Association between Dietary Factors and Breast Cancer Risk among Chinese Females: Meta-analysis

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Abstract

**Background:** Evidence for associations between dietary factors and breast cancer risk is inconclusive among Chinese females. To evaluate this question, we conducted a systematic review of relevant case-control and cohort studies. **Methods:** Studies were systematically searched among 5 English databases (PudMed, ScienceDirect, Wiley, Clinicaltrials.gov, and Cochrane) and 3 Chinese databases (CNKI, WanFang, and VIP) until November 2012. Random effects models were used to estimate summary odds ratios (ORs) and the corresponding 95% confidence intervals (CIs). **Results:** Thirty one case-control studies and two cohort studies involving 9,299 cases and 11,413 controls were included. Consumption of both soy and fruit was significantly associated with decreased risk of breast cancer, with summary ORs of 0.65 (95% CIs: 0.43–0.99; I²=88.9%, P<0.001; N=13) and 0.66 (95% CIs: 0.47–0.91; I²=76.7%, P<0.001; N=7), respectively. Consumption of fat was significantly associated with increased risk of breast cancer (OR=1.36; 95% CIs: 1.13–1.63; I²=47.9%, P=0.088; N=6). There was non-significant association between consumption of vegetables and breast cancer risk (OR=0.72; 95% CIs: 0.51–1.02; I²=74.4%, P>0.001; N=9). However, sensitivity analysis based on adjusted ORs showed decreased risk of breast cancer was also associated with consumption of vegetables (OR=0.49; 95% CIs: 0.30–0.67). **Conclusion:** Both soy food and fruit are significantly associated with decreased risk of breast cancer among Chinese females, and vegetables also seems to be protective while dietary fat exerts a promoting influence.

**Keywords:** Soy - fruit - fat - vegetable - breast cancer - meta-analysis

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Introduction

Breast cancer is one of the most common cancers and the leading cause of cancer death among females, accounting for 23% of all cancer cases and 14% of the cancer deaths all over the world (Ferlay et al., 2010). Incidence rate of breast cancer among Chinese women has long been noted to be substantially lower than that among women in Western nations (Parkin et al., 1992). However, the incidence rate in Chinese women increases rapidly with the improvement of living standard (Ziegler et al., 1993). In China, the breast cancer incidence has been ranked first of all cancers among urban Chinese female from 1989 to 2008 (Chen et al., 2012). Facing the serious situation, to explore preventable strategies is of great importance to reduce the huge burden of breast cancer.

Dietary factors have long been thought to play a major role in the development of breast cancer. With the improvement of living standard in recent years in China, the traditional Chinese dietary pattern has gradually changed to the western dietary pattern, which leads to a rising incidence of many diseases including cancer. According to the national nutrition and health investigation (Wang, 2002), meat intake per capita in China has increased ten times from 1961 to 2000. Daily consumption of fruit per capita among urban residents decreased from more than 80 g in 1992 to less than 70g in 2002, consumption of vegetables per capita decreased from 319.3g to 251.9g. Though soy consumption per capita increased from 8.1g to 11.8g, it is still much less than the recommended 36g (Nan, 2006). Parallel to this great changes in dietary patterns, great concerns on the consequences caused by the changing dietary pattern have been raised.

Though several traditional Chinese foods, such as soy, green vegetables, fruits, are thought to be associated with decreased risk of breast cancer (Dong et al., 2011; Sangrajrang et al., 2013), the conclusion is not consistent among the previous published studies, even in the studies

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conducted in Asian countries (Trock et al., 2006). And two major meta-analyses (Alexander et al., 2010; Turner, 2011) examining the relationship between dietary fat and breast cancer risk have reported inconsistent results. Another study showed that a high consumption of animal fat is associated with a higher breast cancer risk in sedentary women, while consumption of plant fat products may reduce risk in the same group (Kruk et al., 2013). In recent years more and more studies have failed to observe a strong positive association between fat intake and breast cancer risk.

With a large denominator for breast cancer in China, if the case for cancer risk caused by dietary factors is true, the population impact number might be substantial. Thus, as one of the countries experiencing the great changes in dietary pattern, it is very necessary to clarify the association between dietary factors and breast cancer risk among Chinese females.

