

Supplemental Tables

Supplemental Table 1. Details of soy products included in our food frequency questionnaire (FFQ)

Type of soy products	Details	How to use or eat	Nutritional properties*	Amounts asked in our FFQ	Frequency in our FFQ	
Miso	soybeans <u>fermented</u> with <i>Aspergillus oryzae</i>	Seasoning Miso soup	Fiber: 4.9g/100g Protein: 12.5g/100g Potassium: 380mg/100g Other features: high sodium (4900mg/100g)	the number of bowls per day	6 categories as miso soup	almost never, 1–3 days/month, 1–2 days/week, 3–4 days/week, 5–6 days/week, and daily
Tofu	soybean curd (produced by boiling soy beans, filtering soy milk out, and coagulated)	Eat as it is or cooked	Fiber: 0.4g/100g Protein: 6.6g/100g Potassium: 140mg/100g	3 categories (less than half the standard, same as the standard, and more than 1.5 times the standard)	9 categories	almost never, 1–3 times/month, 1–2 times/week, 3–4 times/week, 5–6 times/week, once/day, 2–3 times/day, 4–6 times/day, and 7 times/day or more
Natto	soybeans <u>fermented</u> with <i>Bacillus subtilis</i>	Eat as it is	Fiber: 6.7g/100g Protein: 16.5g/100g Potassium: 660mg/100g Other features: Include fibrinolytic enzyme nattokinase	Same as Tofu	Same 9 categories as Tofu	
Others	yushidofu (pre-drained tofu), koyadofu (freeze-dried tofu), aburage (deep-fried tofu), and soymilk	Eat as it is or cooked		Same as Tofu except soy milk	Same 9 categories as Tofu for products except soy milk 9 categories for soy milk	almost never, 1–2 times/week, 3–4 times/week, 5–6 times/week, 1 glass/day, 2–3 glasses/day, 4–6 glasses/day, 7–9

						glasses/day, and 10 glasses/day or more
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\*These values are according to standard tables of food composition in Japan

Supplemental Table 2. Baseline characteristics of participants according to their fermented soy product intake

Characteristics	Men (n=42,750)					Women (n=50,165)				
	Fermented soy product intake					Fermented soy product intake				
	First	Second	Third	Fourth	Fifth	First	Second	Third	Fourth	Fifth
No of participants	8,550	8,550	8,550	8,550	8,550	10,033	10,033	10,033	10,033	10,033
