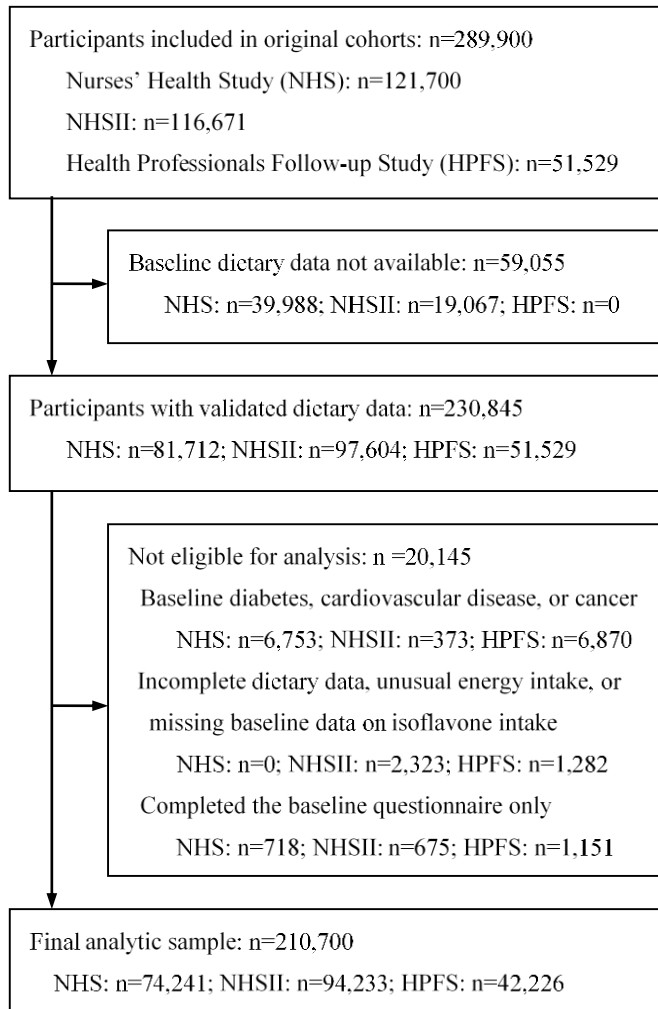


## SUPPLEMENTAL MATERIAL

### Supplemental Figures and Figure Legends

**Supplemental Figure 1.** The flowchart of study participant inclusions and exclusions.



## Supplemental Tables

**Supplemental Table 1.** The top five food contributors to intake of total isoflavones and individual isoflavones in three cohorts (NHS 1998, NHSII 1999, HPFS 2002).

	Rank	NHS		NHSII		HPFS	
		Food group	%	Food group	%	Food group	%
Isoflavones							
	1	Tofu	32.3	Tofu	33.1	Tofu	42.2
	2	Soymilk	23.8	Soymilk	21.7	Soymilk	23.8
	3	Coffee	6.4	Coffee	4.0	Coffee	5.3
	4	Dark bread	3.1	Frozen yogurt, sherbet, non-fat ice cream	2.6	Hotdog	2.7
	5	Frozen yogurt, sherbet, non-fat ice cream	2.9	Cold cereal	2.5	Dark bread	2.4
Daidzein							
	1	Tofu	30.4	Tofu	32.5	Tofu	39.8
	2	Soymilk	22.7	Soymilk	21.7	Soymilk	22.8
	3	Coffee	11.7	Coffee	7.7	Coffee	9.8
	4	Cold cereal	3.1	Cold cereal	3.1	Hotdog	3.5
	5	Hotdog	3.0	Frozen yogurt, sherbet, non-fat ice cream	2.5	Dark bread	2.2
Genistein							
	1	Tofu	32.7	Tofu	32.2	Tofu	43.2
	2	Soymilk	19.2	Soymilk	16.9	Soymilk	19.4
	3	Dark bread	3.6	Frozen yogurt, sherbet, non-fat ice cream	2.8	Coffee	2.9
	4	Coffee	3.5	Cold cereal	2.3	Dark bread	2.8
	5	Frozen yogurt, sherbet, non-fat ice cream	3.4	Coffee	2.1	Frozen yogurt, sherbet, non-fat ice cream	2.6
Glycitein							
	1	Soymilk	43.1	Soymilk	38.7	Soymilk	45.8
	2	Tofu	36.8	Tofu	37.1	Tofu	41.1
	3	Dark bread	2.1	Frozen yogurt, sherbet, non-fat ice cream	1.6	Dark bread	1.5
	4	Frozen yogurt, sherbet, non-fat ice cream	1.9	Cold cereal	1.5	Frozen yogurt, sherbet, non-fat ice cream	1.4
	5	Cold cereal	1.6	Dark bread	1.1	Hotdog	1.0

HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study.

**Supplemental Table 2.** Age-standardized characteristics of participants according to consumption of tofu at the midpoint of follow-up (NHS1998, NHSII 1999, HPFS1998) \*

	NHS			NHSII			HPFS		
	<1 serving/month	<1 serving/week	≥1 serving/week	<1 serving/month	<1 serving/week	≥1 serving/week	<1 serving/month	<1 serving/week	≥1 serving/week
Participants, n	56842	9453	2392	76034	12844	4188	27820	7886	1678
Age ‡, years	63.9 †	63.5	64.1	46.3	46.3	46.8	66.4	64.7	65.0
Caucasians, %	98	96	89	96	93	88	96	93	78
Asian, %	0	2	9	1	4	9	0	3	18
Level education of partner, % of college and above	72	75	71	65	73	72	-	-	-
Self-rated socioeconomic status, % of Top 30%	34	43	40	30	39	37	-	-	-
Current smoker, %	11	7	6	9	6	6	4	3	2
Alcohol intake, g/day	5.0	5.3	4.1	3.6	4.8	4.0	11.1	10.6	8.5
Physical activity, MET/week	16.0	21.2	23.3	19.0	25.7	29.8	30.9	36.2	39.1
BMI, kg/m <sup>2</sup>	26.8	26.2	25.8	27.2	25.4	25.0	26.3	25.9	25.3
Family history of myocardial infarction, %	39	38	35	33	30	31	31	31	31
Multivitamin use, %	53	62	60	45	55	56	47	56	50
Current use of aspirin, %	47	50	44				38	41	31
Hypertension, %	45	42	41	20	9	10	40	39	37
Hypercholesterolemia, %	57	56	54	34	16	21	47	49	46
Postmenopausal women, %	6	6	6	60	66	66	-	-	-
Ever menopausal hormone use, %	63	68	65	25	22	21	-	-	-

Current use of oral-contraceptive, %	-	-	-	7	8	7	-	-	-
Total energy intake, kcal/day	1736	1803	1846	1790	1850	1873	1968	2031	2067
Modified AHEI score	43.4	48.9	51.5	42.7	49.5	54.0	47.0	51.5	55.1
Trans fat intake, % energy	1.7	1.4	1.3	1.7	1.4	1.2	1.5	1.3	1.0
Polyunsaturated fat-to-saturated fat ratio	0.6	0.6	0.7	0.5	0.6	0.7	0.6	0.7	0.8
Total fruits intake, servings/day	2.3	2.7	3.0	1.1	1.5	1.7	2.3	2.8	3.3
Total vegetables intake, servings/day	3.1	3.7	4.3	3.0	4.0	5.1	3.0	3.8	4.5
Red meats intake, servings/day	0.9	0.7	0.6	0.8	0.6	0.4	1.1	0.9	0.7

AHEI, alternative health eating index; BMI, body mass index; HPFS, the Health Professionals Follow-Up Study; MET, metabolic equivalents of task; NHS, Nurses' Health Study.

\* Values were standardized to the age distribution of the study population.

† Data are mean unless otherwise indicated.