Materials and Methods

We followed MOOSE guideline (Stroup et al., 2000) for conducting and reporting this systematic review.

Search strategy

An electronic literature search was conducted in five English databases (PudMed, ScienceDirect, Wiley, Clinicaltrials.gov, Cochrane) and three Chinese databases (CNKI, WanFang, VIP) to identify human studies written in English or Chinese language and published up to June 2013. Three groups of keywords or phrases were used in the searching strategy: (1) “case-control study, cohort study, prospective study, randomized controlled trial”; (2) “risk factor, diet, dietary fiber, vegetable, fruit, soy, fat”; and (3) “breast cancer, breast carcinoma, breast tumor, breast neoplasm.” The reference lists of all included studies, published systematic reviews and meta-analyses were also searched for any potential studies. Only original articles with full-text were considered.

Study selection

We included prospective cohort studies and case-control studies investigating the association between dietary intake and breast cancer. Two independent reviewers read the abstracts retrieved in the initial search to identify potential studies. Any disagreement was adjudicated by a third reviewer. Only studies with complete data of interesting were included.

Data extraction

We extracted all data using a standardized data-collection form. Information was collected as follows: last name of the first author; publication year; type of study; study population; sample size; measurement of exposure and outcome (risk estimates and their 95% CIs or cross-table data); methodological quality of included studies. ORs calculated from both the univariate and multivariate logistic regression models were collected. Due to the different quantiles, in order to get clear conclusion, only the information in the highest and the lowest category of food was collected.

Quality assessment

A quality score was evaluated with Newcastle-Ottawa Scale (NOS) (Wells, 2012) for each study included in the meta-analysis. Two investigators independently scored the studies based upon predetermined methodological standards and any differences were resolved by discussion. The criteria included the provision of details of how the population studied had been assembled, whether histological confirmation of breast cancers had been performed, the evaluation of measurement for exposure, and the methods used to control for potential bias. Quality scores were divided into 3 groups: 8 points and higher, 5-7 points, 4 points and lower.

Statistical analysis

Random effects models were used to calculate the summary ORs and 95% confidence intervals (CIs) for each study. A two-tailed p value less than 0.05 was considered statistically significant.

Homogeneity of ORs across studies was tested by F statistic (significance level at $P < 0.10$), which is a quantitative measure of inconsistency across studies (Higgins et al., 2003). Additional subgroup analysis was used to investigate the sources of heterogeneity, including study design, publication year, sample size and NOS level. Potential publication bias was assessed using a funnel plot by Egger et al. (1997).

Sensitivity analyses on studies reporting multivariate adjusted ORs were conducted to explore the effect of the potential confounding factors. Sensitivity analyses were also conducted to test whether the primary results were affected by the studies which fell outside of the funnel plot.

Stata version 12.0 software was used for the statistical analyses.

Results

A flow chart showing the study selection is presented in Figure 1. Thirty seven potentially eligible full text publications were identified (Yuan et al., 1987; Qi et al., 1990; Cai, 1996; Tan et al., 1998; Xu et al., 1998; Zhao et al., 1999; Wang et al., 2000; Wang, 2000; Dai et al., 2001; Chen, 2002; Tao et al., 2002; Zhang et al., 2003; Zou et al., 2003; Han, 2004; Lee et al., 2005; Shannon et al.,...
### Table 1. Characteristics of Studies for Meta-analysis