Mean (SD) age (years)	56.2 (8.2)	55.9 (7.8)	56.0 (7.6)	56.3 (7.5)	57.2 (7.5)	56.7 (8.5)	56.4 (8.1)	56.4 (7.7)	56.8 (7.5)	57.4 (7.5)
Mean (SD) body mass index (kg/m <sup>2</sup> )	23.6 (2.9)	23.6 (2.9)	23.6 (2.8)	23.5 (2.8)	23.5 (2.8)	23.4 (3.3)	23.4 (3.2)	23.5 (3.1)	23.5 (3.1)	23.5 (3.1)
Current smoker	48.8	46.7	48.4	47.5	43.5	7.9	6.2	5.7	4.8	4.7
Alcohol intake (≥1 day/week)	67.0	70.0	71.1	68.8	65.3	15.9	15.1	13.4	12.8	11.0
Diabetes mellitus	6.1	6.8	6.8	7.1	8.2	3.4	3.6	3.2	3.3	4.5
Antihypertensive drugs	17.4	17.6	18.6	18.0	19.5	18.8	18.4	19.1	19.8	21.1
Health check-up	79.2	81.4	83.3	83.1	84.3	81.1	83.1	85.0	86.5	86.3
Sports or physical exercise (almost every day)	5.5	5.4	5.5	5.2	5.8	5.1	5.5	5.4	5.6	5.7
Postmenopausal	-	-	-	-	-	73.4	73.2	75.1	78.4	80.6
Use of exogenous female hormones	-	-	-	-	-	2.8	2.8	2.4	2.6	2.8
Coffee intake (>once/day)	44.6	39.1	33.2	29.2	23.8	49.1	43.5	36.8	30.7	25.8
Green tea intake (>once/day)	45.7	54.4	59.1	63.6	65.4	52.5	60.5	63.7	65.5	65.6
Median (interquartile range) dietary intake*										
Energy (kcal/day)	2,055 (1,652–2,504)	2,079 (1,680–2,573)	2,166 (1,764–2,615)	2,095 (1,723–2,593)	1,995 (1,632–2,457)	1,756 (1,409–2,164)	1,751 (1,425–2,203)	1,834 (1,512–2,251)	1,822 (1,480–2,240)	1,721 (1,398–2,077)
Fruit (g/day)	123 (57–215)	127 (63–212)	136 (71–224)	145 (78–232)	152 (80–246)	184 (105–295)	194 (117–299)	199 (121–301)	207 (133–304)	210 (132–313)
Vegetables (g/day)	144 (90–216)	160 (106–237)	169 (114–245)	171 (116–246)	177 (119–259)	176 (119–249)	193 (134–270)	201 (143–281)	209 (148–288)	209 (147–291)
Fish (g/day)	73 (48–108)	76 (51–110)	78 (53–111)	81 (56–115)	83 (56–118)	70 (46–102)	74 (50–104)	77 (53–107)	80 (56–109)	80 (57–111)
Meat (g/day)	60 (37–91)	60 (38–88)	56 (35–83)	52 (34–76)	46 (28–68)	53 (33–82)	52 (33–76)	50 (32–73)	47 (30–68)	40 (25–60)
Total soy products (g/day)†	43 (27–70)	65 (49–94)	85 (69–113)	105 (89–132)	142 (118–177)	44 (28–70)	62 (48–89)	82 (65–109)	101 (83–128)	134 (110–170)
Natto (g/day)	1 (1–4)	4 (1–10)	8 (2–15)	14 (6–23)	33 (21–48)	2 (1–4)	5.4 (2–10)	10 (4–16)	17 (9–25)	35 (24–48)

