## **Supplementary Tables**

"Protein intake and functional integrity in aging: The Framingham Heart Study Offspring."

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**Supplementary Table 8.** Sex-specific secondary analyses of the Functional Integrity Score to estimate hazard ratios (95% confidence intervals) of incident loss of functional integrity by quartile category of average protein intake, expressed in grams per kilogram body weight per day, in male and female participants of the Framingham Offspring.

Scale	Short Name	Question Example*	Response Scores**
Katz Activities of Daily Living	ADL Dressing	During the course of a normal day, can you get dressed (undressing redressing) independently or do you need human assistance or the use of a device (such as velcro, elastic laces)?	0 = no help needed, independent 1 = uses device, independent 2 = human assistance needed, minimally dependent 3 = dependent
Katz Activities of Daily Living	ADL Bathing	During the course of a normal day, can you bathe (including getting in and out of the tub or shower) independently or do you need human assistance or the use of a device (such as bath chair, long handled sponge, hand held shower, safety bars)?	Same as above.
Katz Activities of Daily Living	ADL Eating	During the course of a normal day, can you eat independently or do you need human assistance or the use of a device (such as rocking knife, spork, long straw, plate guard)?	Same as above.
Katz Activities of Daily Living	ADL Transferring	During the course of a normal day, can you transfer (getting in and out of a chair) independently or do you need human assistance or the use of a device (such as, sliding board, grab bars, special seat)?	Same as above.
Katz Activities of Daily Living	ADL Toileting	During the course of a normal day, can you do toileting activities (using bathroom facilities and handle clothing) independently or do you need human assistance or the use of a device (such as, special toilet seat, commode)?	Same as above.
Rosow-Breslau	Rosow-Breslau Housework	Are you able to do heavy work around the house, like shoveling snow or washing windows, walls, or floors without help?	0 = no 1 = yes
Rosow-Breslau	Rosow-Breslau Flight of Stairs	Are you able to walk up and down one flight of stairs without help?	Same as above.
Rosow-Breslau***	Rosow-Breslau Walk 1/2 Mile	Are you able to walk half a mile without help? (about 4-6 blocks)	Same as above.
Nagi	Nagi Pulling	Difficulty with Pulling or pushing large objects like a living room chair	0 = no difficulty 1 = a little difficulty 2 = some difficulty 3 = a lot of difficulty / unable to do or don't do on MD orders
Nagi	Nagi Stooping	Difficulty with Either stooping, crouching, or kneeling	Same as above.
Nagi	Nagi Low Arms	Difficulty with Reaching or extending arms below shoulder level	Same as above.
Nagi	Nagi High Arms	Difficulty with Reaching or extending arms above shoulder level	Same as above.
Nagi	Nagi Writing	Difficulty with Either writing, or handling, or fingering small objects	Same as above.
Nagi	Nagi Standing	Difficulty with Standing in one place for long periods, say 15 minutes	Same as above.
Nagi	Nagi Sitting	Difficulty with Sitting for long periods, say 1 hour	Same as above.
Nagi	Nagi Light Weights	Difficulty with Lifting or carrying weights under 10 pounds (like a bag of potatoes)	Same as above.
Nagi	Nagi Heavy Weights	Difficulty with Lifting or carrying weights over 10 pounds (like a very heavy bag of groceries)	Same as above.

\*Questions varied insignificantly between exams. \*\*Responses were subsequently scaled to a 10-point range wherein independence/highest ability/no difficulty was rated 10. \*\*\*This measure was not available at exam 7; however, an ADL flight-of-stairs measure was available and substituted for the Rosow-Breslau measure at exam 7 only.

Supplementary Table 2. Components of the Functional Integrity Score and relationships with the total score.