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Region</th>
<th>Distribution</th>
<th>Design</th>
<th>No of cases</th>
<th>No of controls</th>
<th>Type of controls</th>
<th>Dietary assessment</th>
<th>Items</th>
<th>Intake comparison</th>
<th>NOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDai (2001)</td>
<td>Shanghai</td>
<td>eastern</td>
<td>Case-control</td>
<td>1459</td>
<td>1556</td>
<td>Population</td>
<td>24 h recall</td>
<td>Soy protein</td>
<td>&gt;91.0g/wk vs &lt; Occasionally</td>
<td>A</td>
</tr>
<tr>
<td>Kallianpur et al. (2008)</td>
<td>Shanghai</td>
<td>eastern</td>
<td>Case-control</td>
<td>3452</td>
<td>3474</td>
<td>Population</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Fat</td>
<td>Fourth vs. first quartile</td>
<td>A</td>
</tr>
<tr>
<td>Shannon et al. (2005)</td>
<td>Shanghai</td>
<td>eastern</td>
<td>Cohort</td>
<td>378</td>
<td>1070</td>
<td>Population</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>e13.52 vs e10.5 servings/wk</td>
<td>A</td>
</tr>
<tr>
<td>Tao et al. (2002)</td>
<td>Shanghai</td>
<td>eastern</td>
<td>Case-control</td>
<td>356</td>
<td>925</td>
<td>Population</td>
<td>Diet history</td>
<td>Soy</td>
<td>&gt;37.48 vs &gt;30.0g/day</td>
<td>C</td>
</tr>
<tr>
<td>Wang et al. (2000)</td>
<td>Shanghai</td>
<td>eastern</td>
<td>Multicentral</td>
<td>2063</td>
<td>2063</td>
<td>Population</td>
<td>Diet history</td>
<td>Fruit</td>
<td>&gt;5000 vs &gt;500g/month</td>
<td>B</td>
</tr>
<tr>
<td>Lee et al. (2005)</td>
<td>Taiwan</td>
<td>eastern</td>
<td>Case-control</td>
<td>250</td>
<td>219</td>
<td>Hospital</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Soy rich food</td>
<td>&gt;34 vs &gt;11g/wk</td>
<td>B</td>
</tr>
<tr>
<td>Zhou et al. (2009)</td>
<td>Jiangsu</td>
<td>eastern</td>
<td>Case-control</td>
<td>206</td>
<td>214</td>
<td>Population</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Fruit</td>
<td>&lt;5.75 vs &lt;3.65kg/year</td>
<td>B</td>
</tr>
<tr>
<td>Li et al. (2006)</td>
<td>Sichuan</td>
<td>western</td>
<td>Case-control</td>
<td>121</td>
<td>211</td>
<td>Population</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>1 vs 1 servings/day</td>
<td>B</td>
</tr>
<tr>
<td>Zhao et al. (1999)</td>
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<td>western</td>
<td>Case-control</td>
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<td>265</td>
<td>Population</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Soy</td>
<td>&gt;2500 vs &gt;250g/day</td>
<td>B</td>
</tr>
<tr>
<td>Zhu et al. (2006)</td>
<td>Henan</td>
<td>central</td>
<td>Case-control</td>
<td>246</td>
<td>246</td>
<td>Hospital</td>
<td>Diet history</td>
<td>Soy highFat</td>
<td>no/yes</td>
<td>C</td>
</tr>
<tr>
<td>Tan et al. (1998)</td>
<td>Hunan</td>
<td>central</td>
<td>Case-control</td>
<td>146</td>
<td>146</td>
<td>Hospital</td>
<td>Diet history</td>
<td>Vegetable</td>
<td>yes/no</td>
<td>B</td>
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<td>Cheng et al. (2002)</td>
<td>Qinghai</td>
<td>western</td>
<td>Case-control</td>
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<td>110</td>
<td>Hospital</td>
<td>Diet history</td>
<td>Vegetable</td>
<td>Soy</td>
<td>B</td>
</tr>
<tr>
<td>Zhang et al. (2009)</td>
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<td>eastern</td>
<td>Case-control</td>
<td>438</td>
<td>438</td>
<td>Hospital</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>Fourth vs. first quartile</td>
<td>B</td>
</tr>
<tr>
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<td>Shandong</td>
<td>eastern</td>
<td>Case-control</td>
<td>103</td>
<td>309</td>
<td>Population</td>
<td>Diet history</td>
<td>Fruit</td>
<td>5.7 vs 0 day/wk</td>
<td>B</td>
</tr>
<tr>
<td>Zheng et al. (2010)</td>
<td>Yunnan</td>
<td>western</td>
<td>Case-control</td>
<td>100</td>
<td>100</td>
<td>Hospital</td>
<td>Diet history</td>
<td>Vegetable</td>
<td>Soybean milk</td>
<td>&gt;1000 vs &lt;1000mg/day</td>
