

Supplement 4. Results of the dose-response relationships between baseline vitamin D status and risk of developing total, colorectal, prostate, and breast cancer in prospective cohort studies.

First author, publication year [Country] Study name	Participants /subgroups	Outcome (n/N; Incidence)	Follow-up duration (Time to cancer diagnosis)	Blood 25(OH)D concentration, nmol/L	Number of cases	Number at risk	Adjusted RR	95% CI	P for trend	Study quality			
Michaëlsson, 2010 (37) [Sweden] ULSAM	Adults, males	Total cancer mortality (189/1194; 0.158)	Median 12.7 y	<39	12	59	2.34	1.36, 4.00*	U-shaped	Good			
				(NR)	39 to <46	27	119	1.99			1.29, 3.08*		
				46-93	118	956	1	Reference					
				>93 to 98	19	119	1.56	0.95, 2.56					
				>98	13	59	2.45	1.36, 4.42*					
				Total cancer incidence (373/1194; 0.312)	Median 12.7 y	<39	24	59			1.65	1.08, 2.54*	
						(NR)	39 to <46	38			119	1.34	0.95, 1.91
						46-93	253	956			1	Reference	
						>93 to 98	37	119			1.31	0.92, 1.87	
						>98	21	59			1.68	1.06, 2.65*	
Cawthon, 2010 (35) [US] MrOS	Elderly, males	Total cancer mortality (97/1490; 0.065)	Mean 7.3 y (range 14 d to 9.3 y)	<49.65	NR	372	0.52	0.27, 1.00	Linear 0.09	Fair			
				≥49.65 to 62.9	NR	370	0.90	0.51, 1.60					
				≥62.9 to 74.9	NR	372	0.80	0.45, 1.41					
				≥74.9	NR	376	1	Reference					
				≥74.9	NR	376	1	Reference					
Freedman, 2010 (36) [US] NHANES III	Adults, both sexes	Total cancer mortality (884/16819; 0.053)	Mean 13.4 y	<37.5	116	2689	1	Reference	Linear 0.43	Fair			
				37.5 to <50	174	3056	1.04	0.77, 1.41					
				50 to <62.5	165	3143	1.23	0.89, 1.69					
				62.5 to <80	200	3713	1.19	0.86, 1.65					
				80 to <100	139	2521	1.12	0.80, 1.57					
				≥100	90	1697	1.15	0.79, 1.68					
				Colorectal cancer mortality (95/16819; 0.006)	Mean 13.4 y	<50	38	5745			1	Reference	Linear 0.09
						50 to <80	34	6856			0.56	0.29, 1.09	
						80 to <100	14	2521			0.61	0.26, 1.47	
						≥100	9	1697			0.35	0.11, 1.14	

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	Adults, males	Total cancer mortality (513/7905; 0.059)	Mean 13.4 y	<37.5	47	474	1	Reference	Linear 0.09						
				37.5 to <50	95	806	1.66	0.98, 2.80							
				50 to <62.5	90	1241	1.43	0.90, 2.26							
				62.5 to <80	122	2000	1.52	0.82, 2.80							
				80 to <100	90	1826	1.66	1.06, 2.61*							
				≥100	69	1565	1.85	1.02, 3.35*							
	Prostate cancer mortality (74/7905; 0.009)	Mean 13.4 y	<50	50 to <80	38	3241	1.39	0.70, 2.76	Linear 0.84						
				≥80	20	3391	1.23	0.50, 3.05							
				Adults, females	Total cancer mortality (371/8914; 0.042)	Mean 13.4 y	<37.5	69			1088	1	Reference	Linear 0.29	
								37.5 to <50			79	1408	0.85		
	50 to <62.5	75	1480					1.25	0.82, 1.90						
	62.5 to <80	78	2095					1.11	0.69, 1.79						
	80 to <100	49	1506					0.86	0.50, 1.46						
	≥100	21	1337					0.64	0.35, 1.18						
Breast cancer mortality (53/8914; 0.006)	Mean 13.4 y	<50	50 to <80	24	2496	1	Reference	Linear 0.56							
			50 to <80	19	3575	0.94	0.40, 2.20								
			≥80	10	2843	0.65	0.18, 2.38								

n/N = number of cases/total number of people at risk; 25(OH)D = 25-hydroxyvitamin concentration (conversion factor: 1 ng/mL = 2.495 nmol/L); RR = risk ratio; NR = not reported; y = year(s); ULSAM = the Uppsala Longitudinal Study of Adult Men; MrOS = Osteoporotic Fractures in Men Study; NHANES III = Third National Health and Nutritional Examination Survey

*Statistical significant (P<0.05)