	Exam 5		Exam 6		Exam 7		Exam 8		Exam 9	
	Correlation with total	Cronbach's								
Score Component	FIS	alpha*								
ADL Dressing	0.12	0.82	0.37	0.83	0.13	0.80	0.35	0.83	0.41	0.86
ADL Bathing	0.31	0.81	0.45	0.83	0.40	0.79	0.51	0.83	0.54	0.85
ADL Eating	0.17	0.82	0.29	0.83	0.10	0.80	0.29	0.83	0.20	0.86
ADL Transferring	0.38	0.81	0.45	0.83	0.36	0.80	0.42	0.83	0.44	0.86
ADL Toileting	0.25	0.81	0.35	0.83	0.27	0.80	0.40	0.83	0.48	0.86
Rosow-Breslau Housework	0.60	0.80	0.55	0.82	0.53	0.78	0.61	0.82	0.66	0.85
Rosow-Breslau Flight of Stairs	0.43	0.80	0.40	0.82	0.48	0.79	0.43	0.83	0.57	0.85
Rosow-Breslau Walk 1/2 Mile	0.48	0.80	0.49	0.82	0.43	0.78	0.57	0.82	0.67	0.84
Nagi Pulling	0.64	0.78	0.62	0.81	0.60	0.77	0.59	0.81	0.64	0.85
Nagi Stooping	0.53	0.80	0.51	0.82	0.55	0.77	0.48	0.82	0.58	0.85
Nagi Low Arms	0.19	0.81	0.28	0.83	0.30	0.79	0.46	0.83	0.42	0.86
Nagi High Arms	0.32	0.81	0.39	0.82	0.28	0.79	0.37	0.83	0.38	0.86
Nagi Writing	0.30	0.81	0.37	0.82	0.34	0.79	0.30	0.83	0.39	0.86
Nagi Standing	0.59	0.79	0.60	0.81	0.55	0.77	0.57	0.82	0.61	0.85
Nagi Sitting	0.44	0.80	0.40	0.82	0.33	0.79	0.29	0.83	0.28	0.86
Nagi Light Weights	0.56	0.80	0.64	0.81	0.58	0.78	0.61	0.82	0.59	0.85
Nagi Heavy Weights	0.68	0.78	0.70	0.80	0.65	0.77	0.62	0.81	0.69	0.84

Abbreviation: FIS, Functional Integrity Score. \*Cronbach's alpha is a measure of reliability, or internal consistency of a set of scale or test items (i.e., how closely related a set of items are as a group). For ease of reading, items highlighted in bold are correlations ≥0.60 with the total Functional Integrity Score.

Supplementary Table 3. Odds ratios of reporting a fall or a fracture in the year leading up to the exam, based on the Functional Integrity Score.

	Events/Non-Events	Exposure	Odds Ratio (95% CI) of H Suffered a Fracture in	laving Fallen/ Prior Year*
Falls				
Exam 5**	524/2386	Per 1 point in FIS	0.94 (0.90, 0.98)	
Exam 6	475/2161	Per 1 point in FIS	0.97 (0.95, 0.99)	
	498/2219	FIS >10th percentile	0.64 (0.44, 0.93)	vs. ≤10th percentile
	475/2161	FIS >15th percentile	0.65 (0.47, 0.90)	vs. ≤15th percentile
	457/2086	FIS >20th percentile	0.67 (0.50, 0.89)	vs. ≤20th percentile
Exam 7	460/2086	Per 1 point in FIS	0.95 (0.94, 0.97)	
	486/2139	FIS >10th percentile	0.51 (0.37, 0.73)	vs. ≤10th percentile
	460/2086	FIS >15th percentile	0.53 (0.39, 0.72)	vs. ≤15th percentile
	445/2009	FIS >20th percentile	0.48 (0.36, 0.63)	vs. ≤20th percentile
Fractures				
Exam 5**	159/2750	Per 1 point in FIS	0.97 (0.91, 1.05)	
Exam 6	177/2458	Per 1 point in FIS	0.97 (0.95, 0.99)	
	186/2530	FIS >10th percentile	0.62 (0.36, 1.05)	vs. ≤10th percentile
	177/2458	FIS >15th percentile	0.78 (0.47, 1.29)	vs. ≤15th percentile
	168/2374	FIS >20th percentile	0.82 (0.52, 1.31)	vs. ≤20th percentile
Exam 7	154/2400	Per 1 point in FIS	0.97 (0.95, 0.99)	
	158/2472	FIS >10th percentile	0.56 (0.33, 0.94)	vs. ≤10th percentile
	154/2400	FIS >15th percentile	0.48 (0.31, 0.75)	vs. ≤15th percentile
	150/2312	FIS >20th percentile	0.49 (0.32, 0.74)	vs. ≤20th percentile
Exam 8	241/1964	Per 1 point in FIS	0.97 (0.96, 0.98)	
	247/2024	FIS >10th percentile	0.54 (0.37, 0.78)	vs. ≤10th percentile
	241/1964	FIS >15th percentile	0.53 (0.38, 0.73)	vs. ≤15th percentile
	234/1902	FIS >20th percentile	0.70 (0.51, 0.97)	vs. ≤20th percentile
Exam 9	154/1632	Per 1 point in FIS	0.97 (0.95, 0.98)	
	158/1680	FIS >10th percentile	0.34 (0.22, 0.54)	vs. ≤10th percentile
	154/1632	FIS >15th percentile	0.37 (0.25, 0.55)	vs. ≤15th percentile
	151/1578	FIS >20th percentile	0.46 (0.31, 0.68)	vs. ≤20th percentile

