NUTRITION AND CANCER, *55*(1), 1–12
Copyright © 2006, Lawrence Erlbaum Associates, Inc.

REVIEW

Estimated Asian Adult Soy Protein and Isoflavone Intakes

Mark Messina, Chisato Nagata, and Anna H. Wu

Abstract: *There is substantial interest in the possible anticancer effects of soy foods. In part, this is because of the historically low incidence rates of breast and prostate cancer in Asia. Of the several putative soybean chemopreventive agents, isoflavones have received the most attention. Awareness of this research has led increasing numbers of consumers to use soy foods, isoflavone-fortified foods, and isoflavone supplements. Therefore, there is a need for guidance regarding appropriate isoflavone intake levels. To this end, this article analyzed soy protein (as a surrogate for isoflavones) and isoflavone intake of the major soy food–consuming countries using individual dietary surveys for the bulk of the information. In total, 24 surveys from 4 countries that met the inclusion criteria were identified: Japan (*n *= 11), China (*n *= 7), Hong Kong (*n *= 4), and Singapore (*n *= 2). The results indicate that older Japanese adults consume approximately 6–11 g of soy protein and 25–50 mg of isoflavones (expressed as aglycone equivalents) per day. Intake in Hong Kong and Singapore is lower than in Japan, whereas significant regional intake differences exist for China. Evidence suggests that ≤10% of the Asian population consumes as much as 25 g of soy protein or 100 mg of isoflavones per day. The applicability of these findings for making soy intake recommendations for non-Asians is discussed.*

Introduction

The National Cancer Institute in the United States has been actively investigating the anticancer effects of soy since 1991 when the first request for applications on this subject was issued (1). In part, this interest in soy stems from the historically low incidence rates of breast and prostate cancer in Asia (2,3). Although most focus has been on these two cancers (4,5), limited research suggesting that soy has protective effects against other cancers, including endometrial (6,7) and colon cancer (8,9), also exists.

There are several putative chemopreventive agents in soybeans and soy foods (1). Although the constituents responsible for the hypothesized anticancer effects of soy have not been definitively identified, soybean isoflavones have received the most attention (10), and considerable evidence suggests that they are the primary soy chemopreventive agents (11). The possible health benefits of isoflavones are by no means limited to cancer (12–14), but, of the approximately 600 peer-reviewed articles currently published annually on isoflavones, approximately 20% involve cancer investigations (Medline search).

Over the past 10 yr, soy food consumption has increased approximately fourfold in the United States (15). Isoflavone supplements are also now widely commercially available, and isoflavones are being used as food fortificants (16–18). Thus, increasing numbers of non-Asians are exposed to isoflavones. Clearly, therefore, health professionals need guidance regarding appropriate intake levels for those who partake of these products. This is especially true because of concerns that excessive soy and isoflavone intake may produce adverse health effects (19–21) including stimulating the growth of estrogen-responsive mammary tumors (22–25).

Recently, a rationale was presented for a general soy protein and isoflavone intake recommendation (not specifically for cancer prevention) for healthy adults, but thus far no formal recommendations have been issued by independent health or nutrition organizations (26). In 1999, the U.S. Food and Drug Administration awarded a health claim for the cholesterol-lowering properties of soy protein, concluding that 25 g of soy protein per day was sufficient to lower serum cho-

M. Messina is affiliated with the Department of Nutrition, School of Public Health, Loma Linda University, Loma Linda, CA and Nutrition Matters, Inc., Port Townsend, WA 98368.C. Nagata is affiliated with the Department of Epidemiology & Preventive Medicine, Gifu University Graduate School of Medicine, Gifu 501–1194, Japan. A. H. Wu is affiliated with the University of Southern California, Keck School of Medicine, Department of Preventive Medicine, Los Angeles, CA 90089.

Table 1. Protein and Isoflavone Content of Selected Foods (100 g)[a]

Food (Nutrient Database number)	Isoflavones (μg/g)[b]	Protein/100 g[c]	mg isoflavones/g protein
Tofu			
Firm (16126)	247 ± 38	8.2 ± 0.14	3.0
Regular (16427)	236 ± 63	8.1 ± 0.31	2.9
Silken, firm (16162)	279 ± NA	6.9 ± NA	4.0
Natto (16113)	589 ± 74	17.7 ± NA	3.3
Soymilk (16120)	97 ± 20	4.5 ± NA	2.2
Miso (16112)	426 ± 92	11.7 ± 0.30	3.6
Tempeh (16114)	435 ± 83	18.5 ± NA	2.4
Soynuts, dry roasted (16111)	1,284 ± 334	39.6 ± NA	3.2
Soybeans, cooked (16109)	547 ± NA	16.6 ± NA	3.3

a: U.S. Department of Agriculture, Agricultural Research Service. USDA Nutrient Database for Standard Reference, Release 17, 2004. Nutrient Data Laboratory home page: http://www.nal.usda.gov/fnic/foodcomp. NA, not available.
b: Mean ± standard error of the mean expressed as the aglycone weight.
c: Mean ± standard error of the mean.

lesterol levels (27). However, this claim is unrelated to cancer prevention or treatment and was not intended to provide guidance regarding appropriate isoflavone intake. Furthermore, due to the effects of processing, intake of 25 g of soy protein can provide from approximately 10 to 100 mg of isoflavones (28). The Chinese Nutrition Association recommends a daily intake of 50 g of soy (29), but this recommendation is aimed at improving the general nutrient intake of the population and is not intended to provide guidance regarding isoflavone intake nor soy intake in relation to the prevention of cancer or other chronic diseases (personal communication, Suzanne Ho, January 7, 2004).

Theoretically, cultural and physiological differences between Asians and non-Asians may result in differences in how each group is affected by isoflavones. However, a reasonable supposition is that Asian soy intake can serve as one basis for developing an isoflavone intake recommendation for non-Asians. Therefore, it is necessary to have an accurate understanding of soy consumption in Asia. However, widely varying estimates of Asian soy intake have been reported in the literature, and to date no article has comprehensively reviewed this subject (30,31). Thus, the purpose of this article is to summarize the most relevant Asian, but especially Japanese, soy protein and isoflavone intake data collected on an individual, household, and regional level. Soy protein data are presented for two reasons. First, this nutrient is a surrogate for isoflavone intake. Dietary surveys indicate that the isoflavone (mg):soy protein (g) ratio in traditional soy foods is approximately 3.5:1 (32–35), a ratio that is consistent with that determined by a direct chemical analysis of foods as shown in Table 1). Second, because the constituents responsible for the hypothesized anticancer effects of soy have not been definitively identified, soy protein intake is useful as a general measure of the total amount of traditional soy foods consumed in Asia. Dietary surveys suggest that ~10 g of total soy foods provides ~1 g of soy protein, although this ratio varies considerably among the different soy foods (32,35–42). Before presenting intake data, brief background information on isoflavones is provided.

Background on Isoflavones

Isoflavones are a subclass of flavonoids but have a very limited distribution in nature such that the soybean is essentially the only nutritionally relevant naturally occurring food source of these diphenolic compounds (43,44). The primary isoflavones in soybeans are the glucosides, genistin and daidzin, and their respective aglycones, genistein (4′5,7-trihydroxyisoflavone) and daidzein (4′,7-dihydroxyisoflavone). There are also small amounts of a third isoflavone in soybeans, glycitein (7,4′-dihydroxy-6-methoxyisoflavone), and its glycoside, glycitin. Isoflavones are present in the soybean primarily as glycosides, although as a result of fermentation some of the glycosides are converted to aglycones in soy products such as miso. To avoid confusion over the actual amount of biologically active isoflavone in a product or used in experimental settings (the aglycone isoflavone weight is only approximately 60% of the glycoside), the recommendation has been made to express weight in aglycone units or equivalents (45). This is the case in the text that follows.

