ONLINE SUPPORTING MATERIAL

Associations between dietary protein intake and biomarkers of inflammation and oxidative stress in the Framingham Heart Study Offspring

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Supplemental Figure 1. Participant Flow Chart.

Supplemental Table 1. Number of Framingham Heart Study Offspring participants with measured inflammatory and oxidative stress biomarkers and calculated scores at exam 7 and/or exam 8.

Supplemental Table 2. Adjusted least square means of change in individual biomarkers of inflammation or oxidative stress per averaged total dietary protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.

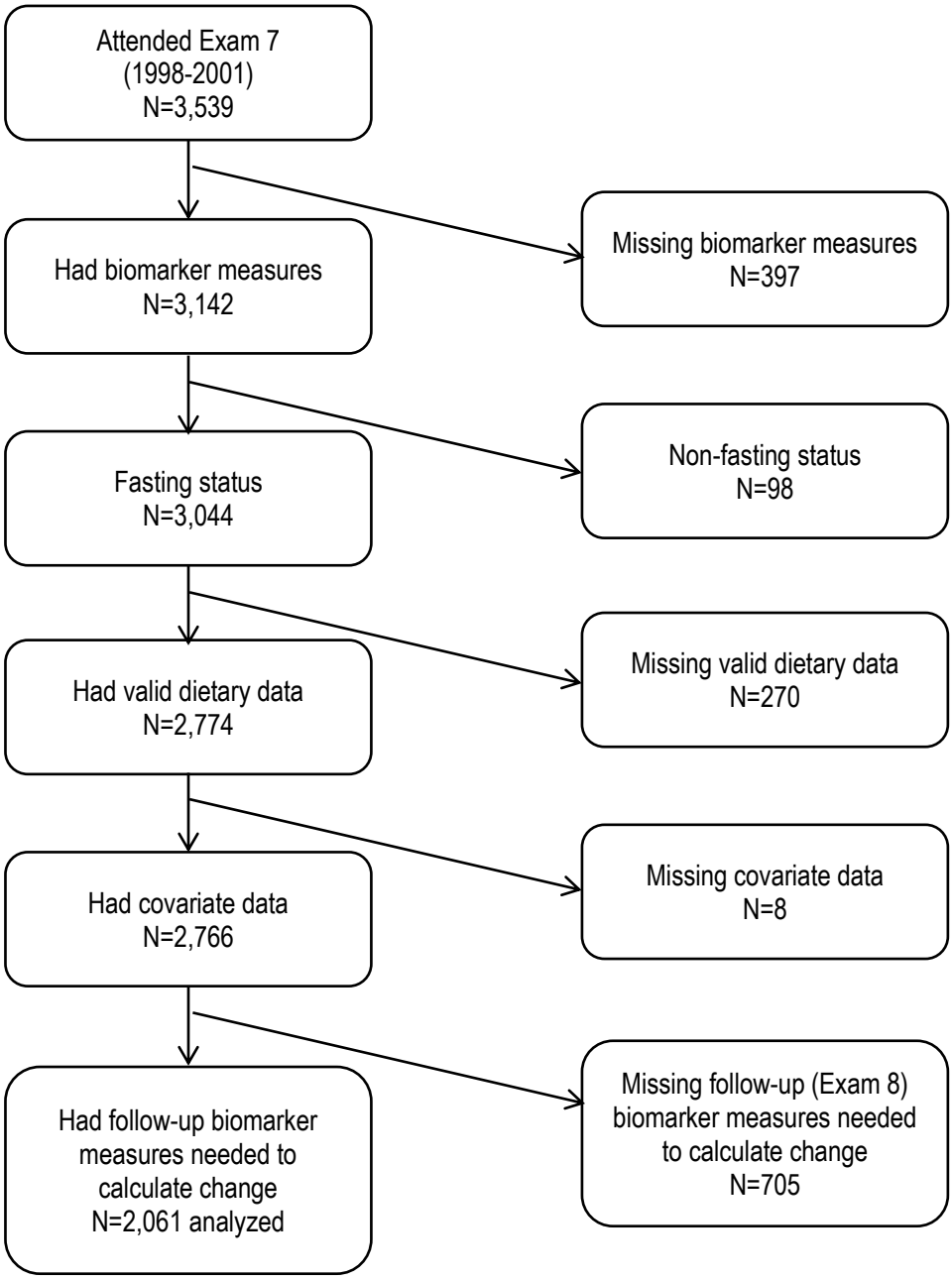
Supplemental Table 3. Adjusted least square means of change in individual biomarkers of inflammation or oxidative stress per averaged plant protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.