Abbreviation: FIS, Functional Integrity Score.

\*Adjusted for age, sex, and body mass index. Reference level for odds ratios is the category below the percentile indicated (e.g., for FIS >10th percentile, the reference category is ≤10th percentile).

\*\*Odds ratios are not available, because participants in the percentile below the cut point were excluded at baseline.

Supplementary Table 4. Odds ratios of being frail at the respective exam, based on the Functional Integrity Score at exams 8 and 9.

Frailty	Events/Non-Events	Exposure	Odds Ratio (95% CI) of Being Frail*		
Exam 8	119/2102	Per 1 point in FIS	0.93 (0.92, 0.95)		
	125/2162	FIS >10th percentile	0.14 (0.09, 0.22)	vs. ≤10th percentile	
	119/2102	FIS >15th percentile	0.14 (0.09, 0.22)	vs. ≤15th percentile	
	116/2036	FIS >20th percentile	0.17 (0.11, 0.26)	vs. ≤20th percentile	
Exam 9	124/1675	Per 1 point in FIS	0.93 (0.92, 0.95)		
	130/1721	FIS >10th percentile	0.12 (0.07, 0.18)	vs. ≤10th percentile	
	124/1675	FIS >15th percentile	0.14 (0.09, 0.22)	vs. ≤15th percentile	
	115/1627	FIS >20th percentile	0.18 (0.12, 0.28)	vs. ≤20th percentile	

Abbreviation: FIS, Functional Integrity Score.

\*Frailty definition adapted from Fried LP, Tangen CM, Walston J, *et al.* Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001; 56(3): M146-156. Odds ratios were adjusted for age, sex, body mass index, and height. Reference level for odds ratios is the category below the percentile indicated (e.g., for FIS >10th percentile, the reference category is  $\leq$ 10th percentile).

**Supplementary Table 5.** Adjusted least square means of objective functional measures  $\leq$  and >15th percentile of the Functional Integrity Score at exams 8 and 9.\*

Objective Functional Measure	a	Mean (SD) at FIS Exam 8		a	Mean (SD) at FIS Exam 9	
	≤10th %ile	>10th %ile	P diff.	≤10th %ile	>10th %ile	P diff.
Gait speed, m/s	1.08 (0.01)	1.19 (0.01)	<0.001	0.91 (0.02)	1.10 (0.004)	<0.001
Quick gait speed, m/s	1.47 (0.02)	1.63 (0.01)	<0.001	1.24 (0.02)	1.48 (0.01)	<0.001
Grip strength, left hand, kg	25.39 (0.45)	27.38 (0.16)	<0.001	22.33 (0.58)	26.58 (0.16)	<0.001
Grip strength, right hand, kg	26.93 (0.44)	29.44 (0.16)	<0.001	22.68 (0.59)	26.84 (0.16)	<0.001
	≤15th %ile	>15th %ile	P diff.	≤15th %ile	>15th %ile	P diff.
Gait speed, m/s	1.11 (0.01)	1.19 (0.01)	<0.001	0.98 (0.01)	1.10 (0.004)	<0.001
Quick gait speed, m/s	1.51 (0.02)	1.64 (0.01)	<0.001	1.32 (0.02)	1.49 (0.01)	<0.001
Grip strength, left hand, kg	25.59 (0.38)	27.94 (0.16)	<0.001	23.32 (0.45)	26.89 (0.16)	<0.001
Grip strength, right hand, kg	27.41 (0.38)	29.65 (0.16)	<0.001	23.83 (0.46)	27.08 (0.17)	<0.001
	≤20th %ile	>20th %ile	<i>P</i> diff.	≤20th %ile	>20th %ile	P diff.
Gait speed, m/s	1.11 (0.01)	1.20 (0.01)	<0.001	0.99 (0.01)	1.11 (0.004)	<0.001
Quick gait speed, m/s	1.53 (0.02)	1.65 (0.01)	<0.001	1.34 (0.01)	1.50 (0.01)	<0.001
Grip strength, left hand, kg	25.92 (0.35)	28.11 (0.17)	<0.001	23.97 (0.40)	27.03 (0.17)	<0.001
Grip strength, right hand, kg	27.81 (0.35)	29.78 (0.17)	<0.001	24.30 (0.41)	27.23 (0.17)	<0.001

