

## Supporting Information

**Supporting Information Table S1. Baseline characteristics of the missing and the remaining participants**

	Placebo ( <i>n</i> = 54)		Daidzein ( <i>n</i> = 55)		Genistein ( <i>n</i> = 56)	
	Missing ( <i>n</i> = 7)	Remaining ( <i>n</i> = 47)	Missing ( <i>n</i> = 5)	Remaining ( <i>n</i> = 50)	Missing ( <i>n</i> = 2)	Remaining ( <i>n</i> = 54)
Age, y	56.4±15.6	56.3±10.5	57.6±16.2	56.2±9.3	56.0±4.2	57.1±9.8
Weight, Kg	55.2±7.7	58.0±9.8	60.1±14.1	59.3±7.7	65.3±1.8	58.3±8.9
BMI, kg/m <sup>2</sup>	22.7±2.6	23.8±3.6	24.4±5.7	24.3±3.0	24.4±2.8	24.1±3.5
SBP, mmHg	116±23	122±15	120±13	121±15	122±9	116±14
DBP, mmHg	73±16	76±8	68±4	75±8	78±4	73±9
Body fat, %	32.5±3.4	31.4±6.8	28.8±15.2	32.3±6.1	33.7±7.9	32.8±6.2
Waist Circumference, cm	84.4±5.7	82.4±8.5	83.6±8.0	83.6±7.0	85.5±7.8	81.6±8.8
Total energy, kcal/d	1969±585	1923±534	1734±760	1880±546	1923±611	1868±514
Total protein, g	96.3±53.4	88.1±29.1	75.4±36.6	89.2±32.7	92.2±34.6	86.2±29.7
Fat, g	74.5±23.2	73.9±28.7	48.8±20.9	68.3±26.4	82.4±20.6	67.6±22.7
Kcal from fat, %	34.4±7.3	34.3±7.4	27.0±9.8	32.5±6.9	39.0±2.7	32.7±6.9
Soy protein, g	2.4±1.3	3.4±4.7	1.6±1.3	3.0±3.8	2.6±0.3	2.8±2.4
Total isoflavones, mg/d	11.5±7.0	15.7±20.4	7.76±6.9	13.9±15.7	11.2±2.8	12.6±9.7
Fasting glucose, mmol/l	5.96±0.89	5.85±0.98	5.59±0.50	5.75±0.82	6.04±0.32	5.91±0.94
120-min postload, mmol/l	11.59±4.50	10.92±3.61	12.83±3.89	11.08±3.53	14.37±1.21	10.61±3.34
HbA <sub>1C</sub> , %	6.24±1.00	6.44±1.08	6.02±0.43	6.49±0.57	7.00±0.42	6.33±0.78

All of the values were presented in Mean ± SD ; No significant difference was observed (t-test) between each set of groups, including in the Placebo group, the Daidzein group and the Genistein group.

**Supporting Information Table S2. Dietary intakes and physical activities at baseline and follow-up in 165 study participants through three arms <sup>a</sup>**