Supplemental Table 4. Adjusted least square means of change in individual biomarkers of inflammation or oxidative stress per averaged animal protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.

Supplemental Table 5. Sensitivity analyses of adjusted least square means of change in individual biomarkers of inflammation or oxidative stress, overall score, and cytokine and oxidative stress subscores between exams 7 and 8, per total, plant, and animal protein in quartile categories of intake averaged from exams 6 and 7, in participants of the Framingham Heart Study Offspring cohort.

Supplemental Table 6. Adjusted least square means of change in cytokine and oxidative stress subscores per averaged total, plant, and animal protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.*

Supplemental Figure 1. Participant Flow Chart.



Supplemental Table 1. Number of Framingham Heart Study Offspring participants with measured inflammatory biomarkers and calculated scores at exam 7 and/or exam 8.

	Biomarker	Biofluid	Unit	Exam 7 (N=3539)	Exam 8 (N=3021)	IS	CY	OX
1	CRP	Serum	mg/L	**3301**	**2744**	X		
2	ICAM-1	Serum	ng/mL	**3303**	**2655**	X		
3	IL-6	Serum	pg/mL	**3297**	**2655**	X	X	
4	LPL-A2 activity concentration	Plasma	nmol/mL/min	**3299**	**2716**	X		X
5	LPL-A2 mass concentration	Plasma	ng/mL	**3298**	**2715**	X		X
6	MCP-1	Serum	pg/mL	**3242**	**2653**	X		
7	OPG	Plasma	pmol/L	**3299**	**2756**	X	X	
8	P-selectin	Plasma	ng/mL	**3304**	**2756**	X		
9	TNFRII	Plasma	pg/mL	**3227**	**2754**	X	X	
	Isoprostanes	Urine	pg/mL	**2828**	**2647**			
	Creatinine	Urine	mg/100mL	**2828**	**2721**			
10	Creatinine-corrected isoprostanes	Urine	ng/mmol	**2828**	**2636**			X

Abbreviations: CY, cytokine subscore; CRP, C-reactive protein; ICAM-1, soluble intracellular adhesion molecule 1; IL-6, interleukin 6; IS, inflammation and oxidative stress score; LPL-A2, lipoprotein-associated phospholipase A2; MCP-1, monocyte chemoattractant protein 1 (also known as CCL, chemokine [C-C motif] ligand); OPG, osteoprotegerin; OX, oxidative stress subscore; TNFRII, tumor necrosis factor receptor II.

Supplemental Table 2. Adjusted least square means of change in individual biomarkers of inflammation or oxidative stress per averaged dietary protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.*

