Supplementary Table 1. Hazard ratios for each year of the trial. (A) Vitamin D; (B) Omega-3 fatty acids.^a (A) Treatment arm: vitamin D

Year	Vitamin D	Placebo	Hazard Ratio	p-value
of Trial	Group	Group	(95% CI)	
Confirmed AD^b	no. of participa	nts with event		
1	30	31	0.97 (0.59 to 1.61)	0.91
2	35	34	1.03 (0.64 to 1.66)	0.89
3	26	35	0.74 (0.45 to 1.23)	0.25
4	18	37	0.49 (0.28 to 0.85)	0.01
5+	8	13	0.61 (0.25 to 1.48)	0.28
Confirmed + Proba	ble AD			
1	50	54	0.93 (0.63 to 1.37)	0.71
2	59	51	1.16 (0.80 to 1.69)	0.43
3	46	57	0.81 (0.55 to 1.19)	0.28
4	31	57	0.54 (0.35 to 0.84)	0.006
5+	13	16	0.81 (0.39 to 1.68)	0.57

(B) Treatment arm: omega-3 fatty acids

Year	n-3 Fatty Acids	Placebo	Hazard Ratio	p-value
of Trial	Group	Group	(95% CI)	
Confirmed AD^b	no. of participants with event			
1	31	30	1.03 (0.63 to 1.71)	0.9
2	27	42	0.64 (0.40 to 1.04)	0.07
3	27	34	0.79 (0.48 to 1.31)	0.37
4	25	30	0.83 (0.49 to 1.41)	0.5
5+	13	8	1.62 (0.67 to 3.91)	0.28
Confirmed + Prob	able AD			
1	41	63	0.65 (0.44 to 0.96)	0.03
2	48	62	0.77 (0.53 to 1.13)	0.18
3	48	55	0.87 (0.59 to 1.28)	0.48
4	43	45	0.95 (0.63 to 1.44)	0.81
5+	16	13	1.23 (0.59 to 2.56)	0.58

^aAdditionally adjusted for age, sex, race, and randomization to other treatment arm.

^bAD: Autoimmune disease.

Supplementary Table 2. Incident diseases included in Main and "Other Autoimmune Diseases" endpoint.

Supplementary Table 2. Incident diseases included in Main and Other Auto		Cases	
	Total	Confirmed	Probable
Disease	N (%)	N	\mathbf{N}
Acute Inflammatory Demyelinating Polyneuropathy/Anti-MAG Peripheral Neuropathy	2 (2)	2	
Alopecia Areata	4 (4)	4	
Autoimmune Hemolytic Anemias	3 (3)	3	
Celiac Sprue	5 (5)	4	1
Circumscribed Scleroderma	5 (5)	5	
Cutaneous Lupus Erythematosus	3 (3)	3	
Erythema Nodosum	1 (1)	1	
Granulomatosis with Polyangiitis	1 (1)	1	
IgA Nephropathy/ Henoch Schonlein Purpura	1 (1)	1	
Immune Thrombocytopenic Purpura	2 (2)	2	
Inflammatory Bowel Disease (Crohn's and Ulcerative Colitis)	14 (13)	12	2
Iridocyclitis / Uveitis	1 (1)	1	
Lichen Planus	7 (6)	5	2
Lymphocytic and Microscopic Colitis	10 (9)	9	1
Membranous Glomerulonephritis	1 (1)	1	
Multiple Sclerosis	1 (1)	1	
Myasthenia Gravis 2	5 (5)	5	
Other Specified Diffuse Diseases of Connective Tissue	1 (1)	1	
Pemphigoid	2 (2)	2	
Pernicious Anemia	3 (3)	1	2
Primary Sclerosing Cholangitis	1 (1)	1	
Retinal Vasculitis	1 (1)	1	
Sarcoidosis	9 (8)	8	1
Sicca Syndrome / Sjogren's Syndrome	10 (9)	10	
Spondyloarthropathy	2 (2)	2	
Systemic Lupus Erythematosus	5 (5)	3	2
Systemic Sclerosis / CREST Syndrome / Scleroderma	4 (4)	3	1
Vitiligo	5 (5)	5	

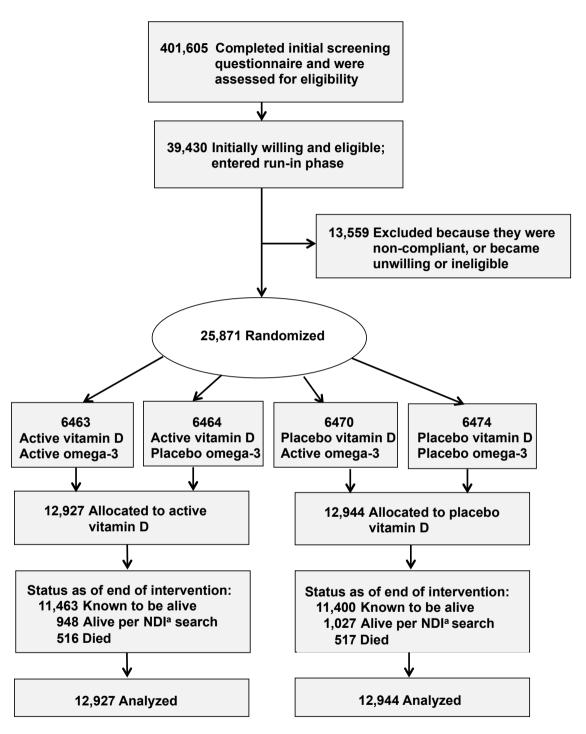
Supplementary Table 3. P-values for interaction terms from models assessing effect modification by relevant continuous variables on the endpoint of confirmed autoimmune disease.^a

Effect modifier	P-value for Interaction		
(continuous variable)	Vitamin D	Omega-3 Fatty Acids	
Age	0.28	0.21	
Body mass index ^b	0.02	0.75	
Baseline serum 25-hydroxyvitamin D, ng/mL	0.31	0.86	
Baseline omega-3 index ^c	0.37	0.33	
Baseline fish consumption, servings/week	0.92	0.55	

^aAdditionally adjusted for age, sex, race, and randomization to other treatment arm.

