

## RESEARCH ARTICLE

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

Xue-Ou Liu<sup>1</sup>, Yu-Bei Huang<sup>1</sup>, Ying Gao<sup>2</sup>, Chuan Chen<sup>1</sup>, Ye Yan<sup>1</sup>, Hong-Ji Dai<sup>1</sup>, Feng-Ju Song<sup>1</sup>, Yao-Gang Wang<sup>2</sup>, Pei-Shan Wang<sup>1</sup>, Ke-Xin Chen<sup>1\*</sup>

### 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 (PubMed, 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;  $I^2=88.9%$ ,  $P<0.001$ ;  $N=13$ ) and 0.66 (95% CIs: 0.47–0.91;  $I^2=76.7%$ ,  $P<0.001$ ;  $N=7$ ), respectively. Consumption of fat was significantly associated with increased risk of breast cancer (OR=1.36; 95% CIs: 1.13–1.63;  $I^2=47.9%$ ,  $P=0.088$ ;  $N=6$ ). There was non-significant association between consumption of vegetables and breast cancer risk (OR=0.72; 95% CIs: 0.51–1.02;  $I^2=74.4%$ ,  $P<0.001$ ;  $N=9$ ). 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; Sangrajang et al., 2013), the conclusion is not consistent among the previous published studies, even in the studies

<sup>1</sup>Department of Epidemiology and Biostatistics, Tianjin Medical University Cancer Hospital and Institute, National Clinical Research Center for Cancer, Tianjin, China; Key Laboratory of Cancer Prevention and Therapy; Key Laboratory of Breast Cancer Prevention and Therapy, Tianjin Medical University, Ministry of Education, <sup>2</sup>Department of Social Medicines and Health Service Management, School of Public Health, Tianjin Medical University, Tianjin, China \*For correspondence: chenxin1963@yahoo.com

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 (PubMed, 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  $I^2$  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.,