Miso (g/day)	5 (2–8)	13 (9–17)	22 (15–26)	27 (18–35)	30 (21–42)	4 (2–7)	11 (7–15)	18 (11–23)	22 (13–29)	25 (17–36)
Tofu (g/day)	28 (16–51)	31 (18–54)	32 (19–55)	33 (20–56)	37 (21–63)	30 (17–51)	33 (20–53)	35 (22–57)	36 (22–59)	39 (24–65)

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\*Food intake were adjusted for energy intake with the residual method.

†Sum of seven soy foods in the questionnaire. Along with total soy products, the table shows the amount of main soy products. The amount of miso was calculated from the amount of miso soup. Total tofu intake was calculated as the sum of the amount of tofu, tofu in miso soup, and other tofu products.

Supplemental Table 3. Baseline characteristics of participants according to their natto intake

Characteristics	Men (n=42,750) <sup>§</sup>					Women (n=50,165) <sup>§</sup>				
	Natto intake					Natto intake				
	First	Second	Third	Fourth	Fifth	First	Second	Third	Fourth	Fifth
No of participants	12450	7575	7575	7575	7575	12227	9484	9485	9484	9485
Mean (SD) age (years)	57.8 (8.2)	55.1 (7.5)	55.0 (7.3)	55.6 (7.4)	57.2 (7.7)	58.9 (8.4)	55.4 (7.6)	55.4 (7.4)	56.2 (7.5)	57.2 (7.5)
Mean (SD) body mass index (kg/m <sup>2</sup> )	23.7 (3.0)	23.5 (2.8)	23.5 (2.8)	23.5 (2.8)	23.5 (2.8)	23.7 (3.4)	23.4 (3.1)	23.3 (3.1)	23.4 (3.0)	23.5 (3.1)
Current smoker	44.7	52.1	51.0	47.1	41.3	6.0	6.2	5.9	5.7	5.3
Alcohol intake (≥1 day/week)	61.3	72.5	74.0	71.4	67.5	9.1	15.3	16.4	15.1	13.2
Diabetes mellitus	6.5	6.3	6.0	7.3	9.2	3.7	2.9	3.3	3.3	4.8
Antihypertensive drugs	18.6	15.4	17.0	18.7	21.2	20.8	16.7	17.8	19.1	22.4
Health check-up	77.0	83.1	83.5	85.0	86.0	79.2	84.5	85.5	86.8	87.5
Sports or physical exercise (almost every day)	5.8	4.6	4.5	5.1	7.2	5.2	4.8	4.9	5.2	7.1
Postmenopausal	-	-	-	-	-	80.5	71.5	71.9	75.9	80.1
Use of exogenous female hormones	-	-	-	-	-	2.7	3.2	2.4	2.4	2.7
Coffee intake (>once/day)	37.9	37.6	34.4	30.1	27.9	40.9	43.4	38.0	33.6	29.2
Green tea intake (>once/day)	44.9	55.1	62.1	64.7	68.7	49.2	59.1	64.6	68.3	69.6
Median (interquartile range) dietary intake*										
Energy (kcal/day)	1,900 (1,531–2,361)	2,128 (1,775–2,584)	2,224 (1,921–2,610)	2,207 (1,683–2,726)	2,029 (1,734–2,526)	1,590 (1,286–1,980)	1,822 (1,521–2,300)	1,967 (1,608–2,217)	1,918 (1,449–2,377)	1,726 (1,474–2,120)
Fruit (g/day)	115 (50–206)	126 (63–207)	136 (75–222)	153 (89–239)	166 (92–261)	174 (93–285)	188 (114–289)	201 (128–302)	213 (138–311)	221 (143–324)
Vegetables (g/day)	161 (100–246)	147 (96–218)	155 (106–225)	172 (121–242)	188 (128–268)	192 (128–275)	184 (128–263)	191 (136–265)	203 (146–279)	219 (157–299)
Fish (g/day)	70 (44–107)	72 (50–105)	80 (57–111)	86 (61–119)	87 (60–121)	68 (43–103)	71 (49–101)	79 (56–106)	82 (59–110)	83 (59–112)
Meat (g/day)	61 (36–95)	54 (34–81)	55 (36–78)	53 (34–76)	47 (30–70)	54 (32–85)	50 (32–75)	50 (32–71)	47 (30–69)	41 (25–60)
Total soy products (g/day) <sup>†</sup>	75 (45–115)	73 (47–107)	85 (60–115)	100 (75–132)	131 (102–168)	69 (43–109)	70 (45–104)	79 (56–109)	94 (70–124)	122 (95–160)
Natto (g/day)	0 (0–0)	4 (3–5)	10 (8–12)	19 (16–22)	38 (31–50)	0 (0–0)	4 (3–6)	10 (9–12)	19 (16–22)	38 (31–49)
Miso (g/day)	14 (7–24)	16 (7–28)	18 (9–28)	19 (10–29)	20 (11–29)	11 (6–21)	12 (6–22)	14 (7–23)	15 (8–23)	16 (9–25)

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Tofu (g/day)	33 (18–62)	28 (16–47)	30 (18–50)	34 (21–54)	38 (23–65)	34 (20–60)	32 (18–56)	32 (20–51)	35 (22–55)	39 (25–65)
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\*Food and nutrient intake were adjusted for energy intake with the residual method.

†Sum of seven soy foods in the questionnaire. Along with total soy products, the table shows the amount of main soy products. The amount of miso was calculated from the amount of miso soup. Total tofu intake was calculated as the sum of the amount of tofu, tofu in miso soup, and other tofu products.

§The first fifth of natto intake included participants who did not eat natto (n=12 450 men and 12 227 women). The remaining participants were divided into quarters and are shown in the second to fifth categories (7575 men and 9484, 9485, 9484, and 9485 women from the second to fifth categories, respectively). The first category comprises the lowest amount of soy product consumption and the fifth category is the highest.

Supplemental Table 4. Baseline characteristics of participants according to their miso intake