		Quartile Category of Total Protein Intake (g/d)				
Change in Outcome	**Model****	**67.4**	**77.3**	**85.0**	**95.9**	***P* trend**
CRP, mg/L	1	-0.152 (0.044)	-0.165 (0.045)	-0.227 (0.046)	-0.195 (0.048)	0.31
	2	-0.278 (0.065)	-0.280 (0.064)	-0.360 (0.065)	-0.320 (0.065)	0.29
	3	-0.295 (0.066)	-0.289 (0.064)	-0.361 (0.065)	-0.305 (0.065)	0.65
ICAM-1, ng/mL	1	0.197 (0.015)	0.188 (0.015)	0.192 (0.015)	0.183 (0.016)	0.48
	2	0.202 (0.022)	0.186 (0.021)	0.191 (0.022)	0.181 (0.021)	0.31
	3	0.199 (0.022)	0.184 (0.022)	0.191 (0.022)	0.185 (0.022)	0.54
IL-6, pg/mL	1	-0.248 (0.032)	-0.230 (0.033)	-0.269 (0.034)	-0.278 (0.035)	0.32
	2	-0.176 (0.048)	-0.165 (0.047)	-0.216 (0.047)	-0.228 (0.047)	0.12
	3	-0.179 (0.048)	-0.166 (0.047)	-0.217 (0.047)	-0.226 (0.048)	0.17
Corrected isoprostanes, ng/mmol***	1	0.030 (0.037)	0.044 (0.038)	0.043 (0.038)	0.020 (0.040)	0.82
	2	0.087 (0.056)	0.103 (0.055)	0.097 (0.055)	0.070 (0.054)	0.69
	3	0.107 (0.056)	0.116 (0.055)	0.098 (0.055)	0.052 (0.055)	0.24
MCP-1, pg/mL	1	0.186 (0.012)	0.195 (0.013)	0.185 (0.013)	0.154 (0.014)	0.03
	2	0.187 (0.019)	0.198 (0.018)	0.188 (0.019)	0.155 (0.018)	0.03
	3	0.188 (0.019)	0.200 (0.018)	0.188 (0.019)	0.153 (0.019)	0.03
OPG, pmol/L	1	-0.076 (0.011)	-0.072 (0.012)	-0.074 (0.012)	-0.085 (0.012)	0.52
	2	-0.038 (0.017)	-0.037 (0.016)	-0.041 (0.017)	-0.056 (0.016)	0.19
	3	-0.033 (0.017)	-0.035 (0.016)	-0.041 (0.017)	-0.060 (0.017)	0.06
LPL-A2 activity, nmol/mL/min	1	0.001 (0.011)	-0.015 (0.011)	-0.017 (0.012)	-0.023 (0.012)	0.09
	2	-0.021 (0.016)	-0.038 (0.016)	-0.038 (0.016)	-0.044 (0.016)	0.11
	3	-0.024 (0.017)	-0.040 (0.016)	-0.039 (0.016)	-0.041 (0.016)	0.30
LPL-A2 mass, ng/mL	1	-0.320 (0.013)	-0.364 (0.013)	-0.347 (0.013)	-0.355 (0.014)	0.07
	2	-0.360 (0.019)	-0.399 (0.019)	-0.382 (0.019)	-0.390 (0.019)	0.15
	3	-0.362 (0.019)	-0.401 (0.019)	-0.382 (0.019)	-0.388 (0.019)	0.25
P-selectin, ng/mL	1	0.144 (0.013)	0.127 (0.013)	0.105 (0.013)	0.139 (0.014)	0.56
	2	0.160 (0.019)	0.139 (0.018)	0.120 (0.019)	0.155 (0.019)	0.60
	3	0.163 (0.019)	0.140 (0.019)	0.120 (0.019)	0.152 (0.019)	0.38
TNFRII, pg/mL	1	0.241 (0.013)	0.250 (0.014)	0.233 (0.014)	0.239 (0.015)	0.74
	2	0.323 (0.020)	0.319 (0.020)	0.297 (0.020)	0.298 (0.020)	0.08
	3	0.318 (0.020)	0.316 (0.020)	0.296 (0.020)	0.303 (0.020)	0.29

*Values are the least square adjusted mean (SE) of the outcome, which is calculated as the change in log value of the biomarker, modeled as exam 8 log value minus exam 7 log value. A higher value of the outcome indicates a larger change (increase) in inflammation, whereas a lower value indicates a smaller change (increase if positive, decrease if negative), and thus less inflammation.
**Models are adjusted as in Table 2.

***N=1,690 for urinary creatinine-corrected urinary isoprostanes.
Abbreviations: BMI, body mass index; CRP, C-reactive protein; CVD, cardiovascular disease; ICAM-1, soluble intracellular adhesion molecule 1; IL-6, interleukin 6; LPL-A2, lipoprotein phospholipase A2; MCP-1, monocyte chemoattractant protein 1; NSAID, non-steroidal anti-inflammatory drug; OPG, osteoprotegerin; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; TNFRII, tumor necrosis factor receptor II.

Supplemental Table 3. Adjusted least square means of change in individual biomarkers of inflammation or oxidative stress per averaged plant protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.*