With regard to both cancer prevention and treatment, the effects of genistein on signal transduction (10), which were first identified by Akiyama et al. (46) in 1987, are of particular interest. However, the possible anti-estrogenic effects of isoflavones—which were first demonstrated in rodents almost 40 yr ago (47)—provide an additional possible mechanism for the hypothesized anticancer effects of soy (see Ref. 48 for general review of proposed mechanisms). Also of potential relevance are recent data showing that isoflavones preferentially bind to (49) and activate estrogen receptor beta (ERβ) (50,51) in comparison with ERα. Some data indicate that, when activated, ERβ inhibits the proliferation of prostate cancer cells (52,53) and estrogen-stimulated growth of breast cancer cells (54). However, as noted previously, despite these potentially beneficial attributes, there is also concern that the estrogen-like effects of isoflavones may stimulate the growth of estrogen-sensitive mammary tumors (22–25).

Sources of Dietary Data

The primary sources of soy protein and isoflavone intake data included in this article were individual dietary surveys. A secondary source was the Food and Agriculture Organization (FAO) of the United Nations and, for Japan only, the Japanese National Nutritional Survey. To identify appropriate dietary surveys, a Medline search was conducted using as keywords soy, isoflavones, consumption, intake, China, Japan, Hong Kong, Indonesia, Korea, and Taiwan. References within those identified articles as well as articles that had come to the attention of the authors through other means were also examined for suitability. To qualify, articles had to include a sample size of at least 100, clearly define the study population (for example, age, gender, and location), and report mean or median total soy protein or total isoflavone intake. Only one survey per cohort was included. Surveys were excluded if they used only broad frequency categories (for example, one to three times per week, at least once per week, etc.) or focused on the intake of individual foods rather than attempting to assess total soy consumption. Generally, only those studies that described in detail the dietary instrument for assessing intake and listed the soy foods assessed were included.

Results

Soy Protein Intake

Food and Agriculture Organization of the United Nations data: It is evident from the FAO food balance sheets (http://apps.fao.org/) that there is considerable variation in soy intake among Asian countries. The FAO data are referred to as disappearance data because they represent the sum of imports minus exports, food used for non-human consumption, and losses during storage and transport. According to the FAO, for the year 2002 daily per capita soy protein intake for the main soy food–consuming countries (China, Hong Kong, Indonesia, Japan, South and North Korea, and Thailand) ranges from 2.0 to 9.6 g (Table 2). In Japan, China, and South Korea, soy provides less than 10% of the overall protein intake, whereas, in North Korea and Indonesia, 15.3% and 12.8% of the protein come from soy, respectively (Table 2).

Daily per capita soy protein intake for Japan between 1961 and 2002 is presented in Fig. 1. Intake remained very constant during this period, ranging from a high of 9.7 g/day in 1961 to a low of 8.4 g/day in 1977. In contrast, there has been a marked decrease in the extent to which soy protein contributes to total protein intake. In 1961, soy protein accounted for 13.4% of total protein, whereas the 2002 value is 9.5%. This decrease results from the steady increase during the past 4 decades in the (primarily animal) protein content of the Japanese diet. This kind of dramatic nutritional transition has been discussed in the literature (55).

Japanese National Nutritional Survey: The Ministry of Health and Welfare in Japan has conducted a National Nutrition Survey (NNS) for more than 50 yr (56). It includes randomly selected prefectures comprised of 10,000–20,000 subjects of all ages. For the NNS, at-home foods and beverages consumed by a family are weighed, meal by meal, for three consecutive days (in the most recent survey a 1-day record was used), excluding weekends and holidays. A dietitian demonstrates the measures to determine food quantities and teaches the survey methods and procedures to a housewife or another person who usually cooks in the family. During the survey, the dietitian makes a call to the subject's home at least once per day and reviews the dietary records. Foods eaten outside the home are also recorded. Dietary intake per capita per day is obtained by dividing the entire amount consumed in a household by the number of family members aged 1 yr and older.

The Japanese NNS (Fig. 2) shows that soy intake (expressed as is or on a wet weight basis) remained fairly constant after 1960 at about 65 g/day (32,57–64). Thus, the NNS is consistent with the FAO data showing a relatively consistent soy intake during the past 4 decades. However, 65 g/day provides approximately 6.5 g of soy protein, which is about 25% lower than the FAO estimate (32). According to the NNS, soy foods provided approximately 8–10% of total protein intake, which is similar to the FAO data (Fig. 1) (32,65,66).

Data from both the Japanese NNS and the FAO are averages across all age groups; therefore, it can be expected that the soy intake of adults, especially older adults consuming traditional

Table 2. Caloric, Total Protein, and Soy Protein Intakes for Selected Countries According to the Food and Agricultural Organization of the United Nations[a]

Country[b]	Total Protein (g)	Soy Protein (g)	% Soy Protein [(soy protein/total protein) × 100]
North Korea	62.8	9.6	15.3
Japan	91.8	8.7	9.5
Indonesia	64.2	8.2	12.8
South Korea	89.6	4.9	5.5
China	81.5	2.7	3.3
Hong Kong	99.8	2.3	2.3
Thailand	57.0	2.0	3.5

a: Food and Agricultural Organization Statistical Database (http://apps.fao.org/).
b: Data for 2002 except Hong Kong (1998).

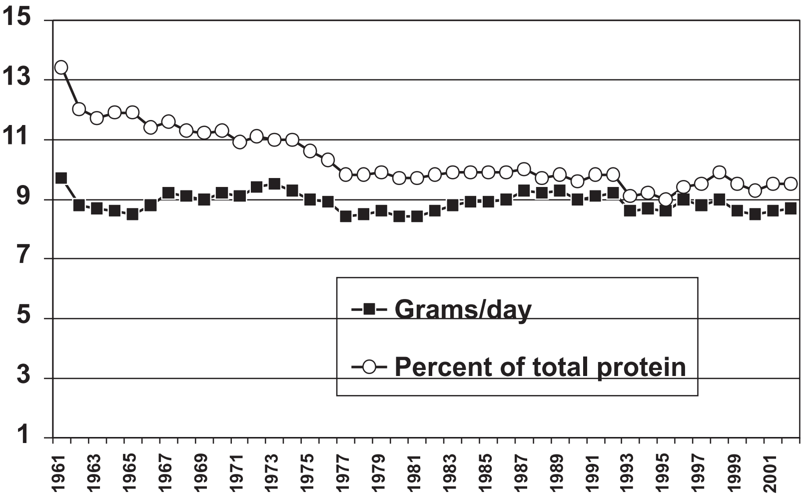

Figure 1. Japanese per capita soy protein intake expressed as grams per day and as a percentage of total protein for the years 1961–2002. (Data taken from the Food and Agriculture Organization of the United Nations.)

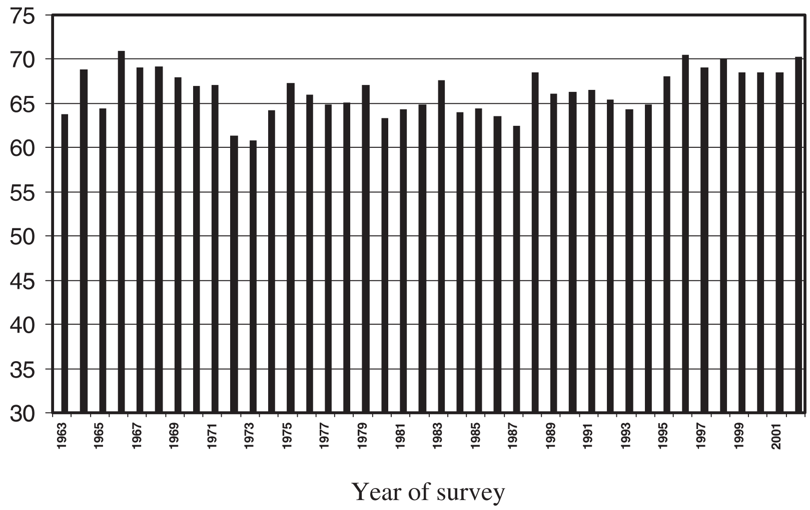

Figure 2. Soy food intake (wet weight or as-is basis, grams per day) as reported by the Japanese National Nutrition Survey for selected years between 1915 and 2002.

diets, would be higher than the values from these two sources of information. This is in fact the case as shown by dietary surveys of individuals discussed in the next section and the NNS when presented according to age. For example, the soy intake of Japanese adults aged 60–69 yr is 91.7 g/day, approximately 50% higher than the mean intake of the Japanese population overall (Fig. 3; information provided by Akio Sato, Professor of Environmental Health, Yamanashi University School of Medicine, Tamaho, Yamanashi 409–3898, Japan).

