

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 of Trial	Vitamin D Group	Placebo Group	Hazard Ratio (95% CI)	p-value
<i>Confirmed AD^b</i>		<i>no. of participants with event</i>		
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
<i>Confirmed + Probable AD</i>				
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 of Trial	n-3 Fatty Acids Group	Placebo Group	Hazard Ratio (95% CI)	p-value
<i>Confirmed AD^b</i>		<i>no. of participants with event</i>		
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
<i>Confirmed + Probable AD</i>				
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.

Disease	Cases		
	Total N (%)	Confirmed N	Probable 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

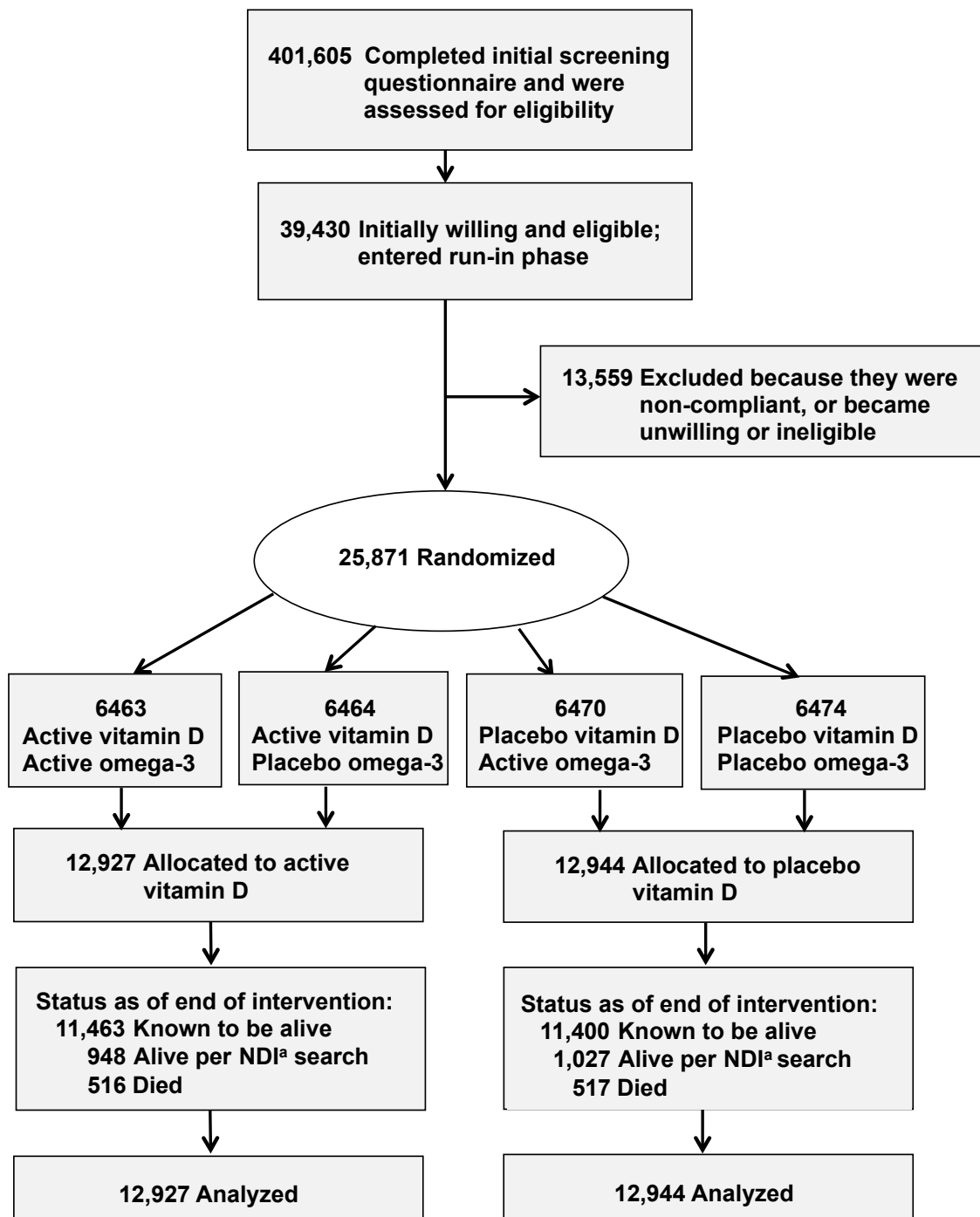
Effect modifier (continuous variable)	<u>P-value for Interaction</u>	
	Vitamin D	Omega-3 Fatty Acids
Age	0.28	0.21
Body mass index ^b	0.02	0.75
Baseline serum 25-hydroxyvitamin D, ng/mL	0.31	0.86
Baseline omega-3 index ^c	0.37	0.33
Baseline fish consumption, servings/week	0.92	0.55

^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.

