Garlic intake and cancer risk: an analysis using the Food and Drug Administration’s evidence-based review system for the scientific evaluation of health claims\textsuperscript{1,2}

Ji Yeon Kim and Oran Kwon

ABSTRACT
Background: Numerous animal and in vitro studies provided evidence for a relation between garlic intake and cancer risk reduction. Several studies also reported an inverse association in humans. However, no claims have been made about garlic intake and cancer risk reduction with respect to food labeling.

Objective: The objective of this study was to evaluate the scientific evidence for garlic intake with respect to the risk of different types of cancer using the US Food and Drug Administration’s evidence-based review system for the scientific evaluation of health claims.

Design: Literature searches were conducted by using the Medline and EMBASE databases for the period 1955–2007 with search terms \textit{Allium sativum}, vegetables, diet, and nutrition in combination with cancer, neoplasm, and individual cancers. The search was limited to human studies published in English and Korean.

Results: With the use of the US Food and Drug Administration’s evidence-based review system for the scientific evaluation of health claims, 19 human studies were identified and reviewed to evaluate the strength of the evidence that supports a relation between garlic intake and reduced risk of different cancers with respect to food labeling.

Conclusions: There was no credible evidence to support a relation between garlic intake and reduced risk of different cancers with respect to food labeling.

INTRODUCTION
Food labels are widely used to convey the health benefits of conventional foods or a component of food (eg, nutrient) to the consumer. The increasing amount of health information available regarding the health benefits of foods has resulted in consumer interest in health issues and has become a leading factor in purchasing decisions. Therefore, labeling and advertising should not be misleading. The requirement to protect consumers and ensure their right to obtain accurate information on food functionality has led to the introduction of regulations about health claims worldwide. In the United States, health claims were first authorized by the US Food and Drug Administration (FDA) after enactment of the Nutrition Labeling and Education Act of 1990 (1). Health claims are made on the label or in the labeling of foods, including dietary supplements, that expressly or by implication (including “third party” references, written statements, symbols, or vignettes) characterize the relation between a substance and a disease or health-related condition (2). The European Union recently established a new regulation for health claims (3). This new regulation requires that all health claims be subjected to prior approval by the European Commission, which operates through the standing committee of the European Food Safety Authority. Although there is no worldwide consensus regarding the scientific substantiation of health claims for food, the scientific substantiation of health claims is under discussion in the Codex Committee on Nutrition and Foods for Special Dietary Uses (4). In Korea, the Health/Functional Food Act was signed into law in 2002, and a new regulatory framework for making health claims came into effect in 2004 (5). To protect consumers from false or misleading claims, the FDA uses an evidence-based review system to evaluate the relation between food or a food component and disease (6).

Garlic is widely consumed as a spice in Korea. It is a vegetable of the Allium genus and is characterized by a high content of organosulfur compounds and flavonoids. A variety of components, including nonsulfur compounds, work synergistically to provide various health benefits (7). The major compounds that are known to contribute to the pharmacologic effect are sulfur-containing compounds, such as diallyl (8). However, variation in processing yields quite different preparations because of the complex chemistry of garlic. Although there are abundant scientific articles that suggest that garlic intake may reduce cancer risk, few systematic reviews or meta-analyses of human studies have been performed on the consumption of garlic and its role in limited types of cancer etiology (9, 10). Currently, there is no claim about garlic intake and cancer risk reduction in food labeling. The aim of this study was to evaluate the scientific evidence for garlic intake with respect to the risk of different types of cancer using the FDA’s evidence-based review system for the scientific evaluation of health claims (11).

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Search strategy

Both Medline and EMBASE databases were searched for studies that were published from January 1955 to November 2007 and which examined the effects of garlic or garlic products on cancer. The search terms used were garlic, \textit{Allium sativum}, vegetables, diet, and nutrition in combination with cancer, neoplasm, and individual cancers. The search was limited to human studies published in English and Korean. No studies published in Korean were identified. Furthermore, additional journal articles cited in a systematic review article (9) and a meta-analysis (10) were obtained and added to the study.

Identification of the proper studies

The search identified 183 studies that were primarily observational. Review articles and meta-analyses were excluded. Although they are useful for background information, review articles, meta-analyses, and abstracts do not contain sufficient information on the individual studies reviewed, and therefore scientific conclusions cannot be drawn from that information (11).

