2-2.3)	2.2 (2.1-2.2)	3.4 (3.2-3.5)	1.2 (0.1)	
30.0-34.9	2.1 (2.0-2.3)	2.1 (2.0-2.3)	2.0 (1.8-2.1)	2.9 (2.7-3.1)	1.0 (0.1)	<.001
≥35.0	1.9 (1.7-2.0)	1.9 (1.7-2.0)	1.8 (1.7-2.0)	2.7 (2.5-2.9)	0.9 (0.1)	







Tobias et al. JAMA Network Open 2023

Zero breast cancer



# Conclusions

- A substantial proportion of women were vitamin D deficient or insufficient at the time of breast cancer diagnosis.
- Maintaining sufficient vitamin D levels after breast cancer diagnosis is advisable for better prognosis, especially for those with advanced stage disease.
- Vitamin D3 supplementation is a safe and effective way to increase vitamin D levels. Patients with higher BMI may need a higher dose.
- Current IOM recommendation of 600 IU for all age up to 70 years and 800 IU for 71+ years may be too low for benefits beyond bone







**MAISER PERMANENTE**