</tr>
<tr>
<td>Cai et al. (1996)</td>
<td>Ningxia</td>
<td>western</td>
<td>Case-control</td>
<td>102</td>
<td>102</td>
<td>Population</td>
<td>Diet history</td>
<td>soy</td>
<td>&gt;100 vs &gt;50g/day</td>
<td>B</td>
</tr>
<tr>
<td>Guo et al. (2010)</td>
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<td>eastern</td>
<td>Case-control</td>
<td>103</td>
<td>103</td>
<td>Population</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;3 vs &gt;3 servings/wk</td>
<td>B</td>
</tr>
<tr>
<td>Xu et al. (1998)</td>
<td>Shandong</td>
<td>eastern</td>
<td>Case-control</td>
<td>186</td>
<td>186</td>
<td>Population</td>
<td>Food freq&lt;sup&gt;abc&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;40 vs &gt;50g/day</td>
<td>B</td>
</tr>
<tr>
<td>Wang et al. (2008)</td>
<td>Beijing</td>
<td>eastern</td>
<td>Case-control</td>
<td>429</td>
<td>781</td>
<td>Hospital</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Soy products</td>
<td>&gt;3 vs &gt;3 servings/wk</td>
<td>C</td>
</tr>
<tr>
<td>Rong et al. (2008)</td>
<td>Hebei</td>
<td>eastern</td>
<td>Case-control</td>
<td>175</td>
<td>175</td>
<td>Hospital</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;1 vs &lt;1 servings/wk</td>
<td>B</td>
</tr>
<tr>
<td>Qi et al. (1990)</td>
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<td>eastern</td>
<td>Case-control</td>
<td>244</td>
<td>244</td>
<td>Hospital</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;600 vs &gt;400g/day</td>
<td>B</td>
</tr>
<tr>
<td>Wang et al. (2010)</td>
<td>Sichuan</td>
<td>western</td>
<td>Case-control</td>
<td>400</td>
<td>400</td>
<td>Population</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Fat</td>
<td>&gt;100 vs &gt;50g/day</td>
<td>A</td>
</tr>
<tr>
<td>Shen et al. (2006)</td>
<td>Shandong</td>
<td>eastern</td>
<td>Case-control</td>
<td>282</td>
<td>298</td>
<td>Population</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;75 vs &gt;75g/day</td>
<td>A</td>
</tr>
<tr>
<td>Ren et al. (2008)</td>
<td>Liaoning</td>
<td>eastern</td>
<td>Case-control</td>
<td>200</td>
<td>200</td>
<td>Hospital</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;14 vs &gt;7 servings/wk</td>
<td>B</td>
</tr>
<tr>
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<td>Zhejiang</td>
<td>eastern</td>
<td>Cohort</td>
<td>84</td>
<td>269</td>
<td>Population</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;36 vs &gt;7.2g/kg/year</td>
<td>A</td>
</tr>
<tr>
<td>Han et al. (2004)</td>
<td>Hubei</td>
<td>central</td>
<td>Case-control</td>
<td>213</td>
<td>430</td>
<td>Hospital</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;3000g vs &gt;300g/d</td>
<td>B</td>
</tr>
<tr>
<td>Zhang et al. (2012)</td>
<td>Ningxia</td>
<td>western</td>
<td>Case-control</td>
<td>107</td>
<td>107</td>
<td>Hospital</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Soy</td>
<td>&gt;150g/d vs &lt;150g/d</td>
<td>B</td>
</tr>
<tr>
<td>Liang et al. (2012)</td>
<td>Guangdong</td>
<td>eastern</td>
<td>Case-control</td>
<td>168</td>
<td>168</td>
<td>Hospital</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Soy</td>
<td>&gt;500g/d vs &lt;500g/d</td>
<td>B</td>
</tr>
<tr>
<td>Yao et al. (2012)</td>
<td>Zhejiang</td>
<td>eastern</td>
<td>Case-control</td>
<td>200</td>
<td>200</td>
<td>Hospital</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Soy</td>
<td>&gt;50/w vs &lt;36/w</td>
<td>B</td>
</tr>
<tr>
<td>Luo et al. (2013)</td>
<td>Sichuan</td>
<td>western</td>
<td>Case-control</td>
<td>116</td>
<td>240</td>
<td>Hospital</td>
<td>Diet history&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Soy</td>
<td>&gt;50/w vs &lt;36/w</td>
<td>B</td>
</tr>
<tr>
<td>Bo et al. (2013)</td>
<td>Sichuan</td>
<td>western</td>
<td>Case-control</td>
<td>210</td>
<td>210</td>
<td>Hospital</td>
<td>Food freq&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Vegetable</td>
<td>&gt;50/w vs &lt;36/w</td>
<td>B</td>
</tr>
</tbody>
</table>