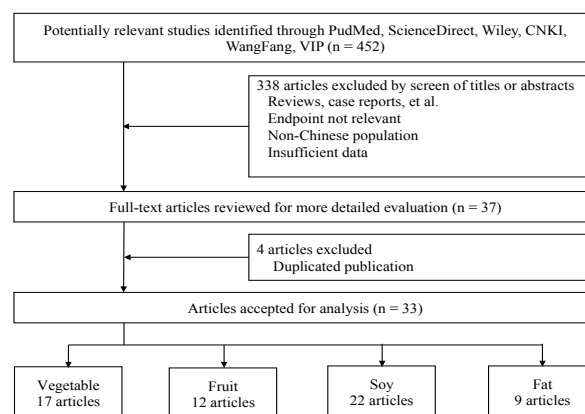


Figure 1. Flow Chart of Study Selection Process

**Table 1. Characteristics of Studies for Meta-analysis**

Author (year)	Region	Distribution	Design	No of cases	No of controls	Type of controls	Dietary assessment	Items	Intake comparison	NOS
DDai (2001)	Shanghai	eastern	Case-control	1459	1556	Population	24 h recall	Soy protein	>91.0g/wk vs < Occasionally	A
Kallianpur(2008)	Shanghai	eastern	Case-control	3452	3474	Population	Food freq <sup>ac</sup>	Fat	Fourth vs. first quartile	A
Shannon(2005)	Shanghai	eastern	Cohort	378	1070	Population	Food freq <sup>ac</sup>	Vegetable Fruit soyfood	≥18.2 vs ≤10.5 servings/wk ≥8.4 vs ≤3.9 servings/wk ≥7.7 vs ≤2.6servings /wk	A
Tao(2002)	Shanghai	eastern	Case-control	356	925	Population	Diet history	Soy	>3748 vs ≤798g/month	C
Yuan(1987)	Shanghai	eastern	Case-control	534	534	Population	Diet history	Fat	>72.5 vs <38.0g/day	B
Wang(2000)	Multicentre	Multicentral	Case-control	2063	2063	Population	Diet history	Fruit soy	>500 vs ≤500g/month >500 vs ≤500g/month	B
Lee(2005)	Taiwan	eastern	Case-control	250	219	Hospital	Food freq <sup>ac</sup>	Soy rich food Fat	>341 vs <114g/wk >98 vs <56g/day	B
Zhou(2009)	Jiangsu	eastern	Case-control	206	214	Population	Diet history <sup>c</sup>	Fruit Soy	>54.75 vs ≤36.5kg/year >6.5 vs ≤2.5kg/year	B
Li(2006)	Sichuan	western	Case-control	121	211	Population	Food freq <sup>ac</sup>	Vegetable Fruit Soy	>1 vs ≤1 servings/day >1 vs ≤1servings/day >1 vs ≤1 servings/day	B
Zhao(1999)	Sichuan	western	Case-control	265	265	Population	Diet history <sup>c</sup>	Vegetable Fruit Soybean Fat	>250 vs <250g/day >250 vs <250g/day >250 vs <250g/day >250 vs <250g/day	B
Zhu(2006)	Henan	central	Case-control	246	246	Hospital	Diet history	Soy highFat	yes/no yes/no	C
Tan(1998)	Hunan	central	Case-control	146	146	Hospital	Diet history	Vegetable Fruit		B
Cheng(2002)	Qinghai	western	Case-control	110	110	Hospital	Diet history	Vegetable Soy Fat		B
Zhang(2009)	Guangdong	eastern	Case-control	438	438	Hospital	Food freq <sup>ac</sup>	Vegetable Fruit	Fourth vs. first quartile Fourth vs. first quartile	B
Yu(2012)	Shandong	eastern	Case-control	103	309	Population	Diet history	Vegetable Bean products	5-7 vs 0 day/wk 5-7 vs 0 day/wk	B
Zheng(2010)	Yunan	western	Case-control	100	100	Hospital	Diet history	Vegetable		B
Cai(1996)	Ningxia	western	Case-control	100	100	Population	Diet history	soy		B
Guo(2010)	Shandong	eastern	Case-control	102	102	Population	Diet history	soy		B
Cheng(2010)	Xinjiang	western	Case-control	103	103	Population	Diet history <sup>c</sup>	Vegetable	>3 vs ≤3 servings/wk	B
Xu(1998)	Shandong	eastern	Case-control	186	186	Population	Food freq <sup>abc</sup>	Vegetable Soya-bean milk Fat	>400 vs <50g/day >100 vs <10ml/day >100 vs <50g/day	B
Wang(2008)	Beijing	eastern	Case-control	429	781	Population	Food freq <sup>ac</sup>	Soy products	>3 vs 0 servings/wk	C
Rong(2008)	Hebei	eastern	Case-control	175	175	Hospital	Food freq <sup>ac</sup>	Vegetable Fruit Soy	>3 vs <1 servings/wk >3 vs <1 servings/wk >3 vs <1 servings/wk	B
Qi(1990)	Tianjin	eastern	Case-control	244	244	Hospital	Food freq <sup>ac</sup>	Vegetable Fat	>600 vs <400g/day >100 vs <60g/day	B
Wang(2010)	Sichuan	western	Case-control	400	400	Population	Food freq <sup>a</sup>	Fat	≥77 vs <77g/day	A
Shen(2006)	Shanghai	eastern	Case-control	282	298	Population	Diet history <sup>c</sup>	Vegetable Fruit	>73 vs ≤73kg/year >41.6 vs ≤41.6kg/year	A
Ren(2008)	Liaoning	eastern	Case-control	200	200	Hospital	Diet history <sup>c</sup>	Vegetable Fruit Soy	>14 vs ≤7 servings/wk >14 vs <7 servings/wk >3 vs <2 servings/wk	B
Wang(2006)	Zhejiang	eastern	Conhort	84	269	Population	Diet history <sup>c</sup>	Vegetable Soy	>36 vs ≤7.2kg/year >4.800 vs ≤0.799kg/year	A
Han(2004)	Hubei	central	Case-control	213	430	Hospital	Diet history <sup>c</sup>	Vegetable Fruit Soy	>300g/d vs ≤300g/d >200g/d vs ≤200g/d >150g/d vs ≤150g/d	B
Zhang(2012)	Ningxia	western	Case-control	107	107	Hospital	Diet history <sup>c</sup>	Soy	>5 t/w vs <1 t/w	B
Liang(2012)	Guangdong	eastern	Case-control	168	168	Hospital	Diet history <sup>c</sup>	Soy	>500g/d vs ≤500g/d	B
Yao(2012)	Zhejiang	eastern	Case-control	200	200	Hospital	Diet history <sup>c</sup>	Fruit	>5t/w vs <3t/w	B
Luo(2013)	Sichuan	western	Case-control	116	240	Hospital	Diet history <sup>c</sup>	Soy		B
Bo(2013)	Sichuan	western	Case-control	210	210	Hospital	Food freq <sup>ac</sup>	Vegetable		B