Characteristics	Men (n=42,750) <sup>§</sup>					Women (n=50,165) <sup>§</sup>				
	Miso intake					Miso intake				
	First	Second	Third	Fourth	Fifth	First	Second	Third	Fourth	Fifth
No of participants	8,550	8,550	8,550	8,550	8,550	10,033	10,033	10,033	10,033	10,033
Mean (SD) age (years)	55.6 (8.1)	56.3 (7.9)	56.2 (7.7)	56.3 (7.4)	57.1 (7.5)	56.1 (8.2)	56.6 (8.2)	57.0 (7.9)	56.7 (7.5)	57.5 (7.5)
Mean (SD) body mass index (kg/m <sup>2</sup> )	23.6 (2.9)	23.6 (2.8)	23.6 (2.9)	23.6 (2.8)	23.6 (2.9)	23.2 (3.2)	23.3 (3.2)	23.5 (3.1)	23.6 (3.1)	23.6 (3.2)
Current smoker	47.7	46.1	46.1	46.8	48.3	9.0	6.0	5.1	4.6	4.5
Alcohol intake (≥1 day/week)	68.2	70.5	70.5	70.0	63.1	18.9	15.8	13.2	11.8	8.5
Diabetes mellitus	7.2	7.1	7.0	7.1	6.6	3.9	3.5	3.8	3.3	3.4
Antihypertensive drugs	18.3	18.9	19.1	17.8	17.1	19.4	19.5	20.3	19.2	18.9
Health check-up	80.4	83.0	83.6	83.7	80.5	81.9	84.3	85.2	86.3	84.2
Sports or physical exercise (almost every day)	6.0	6.1	5.9	5.1	4.4	5.7	6.4	6.0	5.1	4.0
Postmenopausal	-	-	-	-	-	69.3	74.3	75.7	78.9	82.6
Use of exogenous female hormones	-	-	-	-	-	2.7	2.5	2.6	2.8	2.9
Coffee intake (>once/day)	43.0	38.9	33.6	30.2	23.8	48.4	42.7	36.1	32.9	25.5
Green tea intake (>once/day)	49.7	57.9	61.1	61.4	58.2	57.8	64.0	63.8	65.3	57.1
Median (interquartile range) dietary intake*										
Energy (kcal/day)	2,014 (1,648–2,453)	2,085 (1,754–2,509)	2,302 (1,697–2,773)	2,114 (1,777–2,650)	1,990 (1,557–2,394)	1,730 (1,393–2,168)	1,810 (1,495–2,257)	1,780 (1,381–2,115)	1,907 (1,662–2,298)	1,591 (1,354–2,009)
Fruit (g/day)	131 (64–223)	141 (73–232)	140 (73–230)	140 (74–227)	131 (63–218)	193 (113–306)	204 (127–307)	204 (128–307)	202 (127–300)	188 (113–289)
Vegetables (g/day)	146 (93–218)	167 (111–242)	174 (116–250)	174 (118–253)	162 (105–240)	180 (124–256)	199 (140–273)	203 (143–284)	209 (150–289)	197 (135–281)
Fish (g/day)	76 (50–109)	82 (55–116)	80 (54–114)	80 (54–112)	75 (50–110)	73 (49–103)	78 (53–109)	78 (54–107)	78 (53–109)	73 (49–103)
Meat (g/day)	59 (37–88)	56 (36–83)	55 (35–81)	53 (33–78)	49 (30–74)	51 (32–78)	49 (31–72)	49 (31–71)	47 (30–70)	46 (27–69)
Total soy products (g/day)†	46 (28–78)	68 (49–99)	88 (66–121)	105 (84–137)	133 (108–170)	49 (29–80)	67 (47–96)	81 (61–111)	100 (79–132)	129 (103–164)
Natto (g/day)	5 (1–13)	6 (1–19)	9 (2–21)	11 (2–23)	10 (2–22)	6 (2–17)	8 (2–20)	10 (2–22)	12 (4–25)	11 (3–23)
Miso (g/day)	4 (2–6)	11 (10–13)	19 (17–21)	26 (25–29)	38 (34–44)	3 (2–5)	9 (8–11)	15 (13–17)	23 (21–24)	33 (29–38)

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Tofu (g/day)	29 (16–51)	32 (20–53)	34 (20–58)	34 (20–58)	34 (19–59)	30 (17–51)	34 (21–55)	35 (22–57)	36 (22–59)	38 (22–65)
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\*Food intake was adjusted for energy intake with the residual method.

†Sum of seven soy foods in the questionnaire. Along with total soy products, the table shows the amount of main soy products. The amount of miso was calculated from the amount of miso soup. Total tofu intake was calculated as the sum of the amount of tofu, tofu in miso soup, and other tofu products.



