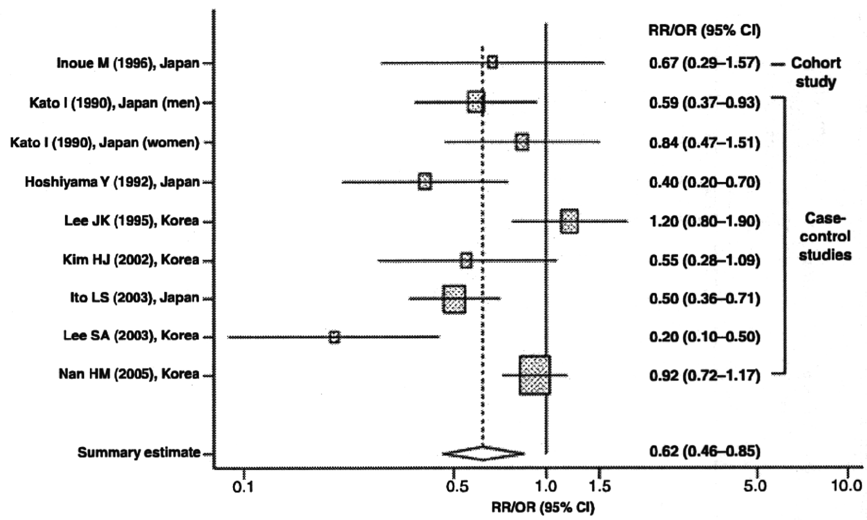

Fig. 1. Summary estimate of the relationships between fresh vegetable intake and gastric cancer risk in Japanese and Korean populations. CI, confidence interval; OR, odds ratio; RR, relative risk. Shaded box, point estimate of each study; horizontal line, 95% CI of each study; diamond, summary point estimate and its 95% CI of studies.

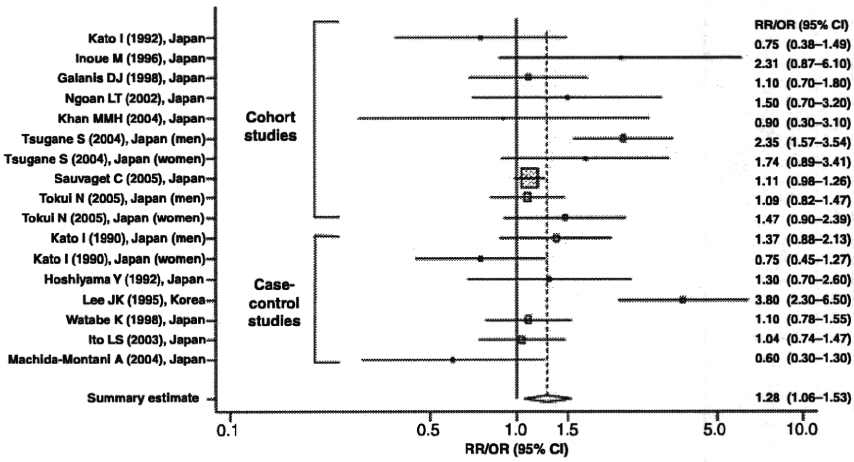

Fig. 2. Summary estimate of the relationships between pickled vegetable intake and gastric cancer risk in Japanese and Korean populations. CI, confidence interval; OR, odds ratio; RR, relative risk. Shaded box, point estimate of each study; horizontal line, 95% CI of each study; diamond, summary point estimate and its 95% CI of studies.

Discussion

The American Institute for Cancer Research reported that the summary relative risks of GC comparing high to low categories for total vegetable consumption were 0.50 (95% CI = 0.38–0.65) for 14 case–control studies and 0.80 (95% CI = 0.54–1.18) for 4 cohort studies through meta-analysis.[16] In a meta-analysis of 8 cohort studies, the summary relative risk of GC in high *versus* low categories for total vegetable intake was 0.88 (95% CI = 0.69–1.13).[24] Similarly, two large European cohort studies[25,26] reported that total vegetable intake was not associated with GC risk, regardless of the anatomic site. Although the protective effects of vegetable consumption on GC risk is widely accepted,[1–6] the results of the above meta-analyses indicate that the evidence from cohort studies does not support the protective effects of total vegetable intake on GC risk.[16,24–26]

Japanese and Korean populations have higher rates of GC incidence,[12] despite the fact that total vegetable consumption is higher in Japan and Korea,[7,8] than those in other countries with a lower intake of vegetables.[9,10] There is a possibility that a higher incidence of GC in Japan and Korea is partly due to the low consumption of fruits in these areas. However, the total consumption of vegetables and fruits is also higher in Korea (414.4 g/day)[7] and Japan (373.1 g/day)[8] than in the USA (358 g/day)[9] or northern Europe (278–288.5).[10] Moreover, Japanese and Korean people tend to consume more cooked, salted, or pickled vegetables than do people from North America or Europe.[7,10,60] Based on this observation, we inferred that the effects of vegetable consumption on GC risk may be different according to the preparation of the vegetables.

In the present meta-analysis, we observed significant inverse associations between a high intake of fresh vegetables and GC risk (overall summary OR = 0.62, 95% CI = 0.46–0.85). It has been suggested that the anticarcinogenic effect of vegetables is attributed in part to the effect of antioxidant vitamins, especially vitamin C and β-carotene, which inhibit the intragastric

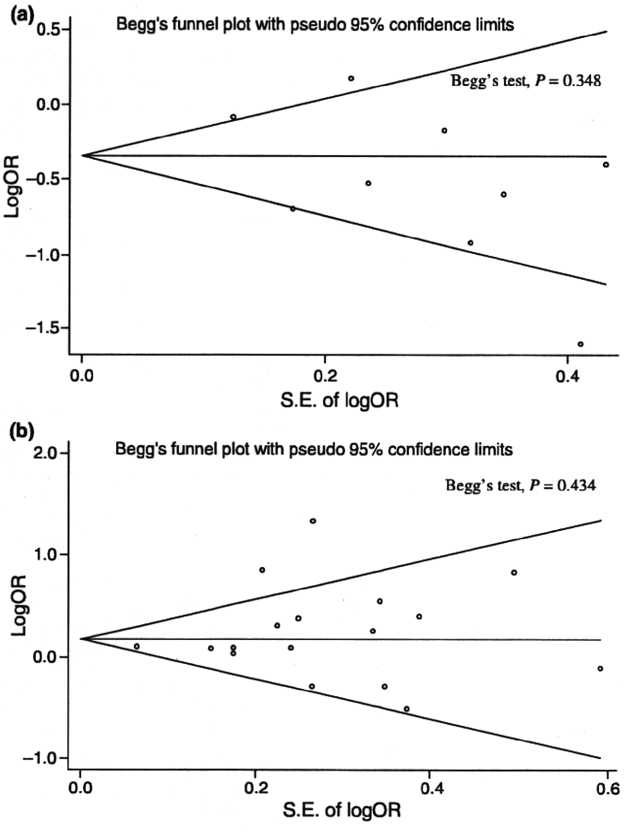

Fig. 3. Begg's funnel plot for publication bias in our overall meta-analysis of published epidemiological reports regarding fresh vegetable intake (a) and pickled vegetable intake (b) and gastric cancer risk. SE of logOR, standard error of log odds ratio.

formation of carcinogens such as *N*-nitroso compounds from secondary amines and nitrite. This inhibition might be caused by the reduction of nitrites into nitric oxide in the presence of reducing equivalents, such as vitamin C, or the combination of antioxidant vitamins with amines.[4,61,62] Another possible mechanism for the anticarcinogenic effects of antioxidants is the neutralization of reactive oxygen free radicals that can damage DNA.[63,64] Fresh vegetables contain a larger amount of antioxidant vitamins, such as vitamin C and β-carotene, than processed vegetables.[20,21,65] As well as antioxidant vitamins, vegetables contain various phytochemicals that act as antioxidants and scavenge free radicals, which could help to prevent cancer that occurs as a result of oxidative stress.[15]