Surveys assessing the soy protein intake of individuals: In Table 3 are listed five recently conducted surveys of individuals in Japan that reported soy protein intake (36,39,67–69). Daily adult female soy protein intake ranged from a low of 6.0 g (69) to a high of 10.5 g (68), whereas the range of intake in males was 8.0 (39) to 11.3 g (68). Soy foods contributed from 6.5% (69) to 12.8% (68) of total protein intake.

Seven studies from China, Hong Kong, and Singapore that provided information on soy protein intake are included in Table 3 (33–35,42,70–72). One of these is a large prospective study from Shanghai that included nearly 46,000 women, which found daily mean soy protein intake to be 8.8 g (72), a value similar to Japanese data discussed previously. In an earlier report (not included in the table) from this cohort, soy protein was found to account for 12.8% of total protein intake (73). In two other studies from Shanghai, mean soy protein intakes were approximately 20% higher (10.3 g) in one (35) but only one-third as high in the other (70). However, the latter study included only a few key soy foods and did not claim to comprehensively assess soy intake.

Studies from Hong Kong published in 2000 and 2003 reported adult female daily soy protein intakes to be 4.9 g (34) and 7.9 g (33), respectively. These values are considerably higher than the FAO values for Hong Kong. The latter value represented 13.6% of total protein intake (33). Finally, two

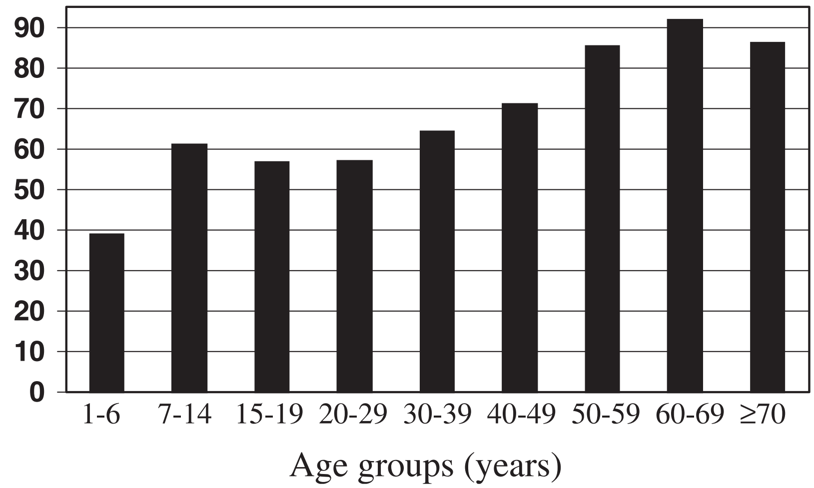

Figure 3. Mean Japanese soy food intake (grams per day) for different age groups according to the Japanese National Nutrition Survey for the years 1995–2002.

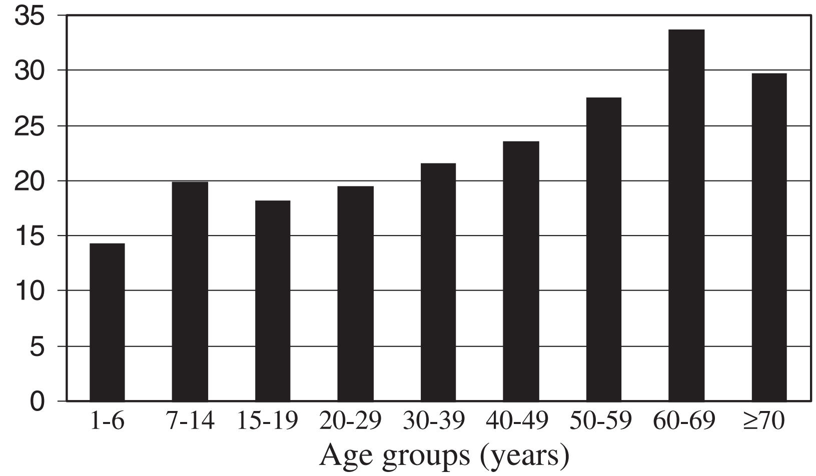

Figure 4. Mean Japanese isoflavone intake (expressed as aglycone weight intake, milligrams per day) according to the National Nutrition Survey for the year 2002 for different age groups.

studies from Singapore show relatively low (≤5.1 g/day) soy protein intakes (42,71). Overall, compared with intake in Japan, soy protein intake appears to be lower among Chinese living in Hong Kong and Singapore, whereas intake for Chinese living in Shanghai appears to be comparable.

Isoflavone Intake

Using the NNS, Nagata estimated overall Japanese mean isoflavone intake to be 28.7 mg/day (32) (Table 3). However, as noted previously, older adults consume more soy than the mean for the overall population; therefore, their isoflavone intake would be expected to be higher as is demonstrated in Fig. 4. The NNS estimate is generally consistent with the results of the eight studies from Japan included in Table 3 that reported intake data from the assessment of individuals (36,69,74–79). Daily isoflavone intake among these studies ranged from a low of 26 mg (69) to a high of about 54 mg (74).

The remaining 11 studies in Table 3 that reported isoflavone intake are from Hong Kong (33,34,80,81), Singapore (71), Shanghai (35,72,82), and elsewhere (29,83,84) in China. Not unexpectedly, with only one exception (80), daily isoflavone intake (<20 mg) in the studies from Singapore and Hong Kong was considerably lower than the intake for Japan (33,34,81). Markedly differing values were reported for Shanghai; in the studies by Dai et al. (35) and Yang et al. (72), daily isoflavone intakes were approximately 41 mg, whereas Frankenfeld et al. (82) reported a mean intake of only 10 mg. However, Frankenfeld et al. (82) commented that their dietary survey may have underestimated actual intake by using the median serving size of the overall Chinese population. The isoflavone intakes for Hebei and Gansu provinces reported by Liu et al. (29) and for Hangzhou reported by Zhang et al. (84) were ~18 mg and ~25 mg, respectively.

The highest reported isoflavone intake of any study comes from a case-control study of prostate cancer that included 12

Table 3. Soy Protein and Isoflavone Intakes Reported From Food-Frequency Questionnaires, Dietary Records, or Dietary Interview Conducted in Japan, China, Singapore, and Hong Kong[a]