Supplemental Table 5. Hazard ratios (HRs) and 95% confidence intervals of all-cause mortality according to quintiles of total soy, fermented soy, and non-fermented soy product intake after excluding participants who died within the first 3 years

	Men (n=42,750)						Women (n=50,165)					
	First	Second	Third	Fourth	Fifth	P <sub>trend</sub>	First	Second	Third	Fourth	Fifth	P <sub>trend</sub>
Total soy products (g/day)												
number of deaths	1,357	1,418	1,461	1,517	1,753		858	877	842	900	1,045	
3 years exclusion Model 2	1.00	0.96 (0.89 to 1.04)	0.95 (0.89 to 1.03)	0.93 (0.86 to 1.00)	1.00 (0.93 to 1.08)	0.88	1.00	1.01 (0.92 to 1.11)	0.95 (0.86 to 1.04)	0.96 (0.87 to 1.06)	0.97 (0.88 to 1.08)	0.38
Fermented soy products <sup>†</sup> (g/day)												
number of deaths	1,489	1,363	1,420	1,596	1,638		924	888	848	893	969	
3 years exclusion Model 2	1.00	0.91 (0.84 to 0.98)	0.90 (0.83 to 0.97)	0.96 (0.89 to 1.04)	0.90 (0.83 to 0.98)	0.13	1.00	0.99 (0.90 to 1.09)	0.93 (0.84 to 1.03)	0.93 (0.84 to 1.03)	0.91 (0.82 to 1.01)	0.05
Non-fermented soy products (g/day)												
number of deaths	1,472	1,360	1,457	1,549	1,668		964	835	805	872	1,046	
3 years exclusion Model 2	1.00	0.94 (0.88 to 1.02)	0.99 (0.92 to 1.07)	1.00 (0.92 to 1.07)	1.03 (0.96 to 1.11)	0.18	1.00	0.92 (0.84 to 1.02)	0.85 (0.77 to 0.94)	0.92 (0.83 to 1.00)	0.98 (0.89 to 1.07)	0.66

Model 2: We excluded participants who died within the first 3 years. Adjusted for age, geographical area, smoking, frequency of alcohol intake, body mass index, sports or physical exercise, history of diabetes or taking drugs for diabetes, taking antihypertensives, health check-up, postmenopausal status (women only), use of exogenous female hormones (women only), total energy intake, and the intake of green tea, coffee, fish, meat, fruit, and vegetables.

Supplemental Table 6. Hazard ratios (HRs) and 95% confidence intervals of all-cause mortality according to categories of soy product intake in Japanese

		Men (n=42,750)					Women (n=50,165)						
		First	Second	Third	Fourth	Fifth	P <sub>trend</sub>	First	Second	Third	Fourth	Fifth	P <sub>trend</sub>
Total soy products (g/day)													
Model 2	1.00	0.96 (0.89 to 1.03)	0.94 (0.87 to 1.01)	0.91 (0.84 to 0.98)	0.98 (0.91 to 1.06)	0.43	1.00	1.01 (0.92 to 1.11)	0.95 (0.86 to 1.04)	0.96 (0.87 to 1.06)	0.98 (0.89 to 1.08)	0.46	
Model 2+area deprivation index	1.00	0.96 (0.89 to 1.03)	0.94 (0.87 to 1.01)	0.91 (0.84 to 0.98)	0.98 (0.91 to 1.06)	0.44	1.00	1.01 (0.92 to 1.11)	0.94 (0.86 to 1.04)	0.96 (0.87 to 1.05)	0.98 (0.89 to 1.08)	0.46	
Fermented soy products <sup>†</sup> (g/day)													
Model 2	1.00	0.92 (0.85 to 0.98)	0.91 (0.85 to 0.98)	0.95 (0.88 to 1.03)	0.90 (0.83 to 0.97)	0.05	1.00	0.95 (0.87 to 1.04)	0.91 (0.83 to 1.00)	0.90 (0.81 to 0.99)	0.89 (0.80 to 0.98)	0.01	
Model 2+area deprivation index	1.00	0.91 (0.85 to 0.98)	0.91 (0.85 to 0.98)	0.95 (0.88 to 1.03)	0.89 (0.83 to 0.97)	0.05	1.00	0.95 (0.87 to 1.04)	0.91 (0.83 to 1.00)	0.89 (0.81 to 0.98)	0.89 (0.80 to 0.98)	0.01	
Non-fermented soy products (g/day)													
Model 2	1.00	0.94 (0.87 to 1.01)	1.00 (0.93 to 1.07)	0.99 (0.92 to 1.06)	1.01 (0.94 to 1.09)	0.32	1.00	0.93 (0.85 to 1.02)	0.84 (0.77 to 0.93)	0.95 (0.86 to 1.04)	1.00 (0.92 to 1.10)	0.80	
Model 2+area deprivation index	1.00	0.94 (0.88 to 1.01)	1.00 (0.93 to 1.07)	0.99 (0.93 to 1.07)	1.01 (0.95 to 1.09)	0.30	1.00	0.93 (0.85 to 1.02)	0.85 (0.77 to 0.93)	0.95 (0.87 to 1.04)	1.00 (0.92 to 1.10)	0.79	
Natto (g/day)													
Model 2	1.00	0.98 (0.91 to 1.05)	1.00 (0.93 to 1.08)	0.96 (0.89 to 1.03)	0.94 (0.87 to 1.02)	0.10	1.00	0.81 (0.74 to 0.89)	0.90 (0.82 to 0.99)	0.81 (0.74 to 0.90)	0.84 (0.76 to 0.93)	0.001	

