pathways
a study of
breast cancer
survivorship

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

Vitamin D May Make A Difference After A Breast Cancer Diagnosis

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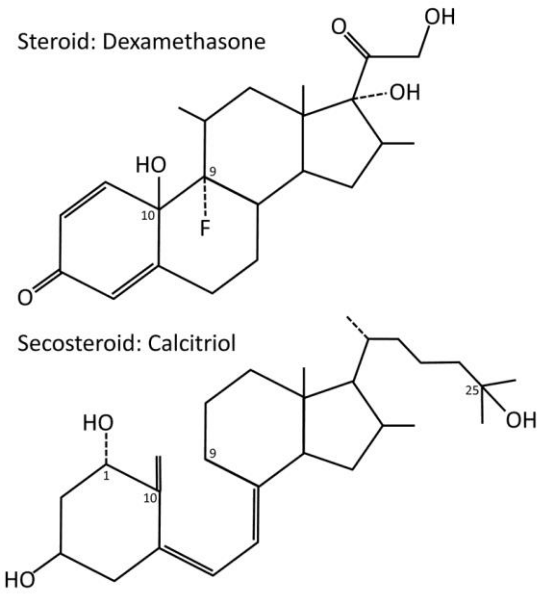
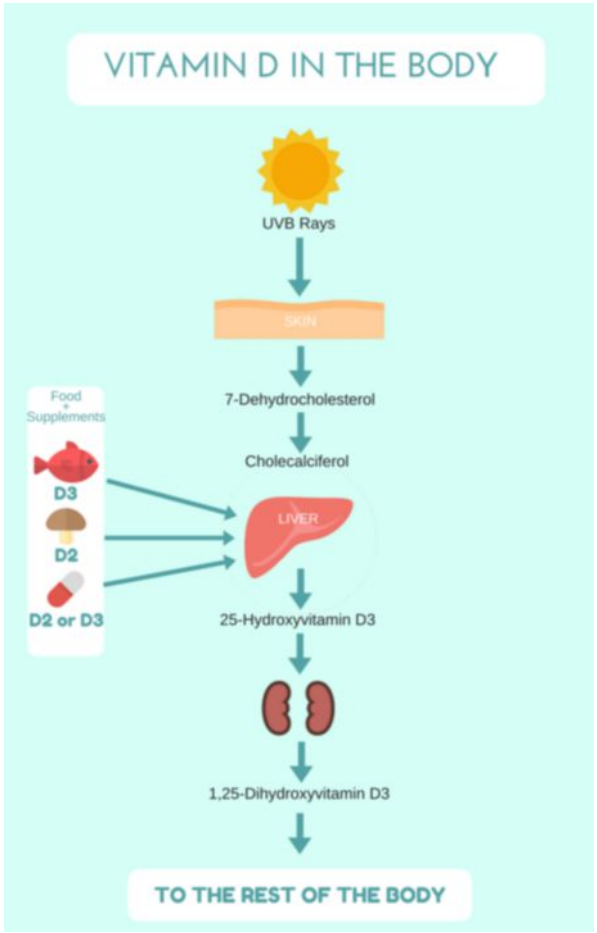
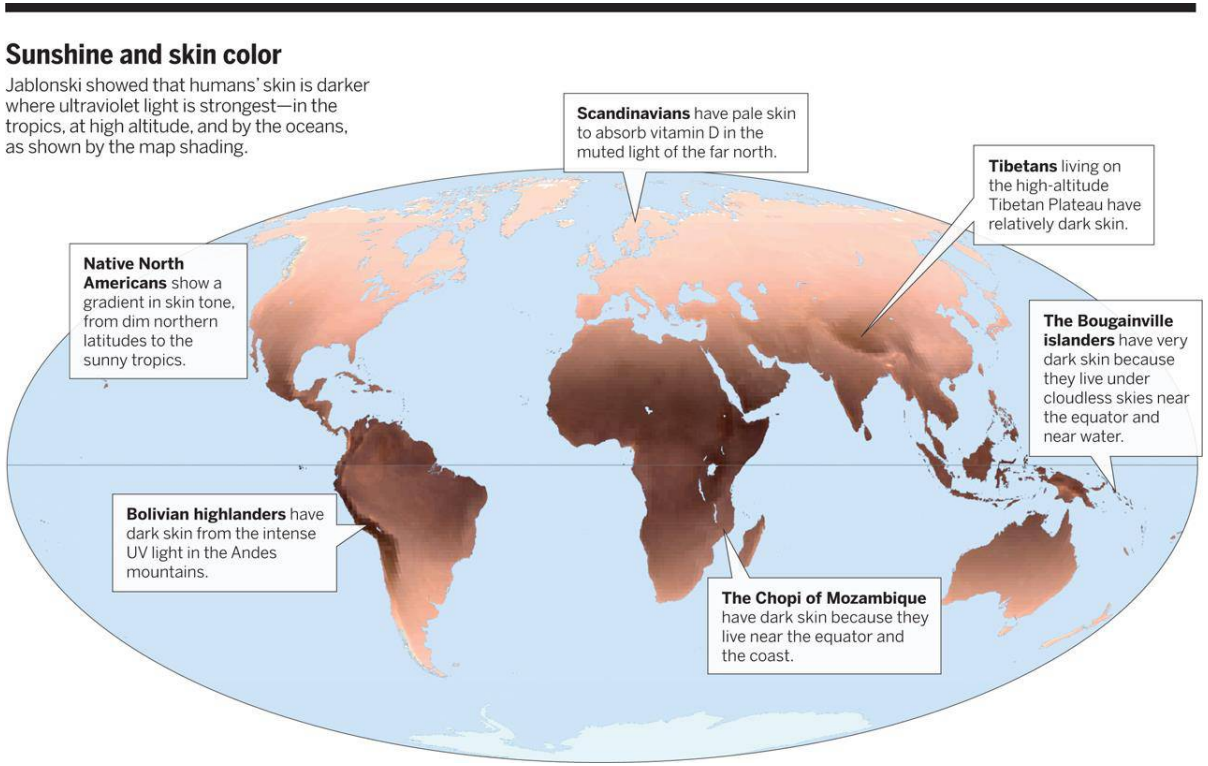
What is Special about Vitamin D?