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

2005; 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; Fang et al., 2009; 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). Four duplicate publications were excluded (Wang, 2000; Zhang et al., 2003; Zou et al., 2003; Fang et al., 2009). In total, 31 case-control studies (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; Dai et al., 2001; Chen, 2002; Tao et al., 2002; Han, 2004; Lee et al., 2005; Li et al., 2006; Shen et al., 2006; Zhu et

al., 2006; 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).

#### Soy

Eleven case-control studies and two cohort studies evaluated the association between soy intake and breast cancer risk. The summary OR for high versus low intake

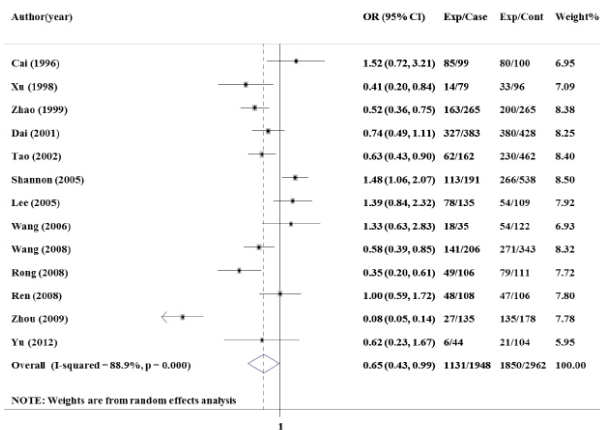


Figure 2. Forest Plot of Studies on the Association Between Soy and Breast Cancer

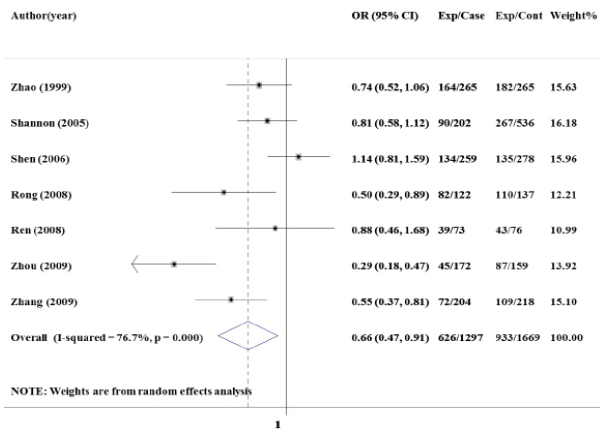


Figure 3. Forest Plot of Studies on the Association Between Fruit and Breast Cancer

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.

**Vegetable**

Seven case-control studies and two cohort studies

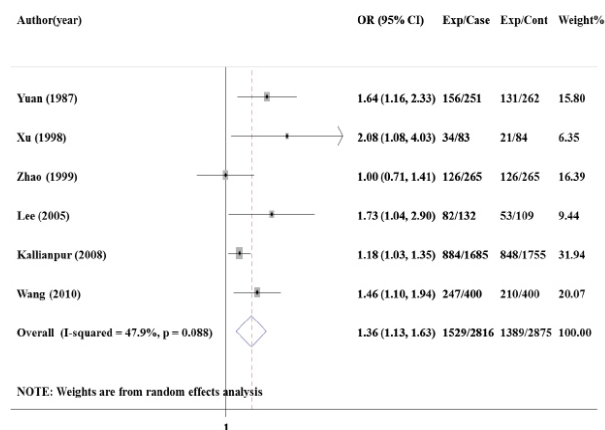


Figure 4. Forest Plot of Studies on the Association Between Fat and Breast Cancer

