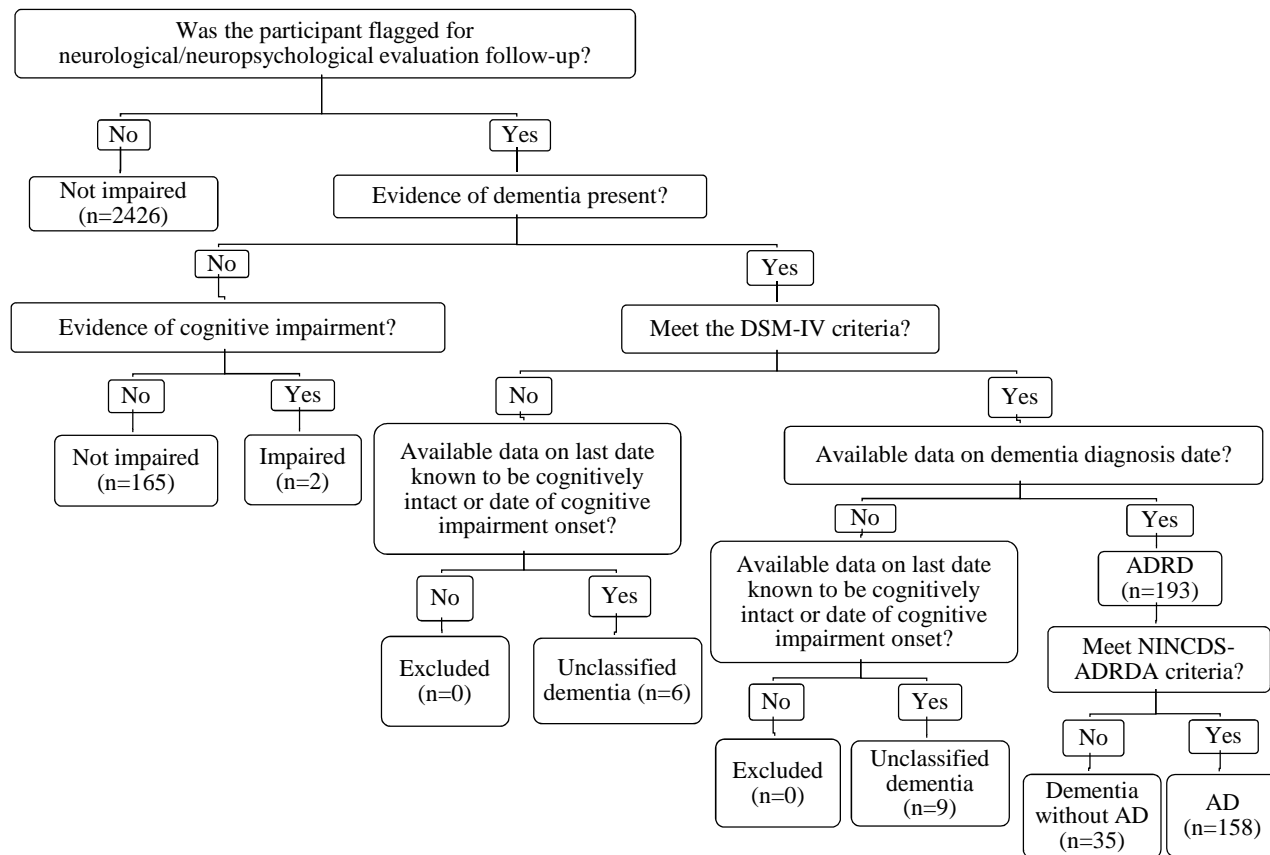# Long-term dietary flavonoid intake and risk of Alzheimer's disease and related dementias in the Framingham Offspring Cohort

Esra Shishtar

Online Supplementary Material

Supplemental Figure 1. Criteria for Alzheimer's disease and related dementias and Alzheimer's disease classification. AD, Alzheimer's disease; ADRD, Alzheimer's disease and related dementias; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; NINCDS-ADRDA, National Institute of Neurological and Communicative Diseases and Stroke and the Alzheimer's Disease and Related Disorders Association.

Supplemental Table 1. Top contributing foods for total flavonoids and each flavonoid class among our population at exam 5

Flavonoid class	Top contributing foods[1] (%)
Flavonols	Tea (17.5) Apples/pears (13.1)
Flavones	Orange juice (39.0) Oranges (12.5)
Flavanones	Orange juice (50.1) Oranges (22.4)
Flavan-3-ols	Tea (30.7) Apples/pears (12.6) Bananas (10.3)
Anthocyanins	Blueberry muffins (25.4) Blueberries (25.1) Strawberries (14.8) Red wine (10.8)
Flavonoid polymers	Tea (25.8) Apples/pears (25.1)
Total flavonoids	Tea (22.0) Apples/pears (16.1) Orange juice (12.3)

[1]Contributing to ≥10% to total intake for total flavonoids and each flavonoid class

Supplemental Table 2. Hazard ratios (95% confidence interval) of Alzheimer's disease and related dementias (ADRD) events over 26 years of follow-up[1] based on a 10-year cutoff between ADRD diagnosis and updated flavonoid intake data