More than a vitamin



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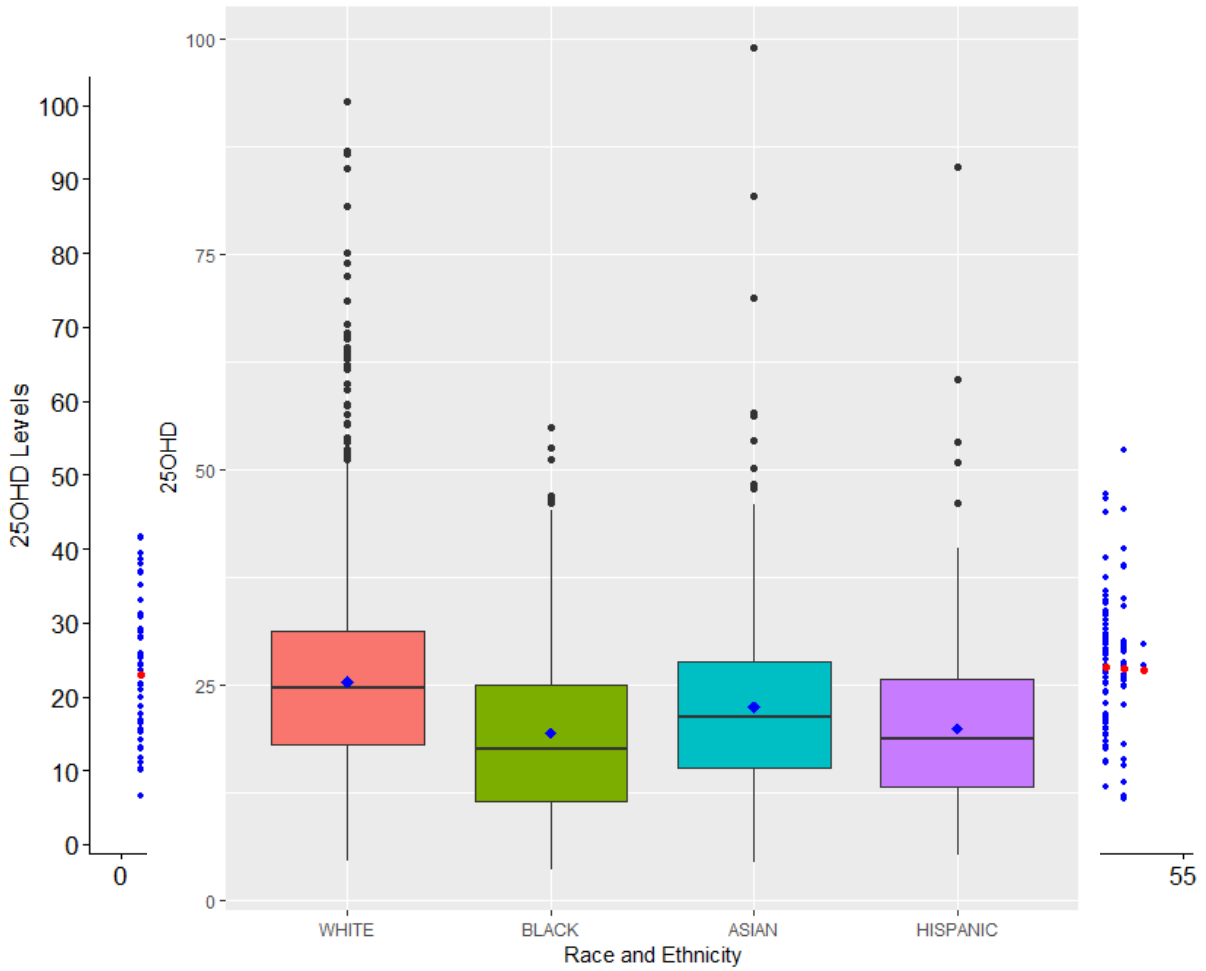
Where Do We Get Vitamin D?