Model 2+area deprivation index	1.00	0.98 (0.91 to 1.05)	1.00 (0.93 to 1.08)	0.96 (0.89 to 1.04)	0.94 (0.87 to 1.02)	0.14	1.00	0.82 (0.74 to 0.90)	0.90 (0.82 to 0.99)	0.82 (0.74 to 0.90)	0.84 (0.77 to 0.93)	0.002
Miso (g/day)												
Model 2	1.00	0.94 (0.87 to 1.01)	0.92 (0.85 to 0.98)	0.91 (0.85 to 0.98)	0.95 (0.87 to 1.02)	0.20	1.00	0.89 (0.81 to 0.97)	0.87 (0.80 to 0.95)	0.89 (0.81 to 0.98)	0.89 (0.81 to 0.97)	0.03
Model 2+area deprivation index	1.00	0.94 (0.87 to 1.01)	0.92 (0.85 to 0.98)	0.91 (0.85 to 0.98)	0.95 (0.88 to 1.02)	0.18	1.00	0.89 (0.81 to 0.97)	0.87 (0.80 to 0.95)	0.89 (0.81 to 0.98)	0.88 (0.80 to 0.97)	0.03
Tofu (g/day)												
Model 2	1.00	0.94 (0.87 to 1.01)	0.97 (0.91 to 1.04)	0.98 (0.91 to 1.05)	0.99 (0.92 to 1.06)	0.88	1.00	0.92 (0.84 to 1.00)	0.86 (0.79 to 0.95)	0.90 (0.82 to 0.99)	0.95 (0.86 to 1.03)	0.21
Model 2+area deprivation index	1.00	0.94 (0.88 to 1.01)	0.98 (0.91 to 1.05)	0.98 (0.91 to 1.05)	0.99 (0.92 to 1.06)	0.85	1.00	0.92 (0.84 to 1.01)	0.87 (0.79 to 0.95)	0.90 (0.82 to 0.99)	0.95 (0.86 to 1.03)	0.21

Model 2 is adjusted for age, geographical area, smoking, frequency of alcohol intake, body mass index, sports or physical exercise, history of diabetes or taking drugs for diabetes, taking antihypertensives, health check-up, postmenopausal status (women only), use of exogenous female hormones (women only), total energy intake, and the intake of green tea, coffee, fish, meat, fruit, and vegetables. Area deprivation index: Areal deprivation indicators for each of the 263 areas by using the 1995 census. Details of this indicator was described in the article by Nakaya et al. (PLoS One. 2014:e97802).

\* Except for natto intake the first to fifth categories comprised 8550 men and 10 330 women. The first fifth of natto intake included participants who did not eat natto (n=12 450 men and 12 227 women). The remaining participants were divided into quarters and are shown in the second to fifth categories (7575 men and 9484, 9485, 9484, and 9485 women from the second to fifth categories, respectively). The first category comprises the lowest amount of soy product consumption and the fifth category is the highest.