	Placebo (n = 54)	Daidzein (n = 55)	Genistein (n = 56)	P value
Baseline dietary intakes <sup>b</sup>				
Total energy ( kJ/d )	8059 ± 2220	7799 ± 2344	7815 ± 2136	0.79
Total protein ( g )	89.2 ± 32.6	88.0 ± 32.9	86.4 ± 29.5	0.90
Fat ( g )	74.0 ± 27.8	66.6 ± 26.4	68.1 ± 22.6	0.29
Kcal from fat ( % )	34.3 ± 7.3	32.0 ± 7.2	32.9 ± 6.8	0.25
Soy protein ( g )	3.3 ± 4.5	2.9 ± 3.6	2.8 ± 2.3	0.76
Total isoflavones (mg/d)	15.1 ± 19.2	13.3 ± 15.2	12.5 ± 9.5	0.65
Daidzein ( mg/d )	6.3 ± 8.0	5.5 ± 6.1	5.2 ± 4.0	0.61
Genistein ( mg/d )	8.6 ± 10.7	7.5 ± 8.5	7.2 ± 5.5	0.65
Glycitein (mg/d)	0.9 ± 1.6	0.7 ± 1.0	0.7 ± 0.6	0.76
Dietary intake at follow-up, on average <sup>c</sup>				
Total energy ( kJ/d )	6499 ± 1287	6461 ± 1630	6660 ± 1801	0.79
Total protein ( g )	71.5 ± 17.7	75. ± 22.8	73.5 ± 24.1	0.67
Fat ( g )	57.7 ± 15.6	57.1 ± 17.0	56.6 ± 17.8	0.95
Kcal from fat ( % )	33.3 ± 5.1	32.7 ± 7.5	31.7 ± 5.0	0.40
Soy protein ( g )	2.4 ± 3.0	3.2 ± 3.0	3.1 ± 3.7	0.46
Total isoflavones (mg/d)	12.0 ± 13.4	13.2 ± 12.2	13.1 ± 13.0	0.88
Daidzein ( mg/d )	4.9 ± 5.2	5.2 ± 4.9	5.5 ± 5.3	0.88
Genistein ( mg/d )	6.9 ± 7.5	7.6 ± 7.1	7.4 ± 7.9	0.82
Glycitein ( mg/d )	0.6 ± 0.9	0.7 ± 0.8	0.8 ± 0.9	0.53
Energy expenditure of PA ( MET-h/d <sup>d</sup> )				
Total PA at baseline	32.2 ± 7.5	31.7 ± 4.6	31.4 ± 5.9	0.72
Total PA at follow-up <sup>e</sup>	29.1 ± 4.3	29.8 ± 3.9	28.9 ± 4.0	0.10
Changes of follow-up and baseline				
Total energy ( kJ/d )	-1446 ± 2499	-1350 ± 2470	-1157 ± 2307	0.82
Total protein ( g )	-13.7 ± 32.7	-13.5 ± 34.4	-13.3 ± 32.7	0.99
Fat ( g )	-15.1 ± 28.8	-9.3 ± 31.4	-11.3 ± 25.5	0.59
Soy protein ( g )	-0.7 ± 4.3	-0.4 ± 4.1	-0.3 ± 3.6	0.34
Total isoflavones (mg/d)	-2.6 ± 17.8	-0.2 ± 16.4	-1.2 ± 14.3	0.50
Daidzein ( mg/d )	-1.1 ± 7.0	-0.3 ± 6.6	-0.4 ± 5.8	0.51
Genistein ( mg/d )	-1.4 ± 9.6	-0.05 ± 9.3	-0.7 ± 8.2	0.49
Glycitein (mg/d)	-0.3 ± 1.7	-0.01 ± 1.2	-0.05 ± 1.0	0.45
Total PA ( MET-h/d <sup>d</sup> )	-3.9 ± 5.8	-2.5 ± 4.6	-1.6 ± 4.4	0.055

<sup>a</sup> All of the values were presented in Mean ± SD; PA, physical activity; METs, average metabolic equivalent tasks ; ANOVA analysis with a post hoc comparison by a Bonferroni test .

<sup>b</sup> Dietary intake on baseline was derived from Food frequency questionnaire ( FFQ ).

<sup>c</sup> Dietary intake at follow-up did not include intervention supplements; the average data was

derived from three 24-hour diet records on 12 week and 24 week.

<sup>d</sup> Energy expenditure of PA was defined as occupational, leisure-time and household-chores activity, and evaluated by metabolic equivalent hours per day (MET-h/d).

<sup>e</sup> The average data was derived from three PA records on 12 week and 24 week.

**Supporting Information Table S3.** 24h urinary isoflavone excretion (mmol/24h) during the 6-mo intervention according to treatment groups in 165 women by intention-to-treat analysis <sup>a</sup>

		Placebo ( <i>n</i> = 46)		Daizein ( <i>n</i> = 52)		Genistein ( <i>n</i> = 50)		<i>P</i> value
Total	ISO	37.1	(28.5,74.5)	99.2 <sup>c</sup>	(89.9, 187)	65.4 <sup>c</sup>	(56.8, 129)	0.000
	Daidzein	11.7 <sup>c</sup>	(10.1, 29.3)	43.5	(36.6, 88.2)	12.0 <sup>c</sup>	(10.4, 31.5)	0.000
	Genistein	4.6 <sup>c</sup>	( 3.7, 9.6)	5.4 <sup>c</sup>	(3.2, 12.3)	16.6	(15.6, 58.2)	0.000
	Equol	1.8 <sup>c</sup>	( 1.5, 7.7)	4.6	(3.3, 25.2)	2.8	(2.34, 13.5)	0.013

<sup>a</sup> All values presented in this table are geometric mean and 95% CI( ); The number of the participants whose urinary isoflavone excretion was measured is the number of participants who collected the 24h urine at 12 weeks; ANOVA analysis with a post hoc comparison by a Bonferroni test. Means in a row with superscripts without a common letter differ,  $P < 0.05$ .

<sup>b</sup> ISO, isoflavones.