<sup>a</sup>Food Frequency Questionnaire; <sup>b</sup>Self-administered; <sup>c</sup>interviewer-administered

### Notes

- Soy
- Fruits
- Vegetable

### References

- Li et al., 2006; Shen et al., 2006; Zhu et al., 2006; Wang, 2007; Kallianpur et al., 2008; Ren, 2008; Rong et al., 2008; Wang et al., 2008; Zhang et al., 2009; Zhou et al., 2009; Cheng et al., 2010; Guo et al., 2010; Zheng et al., 2010; Wang et al., 2011; Liang, 2012; Yao et al., 2012; Yu et al., 2012; Zhang et al., 2012; Bo et al., 2013; Luo et al., 2013 and 2 cohort studies (Shannon et al., 2005; Wang, 2007) were included in the final analysis (Table 1; Figure 1).
was 0.65 (95% CIs: 0.43–0.99) with a high heterogeneity (P < 0.001, $I^2 = 88.9\%$) (Figure 2). There was no evidence of publication bias with Egger’s test (P = 0.867). Funnel plots revealed little evidence of asymmetry (Supplement 1).

**Fruit**

Six case-control studies and one cohort study were included in the analysis of high versus low fruit intake and breast cancer. The summary OR for high versus low intake was 0.66 (95% CI: 0.47–0.91) with a high heterogeneity (P < 0.001, $I^2 = 76.7\%$) (Figure 3). There was no significant publication bias found by Egger test (P = 0.346) among studies with cross-table data. Funnel plots revealed little evidence of asymmetry.

**Fat**

Six case-control studies were included in the analysis of high versus low fat intake and breast cancer. The summary OR for high versus low intake was 1.36 (95% CIs: 1.13–1.63) with a moderate heterogeneity (P = 0.088, $I^2 = 47.9\%$) (Figure 4). There was no evidence of publication bias with Egger’s test (P = 0.090). Funnel plots revealed little evidence of asymmetry and therefore little evidence of publication bias.

**Sensitivity analyses**

16 studies had reported adjusted ORs for these dietary factors. Sensitivity analysis based on these adjusted ORs had got summary ORs of 0.59 (95% CIs: 0.33–0.85, n=10), 0.49 (95% CIs: 0.30–0.67, n=5), 0.38 (95% CIs: 0.28–0.47, n=5), 1.44 (95% CIs: 0.97–1.91, n=4) for soy, vegetable, fruit, and fat respectively.

**Subgroup analyses**

The inverse association between vegetable intake and breast cancer risk was both found among studies published after 2007 (OR=0.49; 95% CIs: 0.27–0.89) and studies with NOS scores of 5-7 points (OR=0.57; 95% CIs: 0.36–0.91), but non-significant association among other subgroup analyses. For fruit consumption, inverse association was found in case-control studies (OR=0.63; 95% CIs: 0.48-0.94), studies published after 2007 (OR=0.50; 95% CIs: 0.33-0.76), studies with sample size less than 530 (OR=0.55; 95% CIs: 0.34-0.90), and studies with high publication bias (P = 0.001).
## Table 2. Subgroup Analyses of Food Intakes and Breast Cancer, High Versus Low Intake