We observed that a high intake of pickled vegetables was significantly associated with an increased risk of GC (overall summary OR = 1.28, 95% CI = 1.06–1.53). Examples of pickled vegetables include Japanese *tsukemono* and Korean *Jangajji*. Japanese *tsukemono* includes *takuan* (daikon), *umeboshi* (ume plum), ginger, turnip, cucumber, and Chinese cabbage.[18] Korean *Jangajji* is a pickled vegetable made by pickling or marinating garlic, daikon, cucumber, chili pepper leaves, and perilla leaves in soy sauce, chili pepper paste, soybean paste, or diluted vinegar.[66] Because they are preserved in brine (a solution of salt in water) or marinated and stored in an acid solution, pickled vegetables contain a substantial amount of salt. Salt is not a directly acting carcinogen, but consumption of salt and salt-preserved foods may cause atrophic gastritis by directly damaging the gastric mucosa, which could induce DNA synthesis and cell proliferation that contributes to stomach carcinogenesis[67] or enhance the penetration of carcinogens.[68] In addition, it has been reported that a high-salt diet enhances *H. pylori* colonization in the stomach.[69] *Helicobacter pylori* infection may increase the endogenous synthesis of nitrate in the stomach and decrease gastric vitamin C concentrations,[70] thereby increasing endogenous *N*-nitroso compound formation.[16] For these reasons, a high intake of salt and salt-preserved foods has been considered a probable cause of GC in many studies.[16,36,40,51,54,71,72] The loss of antioxidants in fresh vegetables as a consequence of processing and storage under acid and oxygen might partially explain the harmful effects of consumption of pickled vegetables on GC risk.[15,20,21] Another possible explanation is that pickled vegetables are a possible food source of nitroso compounds, thereby contributing to gastric carcinogenesis.[22,23]

There are several limitations concerning the interpretation of this meta-analysis. We selected a random-effect model to ameliorate the effect of large heterogeneity between studies in this meta-analysis, but this model has a typical limitation in that it does not strictly rule out the effects of heterogeneity; moreover, the relative weighting of the larger studies becomes reduced, whereas the weighting of the smaller studies is increased.[73] In this meta-analysis, the statistical significance of the results based on a fixed-effect model and random-effect model were not changed (OR = 0.71, 95% CI = 0.61–0.82 in fixed-effect model for fresh vegetables; OR = 1.19, 95% CI = 1.09–1.30 in fixed-effect model for pickled vegetables; data not shown). To explore the possible variables that explain the heterogeneity between studies, we carried out a meta-regression analysis that included nationality, study design, sex, and the year the study started. As a result, only nationality was observed as a source of heterogeneity between studies. Although we carried out a meta-analysis using adjusted RR/OR in order to consider several confounders, a residual confounding effect could remain because the variables included in the multivariate model were different from study to study.

In addition to the above limitations, various types of bias could occur in this meta-analysis. Publication bias is a typical one involved in finding published studies that may lead researchers to draw incorrect conclusions from their meta-analysis, because studies with statistically significant results are more likely to be published.[73] The results of Begg's test suggest that publication bias did not exist in this meta-analysis, but the possibility of publication bias, which is a characteristic inherent to meta-analyses, could still be present. In addition, because most studies were not designed to determine the effects of consumption of fresh or pickled vegetables on GC risk, there is a possibility that an outcome-reporting bias may have influenced the validity of our meta-analysis.[74] That is, non-significant associations between the consumption of fresh or pickled vegetables and GC risk may not have been presented in the results and, therefore, cannot be detected for meta-analysis. The application of strict inclusion criteria for the selection of studies also introduces inclusion criteria bias.[74] However, as the results with the same population can lead to overestimation due to duplication, we excluded these studies. We also excluded one case–control study using death cases,[57] which are more prone to various types of bias in the case–control design than incidence cases. However, even if we include this study of death cases in our meta-analysis, the significance of the overall summary estimate does not change (overall summary OR = 1.26, 95% CI = 1.05–1.50; data not shown). The interpretation and conclusions made from the results of this meta-analysis should be regarded cautiously due to the above limitations and bias.

In conclusion, the results of this meta-analysis provide evidence that high intake of pickled vegetables was associated with an increased GC risk, whereas high intake of fresh vegetables was associated with a decreased GC risk. These

doi: 10.1111/j.1349-7006.2009.01374.x

results may explain why the GC incidence rates in Japan and Korea remain high despite a high consumption of vegetables in these countries. A high consumption of fresh vegetables, rather than the total amount of vegetables, which includes pickled vegetables, should be promoted to reduce GC rates in Japan and Korea.

Acknowledgments

This study was supported by the National Cancer Center, Korea (0731060-1, 0710160-1, 0910221-1) and by a Grant for the Third Term Comprehensive Control Research for Cancer from the Ministry of Health, Labour and Welfare of Japan.

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doi: 10.1111/j.1349-7006.2009.01374.x

JJCO Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2010;40(Supplement 1)i76–i81
doi:10.1093/jjco/hyq131

Cancer Registry and Epidemiological Study Working Group Report

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International Agency for Research on Cancer: The International Agency for Research on Cancer serves as a global reference for cancer information. The Cancer Information Section of the International Agency for Research on Cancer publishes the world's largest information database on cancer incidence and supports cancer registries by providing administrative facilities and training, etc. Many Asian countries have published cancer registries, but Indonesia and Bangladesh have yet to do so.
International Association of Cancer Registries: The International Association of Cancer Registries is a non-governmental organization that promotes information exchange between cancer registries internationally. It supports cancer registries by means of fellowship funds and computer programs.
Cooperative Studies: Asian cooperative studies using cancer registration data are essential for combating cancer in the region. For a cooperative study, countries first need to exchange cancer data and then conduct a comparative study using non-individualized data. The third step is collection of individualized, anonymous data, which would improve comparability.
Collaborative Epidemiological Studies: The Asia Cohort Consortium, which includes investigators from various countries, is a complicated collaboration. Good epidemiological research collaboration requires researchers' comprehension of the significance of multinational collaborative studies, good coordination, adequate funding and balanced collaboration.
Conclusions: Asia faces various problems in relation to cancer registry, including inadequate quality, weak infrastructure, insufficient coverage, etc. Epidemiological studies are hampered by differences in expertise and resources, limited understanding of epidemiology, etc. To alleviate those problems, an organization for Asian cooperation on cancer registration should be established. Adequate funding of registries and activities is essential. Collaborative and comparative epidemiological studies based on data from cancer registries are needed.

Key words: cancer registries – epidemiological studies – collaboration – network

The Cancer Registry and Epidemiological Study Working Group comprised almost 50 members from 19 countries. Its discussions focused on the registry systems and collaborative work necessary for attacking the problem of cancer in the Asia-Pacific region.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

The International Agency for Research on Cancer (IARC)'s mission is cancer research for cancer prevention. It also serves as a global reference for cancer information, including geographical variations, incidence and trends over time. The IARC also provides education and training for low-resource countries. The Cancer Information Section (CIS) includes three groups: biostatistics, data analysis and descriptive epidemiological production. One of the core activities of the CIS is to issue the cancer incidence in five continents series, which is the world's largest database of information on cancer incidence and has been invaluable for conducting cancer research, establishing cancer control programs and determining healthcare policies around the world. The CIS also supports cancer registries by providing administrative facilities, conducting site visits, providing individual and group training, etc. In 2009, Asian Workshops were held in Vietnam and Bhutan.

Various Asian countries have published cancer registries over recent years. Data from 77 registries in 18 countries were submitted for inclusion in the IARC's *Cancer Incidence in Five Continents Vol. IX*, and 44 (55%) of those registries in 15 countries were accepted. (1) Sixty per cent of the world's population lives in Asia, and 6 of the 10 most-populated countries are in Asia, consisting of China, India, Indonesia, Pakistan, Bangladesh and Japan. Unfortunately, there has still been no cancer registry data from two of those Asian countries, Indonesia and Bangladesh (Table 1).