**Supporting Information Table S4. 24-week percentage changes (%) for some of the indices of cardiovascular risk by subgrouping of baseline lipids <sup>a</sup>**

	Placebo	Daidzein	Genistein	P value
<b>normal lipids</b>	<i>n</i> =15	<i>n</i> = 12	<i>n</i> = 10	
<i>TC</i>	2.8 ± 13.0	1.6 ± 9.0	20.9 ± 14 <sup>b</sup>	0.001
<i>TG</i>	22.0 ± 56.8	19.3 ± 41.1	21.2 ± 62.2	0.99
<i>HDL-C</i>	0.3 ± 20.5	0.3 ± 16.9	8.7 ± 18.1	0.49
<i>LDL-C</i>	4.7 ± 20.6	-0.6 ± 13.7	24.6 ± 22.1 <sup>c</sup>	0.01
<i>Lp(a)</i>	0.4 ± 22.0	-0.2 ± 24.2	51.0 ± 87.0	0.39 <sup>d</sup>
<i>hs-CRP</i>	-17.3 ± 52.4	6.8 ± 87.0	-25.4 ± 66.6	0.48
<i>UA</i>	-0.9 ± 19.4	-7.2 ± 17.0	-9.2 ± 16.4	0.48
<b>marginal-dyslipidemia and above</b>	<i>n</i> =39	<i>n</i> =43	<i>n</i> = 46	
<i>TC</i>	2.8 ± 46.6	-1.2 ± 12.6	-5.3 ± 11.8	0.44 <sup>d</sup>
<i>TG</i>	-0.3 ± 39.5	-1.0 ± 37.6	-6.5 ± 31.0	0.68
<i>HDL_C</i>	4.3 ± 20.5	1.7 ± 14.9	0.7 ± 13.5	0.59
<i>LDL_C</i>	-0.3 ± 25.9	-1.0 ± 23.0	-3.1 ± 14.9	0.82
<i>Lp(a)</i>	4.8 ± 50.2	12.2 ± 37.8	6.4 ± 31.2	0.27 <sup>d</sup>
<i>hs-CRP</i>	23.9 ± 88.0	-1.3 ± 71.7	-16.7 ± 54.6 <sup>c</sup>	0.038 <sup>d</sup>
<i>UA</i>	-0.8 ± 21.8	5.2 ± 21.7	2.7 ± 19.6	0.42
<b>Moderate-dyslipidemia</b>	<i>n</i> =22	<i>n</i> =24	<i>n</i> =30	
<i>TC</i>	7.4 ± 61.7	1.2 ± 12.2	-7.2 ± 13.4	0.19 <sup>d</sup>
<i>TG</i>	0.1 ± 42.5	-0.4 ± 36.9	-11.4 ± 31.4	0.43
<i>HDL-C</i>	9.2 ± 24.9	3.9 ± 14.9	3.5 ± 13.6	0.48
<i>LDL-C</i>	2.4 ± 33.0	1.7 ± 24.5	-4.8 ± 16.7	0.51
<i>Lp(a)</i>	4.7 ± 25.3	13.3 ± 43.4	7.7 ± 34.5	0.71
<i>hs-CRP</i>	13.1 ± 71.3	-25.5 ± 36.6	-13.8 ± 50.3	0.74
<i>UA</i>	0.7 ± 26.1	5.5 ± 16.1	1.7 ± 21.8	0.72

<sup>a</sup> All of the values presented in this table were means ± SD except that geometric means were used for which outcomes were abnormal distribution: Lp(a) in the normal lipids status subgroup; TC, Lp(a) and Hs-CRP in the marginal-dyslipidemia and above status subgroup, and TC in the moderated-dyslipidemia status subgroup; ANOVA analysis with a post hoc comparison by a Bonferroni test was used except for the values marked “d” which used Kruskal-Wallis H test of nonparametric test because of abnormal distribution; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol, Lp(a), lipoprotein a, hs-CRP, high sensitive C-creative protein; UA, uric acid; the definitions of different levels of dyslipidemia are based on the standard as below: normal lipids contains TC<5.20mmol/L, TG<1.70mmol/L, LDL-C<3.40mmol/L and HDL-C>1.0mmol/L; marginal

dyslipidemia contains at least one of lipid indices can reach these levels:  $5.20 \leq TC < 6.20 \text{ mmol/L}$ ,  $1.70 \leq TG < 2.30 \text{ mmol/L}$ ,  $3.40 \leq LDL-C < 4.10 \text{ mmol/L}$ , and  $HDL-C < 1.0 \text{ mmol/L}$ ; moderate dyslipidemia contains at least one of lipid indices can reach these levels:  $TC \geq 6.2 \text{ mmol/L}$ ,  $TG \geq 2.3 \text{ mmol/L}$ ,  $LDL-C \geq 4.10 \text{ mmol/L}$ , and  $HDL-C < 1.0 \text{ mmol/L}$ .

<sup>b</sup> Compared with placebo and daidzein group,  $p < 0.01$ .

