

# Adherence to Dietary Recommendations among Long-Term Breast Cancer Survivors and Cancer Outcome Associations

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## ABSTRACT

**Background:** Adherence to dietary recommendations has been shown to be associated with reduced mortality in healthy populations. Little is known about the possible benefits of adherence to dietary recommendations among breast cancer survivors.

**Methods:** Dietary information was collected using food frequency questionnaires at the 5-year postdiagnosis survey in 3,450 5-year breast cancer survivors from the Shanghai Breast Cancer Survival Study. Adherence scores to Chinese Food Pagoda (CHFP)-2007, CHFP-2016, modified Dietary Approaches to Stop Hypertension (DASH), and Healthy Eating Index 2015 (HEI-2015) were created. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for total mortality and breast cancer-specific events according to adherence scores.

**Results:** Participants in the highest quartiles of CHFP-2007, CHFP-2016, and DASH had 25% to 34% lower risk of total

mortality (HR, 0.66; 95% CI, 0.48–0.89 for CHFP-2007; HR, 0.75; 95% CI, 0.55–1.01 for CHFP-2016; HR, 0.66; 95% CI, 0.49–0.91 for DASH), and 36% to 40% lower risk of breast cancer-specific events (HR, 0.64; 95% CI, 0.44–0.93 for CHFP-2007; HR, 0.67; 95% CI, 0.45–0.99 for CHFP-2016; HR, 0.60; 95% CI, 0.40–0.90 for DASH) comparing with the lowest quartiles. Associations did not vary by known prognostic factors. HEI-2015 scores were not significantly associated with breast cancer outcomes.

**Conclusions:** Higher adherence to CHFP and DASH dietary guidelines post-cancer diagnosis was associated with reduced risk of both overall death and breast cancer-specific recurrence or death among long-term breast cancer survivors.

**Impact:** Our study highlights the importance of overall dietary quality among long-term breast cancer survivors.

## Introduction

Breast cancer is one of the most commonly diagnosed malignancies around the world (1). Long-term breast cancer survival is common, with 5-year relative survival rates around 90% in developed countries or regions (2, 3). In 2018, it was estimated that, within the previous 5 years, there were approximately 6.9 million female breast cancer survivors globally, constituting one sixth of all cancer survivors (4).

Worldwide, various dietary recommendations have been developed for general populations, including the Dietary Guidelines for Americans (assessed by the Healthy Eating Index, HEI; ref. 5) and Dietary Approaches to Stop Hypertension (DASH; ref. 6). Better adherence to these recommendations has been associated with lower risk of developing and/or dying from cardiovascular disease, diabetes, and cancer among healthy populations (7, 8). Healthy lifestyles, including healthy

dietary patterns, play an important role in breast cancer prognosis (9) and have been included in several breast cancer survivorship care guidelines (10, 11). However, little empirical evidence is available on whether these dietary recommendations apply to breast cancer survivors. A few studies have suggested that better adherence to HEI-2005 may be associated with reduced overall mortality among breast cancer survivors (12, 13).

In 2007, the Chinese Nutrition Society and Ministry of Health developed the Chinese Food Pagoda (CHFP) guideline for healthy dietary patterns for Chinese populations (14), which was updated in 2016 (15). Previously, we showed that better adherence to the CHFP-2007 in urban populations was associated with lower mortality from cancer, cardiovascular disease, and diabetes among middle aged and elderly Chinese women and men (16). Hereby, using prospective participant data from the Shanghai Breast Cancer Survival Study (SBCSS), we examined associations between adherence to the CHFP-2007/2016 and total mortality, as well as breast cancer-specific recurrence or/and death among 5-year breast cancer survivors, and further compared them with those adhering to American guidelines HEI-2015 and DASH.

## Materials and Methods

### Study population

The SBCSS is a longitudinal, population-based cohort study, including 5,042 women ages 25 to 70 years with a primary breast cancer diagnosis between March 2002 and April 2006 (17). All patients were identified from the population-based Shanghai Cancer Registry and recruited into the study approximately 6-months after breast cancer diagnosis. In-person follow-up surveys were conducted at approximately 1.5, 3, 5, and 10 years after diagnosis, with response rates of 92.8%, 88.2%, 82.5%, and 87.8% for the entire cohort, respectively

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**Note:** Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (<http://cebp.aacrjournals.org/>).