GLOBOCAN 2002 estimated 4.8 million cases of cancer and 3.4 million deaths in Asia, representing almost 45 and 50%, respectively, of the world's cases. (2) GLOBOCAN data are being updated, and the objective is to provide estimates of cancer incidence, mortality and prevalence for 28 major cancers. Estimated data for 2008 showed that the number of cancer cases in Asia had increased by ~10% since 2002, but deaths increased only slightly.

INTERNATIONAL ASSOCIATION OF CANCER REGISTRIES

The International Association of Cancer Registries (IACR) is a non-governmental organization that was founded in 1966 to foster the exchange of information between cancer registries internationally, aimed at improving the quality of data and comparability between registries. The number of member countries has been increasing, especially Asian nations. In 2009, members from 26 countries covered ~20% of the world's population. The IACR is affiliated with two scientific journals, the European Journal of Cancer Prevention and the Asian Pacific Journal of Cancer Prevention. The IACR standards have been presented in a number of publications, aimed at improving the quality of data and comparability between registries. The IACR provides support to cancer registries by means of fellowship funds (the Calum Muir Memorial Fellowship and the Constance Percy Memorial Fund) and also computer programs. Many Asian countries have cancer registries, but some do not, including North Korea, Cambodia and Laos. Meetings to set up an Asian Network of Cancer Registries were held in Korea in 2008 and Thailand in 2009. Then a survey was conducted regarding the establishment of an Asian Network of Cancer Registries, and 22 responses were obtained from 109 Asian registries (Fig. 1). Seven main objectives of networking were favored for the organization, including training for standardization of networking, planning and execution of collaborative research, evaluation of cancer control and treatment outcomes, meetings and discussions, etc. Regarding the name, half of the respondents preferred 'Asian Association of Cancer Registries', whereas the other half preferred 'Asian Network of Cancer Registries'.

Table 1. Cancer Registries in Asia

Eastern (6)	South-Eastern (11)	South-Central (14)	Western (18)
China: 43 + (A)	**Brunei**: N	Afghanistan	Armenia
Japan: 35 + (A)	Cambodia	**Bangladesh**	**Bahrain**: N
South Korea: 8 + N	**Indonesia** (H)	**Bhutan**: N	**Cyprus**: N
North Korea:	Lao	**India**: 10 (A)	**Israel**: N
Mongolia: N	**Malaysia**: 2 + N	**Iran**: 2	**Jordan**: N
Taiwan: N	Myanmar	Kazakhstan	**Kuwait**: N
	Philippines: 4	Kyrgyzstan	**Oman**: N
	Singapore: N	Nepal: 2	**Turkey**: 2
	Timore	**Pakistan**: 2	Others:
	Thailand: 19 + (A)	**Sri Lanka**	
	Vietnam: 6	Others	

Bold: Countries where registries are in operation.

DESIGNING COOPERATIVE STUDIES

A major element in the overall strategy for combating cancer in Asia-Pacific countries in the future is the effective design and execution of cooperative studies using cancer registration data and international comparisons with Asian countries. The rationale is that society, the mass media and health authorities pay more attention to cancer incidence and trend data when they are compared with other countries, rather than only within their own country. Moreover, the results contribute to improved cancer control planning in the participating countries.

Prior to a cooperative study, countries need to exchange data regarding cancer in each of their countries. In Japan, the incidence of hepatocellular carcinoma (HCC) has been decreasing because of reduced hepatitis C virus (HCV) infection rates due to improved hygiene and prevention of

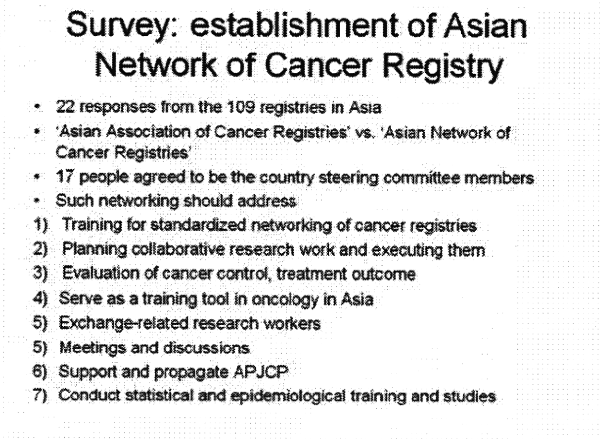

Figure 1. Survey: Establishment of Asian Network of Cancer Registry.

blood-borne infection (3). Information in this regard may be helpful to countries where HCV-related HCC is endemic, such as Mongolia, Myanmar and Taiwan.

Another example is lung cancer. Many Asian countries have high smoking rates in males. Male smoking rates in Japan have been decreasing, and the incidence of lung cancer has been decreasing since 1993, and also reduced incidence of squamous cell carcinoma because of a change from non-filter to filter cigarettes. The incidence rate of squamous cell carcinoma has been decreasing since 1994, whereas the incidence rate of adenocarcinoma increased until 1998, after which it plateaued. It took nearly 30 years for the decrease in non-filtered cigarettes to translate into a decrease in squamous cell carcinoma. Although it takes a long time, anti-smoking policies reduce the incidence of lung cancer. Evidence of this has been presented in Western countries, and it is important to advance such policies in Asia, as well, in order to reduce lung cancer.

A study group financially supported by a Grant-in-Aid for Comprehensive Cancer Control from Japanese Ministry of Health, Labor and Welfare conducted a collaborative study using a population-based cancer registry in East Asia (4). They have reported a 5-year relative survival rate of stomach cancer patients diagnosed between 1997 and 1999. The survival rates were higher in Japan, and even in Korea and Taiwan, than in Europe and the USA. The breast cancer 5-year survival rate was very high in Japan, Korea and Taiwan, and almost the same as in the EU and USA, whereas the survival rate of breast cancer was low in the Philippines, and hence improvement is needed there. The highest cervical cancer 5-year survival rate was seen in Korea, whereas several regions in Japan were not so high. Elucidation of the reasons for the lower rates in Japan is needed. Again, the Philippines had the lowest 5-year survival rate for cervical cancer, as well.

The next stage for cooperative studies is to collect individualized, anonymous data, which would make it possible to elucidate the factors that cause differences between populations, such as age, clinical stage at diagnosis, treatment procedures, etc. Individualized, anonymous data would also improve the comparability of survival data among the participating regions.

In conclusion, designing cooperative studies using cancer registry data involves a first stage in which information is exchanged among the participating countries to facilitate cancer control planning, a second stage consisting of a comparative study using non-individualized data and a third stage using individualized data (Fig. 2). Good human relationships among researchers are also very important, and the APCC represents a good platform for nurturing such good relationships.

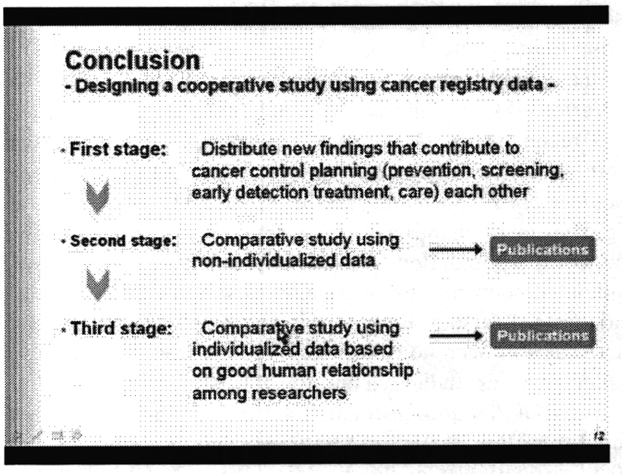

Figure 2. Designing a cooperative study using cancer registry data.