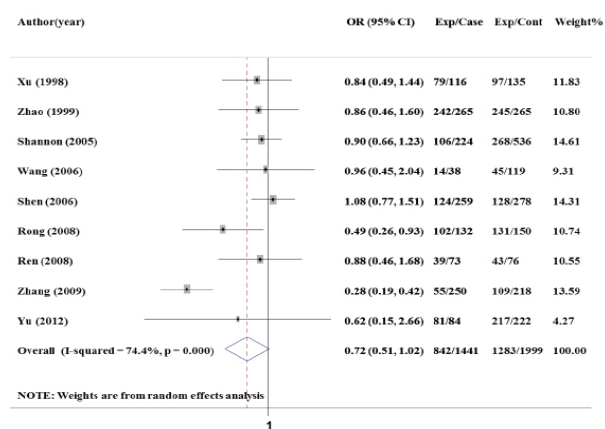


Figure 5. Forest Plot of Studies on the Association Between Vegetable and Breast Cancer

investigated the association between high versus low intake of vegetable and breast cancer risk. The summary OR for high versus low intake of vegetable was 0.72 (95 % CIs: 0.51–1.02), and substantial heterogeneity was observed ( $P < 0.001$ ,  $I^2 = 74.4\%$ ) (Figure 5). There was no evidence of publication bias with Egger’s test ( $P = 0.670$ ). 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=0.60; 95% CIs: 0.37-0.96), but non-significant association among other subgroup analyses. For fruit consumption, inverse association was found in case-control studies (OR=0.63; 95% CIs: 0.42-0.94), 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



Table 2. Subgroup Analyses of Food Intakes and Breast Cancer, High Versus Low Intake

Group	Vegetables				Fruits				Soy				Fat			
	No. of Studies	OR (95% CIs)	P <sub>heterogeneity</sub>	I <sup>2</sup> (%)	No. of Studies	OR (95% CIs)	P <sub>heterogeneity</sub>	I <sup>2</sup> (%)	No. of Studies	OR (95% CIs)	P <sub>heterogeneity</sub>	I <sup>2</sup> (%)	No. of Studies	OR (95% CIs)	P <sub>heterogeneity</sub>	I <sup>2</sup> (%)
Study design																
Cohort	2	0.91(0.68,1.21)	0.875	0	1	0.81(0.58,1.12)	0	0	2	1.46(1.07,1.98)	0.802	0	6	1.36(1.13,1.63)	0.088	47.9
Case-control	7	0.67(0.42,1.06)	0	78.8	6	0.63(0.42,0.94)	0	79.7	11	0.57(0.37,0.87)	0	87.3	2			
NOS level																
>7	3	0.97(0.78,1.21)	0.743	0	2	0.96(0.69,1.33)	0.158	49.9	3	1.12(0.68,1.84)	0.033	70.6	2	1.26(1.04,1.54)	0.18	44.3
5-7	6	0.60(0.37,0.96)	0.004	70.7	5	0.55(0.38,0.79)	0.018	66.4	8	0.54(0.28,1.06)	0	90.8	4	1.48(1.07,2.05)	0.087	54.4
<5									2	0.60(0.46,0.79)	0.765	0				
Sample size																
≤530	6	0.77(0.59,1.02)	0.746	0	4	0.55(0.34,0.90)	0.008	74.8	9	0.60(0.32,1.12)	0	90.2	3	1.45(0.90,2.31)	0.066	63.1
>530	3	0.65(0.31,1.40)	0	93	3	0.80(0.54,1.19)	0.021	74.1	4	0.80(0.51,1.25)	0.001	82.8	3	1.35(1.10,1.65)	0.126	51.7
Publication year																
<2007	5	0.94(0.78,1.15)	0.917	0	3	0.88(0.68,1.14)	0.191	39.7	8	0.88(0.62,1.26)	0	77.9	4	1.48(1.07,2.05)	0.087	54.4
≥2007	4	0.49(0.27,0.89)	0.025	68	4	0.50(0.33,0.76)	0.042	63.4	5	0.39(0.16,0.95)	0	91.9	2	1.26(1.04,1.54)	0.18	44.3

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% CIs = 0.92–1.06) and weak associations for fruits (OR = 0.92, 95% CIs = 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.