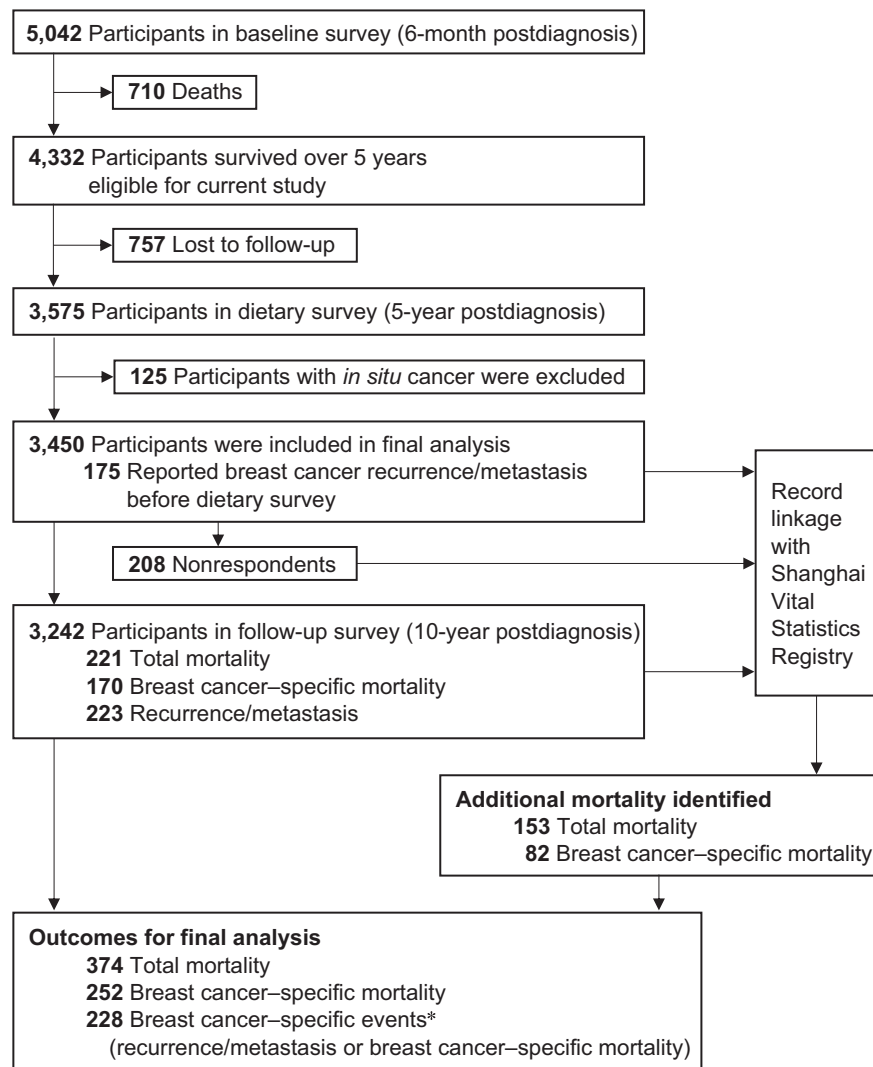
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**Figure 1.**  
Flowchart of study design.



\*Participants who reported breast cancer recurrence/metastasis before dietary survey ( $n = 175$ ) or participants who were lost to follow-up at 10-year postdiagnosis in-person follow-up survey and did not die from breast cancer ( $n = 189$ ) were excluded from breast cancer-specific events analyses, resulting in 3,088 participants and 228 events.

(Fig. 1). A total of 4,332 participants survived 5 years or longer after cancer diagnosis and were eligible for the current study. Among them, 3,575 (participation rate: 82.5%) completed the 5-year postdiagnosis in-person follow-up interview ( $5.3 \pm 0.2$  years after diagnosis) between October 2007 and October 2011 and completed a detailed dietary assessment. After exclusion of 125 cases with *in situ* breast cancer, 3,450 5-year survivors with invasive breast cancer (i.e., stage I to IV) were left for the current study. This study was approved by the Institutional Review Boards of all participating institutions, and written informed consent was acquired for all participants before recruitment. This study was conducted in accordance with the Declaration of Helsinki.