COLLABORATIVE EPIDEMIOLOGICAL STUDIES FOR CANCER PREVENTION

With regard to collaborative epidemiological studies to collect evidence concerning cancer risk and protective factors in the Asian region, recent trends show that the number of studies has been increasing, meta-analysis/pooled analysis of multiple studies has become very popular, and the importance of estimating the population-attributable fraction in each country/region/world has been recognized.

Collaboration between two countries is fairly simple, consisting of securing a research grant/funding, data collection by investigators and co-investigators in each country, and data analysis and manuscript preparation. The data center, data analysis and manuscript preparation are usually in the country of the principal investigator, while the grant is usually executed in the currency of the funding host.

In the case of collaboration between multiple countries, things get more complicated. The principal investigator is in one country, with a network including co-investigators collecting data in each of the participating countries, and the data analysis and manuscript preparation are performed at a data center, usually in the country of the principal investigator. However, the location of the data center and the manuscript writer are flexible.

An even more complicated example of collaboration is the Asia Cohort Consortium, which includes investigators from various countries and who change in accordance with the topic (Fig. 3). Interesting features are that the data center is outside Asia, in the USA, and the researchers include not only Asians but also Europeans and Americans, because they get funding, by topic, from their countries. Also, there is no firm funding base for network maintenance.

The funding agency in support of epidemiological research can be a domestic organization or an international organization. In the case of a domestic organization, the study is based in that country and is usually research topic-oriented. In the case of an international organization, the study base can be anywhere, and it is a potential research platform.

For good epidemiological research collaboration in Asian countries, the following points are important: each researcher must have an understanding of the significance of

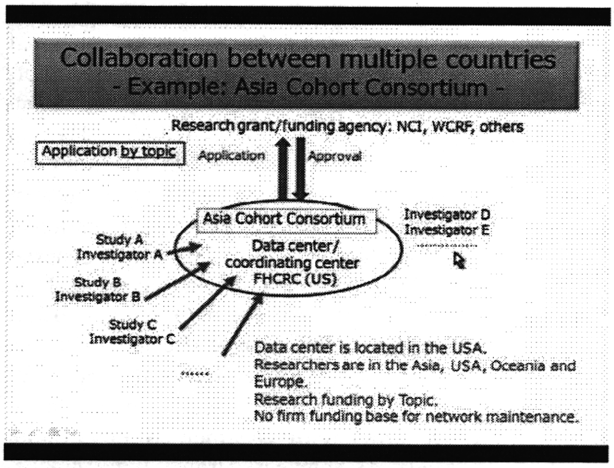

Figure 3. Collaboration between multiple countries: Example: Asia Cohort Consortium.

Problems

Cancer Registry

- Insufficient quality in most cancer registries
  - Quality Index, such as DCO%, MI ratio are MV% are low in Asian countries compared to North America and Europe
- Weak infrastructure
  - Nation wide mortality statistics are not available in some countries
  - Legislative basis is weak in some countries
  - Human and financial resources are insufficient
- Insufficient coverage
  - Some countries have no population based cancer registry at all.
- Difficulties in sustainability
  - Due to insufficient financial support, rapid turn over of trained personnel
- Few occasions of education and training
- Low response rates for the questionnaire surveys from IACR
  - The contact list of the registries is not maintained officially and adequately

Figure 4. Problems: Cancer Registry.

Problems

Epidemiological Study

- Wide variation in the expertise and resources of epidemiological research by country within Asia.
  - Within Asia, there exists wide variation in the availability of resources and expertise between countries, generally more available in Eastern Asia including Japan, Korea and China than the rest of Asia.
- Epidemiologic evidences from Asian population insufficient compared with Western regions
  - Although the number of epidemiological study has increased in Asia, it is still smaller than in Western region and insufficient to formulate public health policy specific to each country/Asian population.
- Limited understanding of epidemiological study
- Limited funding for epidemiological study

Figure 5. Problems: Epidemiological Study.

multinational collaborative studies; the leader must be a good coordinator; funding must be available for network maintenance and a multinational consortium; and the collaboration must be balanced and provide equal opportunity.

CONCLUSIONS

The problems that are faced in relation to cancer registry in Asia are various (Fig. 4). They include insufficient quality of most registries, weak infrastructure, inadequate coverage in some countries, difficulty in sustainability due to insufficient financial support and turnover of trained personnel, few opportunities for education and training, and low response rates to IACR questionnaire surveys. Similarly, problems in relation to epidemiological studies include wide variation in expertise and resources among Asian countries, and limited understanding of epidemiology in some nations, which constrains funding for epidemiological studies (Fig. 5). Other key problems are the lack of opportunity for contact between experts in Asia via collaborative activities and language barriers among Asian countries.

As solutions, from the perspective of researchers, the highest priority should be placed on information-sharing among researchers within the Asia-Pacific region. Newly developed and widely used techniques, such as those for record linkage, should be shared. In addition, there is a need to promote coordination meetings/workshops/symposia, provide training courses, establish international standards and promote collaborative studies, publication and a common database for pooled analysis, both for cancer registries and epidemiological studies. In order to do this, an organization for Asian cooperation on cancer registration should be established in the field of cancer registries. In addition, a common hub for collaborative research will be needed for epidemiological studies. More opportunities for collaborative research projects, activities and publications would improve the research skills and expertise in the region.

From the perspective of international organizations, such as the IARC and IACR, in a 2009 meeting the governing council of the IARC discussed how to provide greater support to cancer registries in developing countries. The IARC/IACR is planning to create a password-protected online system, so that questionnaires can be completed online and updated every year. The website would also allow registries to update their contact information. In October 2010, an Asian session will be held as a post-conference of the IACR annual meeting in Yokohama, Japan and Asian cooperation in cancer registration will be one of the main themes. To maintain a network of cancer registries, or an Asia Cohort Consortium, it will be necessary to maintain funding not only for topic-specific research proposals, but also for the research platform itself. To that end, funding should also be requested of other organizations.

In the future, the Asia-Pacific region must make full use of the platforms afforded by the WHO, IARC/IACR, UICC Headquarters, APFOCC and liaison societies in order to promote and achieve its goals of establishing cancer registries, accumulating cancer statistics, promoting and performing epidemiological studies and formulating regional and national cancer control programs.

With regard to concrete actions, from the perspective of researchers, there must be continued development of collaborative research projects and activities in subregions such as West Asia, Central Asia, Southeast Asia, East Asia and the Pacific. Publication of these activities should be encouraged to improve research skills and expertise in the study of Asia-Pacific populations. In that context, a steering committee for Asian cooperation for cancer registration will be assembled for the kick-off meeting in Yokohama 2010. At the same time, it will be proposed that the IARC supports the administrative work needed to maintain the network. Finally, collaborative and comparative epidemiological studies based on data from cancer registries should be promoted.

Funding

This working group meeting was financially supported by The Health and Labor Sciences Research Grant for Third Term Comprehensive Control Research for Cancer from Ministry of Health, Labor and Welfare, Japan, Grant-in-Aid for Cancer Research on Priority Areas from the Ministry of Education, Science, Sports Culture and Technology, Japan, 20th Asia Pacific Cancer Conference (President: Dr Hideyuki Akaza) and International Union Against Cancer (UICC) Asia Regional Office.

Conflict of interest statement

None declared.