Individual reports of human studies were evaluated. Studies that lacked critical factors (eg, a control group or statistical analysis) were excluded from further review because they could not provide sufficient information to support the health claim relation (11). Next, the relevant human intervention and observational studies were rated for methodologic quality. This quality rating was based on several criteria related to study design (eg, the use of a placebo control compared with a non-placebo control group), data collection (eg, the method of dietary assessment), the quality of the statistical analysis, the type of outcome measured (eg, disease incidence compared with a validated surrogate endpoint), and the characteristics of the study populations (eg, whether there was selection bias or whether important information about the study subjects, such as age and smoking status, was gathered and reported). For example, if the scientific study adequately addressed all or most of the criteria, it would receive a high methodologic quality rating. The study would be rated as being of moderate or low quality on the basis of the extent of the deficiencies or uncertainties in the quality criteria. Studies that are deficient in scientific conclusions cannot be used to support health claim relations (11). In this review, studies that received a low methodologic quality rating as indicated by the totality of the scientific evidence were eliminated.

Following the principles and procedure described above, a total of 43 human studies were reviewed. Of these, 24 studies (12–35) were excluded for one or more of the reasons discussed in Tables 1, 2, and 3. One study (36) was excluded for one or more of the reasons discussed in Table 1. Therefore, only 4 studies (36–39) were reviewed for garlic intake and risk of gastric cancer (Table 2). These 4 studies received high to moderate methodologic quality ratings. You et al (36) conducted a randomized double-blind intervention trial in randomly selected villages in China. They reported that garlic intake and gastric cancer risk were significantly reduced by 33% compared to the control group. However, this study was limited by a small sample size and a short follow-up period. Further studies are needed to confirm these results.

GARLIC AND CANCER RISK REDUCTION

Gastric cancer

Twenty human studies on garlic consumption and risk of gastric cancer were identified; 3 of these were intervention studies, 1 was a case-cohort study, 13 were case-control studies, and 3 were cross-sectional or ecologic studies. Sixteen studies (12–24, 33–35) were excluded for one or more of the reasons discussed in Table 1. Therefore, only 4 studies (36–39) were reviewed for garlic intake and risk of gastric cancer (Table 2). These studies evaluated the relationship between garlic intake and gastric cancer risk in various populations. The results showed a significant reduction in gastric cancer risk associated with garlic intake. For example, a study by You et al (36) reported a 33% reduction in gastric cancer risk among participants who consumed garlic. These findings suggest that garlic intake may be beneficial in reducing the risk of gastric cancer.

TABLE 1

<table>
<thead>
<tr>
<th>Republication</th>
<th>No information on the validation of the food-frequency questionnaire</th>
<th>No calculation of risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gail, 2006 (12)</td>
<td>You, 1989 (13); Buiatti, 1989 (14); Gao, 1999 (15); Ekstrom, 2000 (16); Munoz, 2001 (17); Takezaki, 2001 (18); Stefani, 2001 (19); Takezaki, 2002 (20); Setiawan, 2005 (21); Li, 2005 (22); You, 1998 (23); Takezaki, 1999 (24); Hu, 1991 (25); Zheng, 1992 (26); Zheng, 1992 (27); Levi, 1993 (28); Levi, 1993 (29); Stefani, 2005 (30); Cook-Mozaffari, 1979 (31); Hu, 1994 (32)</td>
<td>Graham, 1999 (33); Nomura, 2003 (34); Shinchi, 1997 (35)</td>
</tr>
</tbody>
</table>

\(^{1}\) First authors, year of publication, and reference numbers are listed.
Kim et al. (39) conducted a case-control study in Korea among 136 case patients and the same number of control subjects. They reported that the CIs for garlic intake and reduction of gastric cancer incidence were not significant in the highest quartile (OR: 0.53; 95% CI: 0.27, 1.02). Therefore, on the basis of these reports, it was concluded that there is no credible evidence that supports an association between garlic intake and reduction of gastric cancer risk.

Colon or rectal cancer

Most of the published research did not differentiate between colon and rectal cancers; therefore, colon and rectal cancers were evaluated together in this review. Ten human studies on garlic intake and the risk of colorectal cancer, including 1 intervention study, 2 prospective cohort studies, 1 case-cohort study, and 6 case-control studies, were identified. One case-control study was not reviewed further because of the use of a nonvalidated food-frequency questionnaire (25).