Reference (dietary instrument)	Location/Study Type[b]	Subject Gender, Age (mean or range)	*n*	Total Protein	Total Soy (g)	Soy Protein (g)	% Soy Protein	Isoflavones (mg) Average	Isoflavones (mg) Range
Japan									
36 (FFQ)	Gifu/CS	F, 42.5	201	92.5[c]	50.7 ± 34.8[c]	9.0 ± 5.4[c]	9.7	29.9 ± 23.5[c]	NA
69 (FFQ)	Gifu/CS	F, 50.9	206	92.0[c]	64.7 ± 49.0[c]	6.0 ± 3.8[c]	6.5	26.0 ± 14.3[c]	NA
79 (FFQ)	Gifu/CS	F, 19–34	189	76.9[c]	60.6 ± 62.4	NA	NA	26.9 ± 26.6[c]	NA
39 (FFQ)	Takayama City/CS	M, 60.0	1,242	94.1[c]	63.6 ± 52.3[c]	8.0 ± 5.0[c]	8.5	NA	NA
		F, 56.7	3,596	83.6[c]	54.4 ± 40.0[c]	6.9 ± 4.1[c]	8.3		
67 (FFQ)	Takayama City/CS	F, 42.7	1,130	83.5[c]	84.4 ± 53.7[c]	9.4 ± 5.8[c]	11.3	NA	NA
68 (FFQ)	Takayama City/Prosp	M, 54.6	13,880	94.3[c]	102.1 ± 72.5[c]	11.3 ± 7.8[c]	12.0	NA	NA
		F, 55.4	16,424	82.0[c]	93.3 ± 64.0[c]	10.5 ± 7.0c	12.8		
77 (FFQ)	Nagoya/CS	M, 54.4	886	NA	NA	NA	NA	31.7[d]	16.2, 51.4[e]
		F, 57.8	346						
74 (DI)	Kyoto/CS	F, 44–80	478	NA	NA	NA	NA	54.3 ± 1.0[c]	81.1 ± 1.8[f]
75 (FFQ)	Takayama City/Prosp	F, 42.9	1,172	NA	84.9 ± 53.6[c]	NA	NA	37.4 ± 22.5[c]	50.1[g]
76 (DR)	Northern/CS	F, 57.9	115	NA	NA	NA	NA	47.2 ± 23.6[c]	12.0, 118.9[h]
78 (FFQ)	12 regions/Prosp	F, 45–74	34,457	64.0[c]	NA	NA	NA	22.6[c]	NA
		M, 45–74	33,195	71.0[c]				23.5[c]	
32 (DR)	National Survey/CS	All ages	6,000 families	79.2[c]	66.8 ± 7.7[c]	6.5 ± 0.8[c]	NA	28.7 ± 4.1[c]	21.3, 35.7[i]

China, Singapore, and Hong Kong									
72 (FFQ)	Shanghai/Prosp	F, 49.9	45,694	NA	NA	8.8 ± 6.3[c]	NA	40.8 ± 28.7[c]	7.4, 145.7[j]
35 (FFQ)	Shanghai/PBCC	F, 47.2	1,556	NA	135.4 ± 127[c]	10.3 ± 10.1[c]	NA	40.9 ± 39.5[c]	18.7, 53.3[d,e]
					93.5[d]	8.0[d]		33.2[d]	
82 (FFQ)	Shanghai/PBCC	F, 30–64	1,823	NA	NA	NA	NA	9.8[k]	
70 (FFQ)	Tianjin/PBCC	F, 43.3	300	50.1[d]	NA	2.8[d]	5.6	NA	NA
	Shanghai/PBCC	F, 50.0	534	67.2[d]		3.5d	5.2		
29 (FFQ)	Hebei and Gansu/CS	F, 20–65	1,188	NA	38.7 ± 58.2[c]	NA	NA	17.7 ± 26.6[c]	NA
					23.5[d]			8.9d	
84 (FFQ)	Hangzhou/PBCC	F, 48.0	652	NA	107.5 ± 93.1[c]	NA	NA	24.7 ± 18.8[c]	NA
83 (FFQ)	12 cities/PBCC	M, 40–70+	265	83.8[c]	NA	NA	NA	75.7[c]	>98.3[l]
				52.9[d]				54.7[d]	
42 (FFQ)	Singapore/HBCC	F, 24–83	420	38.7[d]	35.6[d]	2.5[d]	6.5	NA	NA
71 (FFQ)	Singapore/Prosp	F, M 45–74	26,538	59.5[m]	96.5[m]	5.1[m]	8.6	15.9[m]	NA
33 (FFQ)	Hong Kong/Prosp	F, 55.1	454	58.3[c]	NA	7.9 ± 9.1[c]	13.6	17.3 ± 19.7[2]	42.6[n]
34 (FFQ)	Hong Kong/CS	M, 45.6	500	NA	NA	6.6 ± 7.0[c]	5.7[o]	14.5 ± 15.4[c]	NA
		F, 45.6	510			4.9 ± 5.6c		11.0 ± 12.9c	
80 (FFQ)	Hong Kong/CS	F, 37.5	293	NA	NA		NA	29.7 ± 31.3[c]	5.3, 33.25
		F, 63.0	357					21.9 ± 37.5c	8.8, 40.6[e]
81 (FFQ)	Hong Kong/Prosp	F, 30–40	132	NA	NA	NA	NA	6.2 ± 7.0[c]	NA

a: Abbreviations are as follows: FFQ, food-frequency questionnaire; DI, dietary interview; DR, dietary record. NA, not applicable or not available.
b: CS, cross section; Prosp, prospective; PBCC, population-based case control; HBCC, hospital-based case control.
c: Mean or mean ± standard deviation.
d: Median.
e: 25th and 75th percentiles.
f: Mean ± standard error for the fourth quartile (cutoff, >65 mg; $n = 132$).
g: Median intake for third tertile.
h: Individual low and high intakes.
i: Range based on group means.
j: Mean isoflavone intakes for the 8.8% of women who consumed <2.5 g/day of soy protein and the 2.2% who consumed ≥25 g/day of soy protein.
k: Geometric mean.
l: Value represents the cutoff for the fourth quartile of intake and was determined by summing the individual cutoffs for daidzein and genistein.
m: Value represents estimate based on the unweighted average of data reported for the second and third quartiles of total soy intake.
n: Estimated mean for the fourth quartile of intake based on the stated mean soy protein intake for this quartile.
o: Value for men and women combined.

cities in China (83). Mean daily isoflavone intake was 75.7 mg/day. One cautionary note about this study, however, is that isoflavone intake appears to be much higher than would be predicted on the basis of the reported soy food intake.

Estimates of Upper Soy Protein and Isoflavone Intakes

Several studies provide important insight into the upper levels of soy protein and isoflavone intakes in Asia. For example, in a Japanese study involving over 3,000 subjects, mean fourth-quartile soy protein intakes for men and women were 13.0 g/day and 11.0 g/day, respectively (39). Higher values were reported in a Japanese study involving 30,000 subjects; mean third-tertile soy protein intakes for men and women were 17.4 g/day and 15.9 g/day, respectively (68) (personal communication, Chisato Nagata, March 9, 2004). Mean soy protein intake for the fourth quartile in the Shanghai prospective study involving middle-aged women cited previously (73) was 16.7 g/day (personal communication, Xianglan Zhang, January 10, 2003).

Interestingly, although as noted previously soy protein intake in Hong Kong is low in comparison with Japan, Ho et al. (33) found adult female mean fourth-quartile soy protein intake to be 19.4 g/day, higher than the corresponding values in the three previously cited studies from Japan and Shanghai. Overall, these protein intake data suggest that daily mean isoflavone intake among women in the upper tertile or quartile is approximately 60 mg. This estimate is quite a bit lower, however, than the intake of 83.3 mg reported for women in the fourth quartile in the Japanese study by Somekawa et al. (74).

Four studies are noteworthy for providing insight into the very upper range of soy intake. Two of these studies are from Shanghai; in one, the soy protein intake cutoff for the 90th percentile was ≤19.9 g/day (35), and, in the other, the 95th percentile soy protein intake was 19.7 g/day (73). Also, approximately 2% of women in this cohort consumed ~146 mg/day of isoflavones (72). Finally, two studies from Japan suggest that approximately 5% of adults consume as much as 100 mg of isoflavones per day (76,77).

Intake Trends and Intake According to Age

According to the Japanese NNS, soy (Fig. 3) and isoflavone (Fig. 4) intake increased in each 10-yr age group between 20–29 and 60–69. Thus, the possibility exists that the mean intake reported in the current analysis slightly underestimates the intake of the traditional Japanese diet because much of the data come from subjects ≤59 yr old. There is also the possibility that westernization of the diet has led to a reduction in soy intake among even older Japanese adults and thus the current data underestimate the soy intake of traditional Japanese. However, this appears not to be the case because data from the NNS suggest that soy intake among older Japanese (that is, ≥60 yr) remained constant between 1980 and 1992 (85). In 1980, people who were 60 yr old were born in 1920, prior to the westernization of the Japanese diet. This having been said, because over time different methodologies for assessing intake may have been employed, findings related to intake trends should be regarded with caution.