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**



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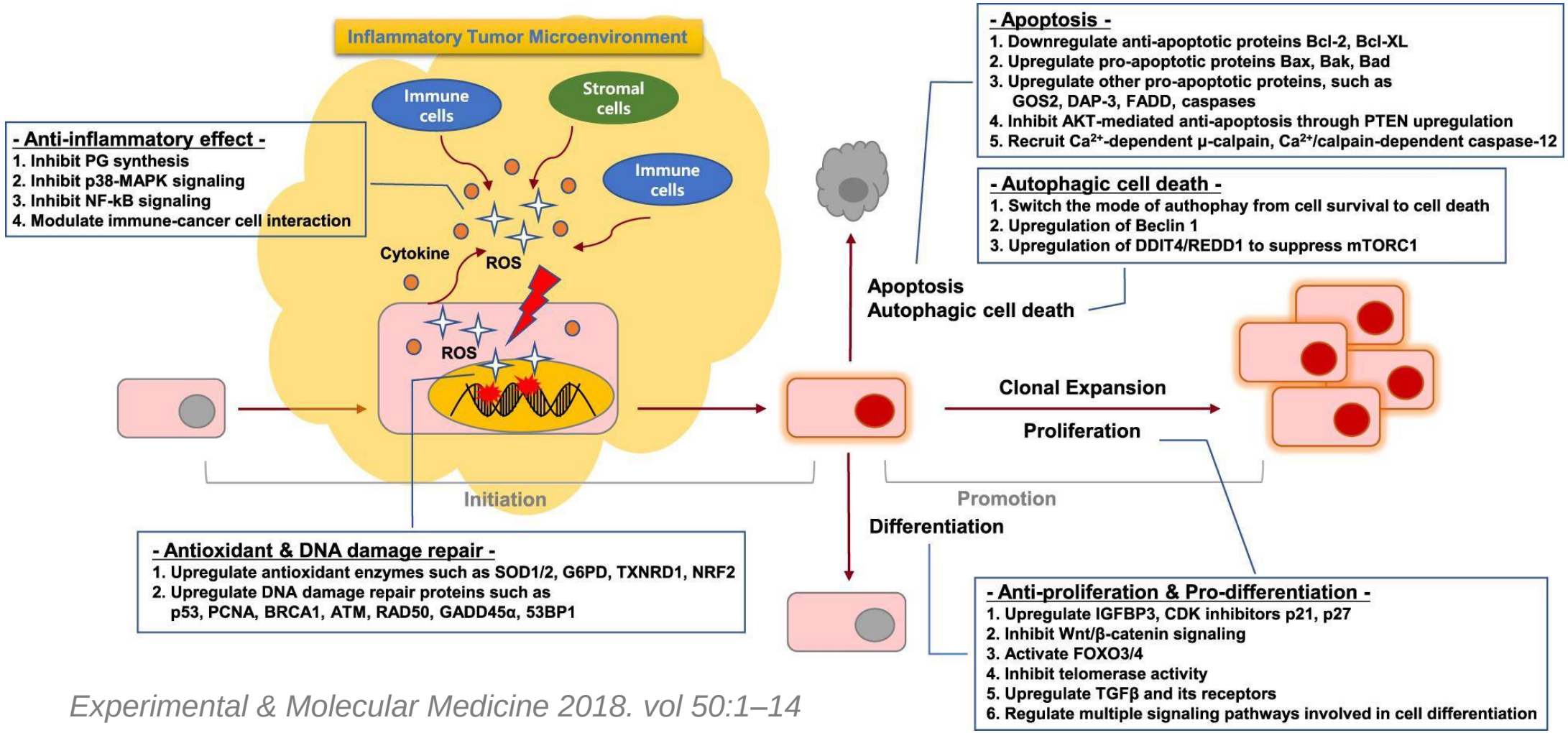
What is the Relevance of Vitamin D and Breast Cancer?