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## References

- Alexander DD, Morimoto LM, Mink PJ, Lowe KA (2010). Summary and meta-analysis of prospective studies of animal fat intake and breast cancer. *Nutr Res Rev*, **23**, 169-79.
- Aune D, Chan DS, Greenwood DC, et al (2012). Dietary fiber and breast cancer risk: a systematic review and meta-analysis of prospective studies. *Ann Oncol*, **23**, 1394-402.
- Aune D, Chan DS, Vieira AR, et al (2012). Fruits, vegetables and breast cancer risk: a systematic review and meta-analysis of prospective studies. *Breast Cancer Res Treat*, **134**, 479-93.
- Bo D, Zheng B, Zhang Y (2013). Analysis of risk factors on 210 patients of breast cancer. *Chin J Curr Adv Gen Surg*, **16**, 470-475.
- Boyd NF, Martin LJ, Noffel M, Lockwood GA, Trichler DL (1993). A meta-analysis of studies of dietary fat and breast cancer risk. *Br J Cancer*, **68**, 627-36.
- Boyd NF, Stone J, Vogt KN, et al (2003). Dietary fat and breast cancer risk revisited: a meta-analysis of the published literature. *Br J Cancer*, **89**, 1672-85.
- Cai SE (1996). An epidemic factor study of breast cancer in women in Ningxia. *Ningxia Medical Journal*, PLEASE SUPPLY, 1-3.
- Chen H (2002). A study of risk factors for female breast cancer in Xining. *Qinghai Med J*, **32**, 57-58.
- Chen WQ, Zheng RS, Zeng HM, et al (2012). Trend analysis and projection of cancer incidence in China between 1989 and 2008. *Zhonghua Zhong Liu Za Zhi*, **34**, 517-24.
- Cheng F, Muke D, Sima Y, et al (2010). A Case-control Study on Risk Factors of Uygur Nationality with Breast Cancer in Xinjiang Area. *Chinese JHealth Statistics*, **27**, 364-65, 368.
- Dai Q, Shu XO, Jin F, et al (2001). Population-based case-control study of soyfood intake and breast cancer risk in Shanghai. *Br J Cancer*, **85**, 372-8.
- Dong JY, Qin LQ (2011). Soy isoflavones consumption and risk of breast cancer incidence or recurrence: a meta-analysis of prospective studies. *Breast Cancer Res Treat*, **125**, 315-23.