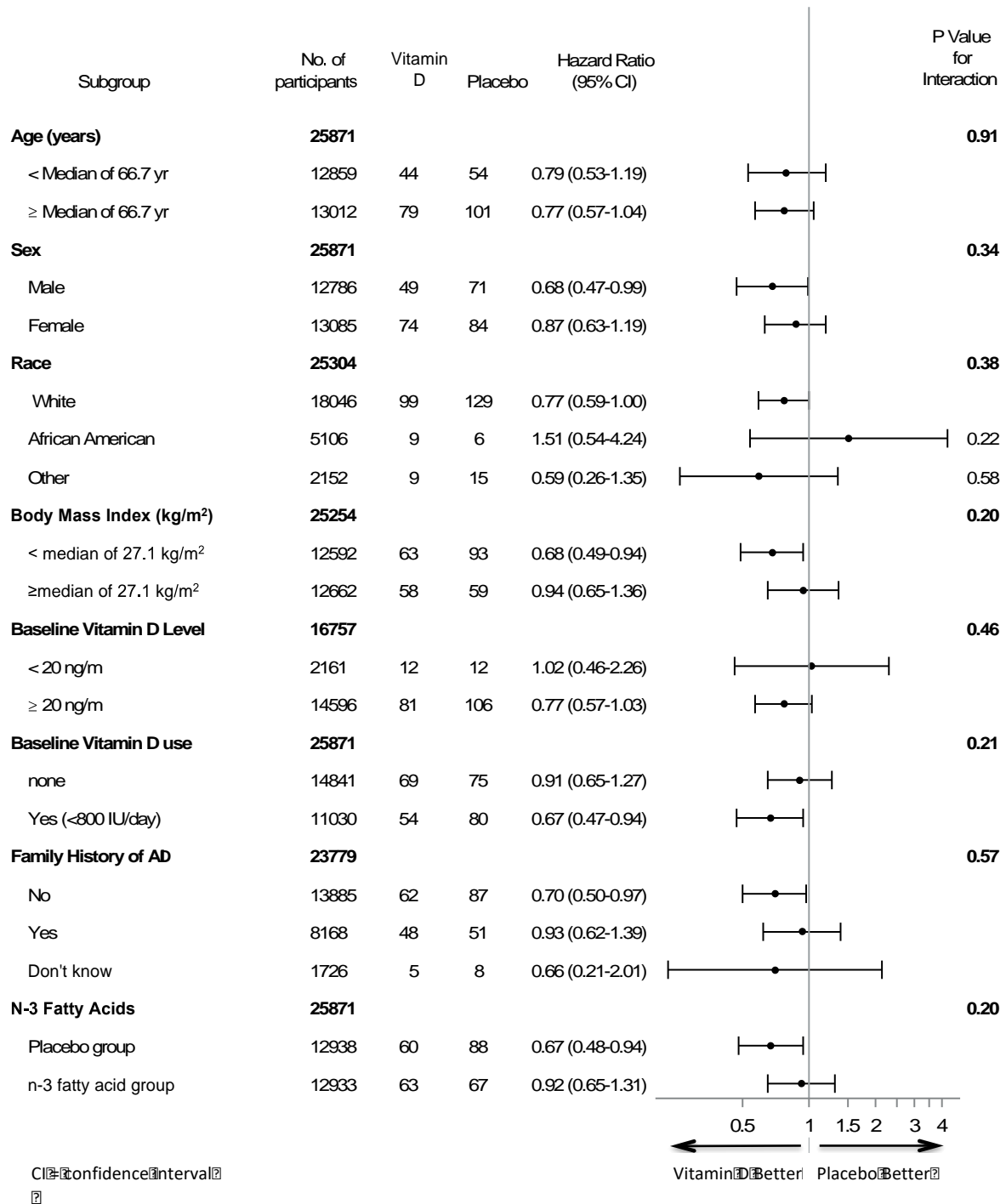
^cSerum EPA +DHA/total lipids

Supplementary Figure 1. Consort diagram for the VITAL trial.