‡ Values were not age adjusted.

**Supplemental Table 3.** Hazard ratio (95% CI) of coronary heart disease according to quintiles of individual isoflavones.

	Quintile of intake					<i>P</i> trend
	1 (low)	2	3	4	5 (high)	
<b>Daidzein</b>						
NHS						
Age-adjusted model *	1	0.90 (0.81, 1.00)	0.87 (0.78, 0.96)	0.98 (0.88, 1.08)	0.90 (0.81, 1.00)	0.30
Multivariable-adjusted model <sup>†</sup>	1	0.89 (0.81, 0.99)	0.83 (0.75, 0.93)	0.86 (0.77, 0.95)	0.85 (0.76, 0.94)	0.02
Fully-adjusted model <sup>‡</sup>	1	0.89 (0.81, 0.99)	0.83 (0.75, 0.93)	0.87 (0.78, 0.96)	0.88 (0.79, 0.98)	0.12
NHS II						
Age-adjusted model *	1	0.95 (0.75, 1.19)	0.87 (0.69, 1.09)	0.83 (0.66, 1.04)	0.58 (0.45, 0.75)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	1.00 (0.79, 1.26)	0.87 (0.69, 1.11)	0.74 (0.59, 0.94)	0.63 (0.48, 0.82)	<0.001
Fully-adjusted model <sup>‡</sup>	1	1.01 (0.80, 1.27)	0.90 (0.71, 1.14)	0.78 (0.61, 0.99)	0.70 (0.54, 0.92)	0.005
HPFS						
Age-adjusted model *	1	0.92 (0.83, 1.01)	0.92 (0.83, 1.01)	0.94 (0.85, 1.03)	0.80 (0.72, 0.89)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.92 (0.84, 1.01)	0.91 (0.83, 1.00)	0.91 (0.83, 1.00)	0.83 (0.75, 0.92)	0.002
Fully-adjusted model <sup>‡</sup>	1	0.92 (0.84, 1.01)	0.91 (0.83, 1.00)	0.92 (0.83, 1.01)	0.89 (0.80, 0.98)	0.09
Pooled results <sup>§</sup>						
Age-adjusted model *	1	0.91 (0.85, 0.97)	0.89 (0.83, 0.95)	0.94 (0.88, 1.01)	0.82 (0.77, 0.88)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.91 (0.86, 0.98)	0.87 (0.82, 0.93)	0.87 (0.82, 0.93)	0.82 (0.76, 0.88)	<0.001
Fully-adjusted model <sup>‡</sup>	1	0.92 (0.86, 0.98)	0.88 (0.82, 0.94)	0.88 (0.82, 0.94)	0.87 (0.81, 0.93)	0.002
<b>Genistein</b>						
NHS						
Age-adjusted model *	1	0.87 (0.78, 0.96)	0.94 (0.84, 1.04)	1.05 (0.95, 1.16)	0.84 (0.75, 0.93)	0.004
Multivariable-adjusted model <sup>†</sup>	1	0.88 (0.79, 0.97)	0.90 (0.81, 1.00)	0.94 (0.85, 1.04)	0.87 (0.78, 0.97)	0.10
Fully-adjusted model <sup>‡</sup>	1	0.88 (0.79, 0.98)	0.91 (0.82, 1.01)	0.95 (0.86, 1.06)	0.92 (0.83, 1.03)	0.65
NHS II						
Age-adjusted model *	1	0.99 (0.79, 1.24)	0.92 (0.74, 1.16)	0.78 (0.61, 0.98)	0.48 (0.37, 0.64)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	1.04 (0.83, 1.31)	0.92 (0.73, 1.15)	0.74 (0.58, 0.94)	0.59 (0.45, 0.78)	<0.001
Fully-adjusted model <sup>‡</sup>	1	1.07 (0.85, 1.34)	0.95 (0.76, 1.20)	0.79 (0.62, 1.01)	0.67 (0.50, 0.90)	0.004
HPFS						
Age-adjusted model *	1	0.91 (0.83, 1.00)	0.96 (0.88, 1.06)	0.96 (0.87, 1.05)	0.77 (0.70, 0.85)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.92 (0.84, 1.01)	0.96 (0.88, 1.06)	0.95 (0.86, 1.04)	0.82 (0.74, 0.91)	<0.001
Fully-adjusted model <sup>‡</sup>	1	0.94 (0.85, 1.03)	0.98 (0.89, 1.08)	0.98 (0.89, 1.08)	0.90 (0.81, 1.00)	0.08
Pooled results <sup>§</sup>						
Age-adjusted model *	1	0.90 (0.84, 0.96)	0.95 (0.89, 1.01)	0.98 (0.92, 1.05)	0.77 (0.72, 0.83)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.91 (0.85, 0.97)	0.93 (0.87, 1.00)	0.93 (0.87, 0.99)	0.82 (0.77, 0.89)	<0.001
Fully-adjusted model <sup>‡</sup>	1	0.93 (0.86, 0.99)	0.95 (0.89, 1.02)	0.95 (0.89, 1.02)	0.89 (0.83, 0.96)	0.01
<b>Glycitein</b>						
NHS						
Age-adjusted model *	1	0.72 (0.62, 0.85)	0.61 (0.51, 0.74)	0.64 (0.54, 0.76)	0.58 (0.49, 0.68)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.88 (0.75, 1.04)	0.80 (0.66, 0.96)	0.80 (0.67, 0.95)	0.80 (0.67, 0.95)	0.03