- Egger M, Davey SG, Schneider M, Minder C (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, **315**, 629-34.
- Fang Y, Hu H (2009). The risk factors and their changes in breast cancer. *Chin J Health Stat*, 241-243+246.
- Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*, **127**, 2893-917.
- Guo Z, Ma S, Li M (2010). Case-control Study on Risk Factors of Breast Cancer in Tengzhou. *Chin J PHM*, **26**, 631-2.
- Han D (2004). The study of epidemiology and estrogen-metabolizing genes in Breast Cancer. PLEASE SUPPLY
- Heber D (2004). Vegetables, fruits and phytoestrogens in the prevention of diseases. *J Postgrad Med*, **50**, 145-9.
- Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003). Measuring inconsistency in meta-analyses. *BMJ*, **327**, 557-60.
- Hooper L, Madhavan G, Tice JA, Leinster SJ, Cassidy A (2010). Effects of isoflavones on breast density in pre- and post-menopausal women: a systematic review and meta-analysis of randomized controlled trials. *Hum Reprod Update*, **16**, 745-60.
- Hooper L, Ryder JJ, Kurzer MS, et al (2009). Effects of soy protein and isoflavones on circulating hormone concentrations in pre- and post-menopausal women: a systematic review and meta-analysis. *Hum Reprod Update*, **15**, 423-40.
- Horn-Ross PL, John EM, Lee M, et al (2001). Phytoestrogen consumption and breast cancer risk in a multiethnic population: the Bay Area Breast Cancer Study. *Am J Epidemiol*, **154**, 434-41.
- Jung S, Spiegelman D, Baglietto L, et al (2013). Fruit and vegetable intake and risk of breast cancer by hormone receptor status. *J Natl Cancer Inst*, **105**, 219-36.
- Kallianpur AR, Lee SA, Gao YT, et al (2008). Dietary animal-derived iron and fat intake and breast cancer risk in the Shanghai Breast Cancer Study. *Breast Cancer Res Treat*, **107**, 123-32.
- Kruk J, Marchlewicz M (2013). Dietary fat and physical activity in relation to breast cancer among Polish women. *Asian Pac J Cancer Prev*, **14**, 2495-502.
- Lee HP, Gourley L, Duffy SW, et al (1991). Dietary effects on breast-cancer risk in Singapore. *Lancet*, **337**, 1197-200.
- Lee MM, Chang IYH, Horng CF, et al (2005). Breast cancer and dietary factors in Taiwanese women. *Cancer Causes Control*, **16**, 929-37.
- Li S, Li J, Lei F, et al (2006). A case-control study on risk factors of breast cancer. *Mod Prev Med*, 2233-5.
- Liang ME (2012). The investigation and analysis of guangdong foshan area breast cancer risk factors. *Chin J Surg Oncol*, **4**, 159-60.
- Limer JL, Speirs V (2004). Phyto-oestrogens and breast cancer chemoprevention. *Breast Cancer Res*, **6**, 119-27.
- Luo E, Yang X, Wang X (2013). A case-control study in groups on risk factors of breast cancer. *J Chengdu Med Coll*, **8**, 269-73.
- Magee PJ, Rowland IR (2004). Phyto-oestrogens, their mechanism of action: current evidence for a role in breast and prostate cancer. *Br J Nutr*, **91**, 513-31.
- Messina M, Nagata C, Wu AH (2006). Estimated Asian adult soy protein and isoflavone intakes. *Nutr Cancer*, **55**, 1-12.
- Nan K (2006). Chinese dietary structure. Food and Nutrition in China.
- Parkin DM, Muir CS (1992). Cancer Incidence in Five Continents. Comparability and quality of data. *IARC Sci Publ*, 45-173.
- Qi X, Zhang A, Wu G, Pang W (1990). The association between breast cancer and diet. *Acta Nutrimenta Sinca*, 221-7.
- Qin LQ, Xu JY, Wang PY, Hoshi K (2006). Soyfood intake in the prevention of breast cancer risk in women: a meta-analysis of observational epidemiological studies. *J Nutr Sci Vitaminol*, **52**, 428-36.
- Ren X (2008). A 1:1 Case-Control Study on Risk Factors Of Breast Cancer. Dalian Medical University, Liaoning, China.
- Rong S, Li J, Zhang Y (2008). Relationship between Dietary Factors and Female Breast Cancer: a Case-control Study. *J Environ Health*, ??, ?? PLEASE SUPPLY
- Sangrajrang S, Chaiwerawattana A, Ploysawang P, et al (2013). Obesity, diet and physical inactivity and risk of breast cancer in thai women. *Asian Pac J Cancer Prev*, **14**, 7023-7.
- Shannon J, Ray R, Wu C, et al (2005). Food and botanical groupings and risk of breast cancer: a case-control study in Shanghai, China. *Cancer Epidemiol Biomarkers Prev*, **14**, 81-90.
- Shen Y, Li DK, Wu J, Zhang Z, Gao E (2006). Joint effects of the CYP1A1 MspI, ERalpha PvuII, and ERalpha XbaI polymorphisms on the risk of breast cancer: results from a population-based case-control study in Shanghai, China. *Cancer Epidemiol Biomarkers Prev*, **15**, 342-7.
- Stroup DF, Berlin JA, Morton SC, et al (2000). Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA*, **283**, 2008-12.
- Tan H, Liu A, Wang J, Li S (1998). A multiple variable analysis about the risk factors of breast cancer in women. *Hunan Yi Ke Da Xue Xue Bao*, **23**, 365-8.
- Tao M, Liu D, Gao L, Jin F (2002). Association between green tea drinking and breast cancer risk. *Tumor*, **22**, 176-80.
- Trock BJ, Hilakivi-Clarke L, Clarke R (2006). Meta-analysis of soy intake and breast cancer risk. *J Natl Cancer Inst*, **98**, 459-71.
- Turner LB (2011). A meta-analysis of fat intake, reproduction, and breast cancer risk: an evolutionary perspective. *Am J Hum Biol*, **23**, 601-8.
- Wang L, Liu L, Tao M, Qiu L, Ding H (2008). Relationship between diet and breast cancer in women. *Maternal Child Health Care China*, ??, ??
- Wang LD (2002). One of China's residents' nutrition and health survey report, People's Medical Publishing House.
- Wang Q, Li H, Tao P, et al (2011). Soy isoflavones, CYP1A1, CYP1B1, and COMT polymorphisms, and breast cancer: a case-control study in southwestern China. *DNA Cell Biol*, **30**, 585-95.
- Wang Q, Li L, Zhu W, Xing X, Zhou Y (2000). Study on risk factors of breast cancer among urban women in China. *Zhonghua Liu Xing Bing Xue Za Zhi*, **21**, 216-20.
- Wang XE (2000). Case-control of factors of breast cancer in Xining. *China Public Health*, **16**, 153-4.
- Wang Y (2007). Case-control Study on the risk Factors of Breast Cancer in Jiashan County. PLEASE SUPPLY
- Warri A, Saarinne NM, Makela S, Hilakivi-Clarke L (2008). The role of early life genistein exposures in modifying breast cancer risk. *Br J Cancer*, **98**, 1485-93.
- Wells GEA (2012). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. ??????
- Wu AH, Yu MC, Tseng CC, Pike MC (2008). Epidemiology of soy exposures and breast cancer risk. *Br J Cancer*, **98**, 9-14.
- Xu G, Lin X, Yu H, Zhao C, Zhao X (1998). The relationship between the dietary and breast cancer- a case control study. *Modern Preventive Medicine*, 427-429.
- Yao X, Ni S, Zhou J, et al (2012). A case-control study on risk