#### Data collection

All in-person surveys were carried out by trained interviewers using structured questionnaires. The 6-month survey collected demographic characteristics, reproductive history, personal and family disease

history, and selected lifestyle factors (alcohol, tea drinking, smoking, physical activity, soy food and cruciferous vegetable intake). Information on post-cancer diagnosis physical activity (i.e., type, frequency, duration and year of participation) was collected using a validated exercise questionnaire (18) at in-person follow-up surveys, and a metabolic equivalent of task (MET)-hours/week score was calculated for each participant (19). Self-reported information on selected diseases such as diabetes mellitus, hypertension, coronary heart disease, and stroke was also collected and used to derive the Charlson Comorbidity Index, with a score of zero indicating no comorbidity at cancer diagnosis (20). Height and weight measurements were taken following standard protocols. The above-mentioned information was updated at postdiagnosis follow-up surveys, at which disease recurrence and survival status were also assessed.

Clinical information, including cancer stage, tumor estrogen receptor (ER) status, progesterone receptor (PR) status, human epidermal growth factor receptor 2 (HER2) status, and primary treatments, was

collected from medical charts obtained from diagnostic hospitals. Breast cancer diagnoses were confirmed by a combination of medical records review and central review of pathological slides.

### Comprehensive dietary assessment at 5-year follow-up

Semiquantitative food frequency questionnaires (FFQ) containing 7 categories (grains; meat; dairy products; vegetables; fruits; nuts; and sugar, salt and oil) of 95 commonly consumed food items in the Shanghai area were administered to study participants. FFQs first asked questions on frequencies (daily, weekly, monthly, yearly or never), followed by quantities (liangs, 50 g) for each item consumed during the 12 months preceding the 5-year postdiagnosis survey. Validity and reproducibility of the FFQ were previously assessed among 191 female participants from the present study's region (21). The correlation coefficients, comparing two FFQs (intervals ranged from 1.65 to 2.66 years), were 0.37 to 0.66 for food group intake and 0.47 to 0.59 for nutrient and energy intakes. The ranges of correlation coefficients comparing FFQ and 24-hour dietary recalls were 0.41 to 0.66 for both food group and nutrient intakes. Energy and nutrient intakes were calculated on the basis of the Chinese Food Composition Table, 2002 (22). Dietary intakes were adjusted for total energy intake using the density method and standardized to 2,000 kcal/d.

### Dietary recommendation adherence scores

Recommendation adherence scores for CHFP-2007, CHFP-2016, DASH and HEI-2015 were created for each participant (5, 6, 14, 15). The CHFP-2007 and CHFP-2016 included the same 11 food groups, but with slightly different recommended intake amounts for: salt; fats and oil; dairy products; beans; meat and poultry; fish; eggs; vegetables; fruits; grains; and water (Supplementary Tables S1 and S2). Because of the lack of daily water intake data in our questionnaire, CHFP scores were calculated on the basis of 10 of the 11 components, with total scores ranging from 0 (lowest adherence) to 45 (highest adherence) points. Following the scoring method used to create the HEI-2005 (23), standards for maximum and 0 points for individual food items were determined by recommended dietary intakes, and intermediate intake scores were proportionately calculated between minimum and maximum (14, 15). For several food groups in the CHFP-2016, which includes a range of recommended intakes, the upper range value was used to derive scores. Similarly, modified DASH scores (0 to 70 points) were calculated on the basis of 7 components in the DASH eating plan: vegetables; fruits; dairy products; poultry, fish and eggs; nuts (nuts, beans, legumes); fats and oil; and sodium (Supplementary Table S3; ref. 6). Serving sizes were estimated by converting the amount consumed in grams, in our FFQ, to DASH servings (16).

Modified HEI-2015 scores included 12 of 13 components from recommendations for: total fruits; whole fruits; total vegetables; greens and beans; dairy; total protein; seafood and plant protein; refined grains; added sugars; fatty acids; sodium; and saturated fats (Supplementary Table S4; ref. 5). Information on whole grains was not collected in our FFQ due to low consumption in the Shanghai area; thus, was excluded in the HEI-2015 calculation. Three steps were used to calculate HEI-2015 (5). First, each FFQ food item was matched to 2015–2020 Dietary Guidelines for Americans (Eighth Edition) to determine the accurate food group, subgroup or nutrient for that item (24). Second, the amount of each relevant dietary subgroup was determined. Intake amounts were estimated by converting the amount consumed in grams, used in the SBCSS, to ounces or cups in the HEI-2015: g/oz was converted following the ratio of 1/28.3; g/cup followed the Food Patterns Equivalents Database, 2015–2016 Methodology and User Guide (25). Finally, component densities (i.e., amount of dietary

component per 1,000 kcal of energy intake) were derived and scored according to HEI-2015 totals (0 to 100 points). We counted legumes toward total vegetables and greens and beans.