Generalizability of the Data

It is important to recognize that the studies presented in this review are not necessarily representative of the intake of all subsets of the Asian population and all regions within the countries discussed. For example, Liu et al. (29) found that, among rural Chinese, education level was positively correlated with soy intake. With regard to China, the importance of the soybean as a crop differs dramatically among different regions within this country (86), and there is about a fourfold range in intake among just the studies reported in Table 3. Liu et al. noted that the national average for total soy food intake in China for the period 1990–1998 was only 17.8 g/day, which likely represents an isoflavone intake of ≤10 mg/day (29). In their specific study, they reported an isoflavone intake of 17.7 mg/day (29). In contrast, Dai et al. (35) and Yang et al. (72) reported daily intakes in Shanghai of approximately 41 mg, and, in a study that included 12 cities in China, Lee et al. (83) reported a daily intake of 75 mg.

Soy intakes reported for several different locations in Japan, including Gifu (36), Nagoya (77), Kyoto (74), Takayama City (75), and Aichi Prefecture (87) (this study reported only total soy foods so it is not included in Table 3), were fairly similar, displaying about a twofold range. However, these locations are all from the central part of Japan. Okinawans have been said to be especially high soy consumers (88), but several small studies suggest that their absolute soy protein intake is similar to that reported in this article, although when expressed as a percentage of total protein it may be somewhat higher (89–93).

There is also the issue of urban versus rural soy intake—a potentially important distinction if rural intake more accurately reflects the traditional Asian diet. However, available data do not suggest consistent differences between rural and urban areas. For example, Adlercreutz et al. (94) reported that isoflavone intake among subjects (age ~48 yr) from a rural village south of Kyoto was similar to that reported for urban Japanese. Similarly, according to the Korean National Household Survey, the mean daily isoflavone intake (15.1 mg) of individuals living in large cities was almost identical to the isoflavone intake (15.2 mg) of individuals living in rural areas (95).

Conclusions and Implications of Findings

Precisely quantifying the intake of any dietary microcomponent is difficult but for at least two reasons may be especially so in the case of isoflavones. First, food processing (96), the environmental conditions under which the soybean is grown, and the soybean variety in question all affect isoflavone content (97–101). Second, there are many commonly consumed dishes throughout Asia that contain small amounts of soy. However, most of the data suggest it is unlikely that intake was substantially underestimated as a result. Wakai et al. (77) found that, among the Japanese subjects in their study, four soy foods (tofu, miso, natto, and fried tofu) accounted for about 90% of total isoflavone intake. Similarly, Somekawa et al. (74) found that soybean curd, fermented soybeans, and soybean paste provided 88% of total isoflavone intake of Japanese women. Among Chinese women, Zhang et al. (73) found that soymilk, tofu, and processed soy products other than tofu accounted for 81% of total soy protein intake consumed. Parenthetically, today, in both Japan and China nonfermented foods provide approximately half of the total soy intake (73,74,77,102,103).

The results from this review can be summarized as follows: average daily soy protein and isoflavone intakes of older Japanese adults are approximately 6–11 g and 25–50 mg, respectively. This isoflavone intake range is consistent with a daily Japanese isoflavone intake of ~35 mg recently estimated using the market basket method (104). Data indicate that soy intake in Hong Kong and Singapore is lower than in Japan, whereas intake in China varies markedly according to region, although two studies from Shanghai found that isoflavone intake in that city is comparable with Japanese intake (35,72). It is likely that a relatively small (≤10%) proportion of the population in Asia consumes daily as much as 25 g of soy protein or 100 mg of isoflavones. Thus, if historical precedent can be used as one measure of safety, then a reasonable upper limit for isoflavone intake from traditional soy foods is approximately 100 mg/day. This having been said, it is worth noting that short-term clinical trials provide little, if any, evidence of harm in response to isoflavone intakes that greatly exceed this level (105–108). Nevertheless, there is a need for long-term safety data.

As noted at the onset, there may be differences between Asians and non-Asians that affect how each group responds to isoflavones. It is interesting to consider whether, in comparison with Asians, the generally larger body size of non-Asians indicates that larger amounts of isoflavones are required by non-Asians to derive any potential benefits. Research comparing isoflavone pharmacokinetics in Asians with non-Asians is needed. The extent, if any, to which soy contributes to the relatively low rates of certain cancers, especially breast and prostate cancer, in Asia is uncertain. Also unclear is whether soy must be consumed throughout life, or during certain periods of life, to exert anticancer effects. In this regard, one of the most intriguing hypotheses is that soy consumption during childhood/adolescence reduces adult breast cancer risk (109–111). Conversely, evidence suggests that late-life influences greatly affect prostate cancer risk (112), and recent preliminary data indicate that isoflavones may help to reduce disease progression in prostate cancer patients (113–115).

If soy does contribute to the lower breast and prostate cancer incidence in Asia, then the current analysis suggests that an average daily isoflavone intake of 25–50 mg may be efficacious. However, epidemiological studies demonstrating inverse associations between soy intake and risk involve comparisons across intake categories, and the largest reductions in risk are typically associated with intakes greater than the mean (83,111,116). Thus, the mean isoflavone intake of 25–50 mg/day may underestimate the amount needed for maximum protection against cancer. Maximum protection might require the consumption of closer to 75 mg of isoflavones per day. This amount is provided by approximately three servings (for example, 250 ml of soymilk, 85–100 g of tofu, and 85 g of cooked soybeans) of traditional soy foods. The daily consumption of this amount of soy undoubtedly represents a significant dietary challenge for most non-Asians. Finally, it should be noted that the intake values presented in this article are not intended to serve as an exact measure but rather as a general estimate and range of soy intake among different Asian populations. Future research may produce more precise data.

Addendum

Subsequent to the completion of this manuscript an additional study fitting the inclusion criteria was identified (117). This study found mean (± SD) daily isoflavone intake among Korean women (n = 178) aged 35 to 60 yr to be 24.4 ± 25.1 mg. Intake among pre-and postmenopausal women was 21.8 and 30.1 mg/day, respectively.

Acknowledgments and Notes

Address correspondence to Mark Messina, Nutrition Matters, Inc., 439 Calhoun Street, Port Townsend, WA 98368. Phone: 360–379–9544. FAX: 360–379–9614. E-mail: markm@olympus.net.

Submitted 13 December 2004; accepted in final form 16 March 2006.

References

1. Messina M and Barnes S: The role of soy products in reducing risk of cancer. *JNCI* **83,** 541–546, 1991.
2. Pisani P, Parkin DM, Bray F, and Ferlay J: Estimates of the worldwide mortality from 25 cancers in 1990. *Int J Cancer* **83,** 18–29, 1999.
3. Ajiki W, Tsukuma H, and Oshima A: Cancer incidence and incidence rates in Japan in 1999: estimates based on data from 11 population-based cancer registries. *Jpn J Clin Oncol* **34,** 352–356, 2004.
4. Adlercreutz H: Phytoestrogens and breast cancer. *J Steroid Biochem Mol Biol* **83,** 113–118, 2002.
5. Messina M: Emerging evidence on the role of soy in reducing prostate cancer risk. *Nutr Rev* **61,** 117–131, 2003.
6. Goodman MT, Wilkens LR, Hankin JH, Lyu LC, Wu AH, et al.: Association of soy and fiber consumption with the risk of endometrial cancer. *Am J Epidemiol* **146,** 294–306, 1997.
7. Xu WH, Zheng W, Xiang YB, Ruan ZX, Cheng JR, et al.: Soya food intake and risk of endometrial cancer among Chinese women in Shanghai: population based case-control study. *Br Med J* **328,** 1285–1290, 2004.
8. Spector D, Anthony M, Alexander D, and Arab L: Soy consumption and colorectal cancer. *Nutr Cancer* **47,** 1–12, 2003.