		Quartile Category of Plant Protein Intake (g/d)				
Change in Outcome	**Model****	**19.8**	**22.9**	**25.5**	**29.9**	***P* trend**
CRP, mg/L	1	-0.142 (0.044)	-0.178 (0.046)	-0.183 (0.046)	-0.246 (0.047)	0.06
	2	-0.277 (0.064)	-0.306 (0.066)	-0.300 (0.065)	-0.353 (0.065)	0.18
	3	-0.278 (0.065)	-0.310 (0.066)	-0.302 (0.065)	-0.356 (0.065)	0.20
ICAM-1, ng/mL	1	0.192 (0.015)	0.187 (0.015)	0.208 (0.015)	0.174 (0.016)	0.44
	2	0.196 (0.021)	0.187 (0.022)	0.205 (0.022)	0.171 (0.022)	0.24
	3	0.197 (0.022)	0.187 (0.022)	0.205 (0.022)	0.169 (0.022)	0.19
IL-6, pg/mL	1	-0.224 (0.032)	-0.225 (0.033)	-0.289 (0.034)	-0.296 (0.035)	0.03
	2	-0.172 (0.047)	-0.169 (0.048)	-0.224 (0.047)	-0.216 (0.047)	0.17
	3	-0.168 (0.047)	-0.168 (0.048)	-0.224 (0.047)	-0.220 (0.047)	0.13
Corrected isoprostanes, ng/mmol***	1	0.053 (0.037)	0.003 (0.038)	0.055 (0.039)	0.023 (0.038)	0.74
	2	0.096 (0.055)	0.053 (0.056)	0.111 (0.055)	0.085 (0.054)	0.92
	3	0.107 (0.055)	0.062 (0.056)	0.115 (0.055)	0.082 (0.054)	0.83
MCP-1, pg/mL	1	0.208 (0.012)	0.181 (0.013)	0.166 (0.013)	0.161 (0.013)	0.003
	2	0.211 (0.018)	0.183 (0.019)	0.168 (0.018)	0.161 (0.018)	0.002
	3	0.215 (0.018)	0.185 (0.019)	0.169 (0.018)	0.158 (0.019)	0.001
OPG, pmol/L	1	-0.070 (0.011)	-0.079 (0.012)	-0.077 (0.012)	-0.080 (0.012)	0.57
	2	-0.034 (0.016)	-0.044 (0.017)	-0.046 (0.016)	-0.050 (0.017)	0.27
	3	-0.028 (0.017)	-0.040 (0.017)	-0.045 (0.016)	-0.054 (0.017)	0.07
LPL-A2 activity, nmol/mL/min	1	-0.014 (0.011)	-0.013 (0.012)	-0.009 (0.012)	-0.012 (0.012)	0.86
	2	-0.035 (0.016)	-0.036 (0.016)	-0.033 (0.016)	-0.038 (0.016)	0.86
	3	-0.034 (0.016)	-0.037 (0.017)	-0.034 (0.016)	-0.040 (0.016)	0.70
LPL-A2 mass, ng/mL	1	-0.331 (0.013)	-0.345 (0.013)	-0.351 (0.013)	-0.358 (0.014)	0.10
	2	-0.368 (0.019)	-0.381 (0.019)	-0.387 (0.019)	-0.397 (0.019)	0.07
	3	-0.366 (0.019)	-0.380 (0.019)	-0.388 (0.019)	-0.400 (0.019)	0.04
P-selectin, ng/mL	1	0.138 (0.013)	0.120 (0.013)	0.134 (0.013)	0.122 (0.014)	0.45
	2	0.157 (0.018)	0.137 (0.019)	0.147 (0.019)	0.131 (0.019)	0.17
	3	0.160 (0.019)	0.139 (0.019)	0.148 (0.019)	0.129 (0.019)	0.10
TNFRII, pg/mL	1	0.247 (0.013)	0.232 (0.014)	0.248 (0.014)	0.236 (0.014)	0.70
	2	0.319 (0.020)	0.300 (0.020)	0.314 (0.020)	0.301 (0.020)	0.44
	3	0.319 (0.020)	0.299 (0.020)	0.313 (0.020)	0.301 (0.020)	0.44

*Values are the least square adjusted mean (SE) of the outcome, which is calculated as the change in log value of the biomarker, modeled as exam 8 log value minus exam 7 log value. A higher value of the outcome indicates a larger change (increase) in inflammation/oxidative stress, whereas a lower value indicates a smaller change (increase if positive, decrease if negative), and thus less inflammation/oxidative stress.
**Models are adjusted as in Table 2; model 3 additionally includes animal protein.

***N=1,690 for urinary creatinine-corrected urinary isoprostanes.
Abbreviations: BMI, body mass index; CRP, C-reactive protein; CVD, cardiovascular disease; ICAM-1, soluble intracellular adhesion molecule 1; IL-6, interleukin 6; LPL-A2, lipoprotein phospholipase A2; MCP-1, monocyte chemoattractant protein 1; NSAID, non-steroidal anti-inflammatory drug; OPG, osteoprotegerin; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; TNFRII, tumor necrosis factor receptor II.

Supplemental Table 4. Adjusted least square means of change in individual biomarkers of inflammation or oxidative stress per averaged animal protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.*