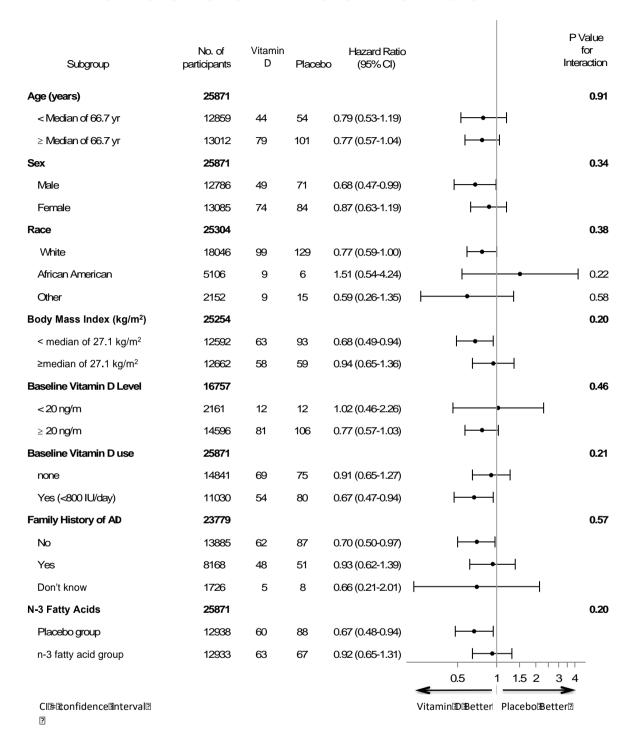
^bBody mass index (BMI) is weight in kilograms divided by the square of height in meters.

^cSerum EPA +DHA/total lipids



^aNational Death Index

Supplementary Figure 2. Hazard ratios and 95% confidence intervals for incidence of confirmed autoimmune diseases, according to subgroup, comparing the vitamin D group with the placebo group in the VITAL trial



Analyses from Cox regression models controlled (unless stratified by the characteristic) for age, sex, race, and randomization group in the n-3 portion of the trial. Analyses were not adjusted for multiple comparisons. Race and ethnic group were reported by the participant.

Supplementary Figure 3. Hazard ratios and 95% confidence intervals for incidence of confirmed autoimmune diseases, according to subgroup, comparing the omega-3 (n-3) fatty acids group with the placebo group in the VITAL trial

Subgroup	No. of participants	N-3 Fatty acids	Placebo	Hazard Ratio (95% CI)		P Value for Interaction
Age (years)	25871					0.42
< Median of 66.7 yr	12859	49	49	0.97 (0.65-1.45)	H	
≥ Median of 66.7 yr	13012	81	99	0.79 (0.59-1.07)	├	
Sex	25871					0.39
Male	12786	58	62	0.97 (0.67-1.39)	H	
Female	13085	72	86	0.78 (0.56-1.07)	├	
Race	25304					0.20
White	18046	101	127	0.79 (0.61-1.03)		
African American	5106	7	8	0.88 (0.32-2.42)	├	0.85
Other	2152	15	9	1.74 (0.76-3.97)	⊢	0.07
Body Mass Index (kg/m²)	25254					0.31
3 O NAK® O Alé& & & O 1	12592	68	88	0.77 (0.56-1.07)	├	
0 NA™ 0 x 1 6 4 6 6 6 6 1 1 1 1 1 1 1 1 1 1 1 1 1	12662	60	57	0.99 (0.69-1.44)	⊢	
Fish consumption	25435					0.15
<median 1.5="" of="" servings="" td="" wk<=""><td>13514</td><td>72</td><td>92</td><td>0.73 (0.53-1.01)</td><td>├•</td><td></td></median>	13514	72	92	0.73 (0.53-1.01)	├ •	
≥ median of 1.5 servings/wk	11921	58	56	1.05 (0.72-1.52)	H-	
Baseline Omega-3 Level	16478					0.81
< Median of 2.5 ng/ml	8118	46	57	0.82 (0.55-1.23)	├	
≥ Median of 2.5 ng/ml	8360	45	57	0.77 (0.52-1.15)	├	
Family History of AD	23779					0.03
No	13885	80	69	1.14 (0.82-1.58)	⊢•	
Yes	8168	40	59	0.66 (0.43-0.99)	—	
Don't know	1726	3	10	0.29 (0.08-1.06)	├	
Vitamin D	25871					0.20
Placebo group	12944	67	88	0.74 (0.54-1.03)	├	
Vitamin D group	12927	63	60	1.02 (0.71-1.46)	<u> </u>	_
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Analyses from Cox regression models controlled (unless stratified by the characteristic) for age, sex, race, and randomization group in the vitamin D portion of the trial (intention-to-treat analyses). Analyses were not adjusted for multiple comparisons. Race and ethnic group were reported by the participant.