<sup>c</sup> Compared with placebo and daidzein group,  $p < 0.05$ .

<sup>d</sup> Kruskal-Wallis H test of nonparametric test for abnormal distribution.

**Supporting Information Table S5. 24-week percentage changes (%) in some of the indices of cardiovascular risk by equol production status in**

**Daidzein group <sup>a</sup>**

	Equol nonproducers (n = 26)	Equol producers (n = 27)	P value <sup>b</sup>
<i>TC</i>	0.54 ± 13.1	-0.9 ± 11.3	0.91
<i>TG</i>	6.7 ± 42.6	-1.7 ± 36.5	0.89
<i>HDL-C</i>	-0.7 ± 17.2	3.2 ± 13.7	0.36
<i>LDL-C</i>	-0.4 ± 26.2	-1.7 ± 16.5	0.83
<i>Lp(a)</i>	13.4 ± 34.4	7.3 ± 37.3	0.54
<i>hs-CRP</i>	-17.6 ± 64.9	19.2 ± 82.2	0.08
<i>UA</i>	7.2 ± 21.8	-2.2 ± 20.8	0.12

<sup>a</sup> All of the values presented in this table are unadjusted and were means ± SD; The definition of equol-producer is based on the standard of Frank: equol status was determined most dependably by overnight urine applying as cutoff the ratio of Equol / Daidzein  $\geq 0.018$  ( $\log_{10}$  Equol / Daidzein = -1.75) with a DE threshold of  $\geq 2$  nmol/mg creatinine; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol, Lp(a), lipoprotein a, hs-CRP, high sensitive C-creative protein; UA, uric acid.

<sup>b</sup> p values derived from T-test.

**Supporting Information Table S6. 24-week percentage changes (%) for some of the indices of cardiovascular risk by subgrouping of menopausal status <sup>a</sup>**

	Placebo	Daidzein	Genistein	<i>P</i> value
<b>Postmenopause</b>	<i>n</i> = 41	<i>n</i> = 39	<i>n</i> = 43	
<i>TC</i>	-1.8 ± 44.9	-2.1 ± 11.9	-0.6 ± 17.2	0.65 <sup>b</sup>
<i>TG</i>	5.2 ± 40.1	5.8 ± 38.6	-2.5 ± 41.9	0.34 <sup>b</sup>
<i>HDL-C</i>	3.0 ± 22.3	0.5 ± 15.5	1.3 ± 12.4	0.81
<i>LDL-C</i>	-1.6 ± 22.8	-4.5 ± 18.8	2.5 ± 21.0	0.32
<i>Lp(a)</i>	2.7 ± 48.5	8.7 ± 38.0	18.1 ± 49.6	0.15 <sup>b</sup>
<i>hs-CRP</i>	19.1 ± 86.2	12.4 ± 81.5	-21.6 ± 50.9 <sup>c</sup>	0.022 <sup>b</sup>
<i>UA</i>	-1.1 ± 23.2	2.7 ± 19.7	2.0 ± 19.7	0.68
<b>Pre-menopause</b>	<i>n</i> = 13	<i>n</i> = 16	<i>n</i> = 13	
<i>TC</i>	6.1 ± 18.1	3.1 ± 11.4	-0.8 ± 10.6	0.44
<i>TG</i>	8.3 ± 61.4	-2.4 ± 40.2	1.4 ± 29.2	0.82
<i>HDL-C</i>	3.9 ± 13.2	3.5 ± 14.8	4.8 ± 20.4	0.98
<i>LDL-C</i>	9.5 ± 28.4	7.7 ± 24.7	-0.2 ± 13.0	0.52
<i>Lp(a)</i>	6.3 ± 26.6	11.5 ± 29.6	2.1 ± 43.3	0.75
<i>hs-CRP</i>	-8.7 ± 62.0	-28.6 ± 43.6	-7.0 ± 72.9	0.55
<i>UA</i>	20.8 ± 22.2	24.9 ± 87.0	3.7 ± 35.4	0.71

<sup>a</sup> All of the values presented in this table were original and unadjusted means±SD except that geometric means were used for TC, TG, Lp(a) and Hs-CRP in the post-menopause status subgroup which were abnormal distribution.. ANOVA analysis with a post hoc comparison by a Bonferroni test was used for HDL-C, LDL-C and UA in the postmenopausal participants and all markers in pre-menopausal participants; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol, Lp(a), lipoprotein a, Hs-CRP, high sensitive C-creative protein; UA, uric acid.

<sup>b</sup> Kruskal-Wallis H test of nonparametric test for abnormal distribution.

<sup>c</sup> Compared with placebo group, *p*<0.05.