Experimental & Molecular Medicine 2018. vol 50:1–14

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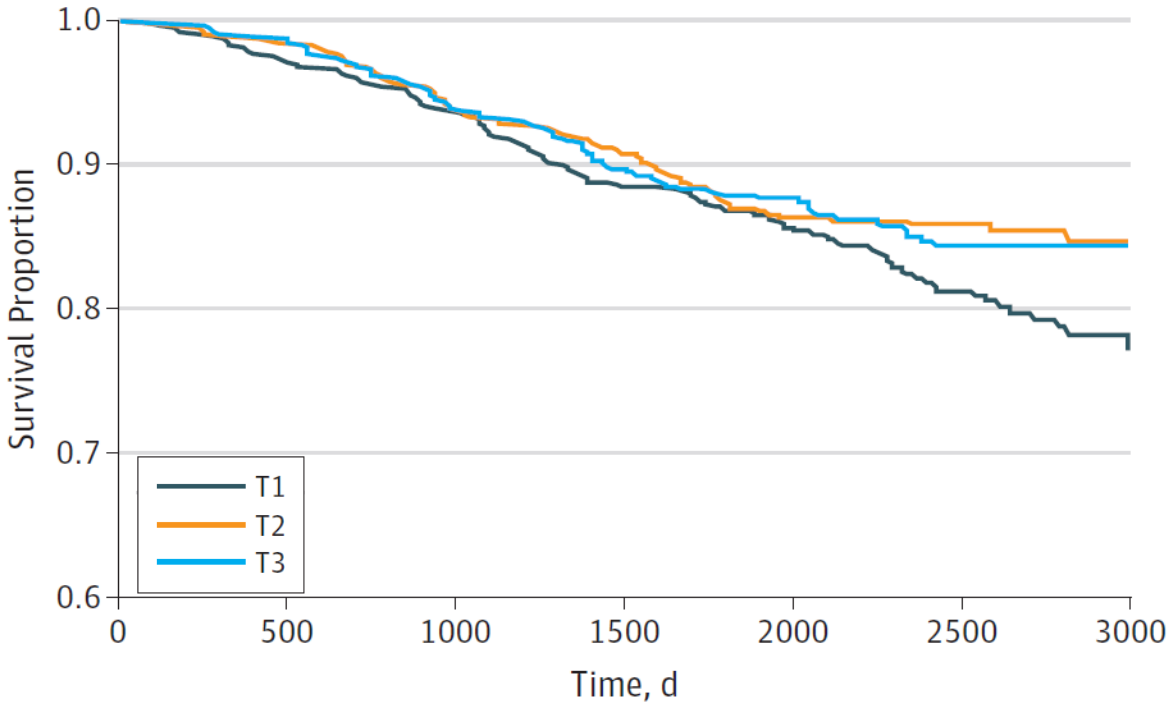
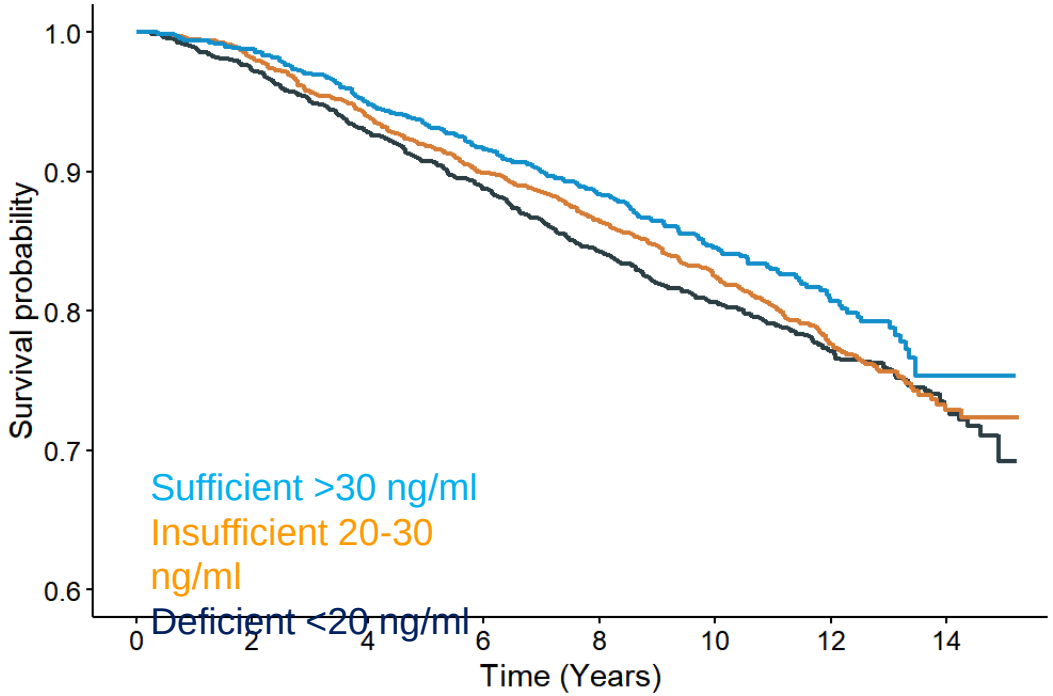
What Do Data from Pathways Study Tell Us?