Flavonoid class	≤15th	>15th – 30th	>30th – 60th	>60th	P-trend[2]
		Flavonoid intake percentile category			
Flavonols	(n[3]=411/28)	(n=412/30)	(n=824/37)	(n=1099/43)	
Model 1[4]	1.00 (ref.)	1.05 (0.62,1.78)	0.64 (0.38,1.07)	0.53 (0.31,0.90)	0.005
Model 2[5]	1.00 (ref.)	1.01 (0.59,1.72)	0.59 (0.35,0.99)	0.50 (0.29,0.85)	0.003
Model 3[6]	1.00 (ref.)	0.96 (0.53,1.71)	0.61 (0.35,1.09)	0.50 (0.27,0.92)	0.02
Flavones	(n=410/29)	(n=414/13)	(n=823/33)	(n=1099/63)	
Model 1[4]	1.00 (ref.)	0.44 (0.23,0.85)	0.43 (0.26,0.71)	0.60 (0.37,0.97)	0.42
Model 2[5]	1.00 (ref.)	0.44 (0.23,0.86)	0.42 (0.25,0.71)	0.59 (0.36,0.96)	0.39
Model 3[6]	1.00 (ref.)	0.47 (0.24,0.95)	0.47 (0.27,0.81)	0.67 (0.39,1.15)	0.75
Flavanones	(n=412/27)	(n=412/8)	(n=824/28)	(n=1098/75)	
Model 1[4]	1.00 (ref.)	0.21 (0.10,0.48)	0.33 (0.19,0.57)	0.56 (0.35,0.90)	0.70
Model 2[5]	1.00 (ref.)	0.22 (0.10,0.49)	0.34 (0.20,0.60)	0.54 (0.34,0.88)	0.92
Model 3[6]	1.00 (ref.)	0.26 (0.12,0.60)	0.40 (0.23,0.72)	0.62 (0.37,1.05)	0.61
Flavan-3-ols	(n=412/28)	(n=412/25)	(n=824/29)	(n=1098/56)	
Model 1[4]	1.00 (ref.)	0.92 (0.53,1.59)	0.52 (0.30,0.88)	0.66 (0.40,1.08)	0.26
Model 2[5]	1.00 (ref.)	0.86 (0.50,1.51)	0.48 (0.27,0.82)	0.61 (0.37,1.00)	0.20
Model 3[6]	1.00 (ref.)	0.73 (0.41,1.32)	0.44 (0.25,0.79)	0.58 (0.34,0.99)	0.33
Anthocyanins	(n=412/39)	(n=412/25)	(n=824/41)	(n=1098/33)	
Model 1[4]	1.00 (ref.)	0.50 (0.30,0.83)	0.40 (0.25,0.63)	0.24 (0.15,0.40)	<0.001
Model 2[5]	1.00 (ref.)	0.46 (0.27,0.76)	0.39 (0.24,0.61)	0.22 (0.13,0.38)	<0.001
Model 3[6]	1.00 (ref.)	0.42 (0.24,0.72)	0.36 (0.22,0.59)	0.22 (0.12,0.39)	<0.001
Flavonoid polymers	(n=412/23)	(n=412/31)	(n=824/31)	(n=1098/53)	
Model 1[4]	1.00 (ref.)	1.15 (0.67,2.00)	0.53 (0.30,0.93)	0.64 (0.37,1.09)	0.09
Model 2[5]	1.00 (ref.)	1.10 (0.63,1.91)	0.50 (0.28,0.88)	0.58 (0.34,1.01)	0.06
Model 3[6]	1.00 (ref.)	1.05 (0.58,1.89)	0.53 (0.29,0.96)	0.61 (0.34,1.10)	0.13

Flavonoid class	≤15th	>15th – 30th	>30th – 60th	>60th	P-trend[2]
Total flavonoids	(n=412/22)	(n=412/29)	(n=823/36)	(n=1099/51)	
Model 1[4]	1.00 (ref.)	1.14 (0.65,2.02)	0.66 (0.38,1.14)	0.61 (0.35,1.07)	0.04
Model 2[5]	1.00 (ref.)	1.11 (0.63,1.97)	0.61 (0.35,1.07)	0.56 (0.32,0.99)	0.02
Model 3[6]	1.00 (ref.)	1.04 (0.57,1.92)	0.64 (0.35,1.16)	0.58 (0.32,1.08)	0.05

Flavonoid intake percentile category (spanning header over the ≤15th through >60th columns)

[1]Mean follow-up time of 19.9 years.

[2]P values for the test of linear trend across percentile categories were based on linear regression models with the median intake of each percentile category assigned to individuals with intake in that category, and this percentile median variable was used as a continuous measure in regression models.

[3]n represents the number of participants/ADRD events per percentile category for model 1.

[4]Model 1 adjusted for age, sex, education, Apolipoprotein E ε4 allele, and total calorie intake; total N 2746; n ADRD events 138.

[5]Model 2 adjusted for model 1 covariates + physical activity index, smoking status, body mass index, prevalent stroke, diabetes, hypertension, and hypercholesterolemia; total N 2746; n ADRD events 138.

[6]Model 3 adjusted for model 1 and model 2 covariates + overall dietary quality, vitamin and mineral supplement use, and dietary intakes of alcohol, omega-3 fatty acids (eicosapentaenoic and docosahexaenoic acid) and lutein and zeaxanthin; total N 2739; n ADRD events 131.