<table>
<thead>
<tr>
<th>Group</th>
<th>Vegetables</th>
<th>Fruits</th>
<th>Soy</th>
<th>Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Studies</td>
<td>OR (95% CIs)</td>
<td>P</td>
<td>F (%)</td>
<td>OR (95% CIs)</td>
</tr>
<tr>
<td>Study design</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case-control</td>
<td>0.67 (0.42, 1.06)</td>
<td>0.802</td>
<td>0</td>
<td>0.63 (0.42, 0.94)</td>
</tr>
<tr>
<td>NOS level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7</td>
<td>0.94 (0.78, 1.15)</td>
<td>0.917</td>
<td>0</td>
<td>0.86 (0.69, 1.13)</td>
</tr>
<tr>
<td>5-7</td>
<td>0.60 (0.37, 0.96)</td>
<td>0.044</td>
<td>70.7</td>
<td>0.55 (0.38, 0.89)</td>
</tr>
<tr>
<td>&gt;7</td>
<td>0.65 (0.31, 1.40)</td>
<td>0.932</td>
<td>0</td>
<td>0.80 (0.54, 1.19)</td>
</tr>
<tr>
<td>Sample size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤530</td>
<td>0.77 (0.59, 1.02)</td>
<td>0.746</td>
<td>0</td>
<td>0.55 (0.34, 0.90)</td>
</tr>
<tr>
<td>&gt;530</td>
<td>0.60 (0.37, 0.96)</td>
<td>0.004</td>
<td>70.7</td>
<td>0.55 (0.38, 0.79)</td>
</tr>
<tr>
<td>Publication year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2007</td>
<td>0.94 (0.78, 1.15)</td>
<td>0.917</td>
<td>0</td>
<td>0.86 (0.69, 1.13)</td>
</tr>
<tr>
<td>≥2007</td>
<td>0.60 (0.37, 0.96)</td>
<td>0.044</td>
<td>70.7</td>
<td>0.55 (0.38, 0.89)</td>
</tr>
</tbody>
</table>

With NOS scores of 5-7 points (OR=0.55; 95% CIs: 0.38-0.79). In terms of soy intake, an inverse relation with breast cancer risk was observed in most subgroups, but not in cohort studies (OR=1.46; 95% CIs: 1.07-1.98) and studies with NOS scores of 8-9 points (OR=1.12; 95% CIs: 0.68-1.84). For fat intake, there was a significant association among all subgroups except studies with sample size less than 530 (OR=1.45; 95% CIs: 0.90-2.31) (Table 2).

## Discussion

The meta-analysis included results from 31 case-control and 2 cohort studies conducted in Chinese female. The results indicate that both soy food and fruit are significantly associated with decreased risk of breast cancer among Chinese females. And vegetable seems also be associated with decreased risk of breast cancer, though non-significant association was found in the primary analysis. These results are consistent with several previously published studies (Boyd et al., 1993; Boyd et al., 2003; Aune et al., 2012; Aune et al., 2012).

The protective effect of soy protein on breast cancer has received a great attention since the first study published on Lancet (Lee et al., 1991). Several experiments studies also support this protective effect of soy food on breast cancer. Experiments on rats indicated that the incidence of chemically induced mammary tumors significantly decreased when prepubertal rats were exposed to soy extracts or the isoflavone genistein (Warri et al., 2008). Soy isoflavone is similar to the structure of endogenous estrogen, thus, it is a competitive inhibitor of endogenous estrogen and then protect against breast cancer (Limer et al., 2004; Magee et al., 2004; Hooper et al., 2010). Soy isoflavones also have other protective effects, including antioxidant, anti-proliferative, anti-inflammatory and anti-angiogenic effect (Heber, 2004). A meta-analysis of 47 studies indicated that soy or soy isoflavone can significantly reduce the level of follicle-stimulating hormone and luteinizing hormone in premenopausal women (Hooper et al., 2009). Several previous studies support the inverse association between soy food and breast cancer risk among Asian people, but a non-significant association is found among Western people (Qin et al., 2006; Wu et al., 2008; Dong et al., 2011). The major reason may come from the less soy food consumed by Western people than Chinese people.