Fully-adjusted model <sup>‡</sup>	1	0.89 (0.76, 1.06)	0.80 (0.67, 0.97)	0.81 (0.68, 0.97)	0.85 (0.72, 1.01)	0.35
NHS II						
Age-adjusted model *	1	0.56 (0.45, 0.70)	0.45 (0.27, 0.76)	0.51 (0.34, 0.77)	0.29 (0.18, 0.47)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.68 (0.54, 0.85)	0.55 (0.33, 0.92)	0.68 (0.45, 1.03)	0.43 (0.27, 0.70)	<0.001
Fully-adjusted model <sup>‡</sup>	1	0.70 (0.56, 0.88)	0.60 (0.36, 1.02)	0.75 (0.49, 1.15)	0.49 (0.30, 0.80)	0.005
HPFS						
Age-adjusted model *	1	0.81 (0.70, 0.94)	0.64 (0.54, 0.76)	0.77 (0.66, 0.89)	0.65 (0.56, 0.76)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.90 (0.78, 1.05)	0.76 (0.64, 0.90)	0.86 (0.74, 1.01)	0.78 (0.67, 0.91)	0.002
Fully-adjusted model <sup>‡</sup>	1	0.93 (0.80, 1.07)	0.77 (0.65, 0.91)	0.90 (0.77, 1.04)	0.86 (0.74, 1.01)	0.17
Pooled results <sup>§</sup>						
Age-adjusted model *	1	0.73 (0.66, 0.80)	0.62 (0.55, 0.70)	0.69 (0.62, 0.77)	0.59 (0.53, 0.66)	<0.001
Multivariable-adjusted model <sup>†</sup>	1	0.85 (0.77, 0.94)	0.76 (0.67, 0.86)	0.82 (0.74, 0.92)	0.76 (0.68, 0.85)	<0.001
Fully-adjusted model <sup>‡</sup>	1	0.87 (0.78, 0.96)	0.77 (0.68, 0.87)	0.85 (0.76, 0.95)	0.83 (0.74, 0.93)	0.003

CI, confidence interval; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; NHS, Nurses' Health Study.

\* Estimates are calculated in Cox proportional hazards models. Age-adjusted model, adjusted for age (years).