		Quartile Category of Animal Protein Intake (g/d)				
Change in Outcome	**Model****	**42.6**	**52.5**	**60.3**	**71.6**	***P* trend**
CRP, mg/L	1	-0.161 (0.045)	-0.189 (0.045)	-0.196 (0.045)	-0.180 (0.047)	0.73
	2	-0.282 (0.065)	-0.307 (0.064)	-0.327 (0.065)	-0.317 (0.065)	0.49
	3	-0.289 (0.066)	-0.314 (0.064)	-0.332 (0.065)	-0.312 (0.066)	0.66
ICAM-1, ng/mL	1	0.203 (0.015)	0.177 (0.015)	0.189 (0.015)	0.195 (0.016)	0.84
	2	0.206 (0.022)	0.175 (0.021)	0.187 (0.022)	0.194 (0.022)	0.73
	3	0.205 (0.022)	0.174 (0.021)	0.186 (0.022)	0.194 (0.022)	0.76
IL-6, pg/mL	1	-0.254 (0.033)	-0.247 (0.033)	-0.250 (0.033)	-0.270 (0.035)	0.67
	2	-0.177 (0.048)	-0.183 (0.047)	-0.195 (0.047)	-0.231 (0.047)	0.16
	3	-0.171 (0.048)	-0.183 (0.047)	-0.198 (0.047)	-0.237 (0.048)	0.12
Corrected isoprostanes, ng/mmol***	1	0.019 (0.038)	0.077 (0.037)	0.017 (0.037)	0.020 (0.040)	0.73
	2	0.077 (0.056)	0.137 (0.054)	0.069 (0.054)	0.069 (0.055)	0.55
	3	0.094 (0.056)	0.144 (0.054)	0.071 (0.054)	0.055 (0.055)	0.24
MCP-1, pg/mL	1	0.176 (0.013)	0.201 (0.013)	0.177 (0.013)	0.172 (0.014)	0.53
	2	0.173 (0.019)	0.200 (0.018)	0.179 (0.018)	0.173 (0.019)	0.69
	3	0.180 (0.019)	0.201 (0.018)	0.176 (0.018)	0.165 (0.019)	0.19
OPG, pmol/L	1	-0.080 (0.011)	-0.062 (0.011)	-0.083 (0.012)	-0.081 (0.012)	0.58
	2	-0.042 (0.017)	-0.029 (0.016)	-0.050 (0.017)	-0.053 (0.017)	0.24
	3	-0.037 (0.017)	-0.027 (0.016)	-0.050 (0.017)	-0.058 (0.017)	0.07
LPL-A2 activity, nmol/mL/min	1	-0.002 (0.011)	-0.001 (0.011)	-0.025 (0.011)	-0.025 (0.012)	0.04
	2	-0.026 (0.016)	-0.024 (0.016)	-0.049 (0.016)	-0.045 (0.016)	0.08
	3	-0.029 (0.017)	-0.025 (0.016)	-0.049 (0.016)	-0.043 (0.017)	0.19
LPL-A2 mass, ng/mL	1	-0.326 (0.013)	-0.352 (0.013)	-0.350 (0.013)	-0.353 (0.014)	0.10
	2	-0.367 (0.019)	-0.389 (0.019)	-0.387 (0.019)	-0.389 (0.019)	0.21
	3	-0.364 (0.019)	-0.390 (0.019)	-0.389 (0.019)	-0.392 (0.019)	0.14
P-selectin, ng/mL	1	0.132 (0.013)	0.130 (0.013)	0.122 (0.013)	0.134 (0.014)	0.97
	2	0.144 (0.019)	0.143 (0.018)	0.136 (0.019)	0.153 (0.019)	0.67
	3	0.149 (0.019)	0.144 (0.018)	0.135 (0.019)	0.148 (0.019)	0.86
TNFRII, pg/mL	1	0.235 (0.014)	0.248 (0.014)	0.240 (0.014)	0.241 (0.015)	0.88
	2	0.316 (0.020)	0.317 (0.020)	0.305 (0.020)	0.299 (0.020)	0.24
	3	0.313 (0.020)	0.315 (0.020)	0.304 (0.020)	0.301 (0.020)	0.45

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Supplemental Table 5. Sensitivity analyses of adjusted least square means of change in individual biomarkers of inflammation or oxidative stress, overall score, and cytokine and oxidative stress subscores between exams 7 and 8, per total, plant, and animal protein in quartile categories of intake averaged from exams 6 and 7, in participants of the Framingham Heart Study Offspring cohort.*