Abbreviations: %ile, percentile; diff., difference; FIS, Functional Integrity Score. \*Least square means in categories of the Functional Integrity Score were adjusted for age, sex, BMI, and height (for gait speeds).

**Supplementary Table 6.** Sensitivity analyses using alternate cut-points of the Functional Integrity Score to estimate hazard ratios (95% confidence intervals) of incident loss of functional integrity by quartile category of average protein intake in participants of the Framingham Offspring.

	Per Quartile Category of Average Protein Intake (median, g/d)				
Outcome: FIS ≤10th percentile	64.5	74.5	82.0	92.1	P trend
Events, N	151	123	135	124	
Person-years	10375	11415	11799	11274	
Crude rate per 100 p-y	1.46	1.08	1.14	1.10	
Model 1	1 (ref)	0.67 (0.53, 0.86)	0.69 (0.54, 0.88)	0.65 (0.51, 0.83)	0.001
Model 2	1 (ref)	0.72 (0.53, 0.98)	0.65 (0.48, 0.88)	0.52 (0.37, 0.72)	<0.001
Model 3	1 (ref)	0.74 (0.55, 1.01)	0.71 (0.52, 0.97)	0.59 (0.42, 0.84)	0.003
Model 4	1 (ref)	0.79 (0.58, 1.08)	0.82 (0.59, 1.13)	0.60 (0.42, 0.86)	0.008
Model 5	1 (ref)	0.80 (0.58, 1.09)	0.82 (0.60, 1.14)	0.61 (0.43, 0.86)	0.009
Outcome: FIS ≤20th percentile	64.3	74.4	81.9	92.2	P trend
Events, <i>N</i>	229	216	224	211	
Person-years	8963	10095	10176	9873	
Crude rate per 100 p-y	2.56	2.14	2.20	2.14	
Model 1	1 (ref)	0.80 (0.66, 0.96)	0.76 (0.63, 0.92)	0.72 (0.59, 0.88)	0.001
Model 2	1 (ref)	0.95 (0.74, 1.22)	0.85 (0.66, 1.09)	0.68 (0.52, 0.89)	0.003
Model 3	1 (ref)	1.00 (0.78, 1.29)	0.95 (0.73, 1.24)	0.80 (0.60, 1.06)	0.11
Model 4	1 (ref)	1.00 (0.78, 1.29)	1.01 (0.78, 1.32)	0.78 (0.59, 1.04)	0.10
Model 5	1 (ref)	1.02 (0.79, 1.32)	1.02 (0.78, 1.33)	0.78 (0.59, 1.04)	0.10

Hazard Ratio (95%CI) of Incident Loss of Functional Integrity Per Quartile Category of Average Protein Intake

Abbreviation: FIS, Functional Integrity Score; p-y, person-years.

Models were adjusted as follows: model 1 was adjusted for baseline age, sex, cumulative average energy intake, and the baseline Functional Integrity Score. Model 2 (risk factor model) was adjusted as for model 1, plus baseline and updated variables of body mass index, waist circumference, systolic blood pressure, treatment for hypertension, total:high-density lipoprotein cholesterol, treatment for hyperlipidemia, smoking status, and physical activity. Model 3 (diet model) was further adjusted for cumulative average intake of saturated fat, monounsaturated fat, polyunsaturated fat, and the Glycemic Index of the overall diet. Model 4 (socioeconomic risk model) was adjusted as for model 3, plus highest education completed and the most recent self-rated health status. Model 5 further adjusted for a cardiovascular event prior to the outcome. All models were stratified by 5-y age groups. *P* values for trend across quartile categories of intake were estimated using the median value in each quartile category, modeled as a continuous variable. **Supplementary Table 7.** Secondary analyses using various cut-points of the Functional Integrity Score to estimate hazard ratios (95% confidence intervals) of incident loss of functional integrity by quartile category of average protein intake, expressed in grams per kilogram body weight per day, in participants of the Framingham Offspring.