<sup>†</sup> Multivariable-adjusted model, further adjusted for ethnicity (Caucasian, African American, Asian, and other ethnicity), self-rated socioeconomic status (top 30%, median 40%, and bottom 30% for women), partner's education (<high school, high school, and above college for women), smoking status (never, former, current [1-14, 15-24, or ≥25 cigarettes/day], or missing), alcohol intake (0, 0.1-4.9, 5.0-14.9, and ≥15.0 g/day for women, 0, 0.1-4.9, 5.0-29.9, and ≥30.0 g/day for men, or missing), physical activity (metabolic equivalents of tasks-hr/week), multivitamin use (yes/no), aspirin use (yes/no), history of hypertension (yes/no) and hypercholesterolemia (yes/no), family history of early myocardial infarction (yes/no), menopausal status and post-menopausal hormone use (pre-menopause, post-menopause [never, former, or current hormone use], or missing, for women), oral contraceptive use (yes, no, or missing, for NHS II), body mass index (kg/m<sup>2</sup>), and total energy intake (kcal/day) based on age-adjusted model.

<sup>‡</sup> Fully-adjusted model, further adjusted for modified alternative health eating index score, based on multivariable-adjusted model.

<sup>§</sup> Results from each cohort were pooled using fixed-effects model.

**Supplemental Table 4.** Stratified hazard ratio (95% CI) of coronary heart disease according to quintiles of isoflavone intake by various characteristics of participants

	Quintile of isoflavone intake					<i>P</i> <sub>trend</sub>	<i>P</i> <sub>interaction</sub> <sup>†</sup>
	1 (low)	2	3	4	5 (high)		
Race							0.18
Caucasians							
No. of case/person years	54/28592	55/31837	35/27620	39/24574	78/65076		
Fully-adjusted HR *	1	0.91 (0.86, 0.98)	0.89 (0.83, 0.95)	0.90 (0.84, 0.97)	0.87 (0.81, 0.94)	0.01	
Other races							
No. of case/person years	1833/934956	1677/937307	1640/933589	1661/938618	1287/903954		
Fully-adjusted HR *	1	0.91 (0.61, 1.36)	0.69 (0.44, 1.08)	0.84 (0.53, 1.31)	0.66 (0.46, 0.96)	0.08	
Age							0.44
< 65 years							
No. of case/person years	966/155262	900/159844	897/155463	973/147206	798/137168		
Fully-adjusted HR *	1	0.88 (0.76, 1.01)	0.82 (0.71, 0.95)	0.79 (0.68, 0.90)	0.79 (0.68, 0.91)	0.02	
≥ 65 years							
No. of case/person years	917/805712	829/806833	775/803681	723/813798	563/829709		
Fully-adjusted HR *	1	0.93 (0.85, 1.00)	0.89 (0.82, 0.97)	0.93 (0.86, 1.02)	0.91 (0.83, 1.00)	0.32	
BMI							0.26
< 30 kg/m <sup>2</sup>							
No. of case/person years	1458/750056	1338/762652	1324/768885	1314/775536	1102/809027		
Fully-adjusted HR *	1	0.93 (0.86, 1.00)	0.92 (0.86, 1.00)	0.94 (0.87, 1.01)	0.93 (0.85, 1.00)	0.22	
≥ 30 kg/m <sup>2</sup>							
No. of case/person years	421/59591	386/53447	342/47358	379/43996	259/34608		
Fully-adjusted HR *	1	0.88 (0.77, 1.01)	0.79 (0.68, 0.91)	0.84 (0.72, 0.96)	0.76 (0.65, 0.89)	0.03	
Modified AHEI score							0.40
< median level							
No. of case/person years	908/488575	808/464812	789/432274	791/391322	425/244194		
Fully-adjusted HR *	1	0.94 (0.85, 1.03)	0.91 (0.83, 1.01)	0.94 (0.85, 1.04)	0.89 (0.79, 1.00)	0.25	
≥ median level							