9. Guo JY, Li X, Browning JD Jr, Rottinghaus GE, Lubahn DB, et al.: Dietary soy isoflavones and estrone protect ovariectomized ERalphaKO and wild-type mice from carcinogen-induced colon cancer. *J Nutr* **134,** 179–182, 2004.
10. Sarkar FH and Li Y: Soy isoflavones and cancer prevention. *Cancer Invest* **21,** 744–757, 2003.
11. Messina M and Flickinger B: Hypothesized anticancer effects of soy: evidence points toward isoflavones as the primary anticarcinogens. *Pharm Biol* **40,** S6–S23, 2002.
12. Nestel P: Isoflavones: their effects on cardiovascular risk and functions. *Curr Opin Lipidol* **14,** 3–8, 2003.
13. Messina M, Ho S, and Alekel DL: Skeletal benefits of soy isoflavones: a review of the clinical trial and epidemiologic data. *Curr Opin Clin Nutr Metab Care* **7,** 649–658, 2004.
14. Messina M and Hughes C: Efficacy of soyfoods and soybean isoflavone supplements for alleviating menopausal symptoms is positively related to initial hot flush frequency. *J Med Food* **6,** 1–11, 2003.
15. Golbitz P: Soyfoods: The U.S. Market 2002. Bar Harbor, ME: Soyatech, 2002.
16. Setchell KD, Brown NM, Desai P, Zimmer-Nechemias L, Wolfe BE, et al.: Bioavailability of pure isoflavones in healthy humans and analysis of commercial soy isoflavone supplements. *J Nutr* **131,** S1362–S1375, 2001.
17. Nurmi T, Mazur W, Heinonen S, Kokkonen J, and Adlercreutz H: Isoflavone content of the soy based supplements. *J Pharm Biomed Anal* **28,** 1–11, 2002.
18. Howes JB and Howes LG: Content of isoflavone-containing preparations. *Med J Aust* **176,** 135–136, 2002.
19. Munro IC, Harwood M, Hlywka JJ, Stephen AM, Doull J, et al.: Soy isoflavones: a safety review. *Nutr Rev* **61,** 1–33, 2003.
20. Siegel-Itzkovich J: Health committee warns of potential dangers of soya. *Br Med J* **331,** 254, 2005.
21. Comité de Nutrition de la Société Française de Pédiatrie: Phytoestrogens and soy foods in infants and children: caution is needed. *Arch Pediatr* **13,** 235–237, 2006.
22. Allred CD, Allred KF, Ju YH, Virant SM, and Helferich WG: Soy diets containing varying amounts of genistein stimulate growth of estrogen-dependent (mcf-7) tumors in a dose-dependent manner. *Cancer Res* **61,** 5045–5050, 2001.
23. Messina MJ and Loprinzi CL: Soy for breast cancer survivors: a critical review of the literature. *J Nutr* **131,** S3095–S3108, 2001.
24. Bouker KB and Hilakivi-Clarke L: Genistein: does it prevent or promote breast cancer? *Environ Health Perspect* **108,** 701–708, 2000.
25. Allred CD, Allred KF, Ju YH, Goeppinger TS, Doerge DR, et al.: Soy processing influences growth of estrogen-dependent breast cancer tumors. *Carcinogenesis* **25,** 1649–1657, 2004.
26. Messina M and Messina V: Provisional recommended soy protein and isoflavone intakes for healthy adults: rationale. *Nutr Today* **38,** 100–109, 2003.
27. U.S. Food and Drug Administration: Food labeling, health claims, soy protein, and coronary heart disease. *Fed Reg* **57,** 699–733, 1999.
28. U.S. Department of Agriculture, Agricultural Research Service: USDA-Iowa State University Database on the Isoflavone Content of Foods, Release 1.3, 2002. Nutrient Data Laboratory Web site: http://www.nal.usda.gov/fnic/foodcomp/Data/isoflav/isoflav.html
29. Liu Z, Li W, Sun J, Liu C, Zeng Q, et al.: Intake of soy foods and soy isoflavones by rural adult women in China. *Asia Pac J Clin Nutr* **13,** 204–209, 2004.
30. Messina M: Isoflavone intakes by Japanese were overestimated. *Am J Clin Nutr* **62,** 645, 1995.
31. Cassidy A, Bingham S, and Setchell KD: Biological effects of a diet of soy protein rich in isoflavones on the menstrual cycle of premenopausal women. *Am J Clin Nutr* **60,** 333–340, 1994.
32. Nagata C: Ecological study of the association between soy product intake and mortality from cancer and heart disease in Japan. *Int J Epidemiol* **29,** 832–836, 2000.
33. Ho SC, Woo J, Lam S, Chen Y, Sham A, et al.: Soy protein consumption and bone mass in early postmenopausal Chinese women. *Osteoporos Int* **14,** 835–842, 2003.
34. Ho SC, Woo JL, Leung SS, Sham AL, Lam TH, et al.: Intake of soy products is associated with better plasma lipid profiles in the Hong Kong Chinese population. *J Nutr* **130,** 2590–2593, 2000.
35. Dai Q, Shu XO, Jin F, Potter JD, Kushi LH, et al.: Population-based case-control study of soyfood intake and breast cancer risk in Shanghai. *Br J Cancer* **85,** 372–378, 2001.
36. Nagata C, Shimizu H, Takami R, Hayashi M, Takeda N, et al.: Soy product intake is inversely associated with serum homocysteine level in premenopausal Japanese women. *J Nutr* **133,** 797–800, 2003.
37. Nagata C, Shimizu H, Takami R, Hayashi M, Takeda N, et al.: Serum concentrations of estradiol and dehydroepiandrosterone sulfate and soy product intake in relation to psychologic well-being in peri- and postmenopausal Japanese women. *Metabolism* **49,** 1561–1564, 2000.
38. Takatsuka N, Nagata C, Kurisu Y, Inaba S, Kawakami N, et al.: Hypocholesterolemic effect of soymilk supplementation with usual diet in premenopausal normolipidemic Japanese women. *Prev Med* **31,** 308–314, 2000.
39. Nagata C, Takatsuka N, Kurisu Y, and Shimizu H: Decreased serum total cholesterol concentration is associated with high intake of soy products in Japanese men and women. *J Nutr* **128,** 209–213, 1998.
40. Nagata C, Kabuto M, Kurisu Y, and Shimizu H: Decreased serum estradiol concentration associated with high dietary intake of soy products in premenopausal Japanese women. *Nutr Cancer* **29,** 228–233, 1997.
41. Horiuchi T, Onouchi T, Takahashi M, Ito H, and Orimo H: Effect of soy protein on bone metabolism in postmenopausal Japanese women. *Osteoporos Int* **11,** 721–724, 2000.
42. Lee HP, Gourley L, Duffy SW, Esteve J, Lee J, et al.: Dietary effects on breast-cancer risk in Singapore. *Lancet* **337,** 1197–2000, 1991.
43. Franke AA, Custer LJ, Wang W, and Shi CY: HPLC analysis of isoflavonoids and other phenolic agents from foods and from human fluids. *Proc Soc Exp Biol Med* **217,** 263–273, 1998.
44. Murphy PA, Song T, Buseman G, Barua K, Beecher GR, et al.: Isoflavones in retail and institutional soy foods. *J Agric Food Chem* **47,** 2697–2704, 1999.
45. Erdman JW Jr, Badger TM, Lampe JW, Setchell KD, and Messina M: Not all soy products are created equal: caution needed in interpretation of research results. *J Nutr* **134,** S1229–S1233, 2004.
46. Akiyama T, Ishida J, Nakagawa S, Ogawara H, Watanabe S, et al.: Genistein, a specific inhibitor of tyrosine-specific protein kinases. *J Biol Chem* **262,** 5592–5595, 1987.
47. Folman Y and Pope GS: The interaction in the immature mouse of potent oestrogens with coumestrol, genistein and other utero-vaginotrophic compounds of low potency. *J Endocrinol* **34,** 215–225, 1966.
48. Wietrzyk J, Grynkiewicz G, and Opolski A: Phytoestrogens in cancer prevention and therapy—mechanisms of their biological activity. *Anticancer Res* **25,** 2357–2366, 2005.
49. Kuiper GG, Lemmen JG, Carlsson B, Corton JC, Safe SH, et al.: Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta. *Endocrinology* **139,** 4252–4263, 1998.
50. An J, Tzagarakis-Foster C, Scharschmidt TC, Lomri N, and Leitman DC: Estrogen receptor beta-selective transcriptional activity and recruitment of coregulators by phytoestrogens. *J Biol Chem* **276,** 17808–17814, 2001.
51. Kostelac D, Rechkemmer G, and Briviba K: Phytoestrogens modulate binding response of estrogen receptors alpha and beta to the estrogen response element. *J Agric Food Chem* **51,** 7632–7635, 2003.
52. Signoretti S and Loda M: Estrogen receptor beta in prostate cancer: brake pedal or accelerator? *Am J Pathol* **159,** 13–16, 2001.
53. Weihua Z, Lathe R, Warner M, and Gustafsson JA: An endocrine pathway in the prostate, ERbeta, AR, 5alpha-androstane-3beta,17beta-diol, and CYP7B1, regulates prostate growth. *Proc Natl Acad Sci USA* **99,** 13589–13594, 2002.
54. Strom A, Hartman J, Foster JS, Kietz S, Wimalasena J, et al.: Estrogen receptor {beta} inhibits 17{beta}-estradiol-stimulated proliferation of