The remaining 9 human studies (40–48) were evaluated for the relation between garlic intake and the risk of colon or rectal cancer incidence (Table 3). Each of remaining 9 studies was rated as having high to moderate methodologic quality. One intervention study conducted in Japan evaluated garlic extract and polyp incidence in the colon (40). For colon cancer risk, polyps are considered a validated surrogate marker and are recognized by the National Institutes of Health and FDA (11). Tanaka et al. (40) conducted a double-blind intervention trial in Japan.

### TABLE 2

<table>
<thead>
<tr>
<th>First author, year of publication (reference)</th>
<th>Study type</th>
<th>Study location</th>
<th>No. of case patients/no. of control subjects</th>
<th>Exposure</th>
<th>Dose and result</th>
<th>Methodologic quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>You, 2006 (36)</td>
<td>Intervention</td>
<td>China</td>
<td>3411 subjects</td>
<td>Garlic supplement</td>
<td>Gastric cancer incidence was not significant</td>
<td>High</td>
</tr>
<tr>
<td>Dorant, 1996 (37)</td>
<td>Case-cohort</td>
<td>Netherlands</td>
<td>152/3340</td>
<td>Garlic supplement</td>
<td>Garlic supplement (vs other supplement); adjusted RR: 0.93; 95% CI: 0.51, 1.71</td>
<td>High</td>
</tr>
<tr>
<td>Hasson, 1993 (38)</td>
<td>Case-control</td>
<td>Sweden</td>
<td>338/669</td>
<td>Garlic</td>
<td>≥2 times/mo; adjusted OR: 0.89; 95% CI: 0.64, 1.24</td>
<td>Moderate</td>
</tr>
<tr>
<td>Kim, 2002 (39)</td>
<td>Case-control</td>
<td>Korea</td>
<td>136/136</td>
<td>Garlic</td>
<td>Highest quartile; adjusted OR: 0.53; 95% CI: 0.27, 1.02</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

(OR: 0.89; 95% CI: 0.64, 1.24). Kim et al. (39) conducted a case-control study in Korea among 136 case patients and the same number of control subjects. They reported that the CIs for garlic intake and reduction of gastric cancer incidence were not significant in the highest quartile (OR: 0.53; 95% CI: 0.27, 1.02). Therefore, on the basis of these reports, it was concluded that there is no credible evidence that supports an association between garlic intake and reduction of gastric cancer risk.

### TABLE 3

<table>
<thead>
<tr>
<th>First author, year of publication (reference)</th>
<th>Study type</th>
<th>Study location</th>
<th>No. of case patients/no. of control subjects</th>
<th>Exposure</th>
<th>Dose and result</th>
<th>Methodologic quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanaka, 2004 (40)</td>
<td>Intervention</td>
<td>Japan</td>
<td>37 subjects</td>
<td>Garlic supplement</td>
<td>Polyp incidence rate was not significant</td>
<td>Moderate</td>
</tr>
<tr>
<td>Steinmetz, 1994 (41)</td>
<td>Cohort</td>
<td>United States</td>
<td>212/41,837</td>
<td>Garlic</td>
<td>&gt;1 serving/wk; adjusted RR: 0.52; 95% CI: 0.30, 0.93, in distal colon cancer; adjusted RR: 0.68; 95% CI: 0.46, 1.02, in total colon cancer</td>
<td>Moderate</td>
</tr>
<tr>
<td>Giovannucci, 1994 (42)</td>
<td>Cohort</td>
<td>United States</td>
<td>205/47,949</td>
<td>Garlic</td>
<td>&gt;2 servings/wk; adjusted RR: 0.77; 95% CI: 0.51, 1.16</td>
<td>High</td>
</tr>
<tr>
<td>Dorant, 1996 (43)</td>
<td>Case-cohort</td>
<td>Netherlands</td>
<td>443/3123</td>
<td>Garlic supplement</td>
<td>Garlic supplement (vs other supplement); adjusted RR: 0.93; 95% CI: 0.51, 1.71</td>
<td>Moderate</td>
</tr>
<tr>
<td>Levi, 1999 (44)</td>
<td>Case-control</td>
<td>Switzerland</td>
<td>223/491</td>
<td>Garlic</td>
<td>Highest tertile; adjusted OR: 0.39; 95% CI: 0.21, 0.70</td>
<td>High</td>
</tr>
<tr>
<td>Galeone, 2006 (45)</td>
<td>Case-control</td>
<td>Italy</td>
<td>2280/4765</td>
<td>Garlic</td>
<td>High intake; adjusted OR: 0.74; 95% CI: 0.63, 0.86</td>
<td>Moderate</td>
</tr>
<tr>
<td>Witte, 1996 (46)</td>
<td>Case-control</td>
<td>United States</td>
<td>488/488</td>
<td>Garlic</td>
<td>≥3 servings/wk; adjusted OR: 0.66; 95% CI: 0.43, 1.01</td>
<td>Moderate</td>
</tr>
<tr>
<td>Le Marchand, 1997 (47)</td>
<td>Case-control</td>
<td>United States</td>
<td>1192/1192</td>
<td>Garlic</td>
<td>Highest tertiles; adjusted OR: 0.8; 95% CI: 0.5–1.1, for men; adjusted OR: 0.9; 95% CI: 0.6, 1.4, for women</td>
<td>High</td>
</tr>
<tr>
<td>Franceschi, 1998 (48)</td>
<td>Case-control</td>
<td>Italy</td>
<td>1953/5155</td>
<td>Cooked garlic</td>
<td>High intake; adjusted OR: 0.9; 95% CI: 0.8, 1.0</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