	Hazard Ratio (95%CI) of Incident Loss of Functional Integrity Per Quartile Category of Average Protein Intake (median, g/kg body weight /d)					
Outcome is FIS ≤10th percentile	0.74	0.93	1.11	1.37	P trend	
Events, N	150	123	145	115		
Person-years	10582	11447	11050	11783		
Crude rate per 100 p-y	1.42	1.07	1.31	0.98		
Model 1	1 (ref)	0.69 (0.54, 0.88)	0.63 (0.49, 0.81)	0.40 (0.31, 0.53)	<0.001	
Model 2	1 (ref)	0.75 (0.54, 1.02)	0.73 (0.50, 1.07)	0.53 (0.33, 0.85)	0.01	
Model 3	1 (ref)	0.81 (0.59, 1.12)	0.89 (0.60, 1.32)	0.67 (0.41, 1.09)	0.14	
Model 4	1 (ref)	0.85 (0.61, 1.17)	0.91 (0.61, 1.35)	0.70 (0.42, 1.14)	0.18	
Model 5	1 (ref)	0.85 (0.61, 1.18)	0.91 (0.61, 1.35)	0.70 (0.43, 1.15)	0.19	
Outcome is FIS ≤15th percentile*	0.75	0.93	1.11	1.37	P trend	
Events, N	208	176	199	148		
Person-years	9802	10794	10163	11212		
Crude rate per 100 p-y	2.12	1.63	1.96	1.32		
Model 1	1 (ref)	0.70 (0.57, 0.86)	0.64 (0.52, 0.80)	0.36 (0.28, 0.46)	<0.001	
Model 2	1 (ref)	0.82 (0.62, 1.07)	0.78 (0.57, 1.08)	0.49 (0.33, 0.73)	<0.001	
Model 3	1 (ref)	0.90 (0.69, 1.19)	0.98 (0.70, 1.36)	0.64 (0.43, 0.98)	0.04	
Model 4	1 (ref)	0.95 (0.72, 1.25)	1.00 (0.72, 1.40)	0.66 (0.43, 1.01)	0.06	
Model 5	1 (ref)	0.95 (0.72, 1.26)	1.01 (0.73, 1.42)	0.67 (0.44, 1.02)	0.07	
Outcome is FIS ≤20th percentile	0.75	0.93	1.11	1.37	P trend	
Events, N	256	190	239	195		
Person-years	9097	10198	9455	10357		
Crude rate per 100 p-y	2.81	1.86	2.53	1.88		
Model 1	1 (ref)	0.61 (0.50, 0.74)	0.63 (0.52, 0.77)	0.41 (0.33, 0.51)	<0.001	
Model 2	1 (ref)	0.69 (0.54, 0.89)	0.77 (0.58, 1.04)	0.55 (0.38, 0.80)	0.004	
Model 3	1 (ref)	0.75 (0.58, 0.97)	0.92 (0.68, 1.26)	0.69 (0.47, 1.01)	0.10	
Model 4	1 (ref)	0.77 (0.60, 1.01)	0.92 (0.68, 1.26)	0.69 (0.47, 1.02)	0.12	
Model 5	1 (ref)	0.77 (0.59, 1.01)	0.93 (0.68, 1.26)	0.70 (0.47, 1.03)	0.12	

Abbreviation: FIS, Functional Integrity Score; p-y, person-years.

\*This cut-point represents the primary outcome in primary analyses.