Appendix

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Cancer Science
The official journal of the Japanese Cancer Association

Fermented and non-fermented soy food consumption and gastric cancer in Japanese and Korean populations: A meta-analysis of observational studies

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(Received July 12, 2010/Revised September 28, 2010/Accepted October 2, 2010/Accepted manuscript online October 8, 2010/Article first published online November 10, 2010)

Soy food is known to contribute greatly to a reduction in the risk of gastric cancer (GC). However, both Japanese and Korean populations have high incidence rates of GC despite the consumption of a wide variety of soy foods. One primary reason is that they consume fermented rather than non-fermented soy foods. In order to assess the varying effects of fermented and non-fermented soy intake on GC risk in these populations, we conducted a meta-analysis of published reports. Twenty studies assessing the effect of the consumption of fermented soy food on GC risk were included, and 17 studies assessing the effect of the consumption of non-fermented soy food on GC risk were included. We found that a high intake of fermented soy foods was significantly associated with an increased risk of GC (odds ratio [OR] = 1.22, 95% confidence interval [CI] = 1.02–1.44, I^2 = 71.48), whereas an increased intake of non-fermented soy foods was significantly associated with a decreased risk of GC (overall summary OR = 0.64, 95% CI = 0.54–0.77, I^2 = 64.27). These findings show that a high level of consumption of non-fermented soy foods, rather than fermented soy foods, is important in reducing GC risk. (*Cancer Sci* 2011; 102: 231–244)

Gastric cancer (GC) is the most common cancer in Japan and Korea and the second leading cause of death from cancer globally, although the incidence and mortality have been declining over the years.[(1)] Dietary factors are known to play an important role in the development of GC.[(2)] Among dietary factors, soy has been of considerable interest in the etiology of GC.[(3)] It is widely known that soy foods may help reduce the risk of developing GC. This might be due to the fact that soy foods are good sources of isoflavones, which are antioxidants known to reduce the risk of GC.[(3)] However, despite the fact that Japanese and Korean populations generally have a high intake of soy foods, they also have a higher risk of GC than other populations, including those in the USA and Europe.

This might be explained by the fact that Japanese and Korean populations consume more fermented soy foods than non-fermented ones. Common fermented soy foods, which generally contain a high content of salt, include soy paste and fermented soybeans.[(3)] The most common non-fermented soy foods include soymilk, tofu, soybeans and soy nuts. There is a contradictory relationship between the intake of soy food and GC; GC risk increases with the intake of fermented soy foods and decreases with the intake of non-fermented soy foods.[(4)] Fermented soy may offer health benefits due to the fermentation process. However, it may have adverse effects on GC risk due to high levels of nitrate or nitrite, large amounts of salt, and the loss of key nutrients under acidic and oxygenic conditions.

An extensive meta-analysis of the relationships between fermented soy foods and GC risk has not been conducted. Thus, we carried out a meta-analysis of the relationships between the consumption of fermented and non-fermented soy foods and GC risk in Japanese and Korean populations.

Materials and Methods

Selection of studies for the meta-analysis. We searched the reference lists of publications concerning diet and GC conducted in Japanese and Korean populations. The search engines used for this study included PubMed, KoreaMed and Ichushi. We used the following keywords: "gastric cancer" or "stomach cancer", "soy" or "fermented soy", and "Japan" or "Korea". We also searched the references cited in the articles and included published works written in Japanese, Korean and English.

Inclusion/exclusion criteria. The inclusion/exclusion criteria for this meta-analysis were as follows:

1 Only results that specified the food item studied was "fermented soy", "non-fermented soy" or were included. The term "fermented soy" included miso (soup) or soybean paste (soup or stew), while "non-fermented soy" included tofu, bean curds or non-fermented soy (bean) products.
2 Only subjects who were Japanese or Korean, including migrants, were included.
3 Cohort or case–control studies were included. Reviews and meta-analyses were excluded.
4 We excluded case–control studies that presented mortality rather than GC incidence.
5 The studies that included adjusted 95% confidence intervals (CI) and either a relative risk (RR) or odds ratio (OR) were included for meta-analysis. We excluded studies that did not present an adjusted 95% CI or those that showed regression coefficients.
6 When multiple studies were published on the same subject population, we included only the most recent study.

Data abstraction. Two reviewers independently examined the studies for inclusion in the meta-analysis.

Disagreements between the reviewers were resolved by consensus. We collected the following information from each study: study design, author, publication year, nation, study period, study subjects (type and sources, definition and numbers of subjects), category of food intake from the lowest to the highest, RR/OR and 95% CI, *P* for trend, and confounding variables.

Statistical analysis. In order to adjust for the confounding factors and to include those studies with missing values

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doi: 10.1111/j.1349-7006.2010.01770.x

Table 1. Intake of fermented soy products and gastric cancer risk in Korean or Japanese populations

Author, year, nation	Study period	Study subjects: Source of subjects	No. subjects	Primary outcome studied	No. incidence or deaths of GC	Category	RR (95% CI)	*P* for trend	Confounding variables considered
Cohort studies									
Kato I *et al.* 1992, Japan[5]	1985–1991	Population-based, Aichi Prefecture	9753	Death	57 (35 men, 22 women)	Miso soup		0.845	Adjusted for age and sex
						<1 cup/day	1.00		
						1 cup/day	0.88 (0.42–1.82)		
						≥2 cups/day	1.04 (0.48–2.25)		
Inoue M *et al.* 1996, Japan[6]	1985–1995	Subjects who underwent gastroscopic examination, Aichi Prefecture	5373 (2552 men, 2821 women)	Incidence	69 (51 men, 18 women)	Soybean paste soup		NA	Adjusted for age and sex
						Rarely	1.00		
						Occasionally	4.68 (0.88–24.99)		
						Daily	3.62 (0.79–16.70)†		
Galanis DJ *et al.* 1998, Japan[7]	1975–1994	Population-based, Japanese–American residents of Hawaii	11 907 (5610 men, 6297 women)	Incidence	108 (64 men, 44 women)	Miso soup		NA	Adjusted for age, years of education, Japanese place of birth and gender
						None	1.0		
						1 or more times/week	1.2 (0.8–1.8)		
Ngoan LT *et al.* 2002, Japan[2]	1986–1989	Population-based, Fukuoka Prefecture	13 250 (5917 men, 7333 women)	Death	116 (77 men, 39 women)	Miso soup		≥0.05	Adjusted for age, sex, smoking, processed meat, liver, cooking or salad oil, and suimono
						2–4 times/week	1.00		
						Once/day	0.9 (0.5–1.8)		
						Twice/day or more	1.7 (0.6–4.5)		
Tsugane S *et al.* 2004, Japan[8]	1990–2001	JPHC Cohort, Iwate, Akita, Nagano, Okinawa Prefectures	18 684 men	Incidence	358 men	Miso soup		0.002	Adjusted for age, smoking, fruit intake and non-green vegetable intake
						Not daily	1.00		
						1 cup/day	1.76 (1.16–2.67)		
						2 cups/day	1.99 (1.39–2.87)		
						3 or more cups/day	1.75 (1.22–2.51)		
			20 381 women	Incidence	128 women	Miso soup		0.65	
						Not daily	1.00		
						1 cup/day	1.15 (0.66–2.01)		
						2 cups/day	0.82 (0.49–1.38)		
						3 or more cups/day	1.11 (0.67–1.84)		
Sauvaget C *et al.* 2005, Japan[9]	1980–1999	Participants in LSS cohort, Hiroshima and Nagasaki Prefectures	38 576 (14 885 men, 23 691 women)	Incidence	1270 (719 men, 551 women)	Miso soup		>0.05	Adjusted for age, sex, city, radiation dose, sex-specific smoking habit and education
						<2 times/week	1.00		
						2–4 times/week	1.01 (0.88–1.16)		
						5 times or more/week	1.01 (0.88–1.16)		

doi: 10.1111/j.1349-7006.2010.01770.x

Table 1. (continued)