### Outcome assessment

Information on breast cancer recurrence/metastasis, mortality and cause of death for current study participants was collected during the 10-year postdiagnosis in-person survey, with a response rate of 93.8%. Survival status and cause of death were supplemented by periodic record linkage to the Shanghai Vital Statistics Registry for SBCSS participants, including 208 non-respondents of the 10-year in-person survey, with the most recent linkage conducted December 31, 2017. Through the linkages, additional 153 total deaths, including 82 breast cancer-specific deaths, were identified for current study participants. Because of the extremely low out-migration rate in Shanghai, follow-up for vital status was approximately 100%.

Primary endpoints included in this study were total mortality (death from any cause), breast cancer-specific events (i.e., new recurrence, metastasis, or death related to breast cancer) and breast cancer-specific mortality occurring 5 years after cancer diagnosis. Participants who had breast cancer recurrence/metastasis before dietary survey ( $n = 175$ ), or participants who did not participate in the 10-year postdiagnosis in-person survey and did not die from breast cancer ( $n = 189$ ) at the latest record linkage were excluded from analyses for breast cancer-specific events. Cardiovascular disease was the most common cause of death other than breast cancer ( $n = 20$ ). Because of the low event rate, cause-specific mortality other than breast cancer was not evaluated.

### Statistical analysis

Participants were classified by quartile distributions of each dietary recommendation adherence score. Descriptive patterns for each group were compared using  $\chi^2$  tests for categorical variables and ANOVA for continuous variables. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for total mortality, breast cancer-specific events and breast cancer-specific mortality, in association with adherence scores, using age as a time scale. Entry time was set as age at dietary survey (i.e., 5-year postdiagnosis survey). Vital status was censored at the date of the last in-person follow-up survey or date of death due to causes other than breast cancer, whichever came first, for breast cancer-specific events and breast cancer-specific mortality analyses, and at date of death or the most recent linkage date for total mortality analyses. Two sets of HRs and 95% CI were presented, first with adjustment for age at dietary survey, interval between diagnosis and dietary survey, and total energy intake; second, with further adjustment for income (monthly personal income >1,000 yuan, or  $\leq 1,000$  yuan), education (high school or above; secondary school or lower), marriage (married or not), menopausal status at diagnosis (premenopausal or postmenopausal), BMI at dietary survey ( $\leq 25.0 \text{ kg/m}^2$  or  $> 25.0 \text{ kg/m}^2$ ), physical activity at dietary survey (categorized by median value, i.e., 9.58 mets-h/wk), ER status (positive, negative, or borderline), PR status (positive, negative, or borderline), HER2 status (positive, negative, borderline, or unknown), TNM stage (I, II, III–IV, or unknown), comorbidity (yes or no), chemotherapy (yes or no), radiation (yes or no), and immunotherapy (yes or no). HRs and 95% CIs for every 5-point increment of adherence scores were calculated by treating the scores as continuous variables. Linearity of the associations between dietary scores and all study endpoints were individually evaluated using restricted cubic spline function, and the linearity assumption was confirmed. Stratified analyses were conducted by ER status, PR status, HER2 status, TNM stage, education

(high school or above), income (monthly personal income >1,000 yuan), BMI at 6-month survey and at dietary survey (25.0 kg/m<sup>2</sup> as the cutoff), age at dietary survey, comorbidity at 6-month survey, and physical activity at dietary survey (median as the cutoff). Multiplicative interaction was evaluated by including both the main effect and interactive terms in Cox models, in which both dietary scores and stratified factors were treated as continuous variables. Sensitivity analyses were carried out by exclusion of participants with breast cancer recurrence/metastasis before dietary survey ( $n = 175$ ).

All statistical tests were based on two-sided probability, with significance level set at  $P < 0.05$ . Statistical analyses were performed using SAS (Version 9.4; SAS Institute Inc.) and R 3.5.1 (R Foundation).

## Results

A total of 3,450 5-year breast cancer survivors were included in the final analysis. In general, participant adherence scores to the 4 recommendations were correlated. Spearman's correlation coefficient was 0.95 between CHFP-2007 and CHFP-2016, 0.67 between CHFP-2007 and DASH, 0.64 between CHFP-2007 and HEI 2015, and 0.50 between DASH and HEI-2015 scores ( $P < 0.001$  for all). Mean ( $\pm$ SD) dietary adherence scores were  $35.2 \pm 5.3$  (range, 14.5–45.0) for CHFP-2007,  $31.5 \pm 5.4$  (range, 13.2–44.6) for CHFP-2016,  $43.4 \pm 8.3$  (range, 8.3–67.7) for DASH, and  $61.9 \pm 5.4$  for HEI-2015 (range, 38.0–78.5; Supplementary Tables S1–S4).