		Quartile Category of Protein Intake**								
		Plant Protein			Animal Protein			Total Protein		
Change in outcome	**Model*** **	**Q1**	**Q4**	***P* trend**	**Q1**	**Q4**	***P* trend**	**Q1**	**Q4**	***P* trend**
Inflammation Score	1	0.677 (0.173)	0.337 (0.183)	0.06	0.639 (0.176)	0.545 (0.180)	0.77	0.795 (0.174)	0.522 (0.182)	0.12
	2	0.715 (0.257)	0.313 (0.251)	0.04	0.649 (0.257)	0.489 (0.250)	0.55	0.858 (0.259)	0.474 (0.250)	0.046
	3	0.711 (0.257)	0.305 (0.251)	0.03	0.674 (0.258)	0.457 (0.252)	0.40	0.890 (0.261)	0.434 (0.252)	0.02
Cytokine Subscore	1	0.314 (0.073)	0.233 (0.079)	0.30	0.274 (0.075)	0.293 (0.077)	0.73	0.314 (0.074)	0.263 (0.078)	0.57
	2	0.652 (0.109)	0.551 (0.107)	0.23	0.639 (0.109)	0.545 (0.106)	0.35	0.702 (0.110)	0.522 (0.106)	0.05
	3	0.653 (0.109)	0.553 (0.107)	0.23	0.638 (0.109)	0.547 (0.107)	0.38	0.703 (0.111)	0.522 (0.107)	0.05
Oxidative Stress Subscore	1	0.253 (0.106)	0.207 (0.111)	0.78	0.218 (0.108)	0.120 (0.110)	0.58	0.264 (0.106)	0.139 (0.112)	0.27
	2	0.007 (0.158)	-0.048 (0.154)	0.71	-0.043 (0.157)	-0.104 (0.154)	0.80	0.011 (0.158)	-0.089 (0.154)	0.39
	3	0.006 (0.158)	-0.052 (0.154)	0.71	-0.010 (0.158)	-0.133 (0.154)	0.50	0.047 (0.159)	-0.119 (0.154)	0.19
CRP	1	-0.180 (0.044)	-0.181 (0.047)	0.74	-0.134 (0.045)	-0.163 (0.046)	0.62	-0.133 (0.044)	-0.192 (0.047)	0.30
	2	-0.326 (0.065)	-0.290 (0.064)	0.74	-0.255 (0.065)	-0.297 (0.064)	0.46	-0.257 (0.065)	-0.319 (0.064)	0.30
	3	-0.326 (0.065)	-0.290 (0.064)	0.73	-0.254 (0.065)	-0.297 (0.064)	0.45	-0.256 (0.066)	-0.320 (0.064)	0.28
ICAM-1	1	0.195 (0.015)	0.191 (0.016)	0.82	0.192 (0.015)	0.177 (0.015)	0.38	0.205 (0.015)	0.186 (0.015)	0.12
	2	0.199 (0.022)	0.187 (0.021)	0.50	0.195 (0.022)	0.176 (0.021)	0.29	0.211 (0.022)	0.184 (0.021)	0.05
	3	0.199 (0.022)	0.187 (0.021)	0.49	0.195 (0.022)	0.176 (0.021)	0.31	0.211 (0.022)	0.184 (0.021)	0.06
IL-6	1	-0.215 (0.032)	-0.269 (0.035)	0.15	-0.230 (0.033)	-0.257 (0.034)	0.62	-0.206 (0.033)	-0.271 (0.034)	0.13
	2	-0.166 (0.048)	-0.194 (0.047)	0.43	-0.159 (0.047)	-0.212 (0.047)	0.23	-0.134 (0.048)	-0.220 (0.047)	0.047
	3	-0.166 (0.048)	-0.192 (0.047)	0.45	-0.161 (0.048)	-0.209 (0.047)	0.30	-0.136 (0.048)	-0.217 (0.047)	0.07
Isoprostanes	1	0.044 (0.037)	0.056 (0.039)	0.91	0.013 (0.038)	0.025 (0.038)	0.71	0.025 (0.037)	0.009 (0.039)	0.80
	2	0.083 (0.056)	0.111 (0.054)	0.68	0.069 (0.056)	0.076 (0.054)	0.81	0.076 (0.056)	0.061 (0.054)	0.79
	3	0.081 (0.056)	0.111 (0.054)	0.65	0.088 (0.056)	0.061 (0.054)	0.65	0.096 (0.056)	0.045 (0.054)	0.33
MCP-1	1	0.205 (0.013)	0.155 (0.013)	0.0006	0.174 (0.013)	0.172 (0.013)	0.61	0.189 (0.013)	0.166 (0.013)	0.04