the breast cancer cell line T47D. *Proc Natl Acad Sci USA* **101,** 1566–1571, 2004.
55. Popkin BM: The nutrition transition in low-income countries: an emerging crisis. *Nutr Rev* **52,** 285–298, 1994.
56. Kobayashi S: Trends in national survey of Japan. *Nutr Health* **8,** 91–96, 1992.
57. Kagawa Y: Impact of westernization on the nutrition of Japanese: changes in physique, cancer, longevity and centenarians. *Prev Med* **7,** 205–217, 1978.
58. Fukutake M, Takahashi M, Ishida K, Kawamura H, Sugimura T, et al.: Quantification of genistein and genistin in soybeans and soybean products. *Food Chem Toxicol* **34,** 457–461, 1996.
59. Watanabe S, Yamaguchi M, Sobue T, Takahashi T, Miura T, et al.: Pharmacokinetics of soybean isoflavones in plasma, urine and feces of men after ingestion of 60 g baked soybean powder (kinako). *J Nutr* **128,** 1710–1715, 1998.
60. Ohta T, Nakatsugi S, Watanabe K, Kawamori T, Ishikawa F, et al.: Inhibitory effects of Bifidobacterium-fermented soy milk on 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine-induced rat mammary carcinogenesis, with a partial contribution of its component isoflavones. *Carcinogenesis* **21,** 937–941, 2000.
61. Fukuba H: Food policy for health in Japan. *Nutr Health* **8,** 177–190, 1992.
62. Nakamura Y, Tsuji S, and Tonogai Y: Determination of the levels of isoflavonoids in soybeans and soy-derived foods and estimation of isoflavonoids in the Japanese daily intake. *J AOAC Int* **83,** 635–650, 2000.
63. Oiso T: Changing food patterns in Japan. In *Nutrition in Health and Disease and International Development: Symposia from the XII International Congress of Nutrition*. New York: Alan R. Liss, 1981.
64. Keys A and Kimura N: Diets of middle-aged farmers in Japan. *Am J Clin Nutr* **23,** 212–223, 1970.
65. Wang M-F, Kishi K, Takahashi T, Komatsu T, Ohnaka M, et al.: Efficiency of utilization of soy protein isolate in Japanese young men. *J Nutr Sci Vitaminol* **29,** 201–216, 1983.
66. Nagaya T: Soy and legume intake. Nagoya City, Japan, 2000.
67. Nagata C, Takatsuka N, Kawakami N, and Shimizu H: Association of diet with the onset of menopause in Japanese women. *Am J Epidemiol* **152,** 863–867, 2000.
68. Nagata C, Takatsuka N, Kawakami N, and Shimizu H: A prospective cohort study of soy product intake and stomach cancer death. *Br J Cancer* **87,** 31–36, 2002.
69. Takata Y, Maskarinec G, Franke A, Nagata C, and Shimizu H: A comparison of dietary habits among women in Japan and Hawaii. *Public Health Nutr* **7,** 319–326, 2004.
70. Yuan JM, Wang QS, Ross RK, Henderson BE, and Yu MC: Diet and breast cancer in Shanghai and Tianjin, China. *Br J Cancer* **71,** 1353–1358, 1995.
71. Sun CL, Yuan JM, Arakawa K, Low SH, Lee HP, et al.: Dietary soy and increased risk of bladder cancer: the Singapore Chinese Health Study. *Cancer Epidemiol Biomarkers Prev* **11,** 1674–1677, 2002.
72. Yang G, Shu XO, Jin F, Zhang X, Li HL, et al.: Longitudinal study of soy food intake and blood pressure among middle-aged and elderly Chinese women. *Am J Clin Nutr* **81,** 1012–1017, 2005.
73. Zhang X, Shu XO, Gao YT, Yang G, Li Q, et al.: Soy food consumption is associated with lower risk of coronary heart disease in Chinese women. *J Nutr* **133,** 2874–2878, 2003.
74. Somekawa Y, Chiguchi M, Ishibashi T, and Aso T: Soy intake related to menopausal symptoms, serum lipids, and bone mineral density in postmenopausal Japanese women. *Obstet Gynecol* **97,** 109–115, 2001.
75. Nagata C, Takatsuka N, Kawakami N, and Shimizu H: Soy product intake and premenopausal hysterectomy in a follow-up study of Japanese women. *Eur J Clin Nutr* **55,** 773–777, 2001.
76. Arai Y, Watanabe S, Kimira M, Shimoi K, Mochizuki R, et al.: Dietary intakes of flavonols, flavones and isoflavones by Japanese women and the inverse correlation between quercetin intake and plasma LDL cholesterol concentration. *J Nutr* **130,** 2243–2250, 2000.
77. Wakai K, Egami I, Kato K, Kawamura T, Tamakoshi A, et al.: Dietary intake and sources of isoflavones among Japanese. *Nutr Cancer* **33,** 139–145, 1999.
78. Ishihara J, Sobue T, Yamamoto S, Sasaki S, and Tsugane S: Demographics, lifestyles, health characteristics, and dietary intake among dietary supplement users in Japan. *Int J Epidemiol* **32,** 546–553, 2003.
79. Nagata C, Hirokawa K, Shimizu N, and Shimizu H: Soy, fat and other dietary factors in relation to premenstrual symptoms in Japanese women. *BJOG* **111,** 594–599, 2004.
80. Mei J, Yeung SS, and Kung AW: High dietary phytoestrogen intake is associated with higher bone mineral density in postmenopausal but not premenopausal women. *J Clin Endocrinol Metab* **86,** 5217–5221, 2001.
81. Ho SC, Chan SG, Yi Q, Wong E, and Leung PC: Soy intake and the maintenance of peak bone mass in Hong Kong Chinese women. *J Bone Miner Res* **16,** 1363–1369, 2001.
82. Frankenfeld CL, Lampe JW, Shannon J, Gao DL, Ray RM, et al.: Frequency of soy food consumption and serum isoflavone concentrations among Chinese women in Shanghai. *Public Health Nutr* **7,** 765–772, 2004.
83. Lee MM, Gomez SL, Chang JS, Wey M, Wang RT, et al.: Soy and isoflavone consumption in relation to prostate cancer risk in China. *Cancer Epidemiol Biomarkers Prev* **12,** 665–668, 2003.
84. Zhang M, Xie X, Lee AH, and Binns CW: Soy and isoflavone intake are associated with reduced risk of ovarian cancer in southeast China. *Nutr Cancer* **49,** 125–130, 2004.
85. Saio K: Soybean food industry for the 21st century. *Korean Soybean Digest* **15,** 94–105, 1998.
86. Simoons: *Food in China. A Cultural and Historical Inquiry*. Boca Raton, FL: CRC Press, 1991.
87. Tokudome S, Imaeda N, Tokudome Y, Fujiwara N, Nagaya T, et al.: Relative validity of a semi-quantitative food frequency questionnaire versus 28 day weighed diet records in Japanese female dietitians. *Eur J Clin Nutr* **55,** 735–742, 2001.
88. Matsuzaki T: Longevity, diet, and nutrition in Japan: epidemiological studies. *Nutr Rev* **50,** 355–359, 1992.
89. Willcox BJ, Fuchigami K, Willcox DC, Kendall CWC, Suzuki M, et al.: Isoflavone intake in Japanese and Japanese-Canadians. *Am J Clin Nutr* **61,** 901 (abstract 58), 1995.
90. Willcox BJ, Jenkins DJA, Fuchigami K, Willcox DC, Suzuki M, et al.: Dietary westernization and chronic disease in Japan. *FASEB J* 1995.
91. Willcox BJ, Hensrud WW, Jenkins DJA, Fuchigami K, Willcox DC, et al.: The dietary habits of Japan's longest-lived women. *Am J Clin Nutr* **66,** 210 (abstract 42), 1997.
92. Wakai K, Ohno Y, Genka K, Ohmine K, Kawamura T, et al.: Risk modification in lung cancer by a dietary intake of preserved foods and soyfoods: findings from a case-control study in Okinawa, Japan. *Lung Cancer* **25,** 147–159, 1999.
93. Kanke Y, Iitoi Y, Twasaki M, Iwase Y, Iwama M, et al.: Effects of human diets of two different Japanese populations on cancer incidence in rat hepatic drug-metabolizing and antioxidant enzyme systems. *Nutr Cancer* **26,** 63–71, 1996.
94. Adlercreutz H, Honjo H, Higashi A, Fotsis T, Hamalainen E, et al.: Urinary excretion of lignans and isoflavonoid phytoestrogens in Japanese men and women consuming a traditional Japanese diet. *Am J Clin Nutr* **54,** 1093–1100, 1991.
95. Kim J and Kwon C: Estimated dietary isoflavone intake of Korean population based on National Nutrition Survey. *Nutr Res* **21,** 947–953, 2001.
96. Wang H-J and Murphy PA: Mass balance study of isoflavones during soybean processing. *J Agric Food Chem* **44,** 2377–2383, 1996.
97. Wang H-J and Murphy PA: Isoflavone composition of American and Japanese soybeans in Iowa: effects of variety, crop year, and location. *J Agric Food Chem* **42,** 1674–1677, 1994.
98. Eldridge AC and Kwolek WF: Soybean isoflavones: effects of environment and variety on composition. *J Agric Food Chem* **31,** 394–396, 1983.
99. Tsukamoto C, Shimada S, Igita K, Kudou S, Kokubun M, et al.: Factors affecting isoflavone content in soybean seeds: changes in