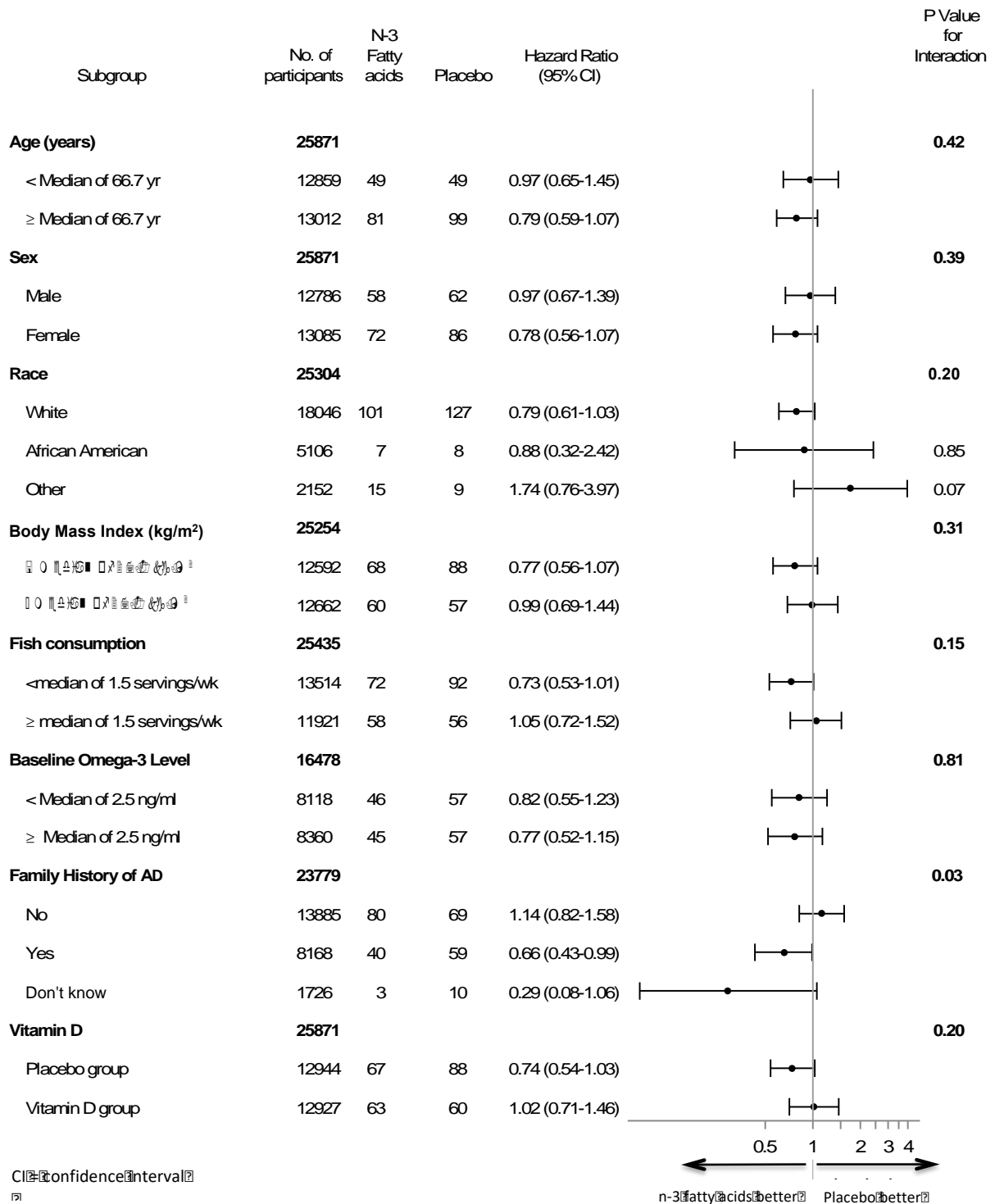
^aNational Death Index

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



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.