Higher adherence to CHFP-2007 was observed among younger participants (Table 1). Compared with participants within the lowest CHFP-2007 quartile (i.e., 14.5–31.6), those within the highest quartile (i.e., 39.2–45.0) had better education, higher income, and a higher rate of family history of breast cancer. These participants were also less likely to smoke or drink, and more likely to have higher physical activity and lower BMI. Higher proportions of early-stage cancer were observed among participants within the highest quartile, who were more likely to receive endocrine therapy and immunotherapy comparing with those with lowest adherence scores.

Over 8 years following the dietary survey, 374 deaths occurred, with 252 attributed to breast cancer (67.4%). Among participants who had no breast cancer recurrence/metastasis within 5 years post-cancer diagnosis, 228 developed a new breast cancer-specific event. Higher CHFP-2007, CHFP-2016, and DASH scores were associated with lower risk of total mortality, after adjustment for age, daily energy intake, interval between diagnosis and dietary survey, and additional potential confounders (i.e., BMI and physical activity at dietary survey). HRs of total mortality, comparing highest with lowest quartiles, were 0.66 (95% CI, 0.48–0.89) for CHFP-2007, 0.75 (95% CI, 0.55–1.01) for CHFP-2016, and 0.66 (95% CI, 0.49–0.91) for DASH. Every 5-point increment in adherence scores of the above CHFP-2007, CHFP-2016 and DASH recommendations was associated with an 7% to 13% reduction in total mortality risk. A similar tendency was observed for HEI-2015, though not significant (Table 2).

A total of 3,088 participants were included in the breast cancer-specific event analysis. Higher CHFP-2007 and DASH scores were associated with lower risk of breast cancer-specific events, with fully adjusted HRs of 0.64 (95% CI, 0.44–0.93) for CHFP-2007, and 0.60 (95% CI, 0.40–0.90) for DASH, comparing highest to lowest quartiles. Every 5-point increment in CHFP-2007, CHFP-2016, and DASH scores was associated with an 8% to 16% lower risk of breast cancer-specific events. HEI-2015 was not significantly associated with breast cancer-specific events (Table 3). Similar association patterns and point estimates were observed for breast cancer-specific mortality analyses (Supplementary Table S5, online only).

We found little evidence of modification from known/suspected prognostic factors in the stratified analyses for both dietary scores (Figs. 2 and 3; Supplementary Table S6, online only). Associations of adherence to individual dietary items with cancer outcomes were only significant for a few items (i.e., dairy product; fruits; and poultry, fish and eggs; Supplementary Tables S1–S4, online only). After excluding survivors who had breast cancer recurrence/metastasis before the dietary survey (e.g., within 5 years post-cancer diagnosis), associations of dietary adherence scores with total mortality or breast cancer-specific mortality remained essentially unchanged (Supplementary Tables S7, online only).

## Discussion

In this population-based prospective cohort study, we found that higher adherence to dietary recommendations, including CHFP and DASH, was similarly associated with reduced total mortality risk and breast cancer-specific recurrence and death among female, Chinese breast cancer long-term survivors. Associations with adherence to HEI-2015 were not significant.

Herein, we showed that dietary guidelines, originally designed toward general populations for the prevention of chronic disease (16), may also benefit female breast cancer survivors. It is worth mentioning that, compared with our previous study among healthy women in the same area (16), the mean CHFP-2007 score among 5-year breast cancer survivors was higher ( $35.2 \pm 5.3$  vs.  $33.4 \pm 4.2$ ), indicating possible improvements to dietary quality after breast cancer diagnosis. This is consistent with previous reports that cancer survivors tend to make healthier lifestyle choices following cancer diagnosis (26, 27). However, participants with low education or income showed lower adherence scores, indicating the importance of enhancing health promotion among these populations.