No. of case/person years	914/458944	881/488710	822/513089	839/556250	903/708866		
Fully-adjusted HR *	1	0.94 (0.85, 1.03)	0.90 (0.82, 0.99)	0.90 (0.82, 0.99)	0.87 (0.79, 0.95)	0.03	
Physical activity							0.27
< median level							
No. of case/person years	1099/487484	1021/482855	940/471862	971/473114	704/405824		
Fully-adjusted HR *	1	0.95 (0.87, 1.03)	0.88 (0.81, 0.96)	0.91 (0.83, 0.99)	0.86 (0.78, 0.95)	0.02	
≥ median level							
No. of case/person years	756/461488	689/473338	717/477088	709/475549	645/550874		
Fully-adjusted HR *	1	0.88 (0.79, 0.98)	0.90 (0.81, 1.00)	0.91 (0.82, 1.01)	0.89 (0.80, 0.99)	0.29	
Smoking status							0.15
Never							
No. of case/person years	1727/907150	1533/903075	1402/866298	1340/822461	1113/862930		
Fully-adjusted HR *	1	0.90 (0.84, 0.97)	0.88 (0.82, 0.94)	0.93 (0.86, 1.00)	0.87 (0.80, 0.94)	0.01	
Ever							
No. of case/person years	160/56398	199/66067	273/94911	360/140731	252/106102		
Fully-adjusted HR *	1	1.07 (0.87, 1.32)	1.01 (0.83, 1.23)	0.92 (0.76, 1.11)	0.95 (0.78, 1.17)	0.49	
Alcohol consumption							0.98
Never							
No. of case/person years	929/463030	708/380240	576/302846	648/294132	546/336474		
Fully-adjusted HR *	1	0.94 (0.85, 1.04)	0.88 (0.80, 0.98)	0.95 (0.86, 1.05)	0.85 (0.77, 0.95)	0.03	
Ever							
No. of case/person years	958/500518	1024/588903	1099/658362	1052/669060	819/632557		
Fully-adjusted HR *	1	0.91 (0.83, 1.00)	0.91 (0.83, 0.99)	0.90 (0.82, 0.98)	0.88 (0.80, 0.97)	0.06	

AHEI, alternative health eating index; CI, confidence interval; BMI, body mass index; HR, hazard ratio.

\* Estimates are calculated in Cox proportional hazards models, adjusted for ethnicity (Caucasian, African American, Asian, and other ethnicity), self-rated socioeconomic status (top 30%, median 40%, or bottom 30%, for women), partner's education (<high school, high school, or above college, for women), smoking status (never, former, current [1-14, 15-24, or ≥25 cigarettes/day], or missing), alcohol intake (0, 0.1-4.9, 5.0-14.9, and ≥15.0 g/day for women, 0, 0.1-4.9, 5.0-29.9, and ≥30.0 g/day for men, or missing), physical activity (metabolic equivalents of tasks-hr/week), multivitamin use (yes/no), aspirin use (yes/no), history of hypertension (yes/no) and hypercholesterolemia (yes/no), family history of early myocardial infarction (yes/no), menopausal status and post-menopausal hormone



use (pre-menopause, post-menopause [never, former, or current hormone use], or missing, for women), oral contraceptive use (yes, no, or missing, for Nurses' Health Study II), BMI (kg/m<sup>2</sup>), total energy intake (kcal/day), and the modified alternative health eating index score.

<sup>†</sup>  $P_{\text{interaction}}$  was calculated using likelihood-ratio test.