Author, year, nation	Study period	Study subjects: Source of subjects	No. subjects	Primary outcome studied	No. incidence or deaths of GC	Category	RR (95% CI)	*P* for trend	Confounding variables considered
Tokui N *et al.* 2005, Japan(10)	1988–1999	Participants in JACC study (45 areas)	110 792	Death	574 men	Miso soup			Adjusted for age
						None	1.00	0.36	
						Several times/ month	1.42 (0.79–2.56)		
						Several times/ week	1.50 (0.85–2.65)		
						Every day	1.44 (0.86–2.42)		
				Death	285 women	Miso soup			
						None	1.00	0.19	
						Several times/ month	1.38 (0.69–2.74)		
						Several times/ week	1.18 (0.60–2.31)		
						Every day	1.46 (0.81–2.61)		
Nagata C *et al.* 2002, Japan(11)	1992–1999	Community-based, Takayama	13 880 men	Death	81 men	Fermented soy products		0.76	Adjusted for age, total energy, smoking and BMI at age approximately 21 years
						Low	1.00		
						Middle	1.17 (0.69–2.01)		
						High	0.91 (0.53–1.58)		
			16 424 women	Death	40 women	Fermented soy products		0.1	Adjusted for age, total energy, marital status, age at menarche, BMI at age approximately 21 years
						Low	1.00		
						Middle	0.78 (0.38–1.61)		
						High	0.52 (0.24–1.13)		
Khan MMH *et al.* 2004, Japan(12)		Population-based, Hokkaido	1524 men	Death	36 men	Miso soup		<0.05	Adjusted for age and smoking
						≤Several times/ month	1.0		
						≥Several times/ week	0.2 (0.1–0.8)		

Table 1. (continued)

Author, year, nation	Study period	Study subjects: Source of subjects	No. subjects	Primary outcome studied	No. incidence or deaths of GC	Category	RR (95% CI)	P for trend	Confounding variables considered
Case–control studies									
Kono S *et al.* 1988, Japan[13]	1979–1982	Hospital-based, Karatsu Stomach Institute	Cases: newly diagnosed as having gastric cancer at the institute General population controls: random sampling from the computerized file of residents		General population controls: 148 men, 130 women	Miso soup		≥0.05	Matched for sex, year of birth
						None or 1–3 times/month	1.00		
						1–3 times/week	0.49 (0.19–1.29)		
						≥1 time/day	0.52 (0.22–1.26)		
			Hospital controls: patients without gastric cancer		Hospital control: 1171 men, 1474 women	Miso soup		≥0.05	
						None or 1–3 times/month	1.00		
						1–3 times/week	0.62 (0.30–1.33)		
						≥1 time/day	0.71 (0.39–1.42)		
Kato I *et al.* 1990, Japan[14]	1985–1989	Hospital-based Aichi Cancer Center Hospital	Cases: histologically confirmed cases who received gastroscopic examination		1247 men	Soybean paste soup		NA	Adjusted for age, residence
						<1–2/month	1.00		
						2–3 times/week	0.91 (0.50–1.65)		
						Daily	1.04 (0.60–1.81)		
			Controls: patients with normal gastric mucosa		1767 women	Soybean paste soup		NA	
						<1–2/month	1.00		
						2–3 times/week	0.79 (0.40–1.54)		
						Daily	0.83 (0.44–1.58)		
Hoshiyama Y *et al.* 1992, Japan[15]	1984–1990	Hospital-based, Saitama Cancer Center Hospital	Cases: newly histologically confirmed cases who received gastroscopic examination in the institute. Population controls: residents in the study area		206 men, 88 women	Miso soup		<0.01	Matched for sex, age, administrative division Adjusted for sex, age, administrative division, smoking status
						<1 cup/day	1.00		
						1 cup/day	1.4 (0.8–2.5)		
						≥2 cups/day	2.0 (1.2–3.5)		
			Hospital controls: inpatients without cancer		104 men, 98 women	Miso soup		0.08	Adjusted for sex, age (three categories), area (three categories), smoking status
						<1 cup/day	1.0		
						1 cup/day	1.5 (0.8–2.9)		
						≥2 cups/day	1.8 (1.0–3.4)		

doi: 10.1111/j.1349-7006.2010.01770.x

Table 1. (continued)

Author, year, nation	Study period	Study subjects: Source of subjects	Study subjects: No. subjects	Study subjects: Primary outcome studied	Study subjects: No. incidence or deaths of GC	Category	RR (95% CI)	P for trend	Confounding variables considered
Hoshiyama Y. and Sasaba T 1992, Japan[16]	1984–1990	Hospital-based, Saitama Cancer Center Hospital	Cases: single and multiple gastric cancer cases, newly diagnosed and of adenocarcinoma type in the institute Population controls: residents in the study area		483 men	Miso soup ≤1 cup/day 2 cups/day ≥3 cups/day Miso soup ≤1 cup/day 2 cups/day ≥3 cups/day	 1.0 1.3 (0.9–1.9) 2.3 (1.5–3.7) 1.0 1.6 (0.7–3.5) 3.4 (1.4–8.3)	0.00 0.01	Matched for age, sex. Adjusted for age, smoking status Adjusted for age, smoking status
Iwasaki J et al. 1992, Japan[17]	1980–1986	Population-based, mountain villages in the Shizuoka Prefecture and farming-fishing villages in the Chiba Prefecture	Cases: gastric cancer death Controls: general population control		83 men	Miso soup Not frequently Frequently	 1.000 1.235 (0.594–2.590)	NA	Matched for sex, age (±2 years), district and year of death (±6 years)
Inoue M et al. 1994, Japan (18)	1988–1991	Hospital-based, Aichi Cancer Center Hospital	Cases: histologically confirmed incident case Controls: outpatients of the same hospital		420 men, 248 women	Miso soup 3–4 times or more/week *vs* less	 0.95 (0.75–1.20)	<0.05	Matched for sex, age (±2 years), time of first hospital visit (±2 months) Adjusted for sex
Watabe K et al. 1998, Japan[19]	1996–1997	Hospital-based, Sapporo Medical University	Cases: histologically confirmed Control: randomly selected from the telephone book		242 cases and 484 controls	Miso soup ≥3/day	 2.14 (1.43–3.15)	NA	Matched for sex, age (±3 years), registered residence
Ito LS et al. 2003, Japan[20]	1988–1998	Hospital-based, Aichi Cancer Center Hospital	Cases: histologically confirmed cases Controls: cancer-free first visit outpatients at the center		36 490 women	Soybean paste soup Almost never Occasionally 3–4 times/week Every day	 1.00 0.62 (0.42–0.92) 0.69 (0.47–1.01) 0.74 (0.47–1.14)	NS	Adjusted for age, year and season of first hospital visit, smoking habit, family history of gastric cancer

Table 1. (continued)

Author, year, nation	Study period	Study subjects: Source of subjects	Study subjects: No. subjects	Study subjects: Primary outcome studied	Study subjects: No. incidence or deaths of GC	Category	RR (95% CI)	*P* for trend	Confounding variables considered.
Machida-Montani A 2004, Japan[21]	1998–2002	Hospital-based, four hospitals in Nagano prefecture	Cases: non-cardia gastric cancer. Control: participants of a health check-up program at the same hospitals		235	Miso soup <3 cups/day 3 cups/day ≥4 cups/day	 1.0 1.8 (1.0–3.3) 2.1 (0.9–5.1)	0.04	Matched by age (within 3 years), sex, residential area Adjusted for *H. pylori* infection, smoking status, JA membership, family history of gastric cancer, total vegetable intake, total fruits intake, salt intake and total energy intake
Lee JK *et al.* 1995, Korea[22]	1990–1991	Hospital-based, Hanyang University Hospital, Asan Medical Center, Seoul	Cases: histologically confirmed gastric cancer. Hospital controls: orthopedic, urological, ophthalmological, gynecological wards, ambulatory patients		132 men, 81 women	Soybean paste stew 1–3/months ≥2–3/week	 1.0 5.5 (2.5–12.1)	<0.001	Matched by age (within 2 years), sex. Adjusted for age, sex, education, economic status and residence
Park HS *et al.* 1998, Korea[23]	1996	Hospital-based, Korea Cancer Center Hospital, Seoul	Cases: histologically confirmed gastric cancer. Hospital controls: patients without gastric cancer		87 men, 39 women	Soybean paste ≤1/week ≥2/week	 1.0 0.8 (0.5–1.2)	NS	Matched by age (within 5 years), sex, admission date. Adjusted for age, sex, education, economic status, residence
Zhang YW *et al.* 2009, Korea[24]	2000–2005	Hospital-based, Chungbuk National University Hospital, Eulji University Hospital	Cases: histologically confirmed gastric cancer. Hospital controls: patients without gastric cancer		315 men, 156 women	Soybean paste Low High	 1.0 1.63 (1.24–2.14)	<0.05	Matched by age (within 3 years), sex. Adjusted for age, sex and energy intake
Kim HJ *et al.* 2002, Korea[25]	1997–1998	Hospital-based, Hanyang and Hallim University Hospital	Cases: histologically confirmed gastric cancer. Hospital controls: patients without gastric cancer		93 men, 43 women	Soybean paste Low Medium High	 1.00 0.86 (0.48–1.55) 0.84 (0.43–1.63)	NA	Matched by age (within 2 years), sex, during same period in the same hospital. Adjusted for sex, age, socioeconomic status, family history, refrigerator use