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



Yao, et al, Kushi. JAMA Oncol 2017

2020: 3,995 patients median f/u 137 months



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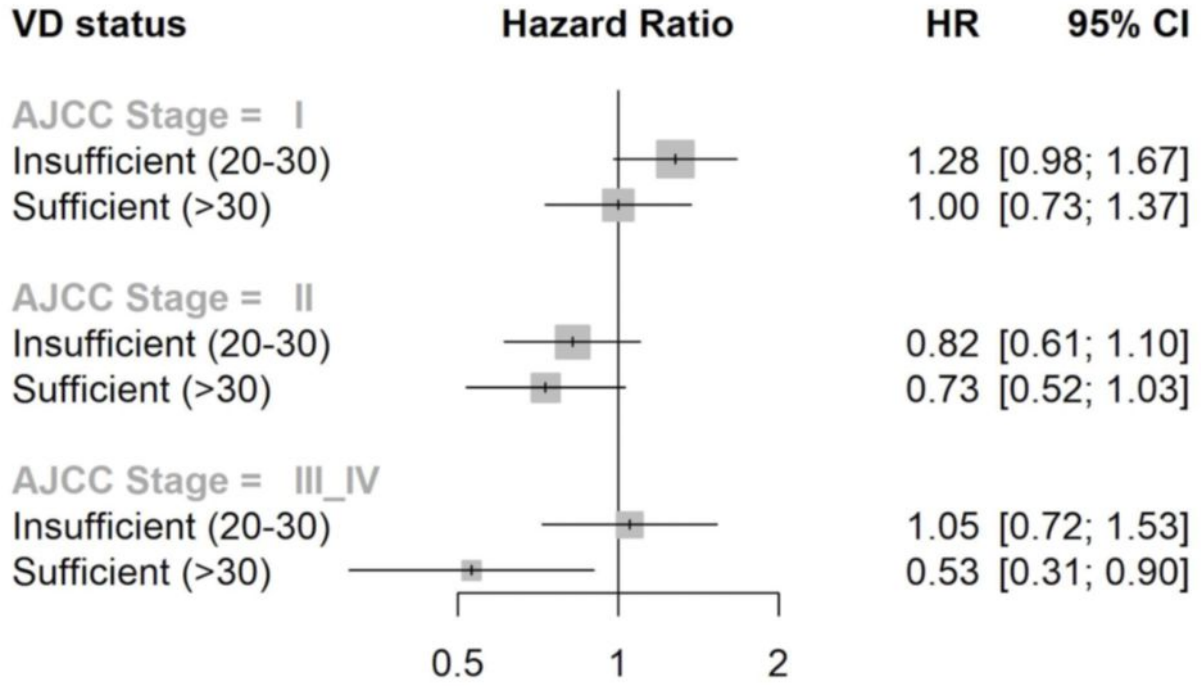
What Do Data from Pathways Study Tell Us?