isoflavones, saponins, and composition of fatty acids at different temperatures during seed development. *J Agric Food Chem* **43,** 1184–1192, 1995.
100. Carrão-Panizzi MC and Kitamura K: Isoflavone content in Brazilian soybean cultivars. *Breed Sci* **45,** 295–300, 1995.
101. Setchell KD and Cole SJ: Variations in isoflavone levels in soy foods and soy protein isolates and issues related to isoflavone databases and food labeling. *J Agric Food Chem* **51,** 4146–4155, 2003.
102. Yamamoto S, Sobue T, Sasaki S, Kobayashi M, Arai Y, et al.: Validity and reproducibility of a self-administered food-frequency questionnaire to assess isoflavone intake in a Japanese population in comparison with dietary records and blood and urine isoflavones. *J Nutr* **131,** 2741–2747, 2001.
103. Arai Y, Uehara M, Sato Y, Kimira M, Eboshida A, et al.: Comparison of isoflavones among dietary intake, plasma concentration and urinary excretion for accurate estimation of phytoestrogen intake. *J Epidemiol* **10,** 127–135, 2000.
104. Kikuchi Y, Shimamura Y, Hirokado M, Yasuda K, and Nishijma M: Daily intake of isoflavones based on the market basket method. *J Food Hygenics Soc Jpn* **42,** 122–127, 2001.
105. Miltyk W, Craciunescu CN, Fischer L, Jeffcoat RA, Koch MA, et al.: Lack of significant genotoxicity of purified soy isoflavones (genistein, daidzein, and glycitein) in 20 patients with prostate cancer. *Am J Clin Nutr* **77,** 875–882, 2003.
106. Busby MG, Jeffcoat AR, Bloedon LT, Koch MA, Black T, et al.: Clinical characteristics and pharmacokinetics of purified soy isoflavones: single-dose administration to healthy men. *Am J Clin Nutr* **75,** 126–136, 2002.
107. Bloedon LT, Jeffcoat AR, Lopaczynski W, Schell MJ, Black TM, et al.: Safety and pharmacokinetics of purified soy isoflavones: single-dose administration to postmenopausal women. *Am J Clin Nutr* **76,** 1126–1137, 2002.
108. Fischer L, Mahoney C, Jeffcoat AR, Koch MA, Thomas BE, et al.: Clinical characteristics and pharmacokinetics of purified soy isoflavones: multiple-dose administration to men with prostate neoplasia. *Nutr Cancer* **48,** 160–170, 2004.
109. Lamartiniere CA, Zhao YX, and Fritz WA: Genistein: mammary cancer chemoprevention, in vivo mechanisms of action, potential for toxicity and bioavailability in rats. *J Womens Cancer* **2,** 11–19, 2000.
110. Wu AH, Wan P, Hankin J, Tseng CC, Yu MC, et al.: Adolescent and adult soy intake and risk of breast cancer in Asian-Americans. *Carcinogenesis* **23,** 1491–1496, 2002.
111. Shu XO, Jin F, Dai Q, Wen W, Potter JD, et al.: Soyfood intake during adolescence and subsequent risk of breast cancer among Chinese women. *Cancer Epidemiol Biomarkers Prev* **10,** 483–488, 2001.
112. Shimizu H, Ross RK, Bernstein L, Yatani R, Henderson BE, et al.: Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles County. *Br J Cancer* **63,** 963–966, 1991.
113. Hussain M, Banerjee M, Sarkar FH, Djuric Z, Pollak MN, et al.: Soy isoflavones in the treatment of prostate cancer. *Nutr Cancer* **47,** 111–117, 2003.
114. Dalais FS, Meliala A, Wattanapenpaiboon N, Frydenberg M, Suter DA, et al.: Effects of a diet rich in phytoestrogens on prostate-specific antigen and sex hormones in men diagnosed with prostate cancer. *Urology* **64,** 510–515, 2004.
115. Jarred RA, Keikha M, Dowling C, McPherson SJ, Clare AM, et al.: Induction of apoptosis in low to moderate-grade human prostate carcinoma by red clover-derived dietary isoflavones. *Cancer Epidemiol Biomarkers Prev* **11,** 1689–1696, 2002.
116. Yamamoto S, Sobue T, Kobayashi M, Sasaki S, and Tsugane S: Soy, isoflavones, and breast cancer risk in Japan. *JNCI* **95,** 906–913, 2003.
117. Lee S-K, Lee M-J, Yoon S, Kwon D-J: Estimated isoflavone intake from soy products in Korean middle-aged women. *J Korean Soc Food Sci Nutr* **29,** 948–956, 2000.

Copyright of Nutrition & Cancer is the property of Lawrence Erlbaum Associates and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.