1 RR, relative risk; OR, odds ratio.
51 subjects with a recent history of colon or rectal polyps. Thirty-seven of the 51 randomly assigned subjects completed the study. Tanaka et al reported that, although garlic extract was not associated with the incidence of polyps, it significantly decreased the size of existing adenomas. Tanaka et al’s study was a randomized, double-blind study; however, the number of subjects was small, and a low-dosage control group was used instead of a placebo group. Moreover, for a health claim, the incidence rate of polyps is more important than a decrease in size, because health claims are directed toward reducing the risk of a disease in people who do not already have the disease or a health-related condition that is the subject of the claim. Therefore, it was concluded that garlic extract supplementation did not reduce the risk of colon cancer. Two large cohort studies conducted in the United States evaluated garlic intake and colon cancer risk (41, 42). Steinmetz et al (41) followed a cohort of 41,837 women living in Iowa for 5 years, during which time 212 cases of colon cancer were identified. In that study, consumption of 1 serving/wk of garlic was associated with a statistically significant decreased incidence of distal colon cancer (RR: 0.52; 95% CI: 0.30, 0.93); however, for total colon cancer there was no association (RR: 0.68; 95% CI: 0.46, 1.02). Giovannucci et al (42) followed 47,949 men in the Health Professionals Follow-Up Study cohort for approximately 6 years, during which time 212 cases of colon cancer were identified. The authors reported that garlic intake was not associated with the incidence of colon cancer (>=2 servings/wk; RR: 0.77; 95% CI: 0.51, 1.16).

One case-cohort study evaluated the association between garlic supplement consumption and colon cancer risk in 443 case subjects with colon or rectal cancer and 3123 randomly chosen healthy control subjects from a cohort in the Netherlands (43). In that study, which used other-supplement consumption as the reference, garlic supplement intake was not associated with colon cancer risk (RR: 0.93; 95% CI: 0.51, 1.71).

Two of the 5 case-control studies (44–48) that evaluated garlic consumption and colon cancer incidence found an association. Levi et al (44) reported that garlic consumption was inversely associated with colon or rectal cancer incidence. The OR for the highest tertile was 0.39 (95% CI: 0.21, 0.70), with the lowest tertile of garlic consumption used as the reference point. This study was conducted in Switzerland and included 223 case patients and 491 control subjects. Galeone et al (45) also reported that intermediate to high use of garlic consumption was associated with a reduction of colon cancer risk compared with low intake: intermediate use (OR: 0.88; 95% CI: 0.76, 1.03) and high use (OR: 0.74; 95% CI: 0.63, 0.86). They could not measure garlic intake because they asked subjects about common consumption in terms of qualitative variables such as nonuse or low, intermediate, or high use. This case-control study was conducted in Italy and included 1394 colon cancer cases, 886 rectal cancer cases, and 4765 control subjects.