†Compared with subjects without atrophic gastritis. §LSS (Life Span Study cohort) includes atomic bomb survivors and unexposed subjects in Hiroshima and Nagasaki. ¶Compared with the general population control. BMI, body mass index; CI, confidence interval; GC, gastric cancer; JACC, The Japan Collaborative Cohort Study for Evaluation of Cancer Risk; JPHC cohort, The Japan Public Health Center-based prospective study; NA, not available; NS, not significant; RR, relative risk.

doi: 10.1111/j.1349-7006.2010.01770.x

Table 2. Intake of non-fermented soy products and gastric cancer risk in Korean or Japanese populations

Author, year, nation	Study period	Study subjects: Source of subjects	Study subjects: No. subjects	Study subjects: Primary outcome studied	Study subjects: No. incidence or deaths of GC	Category	OR (95% CI)	*P* for trend	Confounding variables considered
Cohort studies									
Ngoan LT et al. 2002, Japan[2]	1986–1989	Population-based Fukuoka Prefecture	13 250 (5917 men, 7333 women)	Death	116 (77 men, 37 women)	Tofu		≥0.05	Adjusted for age, sex, smoking, processed meat, liver, cooking or salad oil, and suimono
						≤2–4 times/month	1.0		
						2–4 times/week	0.6 (0.3–1.1)		
						Once/day or more	0.4 (0.2–0.9)		
Sauvaget C et al. 2005, Japan[9]	1980–1999	Participants in LSS cohort§, Hiroshima and Nagasaki Prefectures	38 576 (14 885 men, 23 691 women)	Incidence	1270 (719 men, 551 women)	Tofu		0.492	Adjusted for age, sex, city, radiation dose, sex-specific smoking habit and education
						<2 times/week	1.00		
						2–4 times/week	0.94 (0.83–1.06)		
						5 times or more/week	1.01 (0.85–1.20)		
Tokui N et al. 2005, Japan[10]	1988–1999	Participants in JACC study (45 areas)	110 792	Death	574 men	Bean curds		0.97	Adjusted for age
						1–2/month or less	1.0		
						1–2/week	1.12 (0.76–1.65)		
						3–4/week	1.09 (0.74–1.60)		
						1+/day	1.07 (0.73–1.58)		
				Death	285 women	Bean curds		0.25	
						1–2/month or less	1.00		
						1–2/week	1.24 (0.65–2.36)		
						3–4/week	1.38 (0.74–2.59)		
						1+/day	1.41 (0.75–2.64)		
Nagata C et al. 2002, Japan[11]	1992–1999	Community-based, Takayama study	13 880 men	Death	81 men	Non-fermented soy products		0.0006	Adjusted for age, total energy, smoking and BMI at age approximately 21 years
						Low	1.00		
						Middle	0.73 (0.44–1.23)		
						High	0.46 (0.26–0.81)		
			16 424 women	Death	40 women	Non-fermented soy products		0.09	Adjusted for age, total energy, marital status, age at menarche, BMI at age approximately 21 years
						Low	1.00		
						Middle	0.97 (0.48–1.96)		
						High	0.48 (0.21–1.10)		
Kurosawa M et al. 2006, Japan[26]	1989–1999	Population-based, three municipalities of Higashi-Yamanashi Country	8035 (3652 men, 4383 women)	Death	76 (54 men, 22 women)	Bean and bean products		0.66	Multivariate, adjusted by backward elimination method
						Low (2–7/week)	1.00		
						Intermediate (8/week)	1.79 (0.81–3.96)		
						High (9–10/week)	0.88 (0.31–2.56)		

Table 2. (continued)

Author, year, nation	Study period	Study subjects: Source of subjects	No. subjects	Primary outcome studied	No. incidence or deaths of GC	Category	OR (95% CI)	*P* for trend	Confounding variables considered
Khan MMH *et al.* 2004, Japan[12]		Population-based, Hokkaido	1524 men	Death	36 men	Tofu		>0.05	Adjusted for age and smoking
						≤Several times/month	1.0		
						≥Several times/week	3.6 (0.5–26.0)		
			1634 women	Death	15 women	Tofu		>0.05	Adjusted for age, health status, health education, health screening and smoking
						≤Several times/month	1.0		
						≥Several times/week	1.1 (0.1–8.5)		
Case–control studies									
Hoshiyama Y *et al.* 1992, Japan[15]	1984–1990	Hospital-based, Saitama Cancer Center Hospital	Cases: newly histologically confirmed cases who received gastroscopic examination in the institute. Population controls: residents in the study area		206 men, 88 women	Soybean products (except miso soup)		<0.01	Matched for sex, age, administrative division. Adjusted for sex, age, administrative division, smoking status
						≤4/week	1.0		
						5–7/week	0.5 (0.4–0.8)		
						≥8/week	0.6 (0.4–1.0)		
			Hospital controls: inpatients without cancer		104 men, 98 women	Soybean products (except miso soup)		0.36	Adjusted for sex, age (three categories), area (three categories), smoking status
						≤4/week	1.0		
						5–7/week	0.9 (0.6–1.3)		
						≥8/week	0.8 (0.4–1.4)		
Hoshiyama Y. and Sasaba T 1992, Japan[16]	1984–1990	Hospital-based, Saitama Cancer Center hospital	Cases: single and multiple gastric cancer cases newly diagnosed and of adenocarcinoma type in the institute. Population controls: residents in the study area		483 men	Soybean products (except miso soup)		0.00	Match for age, sex. Adjusted for age, smoking status
						≤4/week	1.0		
						5–7/week	0.6 (0.4–0.8)		
						≥8/week	0.6 (0.3–0.9)		
						Soybean products (except miso soup)		0.28	Adjusted for age, smoking status
						≤4/week	1.0		
						5–7/week	0.8 (0.4–1.7)		
						≥8/week	0.5 (0.2–1.7)		
Inoue M *et al.* 1994, Japan[18]	1988–1991	Hospital-based, Aichi Cancer Center Hospital	Cases: histologically confirmed incident case. Controls: outpatients of the same hospital		420 men, 248 women	Bean curds		NA	Matched for sex, age (±2 years), time of first hospital visit (±2 months). Adjusted for sex
						3–4 times or more/week *vs* less	0.89 (0.71–1.11)		
Watabe K *et al.* 1998, Japan[19]	1996–1997	Hospital-based, Sapporo Medical University	Cases: histologically confirmed. Controls: randomly selected from the telephone book		242 cases and 484 controls	Tofu		NA	Matched for sex, age (±3 years), registered residence
						≥1/week	0.69 (0.45–1.07)		

doi: 10.1111/j.1349-7006.2010.01770.x

Table 2. (continued)