	2	0.209 (0.019)	0.157 (0.018)	0.0004	0.172 (0.019)	0.173 (0.018)	0.81	0.188 (0.019)	0.168 (0.018)	0.07
	3	0.209 (0.019)	0.157 (0.018)	0.0005	0.174 (0.019)	0.171 (0.018)	0.64	0.191 (0.019)	0.165 (0.018)	0.04
OPG	1	-0.073 (0.011)	-0.085 (0.012)	0.25	-0.072 (0.011)	-0.073 (0.012)	0.99	-0.068 (0.011)	-0.081 (0.012)	0.33
	2	-0.035 (0.017)	-0.053 (0.016)	0.14	-0.036 (0.017)	-0.046 (0.016)	0.51	-0.028 (0.017)	-0.054 (0.016)	0.07
	3	-0.035 (0.017)	-0.054 (0.016)	0.12	-0.034 (0.017)	-0.048 (0.016)	0.32	-0.025 (0.017)	-0.057 (0.016)	0.03
LPL-A2 Activity	1	-0.016 (0.011)	-0.024 (0.012)	0.52	-0.011 (0.011)	-0.015 (0.012)	0.68	-0.006 (0.011)	-0.015 (0.012)	0.38
	2	-0.035 (0.016)	-0.050 (0.016)	0.26	-0.035 (0.016)	-0.035 (0.016)	0.85	-0.028 (0.016)	-0.036 (0.016)	0.40
	3	-0.035 (0.016)	-0.050 (0.016)	0.25	-0.035 (0.016)	-0.036 (0.016)	0.84	-0.028 (0.017)	-0.037 (0.016)	0.37
LPL-A2 Mass	1	-0.339 (0.013)	-0.368 (0.014)	0.08	-0.333 (0.013)	-0.349 (0.013)	0.54	-0.329 (0.013)	-0.347 (0.014)	0.23
	2	-0.375 (0.019)	-0.403 (0.019)	0.09	-0.372 (0.019)	-0.386 (0.019)	0.68	-0.367 (0.019)	-0.383 (0.019)	0.33
	3	-0.375 (0.019)	-0.403 (0.019)	0.09	-0.371 (0.019)	-0.387 (0.019)	0.54	-0.365 (0.019)	-0.385 (0.019)	0.23
P-Selectin	1	0.125 (0.013)	0.131 (0.014)	0.99	0.138 (0.013)	0.142 (0.013)	0.51	0.137 (0.013)	0.145 (0.013)	0.56
	2	0.145 (0.019)	0.140 (0.018)	0.52	0.150 (0.019)	0.157 (0.018)	0.36	0.152 (0.019)	0.159 (0.018)	0.55
	3	0.144 (0.019)	0.138 (0.018)	0.48	0.153 (0.019)	0.153 (0.019)	0.71	0.155 (0.019)	0.154 (0.019)	0.98
TNFRII	1	0.250 (0.013)	0.252 (0.014)	0.78	0.234 (0.014)	0.258 (0.014)	0.18	0.240 (0.014)	0.263 (0.014)	0.20
	2	0.322 (0.020)	0.316 (0.020)	0.87	0.310 (0.020)	0.314 (0.019)	0.94	0.319 (0.020)	0.318 (0.019)	0.85
	3	0.322 (0.020)	0.317 (0.020)	0.89	0.309 (0.020)	0.316 (0.020)	0.78	0.317 (0.020)	0.320 (0.020)	0.98

*Values are the least square adjusted mean (SE) of the outcome in quartile categories 1 and 4 (2 and 3 omitted), which is calculated as the change in log value of the biomarker, modeled as exam 8 log value minus exam 7 log value. A higher value of the outcome indicates a larger change (increase) in inflammation/oxidative stress, whereas a lower value indicates a smaller change (increase if positive, decrease if negative), and thus less inflammation/oxidative stress. The cytokine score is the sum of rank-normalized values of IL-6, TNFRII, and OPG (N=2,061). The oxidation subscore is the sum of rank-normalized values of LPL-A2 mass and activity, and urinary creatinine-corrected isoprostanes (N=1,690). A higher value of the outcome indicates a larger change (increase) in inflammation/oxidative stress, whereas a lower value indicates a smaller change (increase if positive, decrease if negative), and thus less inflammation/oxidative stress.

**Median values in quartile categories 1 and 4 of intake were for plant protein, 18.6 and 28.7 g/d; for animal protein, 40.9 and 70.0 g/d; for total protein, 64.9 and 92.6 g/d.

***Models are adjusted as in Table 2; model 3 additionally includes plant protein or animal protein, in animal and plant protein models, respectively.

Abbreviations: BMI, body mass index; CRP, C-reactive protein; CVD, cardiovascular disease; ICAM-1, soluble intracellular adhesion molecule 1; IL-6, interleukin 6; LPL-A2, lipoprotein phospholipase A2; MCP-1, monocyte chemoattractant protein 1; NSAID, non-steroidal anti-inflammatory drug; OPG, osteoprotegerin; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; TNFRII, tumor necrosis factor receptor II.