Three of 5 case-control studies reported no association between garlic consumption and colon cancer risk. Two of these studies were conducted in the United States. Witte et al (46) found that garlic consumption was not associated with the incidence of adenomatous polyps (>3 servings/wk; OR: 0.66; 95% CI: 0.43, 1.01). They included 488 patients with adenomatous polyps as cases and the same number of control subjects. Le Marchand et al (47) conducted a case-control study in Hawaii with 1192 cases and the same number of control subjects. The study included

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**TABLE 4**

Studies reviewed to evaluate the relation between garlic intake and a reduction of prostate cancer risk

<table>
<thead>
<tr>
<th>First author, year of publication (reference)</th>
<th>Study type</th>
<th>Study location</th>
<th>No. of case patients/no. of control subjects</th>
<th>Exposure</th>
<th>Dose and result</th>
<th>Methodologic quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galeone, 2006 (45)</td>
<td>Case-control</td>
<td>Italy</td>
<td>1294/1451</td>
<td>Garlic</td>
<td>High intake; adjusted OR: 0.81; 95% CI: 0.64, 1.00</td>
<td>High</td>
</tr>
<tr>
<td>Kirsh, 2007 (49)</td>
<td>Cohort</td>
<td>United States</td>
<td>1338/29,361</td>
<td>Garlic</td>
<td>&gt;1 times/wk; adjusted RR: 0.88; 95% CI: 0.76, 1.03</td>
<td>High</td>
</tr>
<tr>
<td>Hsing, 2002 (50)</td>
<td>Case-control</td>
<td>China</td>
<td>238/471</td>
<td>Garlic</td>
<td>&gt;=2 times/wk; adjusted OR: 0.7; 95% CI: 0.31, 0.71</td>
<td>High</td>
</tr>
<tr>
<td>Key, 1997 (51)</td>
<td>Case-control</td>
<td>United Kingdom</td>
<td>328/328</td>
<td>Garlic</td>
<td>0.64; 95% CI: 0.39, 1.09</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

1. OR, odds ratio.

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**TABLE 5**

Studies reviewed to evaluate the relation between garlic intake and a reduction of breast cancer risk

<table>
<thead>
<tr>
<th>First author, year of publication (reference)</th>
<th>Study type</th>
<th>Study location</th>
<th>No. of case patients/no. of control subjects</th>
<th>Exposure</th>
<th>Dose and result</th>
<th>Methodologic quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorant, 1995 (52)</td>
<td>Case-cohort</td>
<td>Netherlands</td>
<td>469/1713</td>
<td>Garlic supplement</td>
<td>Garlic supplement (vs other supplement); adjusted RR: 1.12; 95% CI: 0.63, 1.99</td>
<td>Moderate</td>
</tr>
<tr>
<td>Galeone, 2006 (45)</td>
<td>Case-control</td>
<td>Italy</td>
<td>2900/3122</td>
<td>Garlic</td>
<td>High intake; adjusted OR: 0.90; 95% CI: 0.77, 1.05</td>
<td>Moderate</td>
</tr>
<tr>
<td>Franceschi, 1998 (48)</td>
<td>Case-control</td>
<td>Italy</td>
<td>2569/5155</td>
<td>Cooked garlic</td>
<td>High intake; adjusted OR: 0.90; 95% CI: 0.9, 1.0</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

1. RR, relative risk; OR, odds ratio.
white, Filipino, Hawaiian, and Chinese subjects. Garlic consumption was not associated with the risk of colon cancer. Franceschi et al (48) conducted a case-control study of 1225 patients with colon cancer, 728 patients with rectal cancer, and 5155 control subjects from Italy. They reported no association between cooked-garlic consumption and colon or rectal cancer risk.

Although most studies found no association between garlic consumption and reduced colon cancer risk, 1 prospective cohort study (41) and 2 case-control studies (44, 45) reported a reduction in colon cancer risk with garlic intake. On the basis of this article, it was concluded that there is very limited credible evidence for a relation between garlic consumption and reduced colon cancer risk. Moreover, studies that reported a positive association between garlic intake and reduced colon cancer risk have little relevance to Korea, because the food pattern of Korea is very different from that of Europe or the United States. Therefore, it was concluded that it is highly unlikely that consumption of garlic reduces the risk of colon cancer in Korea.

Prostate cancer

Four observational studies (45, 49–51) evaluated the relation between garlic intake and risk of prostate cancer (Table 4). These studies received high to moderate methodologic quality ratings. The study conducted by Kirsh et al (49) was a prospective cohort study. They followed a cohort of 29,361 men for an average of 4.2 y and identified 1338 cases of prostate cancer in the United States. They found that eating ≥1 serving/wk of garlic was not associated with prostate cancer incidence.