Hazard Ratios (and 95 CI) for Overall Survival by Serum Vitamin D Levels				
Vitamin D levels	N events / Total	M1: non-clinical factors	M2: M1+ clinical factors	M3: M2 + treatment factors
		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

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.

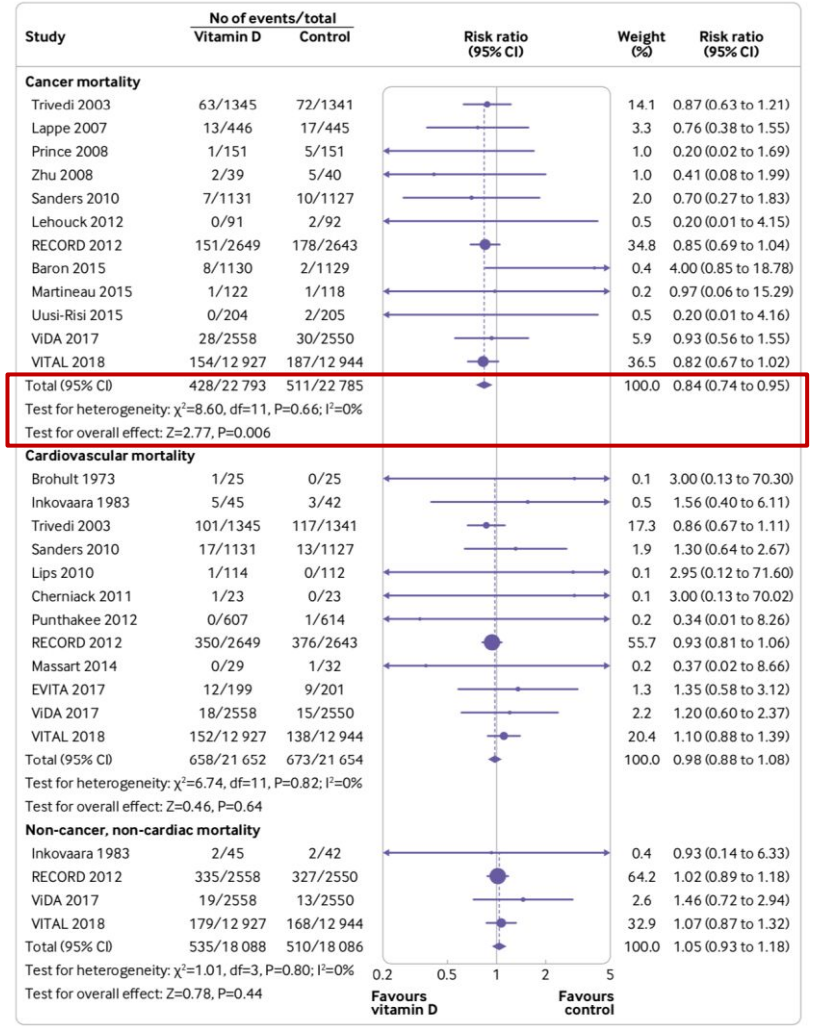
The Impact of Breast Cancer Stage

Stage	No. (%)	Mean ± 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)	