**Supplemental Table 5.** Stratified hazard ratio (95% CI) of coronary heart disease according to consumption of tofu by various characteristics of participants \*

	Consumption of tofu			<i>P</i> <sub>trend</sub>	<i>P</i> <sub>interaction</sub> <sup>†</sup>
	<1 serving/month	<1 serving/week	≥1 serving/week		
Race					0.18
Caucasians					
No. of case/person years	6749/3890016	981/624525	192/165688		
Fully-adjusted HR *	1	0.92 (0.86, 0.98)	0.86 (0.73, 1.01)	0.01	
Other races					
No. of case/person years	173/112819	53/39358	27/27047		
Fully-adjusted HR *	1	1.05 (0.96, 1.16)	0.58 (0.37, 0.92)	0.03	
Age					0.02
< 65 years					
No. of case/person years	2739/3061596	335/463209	63/143145		
Fully-adjusted HR *	1	0.76 (0.63, 0.91)	0.74 (0.51, 1.08)	0.01	
≥ 65 years					
No. of case/person years	4183/941239	699/200674	156/49591		
Fully-adjusted HR *	1	0.95 (0.87, 1.03)	0.96 (0.80, 1.15)	0.37	
BMI					0.51
< 30 kg/m <sup>2</sup>					
No. of case/person years	5324/3172993	857/558639	184/164864		
Fully-adjusted HR *	1	0.94 (0.87, 1.01)	0.83 (0.71, 0.98)	0.02	
≥ 30 kg/m <sup>2</sup>					
No. of case/person years	1567/808721	174/103233	35/27021		
Fully-adjusted HR *	1	0.89 (0.76, 1.04)	0.81 (0.56, 1.19)	0.10	
Modified AHEI score					0.96
< median level					
No. of case/person years	3582/1922247	307/149716	41/26659		
Fully-adjusted HR *	1	0.90 (0.80, 1.01)	0.77 (0.54, 1.10)	0.06	
≥ median level					

No. of case/person years	3103/2018092	699/502734	173/163088		
Fully-adjusted HR *	1	0.91 (0.84, 0.99)	0.82 (0.69, 0.98)	0.01	
Physical activity					0.83
< median level					
No. of case/person years	4032/2022452	487/252658	100/70216		
Fully-adjusted HR *	1	0.91 (0.82, 1.00)	0.80 (0.64, 1.00)	0.02	
≥ median level					
No. of case/person years	2790/1918785	543/408091	117/120672		
Fully-adjusted HR *	1	0.93 (0.85, 1.02)	0.85 (0.69, 1.04)	0.10	
Smoking status					0.78
Never					
No. of case/person years	5802/3588736	940/625613	204/182331		
Fully-adjusted HR *	1	0.92 (0.86, 0.99)	0.84 (0.72, 0.98)	0.006	
Ever					
No. of case/person years	1120 /414100	94/38268	15/10404		
Fully-adjusted HR *	1	0.96 (0.77, 1.19)	0.73 (0.39, 1.39)	0.76	
Alcohol consumption					0.73
Never					
No. of case/person years	2867/1505615	384/202964	91/78803		
Fully-adjusted HR *	1	0.97 (0.87, 1.08)	0.71 (0.55, 0.90)	0.05	
Ever					
No. of case/person years	4055/2497220	650/460918	128/113934		
Fully-adjusted HR *	1	0.89 (0.81, 0.96)	0.89 (0.73, 1.08)	0.02	

AHEI, alternative health eating index; CI, confidence interval; BMI, body mass index.

\* Estimates are calculated in Cox proportional hazards models, adjusted for ethnicity (Caucasian, African American, Asian, and other ethnicity), self-rated socioeconomic status (top 30%, median 40%, or bottom 30%, for women), partner's education (<high school, high school, or above college, for women), smoking status (never, former, current [1-14, 15-24, or ≥25 cigarettes/day], or missing), alcohol intake (0, 0.1-4.9, 5.0-14.9, and ≥15.0 g/day for women, 0, 0.1-4.9, 5.0-29.9, and ≥30.0 g/day for men, or missing), physical activity (metabolic equivalents of tasks-hr/week), multivitamin use (yes/no), aspirin use (yes/no), history of hypertension (yes/no) and hypercholesterolemia (yes/no), family history of early myocardial infarction (yes/no), menopausal status and post-menopausal hormone

use (pre-menopause, post-menopause [never, former, or current hormone use], or missing, for women), oral contraceptive use (yes, no, or missing, for Nurses' Health Study II), BMI (kg/m<sup>2</sup>), total energy intake (kcal/day), and the modified alternative health eating index score.