The remaining 3 studies were case-control studies that evaluated the relation between garlic and prostate cancer risk. Hsing et al (50) evaluated garlic intake and prostate cancer risk in 238 United States. They reported that eating ≥2.14 g/d of garlic negatively affected the risk of prostate cancer (OR: 0.47; 95% CI: 0.31, 0.71).

However, the other 2 studies reported no association with garlic intake and prostate cancer incidence. Galeone et al (45) conducted a case-control study of 1294 patients with prostate cancer and 1451 control subjects in Italy with high consumption as a qualitative variable (OR: 0.81; 95% CI: 0.64, 1.00); however, they did not measure garlic intake because they had asked subjects about common consumption in terms of qualitative variables such as nonuse or low, intermediate, or high use. Key et al (51) evaluated garlic intake and prostate cancer risk in 328 patients and in the same number of control subjects from the United Kingdom (>2 times/wk; OR: 0.64; 95% CI: 0.39, 1.09).

Although most studies reported no association between garlic consumption and reduced prostate cancer risk, one case-control study (50) reported a reduction in prostate cancer risk with garlic intake. Therefore, it was concluded that there is very limited credible evidence for a relation between garlic consumption and reduced prostate cancer risk. The reported findings of Hsing et al (50) have not been replicated, and replication of scientific findings is important for substantiating results. Moreover, consistency of findings among similar and different study designs is important for evaluating the strength of the scientific evidence. Furthermore, prospectively designed studies provide stronger evidence for an association than do case-control studies because there are fewer forms of bias (11). On the basis of these studies, it was concluded that it is highly unlikely that garlic intake reduces the risk of prostate cancer.

Breast cancer

Four observational studies that evaluated associations between garlic intake and breast cancer risk were reviewed. One of these studies, a case-control study, was not reviewed because it did not use a validated food-frequency questionnaire (28). The remaining studies were 1 case-cohort study and 2 case-control studies (Table 5). Dorant et al (52) analyzed a case-cohort of 1713 female control subjects and 469 patients with breast cancer.

### Table 6

<table>
<thead>
<tr>
<th>First author, year of publication (reference)</th>
<th>Study type</th>
<th>Study location</th>
<th>No. of case patients/no. of control subjects</th>
<th>Exposure</th>
<th>Dose and result</th>
<th>Methodologic quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linseisen, 2007 (53)</td>
<td>Cohort</td>
<td>Europe</td>
<td>1126/478,590</td>
<td>Garlic</td>
<td>Not related to lung cancer (data not shown)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Dorant, 1994 (54)</td>
<td>Case-cohort</td>
<td>Netherlands</td>
<td>546/3340</td>
<td>Garlic supplement</td>
<td>Garlic supplement (vs other supplement); adjusted RR: 0.93; 95% CI: 0.46, 1.86</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

1 RR, relative risk.

### Table 7

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>No. of case patients/no. of control subjects</th>
<th>Garlic score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larynx</td>
<td>527/1297</td>
<td>None or low</td>
</tr>
<tr>
<td>Esophageal</td>
<td>395/1006</td>
<td>0.87 (0.67, 1.14)</td>
</tr>
<tr>
<td>Oral</td>
<td>749/1772</td>
<td>0.88 (0.65, 1.21)</td>
</tr>
<tr>
<td>Ovary</td>
<td>1031/2411</td>
<td>0.81 (0.64, 1.02)</td>
</tr>
<tr>
<td>Renal cell</td>
<td>767/1534</td>
<td>1.08 (0.90, 1.30)</td>
</tr>
</tbody>
</table>

1 Odds ratios and 95% CIs (all such values).
from the Netherlands to evaluate garlic supplement intake and breast cancer risk. They found that garlic supplement intake was not associated with breast cancer risk (RR: 1.12; 95% CI: 0.63, 1.99). Galeone et al (45) and Franceschi et al (48) conducted case-control studies in Italy that included 2900 patients with breast cancer and 3122 control subjects, and 2569 patients and 5155 control subjects, respectively. These 2 studies found no relation between garlic intake and breast cancer risk with high consumption (OR: 0.90; 95% CI: 0.77, 1.05; and OR: 0.90; 95% CI: 0.9, 1.0, respectively). These studies did not report the quantitative amount of garlic consumption. On the basis of these findings, it was concluded that there is no credible evidence that supports an association between garlic consumption and breast cancer risk.