- factors of female breast cancer in Zhejiang province. *J Zhejiang Univ Medical Sciences*, **41**, 512-8.
- Yu SZ, Lu RF, Xu DD, Howe GR (1990). A case-control study of dietary and nondietary risk factors for breast cancer in Shanghai. *Cancer Res*, **50**, 5017-21.
- Yu ZG, Jia CX, Geng CZ, et al (2012). Risk factors related to female breast cancer in regions of Northeast China: a 1:3 matched case-control population-based study. *Chin Med J (Engl)*, **125**, 733-40.
- Yuan J, Gao Y, Yu MC, Henderson BE (1987). Risk factors for female breast cancer in Shanghai. *Tumor*, **7**, 244-8.
- Yuan JM, Wang QS, Ross RK, Henderson BE, Yu MC (1995). Diet and breast cancer in Shanghai and Tianjin, China. *Br J Cancer*, **71**, 1353-8.
- Zhang CX, Ho SC, Chen YM, et al (2009). Greater vegetable and fruit intake is associated with a lower risk of breast cancer among Chinese women. *Int J Cancer*, **125**, 181-8.
- Zhang H, Yu JJ, Liu L, Zhang PJ, Ni WS (2012). A Case-control Study on the Risk of Female Breast Cancer in Ningxia Areas. *JNingxia Med Univ*, **34**, 470-2.
- Zhang J, Xie Z, Zai S, et al (2003). Matched Case-Control Study for Detecting Risk Factors of Breast Cancer in Women Living in Xinxiang, Henan Province. *Henan J Oncol*, 201-203.
- Zhao Y, Shi Z, Liu L, et al (1999). Matched case-control study for detecting risk factors of Breast Cancer in women living in Chengdu. *Chin J Epidemiol*, **20**, 91-94.
- Zheng K, Zou T (2010). Case-control study on influential factors for breast cancer in women. *Med Pharm Yunnan*, **31**, 279-82.
- Zhou L, He T, Jin Y, Liu N, Shen Y (2009). A Case-control Study on Risk Factors of Breast Cancer. *Bull Chin Cancer*, **18**, 27-30.
- Zhu L, Li X (2006). A case-control study of risk factors for female breast cancer in Zhengzhou City. *Chin J Prim Med Pharm*, **13**, 679-80.
- Ziegler RG, Hoover RN, Pike MC, et al (1993). Migration patterns and breast cancer risk in Asian-American women. *J Natl Cancer Inst*, **85**, 1819-27.
- Zou L, Tian J, Wu H (2003). Case-control study on the risk factors of female breast cancer in Qingshan district of Wuhan city, China. Compilation Of National Oncology Nursing Academic Exchange Meeting, Dalian, Liaoning, China.