Author, year, nation	Study period	Study subjects: Source of subjects	Study subjects: No. subjects	Study subjects: Primary outcome studied	Study subjects: No. incidence or deaths of GC	Category	OR (95% CI)	*P* for trend	Confounding variables considered
Ito LS *et al.* 2003, Japan[20]	1988–1998	Hospital-based, Aichi Cancer Center Hospital	Cases: histologically confirmed cases Controls: cancer-free first visit outpatients at the center		36 490 women	Tofu <1 times/week 1–2 times/week 3–4 times/week ≥5 times/week	 1.00 0.84 (0.63–1.11) 0.81 (0.61–1.09) 0.86 (0.63–1.17)	NS	Adjusted for age, year and season of first hospital visit, smoking habit, family history of gastric cancer
Hamada GS *et al.* 2002, Japan[27]	1991–1994	Hospital-based, Japanese–Brazilians, Sao Paulo	Cases: histologically confirmed cases Controls: preferably identified from among the inpatients of the same hospital		120 men, 72 women	Soybean products <1 day/week 1–2 day/week 3–4 day/week Daily	 1.0 0.6 (0.3–1.2) 0.7 (0.3–1.5) 0.4 (0.1–1.1)	0.33	Adjusted for country of birth
Lee SA *et al.* 2002, Korea[28]	2000	Hospital-based, Asan Medical Center, Seoul	Cases: newly diagnosed as having gastric cancer at the institute Hospital controls: patients without gastric cancer		116 men, 83 women	Soybean curds <1/month ≥1/month	 1.0 0.3 (0.1–0.5)	<0.001	Adjusted for age, sex, and *H. pylori* infection
Lee JK *et al.* 1995, Korea[22]	1990–1991	Hospital-based, Hanyang University Hospital, Asan Medical Center, Seoul	Cases: histologically confirmed gastric cancer Hospital controls: orthopedic, urological, ophthalmological, gynecological wards, ambulatory patients		132 men, 81 women	Soybean curds None or 4–5/year 1–3/months ≥2–3/week	 1.0 0.5 (0.1–1.5) 0.2 (0.1–0.8)	<0.01	Matched by age (within 2 years), sex. Adjusted for age, sex, education, economic status and residence
Park HS *et al.* 1998, Korea[23]	1996	Hospital-based, Korea Cancer Center Hospital, Seoul	Cases: histologically confirmed gastric cancer Hospital controls: patients without gastric cancer		87 men, 39 women	Soybean curds ≤2–3/month 1–2/week ≥3/week	 1.0 0.7 (0.4–1.2) 0.3 (0.2–0.7)	<0.05	Matched by age (within 5 years), sex, admission date Adjusted for age, sex, education, economic status, residence
Zhang YW *et al.* 2009, Korea[24]	2000–2005	Hospital-based, Chungbuk National University Hospital, Eulji University Hospital	Cases: histologically confirmed gastric cancer Hospital controls: patients without gastric cancer		315 men, 156 women	Non-fermented soybean foods Low High	 1.0 0.57 (0.43–0.75)	<0.05	Matched by age (within 3 years), sex. Adjusted for age, sex, and energy intake

Table 2. (continued)

Author, year, nation	Study period	Study subjects: Source of subjects	Study subjects: No. subjects	Study subjects: Primary outcome studied	Study subjects: No. incidence or deaths of GC	Category	OR (95% CI)	P for trend	Confounding variables considered
Kim HJ *et al.* 2002, Korea[25]	1997–1998	Hospital-based, Hanyang and Hallim University Hospital	Cases: histologically confirmed gastric cancer. Hospital controls: patients without gastric cancer		93 men, 43 women	Soybean products Low Medium High	 1.00 0.81 (0.46–1.42) 0.35 (0.16–0.75)	NA	Matched by age (within 2 years), sex, during same period in the same hospital Adjusted for sex, age, socioeconomic status, family history, refrigerator use
Ko KP *et al.* 2009, Korea[29]	1993–2004	Community-based, Korean multi-center cancer cohort	Cases: Linkages to the Korean cancer registry and National death certificate databases Community control		236 men, 100 women	Soybean ≥3–4 times/week <3–4 times/ month	 1.00 0.54 (0.26–1.12)	NA	Matched by age (within 5 years), sex, residence area, year of recruitment; 1 case : 4 control

†Compared with subjects without atrophic gastritis. §LSS (Life Span Study cohort) includes atomic bomb survivors and unexposed subjects in Hiroshima and Nagasaki. ¶Compared with the general population control.BMI, body mass index; CI, confidence interval; GC, gastric cancer; JACC, The Japan Collaborative Cohort Study for Evaluation of Cancer Risk; NA, not available; NS, not significant; OR, odds ratio.

(cross-tabulation) in the tables, we used an unconditional logistic regression analysis to compute the RR or OR with a 95% CI. We assessed statistical heterogeneity across the studies by calculating the variation between studies (τ^2) from the Q statistic. Based on these results for heterogeneity, we used either a fixed-effect or random-effect model to compute the summary OR and 95% CI. For assessing publication bias, asymmetry was tested using Begg's funnel plot. A P-value <0.05 was considered statistically significant. We carried out all analyses using STATA 10 software (STATA, College Station, TX, USA).

Results

We identified a total of 69 articles in the initial computerized search of published work. After screening the articles according to title and abstract, 43 articles (two review papers, one meta-analysis, 27 experimental studies or clinical trials, two studies of populations from countries other than Japan or Korea, four studies with the same subject population, and seven studies on other foods, soy foods or non-dietary factors) were excluded. Twenty-two articles (nine cohort studies[2,5–12] and 13 case–control studies[13–25]) assessing the effect of consumption of fermented soy foods on GC risk were included in the meta-analysis. Eighteen articles (six cohort studies[2,9–11,26] and 12 case–control studies[15,16,18–20,22–25,27–29]) assessing the effect of consumption of non-fermented soy food on GC risk were included in the meta-analysis.

Table 1 lists the included cohort and case–control studies on the effect of fermented soy products on GC risk. Similarly, Table 2 lists the included cohort and case–control studies on the effect of non-fermented soy products on GC risk. Most studies adjusted for confounding factors, including age and sex. We obtained statistically significant results when testing for heterogeneity between studies of fermented soy foods (overall summary $Q = 98.18$ with 28 degrees of freedom (df), $P < 0.001$; cohort studies $Q = 27.36$ with 11 df, $P = 0.004$; case-control studies $Q = 66.51$ with 16 df, $P < 0.001$) and non-fermented soy foods (overall summary $Q = 61.58$ with 22 df, $P < 0.001$; cohort studies $Q = 18.07$ with eight df, $P = 0.021$; case-control studies $Q = 30.08$ with 13 df, $P = 0.005$). Therefore, we selected a random-effect model to produce the summary statistics. The results of the meta-analysis of the relationships between GC risk and non-fermented soy food intake and fermented soy food intake are summarized in Figures 1 and 2, respectively. A high intake of non-fermented soy foods was significantly associated with a decreased risk of GC (overall summary OR = 0.64, 95% CI = 0.54–0.77, $I^2 = 64.27$; cohort studies OR = 0.83, 95% CI = 0.60–1.13, $I^2 = 55.73$; case–control studies OR = 0.57, 95% CI = 0.46–0.71, $I^2 = 56.78$), whereas a high intake of fermented soy foods was significantly associated with an increased risk of GC (overall summary OR = 1.22, 95% CI = 1.02–1.44, $I^2 = 71.48$; cohort studies OR = 1.12, 95% CI = 0.88–1.41, $I^2 = 59.79$; case–control studies OR = 1.34, 95% CI = 1.04–1.73, $I^2 = 75.94$). In order to assess for publication bias, Begg's funnel plot[30,31] for the assessment of publication bias is presented in Figure 3 for fermented soy food and in Figure 4 for non-fermented soy food. The funnel plots did not detect a publication bias in the meta-analyses of the effect of fermented ($Z = 0.11$, $P = 0.910$) or non-fermented soy foods ($Z = 0.95$, $P = 0.342$) on GC risk.

Discussion

Soy food has been a major plant source of dietary protein for Asians, especially Japanese and Koreans, and many epidemiological studies suggest that soy intake may be a strong protective

doi: 10.1111/j.1349-7006.2010.01770.x