<sup>†</sup>  $P_{\text{interaction}}$  was calculated using likelihood-ratio test.

**Supplemental Table 6.** Sensitivity analyses for the association between total isoflavone/tofu intake and coronary heart disease in three cohorts \*

	Consumption levels					<i>P</i> trend
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	
Isoflavones						
Using baseline isoflavone intake as an exposure	1	0.99 (0.92, 1.06)	1.02 (0.96, 1.10)	0.98 (0.91, 1.05)	0.95 (0.88, 1.02)	0.09
Adjustment for major dietary factors instead of modified AHEI score	1	0.91 (0.85, 0.97)	0.87 (0.81, 0.93)	0.87 (0.81, 0.93)	0.83 (0.78, 0.90)	<0.001
Using a 4-year lag period	1	0.91 (0.85, 0.98)	0.88 (0.82, 0.94)	0.88 (0.82, 0.94)	0.86 (0.80, 0.93)	0.04
Using an 8-year lag period	1	0.92 (0.86, 0.99)	0.86 (0.80, 0.92)	0.91 (0.85, 0.98)	0.88 (0.81, 0.95)	0.07
Excluding Asians	1	0.92 (0.86, 0.99)	0.89 (0.83, 0.95)	0.90 (0.84, 0.96)	0.88 (0.82, 0.94)	0.01
Excluding probable CHD cases	1	0.92 (0.85, 1.00)	0.88 (0.81, 0.95)	0.88 (0.81, 0.95)	0.87 (0.80, 0.95)	0.03
Excluding soy/isoflavone supplement users	1	0.92 (0.86, 0.99)	0.89 (0.83, 0.95)	0.90 (0.84, 0.96)	0.88 (0.82, 0.94)	0.01
Tofu	<1 serving/month	<1 serving/week	≥1 serving/week			
Using baseline isoflavone intake as an exposure	1	0.91 (0.83, 0.99)	0.81 (0.68, 0.97)			0.02
Adjustment for major dietary factors instead of modified AHEI score	1	0.87 (0.82, 0.94)	0.75 (0.65, 0.88)			0.008
Using a 4-year lag period	1	0.93 (0.87, 1.00)	0.82 (0.70, 0.96)			0.008
Using an 8-year lag period	1	0.91 (0.83, 0.98)	0.84 (0.70, 1.00)			0.01
Excluding Asians	1	0.92 (0.86, 0.99)	0.84 (0.72, 0.99)			0.01
Excluding probable CHD cases	1	0.90 (0.83, 0.98)	0.79 (0.65, 0.95)			0.009
Excluding soy/isoflavone supplement users	1	0.93 (0.86, 0.99)	0.81 (0.70, 0.95)			0.005

AHEI, alternative health eating index

\* Estimates are calculated in Cox proportional hazards models, adjusted for ethnicity (Caucasian, African American, Asian, and other ethnicity), self-rated socioeconomic status (top 30%, median 40%, or bottom 30%, for women), partner's education (<high school, high school, or above college, for women), smoking status (never, former, current [1-14, 15-24, or ≥25 cigarettes/day], or missing), alcohol intake (0, 0.1-4.9, 5.0-14.9, and ≥15.0 g/day for women, 0, 0.1-4.9, 5.0-29.9, and ≥30.0 g/day for men, or missing), physical activity (metabolic equivalents of tasks-hr/week), multivitamin use (yes/no), aspirin use (yes/no), history of hypertension (yes/no) and hypercholesterolemia (yes/no), family history of early myocardial infarction (yes/no), menopausal status and post-menopausal hormone use (pre-menopause, post-menopause [never, former, or current hormone use], or missing, for women), oral contraceptive use (yes, no, or missing, for Nurses' Health Study II), body mass index (kg/m<sup>2</sup>), total energy intake (kcal/day), and the modified alternative health eating index score.