P for interaction = 0.006

Put the Results in the Context



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.*

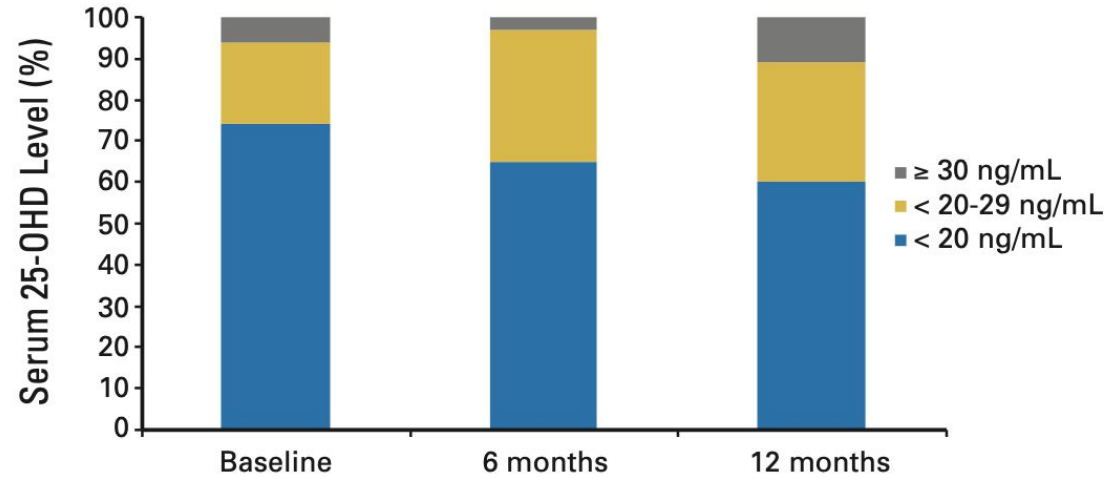
End Point	Vitamin D Group (N=12,927)	Placebo Group (N=12,944)	Hazard Ratio (95% CI)
	no. of participants with event		
Cancer			
Primary end point: invasive cancer of any type	793	824	0.96 (0.88–1.06)
Breast cancer	124	122	1.02 (0.79–1.31)
Prostate cancer	192	219	0.88 (0.72–1.07)
Colorectal cancer	51	47	1.09 (0.73–1.62)
Death from cancer	154	187	0.83 (0.67–1.02)
Cardiovascular disease			
Primary end point: major cardiovascular event†	396	409	0.97 (0.85–1.12)
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)

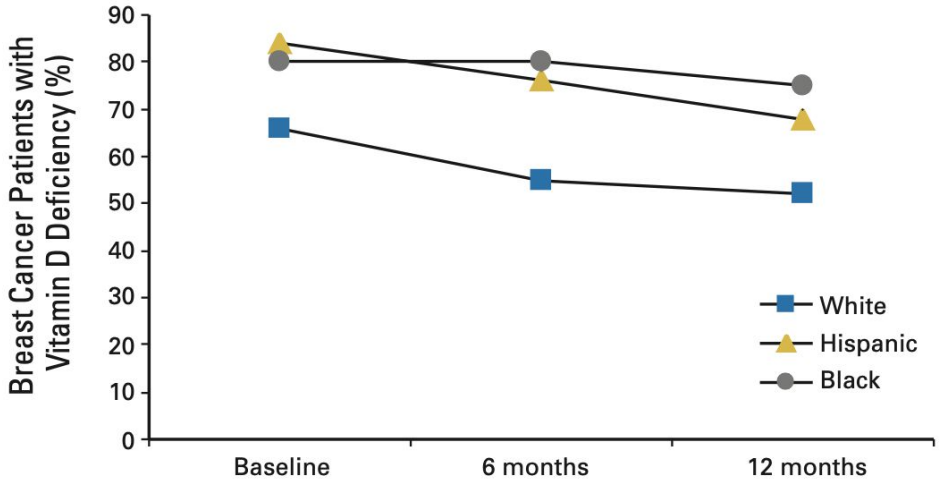
Manson et al. N Engl J Med 2019

Put the Results in the Context

Pathways Patients at Cancer Dx

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





Crew et al. JCO 2009

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[a]

Biomarker, BMI category[b]	Multivariable-adjusted mean (SEM)				Treatment effect, mean (SE)	*P* value for treatment effect interaction by BMI
	Placebo		Vitamin D			
	Baseline	Year 2	Baseline	Year 2		
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)	<.001
25.0-29.9	29.9 (0.4)	28.9 (0.4)	28.7 (0.4)	41.2 (0.4)	12.7 (0.5)	
30.0-34.9	29.0 (0.5)	28.7 (0.6)	28.9 (0.5)	39.4 (0.5)	10.5 (0.7)	
≥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)	<.001
25.0-29.9	29.4 (0.4)	28.1 (0.4)	28.0 (0.4)	40.9 (0.4)	13.4 (0.5)	
30.0-34.9	28.4 (0.5)	27.9 (0.6)	28.1 (0.5)	39.4 (0.6)	11.6 (0.7)	
≥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)	<.001
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)	
≥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, geometric mean (95% CI), ng/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)	<.001
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)	
≥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

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 health.