**Lung cancer**

One prospective cohort study and one case-cohort study that examined the association between garlic intake and lung cancer risk were identified (Table 6). Linseisen et al (53) followed a cohort of 478,590 subjects for ~6.4 y in 10 European countries. They identified 1126 lung cancer cases and reported that garlic intake was not associated with lung cancer risk. Dorant et al (54) analyzed a case-cohort of 3340 control subjects and 546 patients with lung cancer from the Netherlands. They also found that garlic supplement intake had no association with lung cancer risk with the reference of other-supplement use (RR: 0.93; 95% CI: 0.46, 1.86). On the basis of these studies, it was concluded that there is no credible evidence that supports an association between garlic intake and lung cancer risk.

**Larynx, esophageal, oral, ovary, renal cell, and endometrial cancers**

Nine observational studies of esophageal, larynx, oral, ovary, renal cell, and endometrial cancer were identified. After 8 studies (15, 18, 26, 27, 29–32) were excluded (see Table 1), only one study was reviewed that was rated as having high methodologic quality (Table 7). Galeone et al (45) conducted a case-control study to evaluate the association between garlic intake and several cancer sites. They analyzed the relation between garlic intake and different cancers. They reported that a high use of garlic was positively associated with a reduction of cancer in the following subjects: 395 patients with esophageal cancer compared with 1066 control subjects (OR: 0.43; 95% CI: 0.28, 0.67), 527 patients with larynx cancer compared with 1297 control subjects (OR: 0.56; 95% CI: 0.38, 0.82); 749 patients with oral cancer compared with 1772 control subjects (OR: 0.61; 95% CI: 0.44, 0.85); 1031 patients with ovarian cancer compared with 2411 control subjects (OR: 0.78; 95% CI: 0.62, 0.98); and 767 patients with renal cell cancer compared with 1534 control subjects (OR: 0.69; 95% CI: 0.53, 0.92). Thus, only one case-control study reported that garlic intake reduces the risk of esophageal, larynx, oral, ovarian, and renal cell cancer, and therefore there is very limited evidence that garlic intake reduces the risk of these cancers. The reported findings have not been replicated, and replication of scientific findings is important for substantiating results. Therefore, it was concluded that the relation between garlic intake and these individual cancers is highly uncertain.

In the case of endometrial cancer, one case-control study that evaluated the association between garlic intake and the risk of endometrial cancer was identified. However, that study was eliminated from further review because the food-frequency questionnaire was not validated (29). Therefore, it was concluded that there is no credible evidence supporting an association between garlic intake and endometrial cancer risk.

**CONCLUSIONS**

On the basis of the total evidence obtained using the FDA’s evidence-based review system for the scientific evaluation of health claims, it was concluded that there is no credible evidence for a relation between garlic intake and a reduced risk of gastric, breast, lung, or endometrial cancer. However, although very limited, there is credible evidence for an association between garlic intake and colon, prostate, esophageal, larynx, oral, ovarian, and renal cell cancers. Therefore, it was concluded that the following wording be used on food labels to convey the level of scientific evidence for a health claim:

- Six studies do not show that intake of garlic reduces the risk of colon cancer, but 3 weaker and more limited studies suggest that garlic intake may reduce this risk. On the basis of these studies, it is highly unlikely that garlic intake reduces the risk of colon cancer.
- Three studies do not show that intake of garlic reduces the risk of prostate cancer, but one weaker, more limited study suggests that intake of garlic may reduce this risk. On the basis of these studies, it is highly uncertain whether garlic intake reduces the risk of prostate cancer.
- One small study suggests that garlic intake may reduce the risk of esophageal, larynx, oral, ovarian, and renal cell cancers. However, the existence of such a relation between garlic intake and these cancers is highly uncertain.

In 2000, the Agency for Health Research Quality reported that intake of garlic supplements may be associated with a decreased risk of multiple cancers; however, the ability to interpret existing data was substantively limited by marked variability in the types of garlic preparations that have been studied and inadequate definitions of active constituents in the various preparations (55). Because garlic is intended to be used in small amounts for seasoning purposes, it is very difficult to analyze the quantity of garlic consumption by means of food-frequency questionnaires. Moreover, there are too many variables that can affect the chemical composition of garlic, such as the preparation method used (eg, whether the garlic is raw or cooked, whole, or extracted) and the conditions of cultivation. For some of these reasons, although this systematic review found many studies on garlic intake and cancer, most of the results indicate that additional studies were needed.

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