Though the primary analysis and several subgroup analyses had shown high intake of soy and fruit was associated with decreased risk of breast cancer, 2 cohort studies had showed an increase in breast cancer risk (Shannon et al., 2005; Wang, 2007). After revising the 2 cohort studies, we had found a similar and more obvious aggregation of risk factors of breast cancer among the case group compared with the control group, including early age at menarche, less number of live births, late age at 1st live birth, less duration of breast-feeding, more length of oral contraceptive use, and so on. The imbalance distribution of these risk factors among the two groups inevitably can lead to confounding bias when the focus have shift to the dietary pattern. After adjusting age, total energy intake, and total years of breast-feeding, intake of fruit were still non-significantly associated with breast cancer risk. This indicates that other residual confounding may still exist and need more clarification.

As for vegetables and fruits, our results are in agreement with a recent meta-analysis of the prospective studies on fruit and vegetable intake and the risk of breast cancer (Aune et al., 2012),
which found non-significant associations for vegetables (OR = 0.99, 95% CI = 0.92–1.06) and weak associations for fruits (OR = 0.92, 95% CI = 0.86–0.98). However, a study of 20 cohort studies in European countries followed for 11 to 20 years showed non-significant associations for both vegetables and fruits with breast cancer (Jung et al., 2013). The previous report from the WCRF/AICR judged that diets high in vegetables and fruits probably protected against breast cancer. But in the 2nd report, it was stated that the evidence for an association between intake of fruits and non-starchy vegetables and breast cancer risk was too limited or inconsistent for a conclusion. With additional studies in Chinese population published after the report we found significant inverse associations between high versus low intake of fruits and breast cancer risk.

For fat, our finding showed that total fat intake was significantly associated with increased breast cancer risk in Chinese female. A previous meta-analysis included 45 studies (Boyd et al., 2003) reported that the association between total fat intake and breast cancer risk was significant in all women but non-significant in Asian women. But 6 Asian studies were included, and only 2 studies were conducted among Chinese female (Yu et al., 1990; Yuan et al., 1995). Furthermore, there was strong heterogeneity among the included study (Boyd et al., 1993). Though a recent systematic review (Turner, 2011) included more studies (57 studies in total) and also showed a non-significant association between total fat and breast cancer risk, only the 2 same Chinese studies (Yu et al., 1990; Yuan et al., 1995) were included.

Difference exists between our study and other studies may largely be attributed to the different amount of food consumption between Asian and Western populations. Our vegetables and soy intake is much higher than the west, while fruits and fat intake is lower than the west (Nan, 2006). In China, Japan, Singapore and other Asian countries and regions, the average daily intake of soy isoflavones is 25-50mg (Messina et al., 2006), while in the U.S. and Europe, the average daily intake of soy isoflavones is less than 1mg (Horn-Ross et al., 2001). What’s more, there is great difference in the type of soy food between Asia, U.S. and Europe. In Asia, soy food is consumed traditionally as tofu and soy milk, while in the U.S. and Europe, soy food is consumed mainly through adding soy ingredients intake to traditional western food (Wu et al., 2008).

There are potential limitations to our meta-analysis. First, substantial heterogeneity were both observed among included studies on vegetables, fruit, soy, and dietary fat. Though several subgroup analysis was used to explore the potential source of heterogeneity, no significant improvement were found on the heterogeneity. Second, the current systematic review cannot overcome the limitations in the original studies. Though a detailed protocol with explicit criteria for study selection and strict strategies for data extraction were developed before the study, the limitations in exposure definitions, dietary assessment, and population selection in the original will still affect the current results. Third, due to lack of individual information as in other systematic review, the current systematic review cannot control the potential confounding bias caused by other genetic and environmental factors of breast cancer, such as family history of cancer, voluntary and involuntary physical activity, as well as exposure to tobacco smoke and alcohol, et al. Therefore, it’s very necessary to interpret the current results carefully.

In conclusion, our results suggest that both soy food and fruit are significantly associated with decreased risk of breast cancer among Chinese females. And vegetable seems also be associated with decreased risk of breast cancer.

Acknowledgements

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