Supplemental Table 6. Adjusted least square means of change in cytokine and oxidative stress subscores per averaged total, plant, and animal protein in quartile categories of intake in 2,061 participants of the Framingham Heart Study Offspring cohort.*

		Quartile Category of Protein Intake**				
Protein Source	**Model*** **	**Q1**	**Q2**	**Q3**	**Q4**	***P* trend**
Cytokine Subscore						
Total, g/d	1	0.248 (0.073)	0.296 (0.075)	0.193 (0.077)	0.188 (0.080)	0.35
	2	0.637 (0.110)	0.630 (0.107)	0.493 (0.108)	0.458 (0.107)	0.02
	3	0.633 (0.111)	0.629 (0.108)	0.493 (0.108)	0.461 (0.109)	0.04
Animal, g/d	1	0.217 (0.075)	0.295 (0.075)	0.220 (0.076)	0.202 (0.079)	0.69
	2	0.602 (0.110)	0.621 (0.107)	0.527 (0.108)	0.459 (0.108)	0.07
	3	0.616 (0.111)	0.621 (0.107)	0.520 (0.108)	0.446 (0.110)	0.05
Plant, g/d	1	0.299 (0.073)	0.238 (0.076)	0.198 (0.077)	0.175 (0.079)	0.16
	2	0.635 (0.107)	0.561 (0.109)	0.511 (0.108)	0.496 (0.108)	0.12
	3	0.659 (0.108)	0.572 (0.110)	0.513 (0.108)	0.477 (0.109)	0.05
Oxidation Subscore						
Total, g/d	1	0.343 (0.105)	0.125 (0.108)	0.315 (0.107)	0.062 (0.114)	0.09
	2	0.092 (0.157)	-0.097 (0.155)	0.097 (0.155)	-0.156 (0.154)	0.16
	3	0.102 (0.159)	-0.090 (0.156)	0.098 (0.155)	-0.166 (0.156)	0.14
Animal, g/d	1	0.285 (0.108)	0.287 (0.106)	0.208 (0.106)	0.080 (0.114)	0.09
	2	0.019 (0.157)	0.048 (0.154)	-0.023 (0.154)	-0.138 (0.156)	0.19
	3	0.036 (0.160)	0.053 (0.155)	-0.025 (0.154)	-0.153 (0.158)	0.15
Plant, g/d	1	0.307 (0.105)	0.159 (0.109)	0.237 (0.110)	0.177 (0.110)	0.44
	2	0.068 (0.154)	-0.090 (0.158)	-0.010 (0.156)	-0.083 (0.154)	0.36
	3	0.104 (0.156)	-0.070 (0.158)	-0.005 (0.156)	-0.107 (0.155)	0.18

*Values are the least square adjusted mean (SE) of the outcome, which is the change in the score, modeled as the difference in the score between exam 8 and exam 7. The cytokine score is the sum of rank-normalized values of IL-6, TNFRII, and OPG (N=2,061). The oxidation subscore is the sum of rank-normalized values of LPL-A2 mass and activity, and urinary creatinine-corrected isoprostanes (N=1,690). A higher value of the outcome indicates a larger change (increase) in inflammation/oxidative stress, whereas a lower value indicates a smaller change (increase if positive, decrease if negative), and thus less inflammation/oxidative stress.

**Median values in quartile categories of intake were as follows: for total protein, 67.4, 77.3, 85.0, and 95.9 g/d; for animal protein, 42.6, 52.5, 60.3, and 71.6 g/d; and for plant protein, 19.8, 22.9, 25.5, and 29.9 g/d.

***Models were adjusted as follows: 1) age, sex, energy intake, smoking status, and the baseline (exam 7) value of the score; 2) baseline physical activity, NSAID use, BMI, cardiovascular disease history, treatment for hypertension, diabetes, and/or dyslipidemia, and alcohol intake; 3) Glycemic Index, and the PUFA:SFA ratio. For animal and plant protein, model 3 was also adjusted for the other protein source (e.g., animal protein adjusted for plant protein as well as Glycemic Index and the PUFA:SFA ratio).

Abbreviations: BMI, body mass index; CRP, C-reactive protein; CVD, cardiovascular disease; ICAM-1, soluble intracellular adhesion molecule 1; IL-6, interleukin 6; LPL-A2, lipoprotein phospholipase A2; MCP-1, monocyte chemoattractant protein 1; NSAID, non-steroidal anti-inflammatory drug; OPG, osteoprotegerin; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; TNFRII, tumor necrosis factor receptor II.