Models were adjusted as in the analyses for protein expressed in grams per day, except that updated body mass index was replaced with weight change owing to confounding by body mass index because of units (i.e., kg in the numerator of body mass index), as follows: model 1 was adjusted for baseline age, sex, cumulative average energy intake, and the baseline functional integrity score. Model 2 (risk factor model) was adjusted as for model 1, plus baseline body mass index, waist circumference, systolic blood pressure, treatment for hypertension, total:high-density lipoprotein cholesterol, treatment for hyperlipidemia, smoking status, weight change, and physical activity. Model 3 (diet model) was further adjusted for cumulative average intake of saturated fat, monounsaturated fat, polyunsaturated fat, and the Glycemic Index of the overall diet. Model 4 (socioeconomic risk model) was adjusted as for model 3, plus highest education completed and the most recent self-rated health status. Model 5 further adjusted for a cardiovascular event prior to the outcome. All models were stratified by 5-y age groups. *P* values for trend across quartile categories of intake were estimated using the median value in each quartile category, modeled as a continuous variable.

**Supplementary Table 8.** Sex-specific secondary analyses of the Functional Integrity Score to estimate hazard ratios (95% confidence intervals) of incident loss of functional integrity (<15th percentile of the Functional Integrity Score) by quartile category of average protein intake, expressed in grams per kilogram body weight per day, in male and female participants of the Framingham Offspring.

Hazard Ratio (95%CI) of Incident Loss of Functional Integrity Per Quartile Category of Average Protein Intake (median, g/kg body weight/d)							
Sex	0.75	0.93	1.11	1.37	P trend		
Female							
Events, N	72	97	146	137			
Person-years	1427	3409	6251	10020			
Crude rate per 100 p-y	5.04	2.85	2.34	1.37			
Model 1	1 (ref)	0.65 (0.48, 0.89)	0.53 (0.39, 0.70)	0.31 (0.23, 0.41)	<0.001		
Model 2	1 (ref)	0.84 (0.53, 1.33)	0.62 (0.38, 1.00)	0.39 (0.23, 0.67)	<0.001		
Model 3	1 (ref)	1.02 (0.63, 1.63)	0.83 (0.50, 1.39)	0.56 (0.31, 1.01)	0.007		
Model 4	1 (ref)	1.09 (0.67, 1.76)	0.89 (0.53, 1.51)	0.59 (0.32, 1.08)	0.009		
Model 5	1 (ref)	1.10 (0.68, 1.78)	0.89 (0.53, 1.51)	0.60 (0.33, 1.09)	0.01		
Male							
Events, N	136	79	53	11			
Person-years	8374	7385	3912	1192			
Crude rate per 100 p-y	1.62	1.07	1.35	0.92			
Model 1	1 (ref)	0.67 (0.51, 0.89)	0.82 (0.59, 1.14)	0.60 (0.32, 1.12)	0.04		
Model 2	1 (ref)	0.76 (0.53, 1.10)	1.14 (0.73, 1.78)	0.83 (0.37, 1.88)	0.92		
Model 3	1 (ref)	0.80 (0.55, 1.16)	1.37 (0.85, 2.19)	0.88 (0.38, 2.01)	0.72		
Model 4	1 (ref)	0.80 (0.55, 1.16)	1.30 (0.80, 2.12)	1.00 (0.43, 2.31)	0.64		
Model 5	1 <i>(ref)</i>	0.78 (0.54, 1.14)	1.34 (0.83, 2.17)	0.95 (0.41, 2.20)	0.65		

Abbreviation: p-y, person-years.

*P* interaction between protein and sex <0.05. Models were adjusted as in the analyses for protein expressed in grams per day, except that updated body mass index was replaced with weight change owing to confounding by body mass index because of units (i.e., kg in the numerator of body mass index), as follows: model 1 was adjusted for baseline age, cumulative average energy intake, and the baseline functional integrity score. Model 2 (risk factor model) was adjusted as for model 1, plus baseline body mass index, waist circumference, systolic blood pressure, treatment for hypertension, total:high-density lipoprotein cholesterol, treatment for hyperlipidemia, smoking status, weight change, and physical activity. Model 3 (diet model) was further adjusted for cumulative average intake of saturated fat, monounsaturated fat, polyunsaturated fat, and the Glycemic Index of the overall diet. Model 4 (socioeconomic risk model) was adjusted as for model 3, plus highest education completed and the most recent self-rated health status. Model 5 further adjusted for a cardiovascular event prior to the outcome. All models were stratified by 5-y age groups. *P* values for trend across quartile categories of intake were estimated using the median value in each quartile category, modeled as a continuous variable.