In general, our findings are supported by the Women's Health Initiative (WHI), which included 2,317 patients, with dietary intake assessed at 1.5 years after breast cancer diagnosis (12), as well as the Health, Eating, Activity, and Lifestyle (HEAL) Study, which conducted 30-month postdiagnosis dietary assessments among 670 breast cancer patients (13). Both studies, with median follow-ups of 6 (HEAL) and 9.6 (WHI) years, found that higher postdiagnosis adherence to HEI-2005 was associated with reduced risk of overall mortality among breast cancer survivors, by 60% (HR<sub>Q4:Q1</sub>:0.40; 95% CI, 0.17–0.94) in the HEAL Study, and 26% (HR<sub>Q4:Q1</sub>:0.74; 95% CI, 0.55–0.99) in the WHI. Similarly, the Life After Cancer Epidemiology (LACE) Study (28), which recruited 1,901 breast cancer survivors 11 to 39 months after cancer diagnosis, showed that increasing adherence to prudent dietary patterns was associated with decreasing risk of overall death (HR, 0.57; 95% CI, 0.36–0.90).

Furthermore, our study showed a 33% to 41% lower risk of breast cancer recurrence/metastasis or death and 30% to 42% lower breast cancer-specific mortality for 5-year breast cancer survivors with the highest adherence scores to dietary guidelines. This is consistent with the HEAL Study (13), but different from most other previous research studies (12, 28, 29), which showed no association at or beyond a 6-year follow-up period. However, none of these previous studies focused on long-term survivors (from 1.5 to 3.25 years after cancer diagnosis). It is possible that dietary intake has different effects on short- and long-term breast cancer outcomes. Events occurring shortly after cancer diagnosis may be heavily influenced by disease biology and cancer treatments, whereas influence of dietary intake may be too small to be identified. Plus, dietary intake is more variable and difficult to assess accurately during the period close to cancer diagnosis and treatment.

**Table 1.** Characteristics according to quartiles of CHFP-2007 score.

Characteristics	1st quartile (N = 870)	2nd quartile (N = 872)	3rd quartile (N = 843)	4th quartile (N = 865)	P
Age at survey (y)	60.7 ± 10.4 <sup>a</sup>	59.0 ± 10.0	58.3 ± 9.4	57.5 ± 8.9	<0.001
Interval between diagnosis and dietary survey (y)	5.3 ± 0.2	5.3 ± 0.2	5.3 ± 0.2	5.3 ± 0.2	0.25
CHFP-2007 score (median, [range]) <sup>b</sup>	28.9 (14.5–31.6)	33.8 (31.6–35.6)	37.4 (35.6–39.2)	41.3 (39.2–45.0)	<0.001
Total mortality	136	87	84	67	<0.001
Breast cancer-specific events	118	77	67	59	<0.001
Breast cancer-specific mortality	94	56	57	45	<0.001
High education (%) <sup>c</sup>	39.9	51.0	58.2	64.1	<0.001
High income (%) <sup>d</sup>	32.1	39.0	47.7	51.0	<0.001
Marriage (%)					<0.001
Married	84.7	86.7	89.6	91.3	
Otherwise	15.3	13.3	10.4	8.7	
Menopause at diagnosis (%)					<0.001
No	44.1	50.3	51.0	56.3	
Yes	55.9	49.7	49.0	43.7	
ER (%)					0.003
Positive	68.9	62.6	67.9	63.0	
Negative	30.1	35.6	31.7	36.3	
Unknown	1.0	1.8	0.5	0.7	
PR (%)					0.10
Positive	61.2	57.5	59.8	59.4	
Negative	37.4	40.5	39.6	39.7	
Unknown	1.5	2.1	0.6	0.9	
HER2 (%)					0.30
Positive	21.3	20.8	22.4	22.3	
Borderline	8.1	6.2	6.4	5.0	
Negative	50.7	51.8	53.0	51.2	
Unknown	20.0	21.2	18.2	21.5	
TNM stage (%)					0.06
I	34.1	38.9	38.2	39.7	
II	52.4	48.4	52.2	50.8	
III/IV	7.7	7.2	6.1	5.3	
Unknown	5.8	5.5	3.6	4.3	
Surgery (%)					0.29
Mastectomy	96.0	94.2	94.7	94.2	
Conservation	4.0	5.9	5.3	5.8	
Chemotherapy (%)	91.5	91.6	92.4	93.5	0.37
Endocrine therapy (%)	42.3	46.4	48.2	47.8	0.06
Radiotherapy (%)	29.4	29.8	31.1	30.6	0.87
Immunotherapy (%)	12.6	13.1	17.1	17.1	0.01
Family history of breast cancer (%)	5.9	4.2	5.3	6.9	0.10
Family history of cancer (%)	35.8	35.0	35.7	33.9	0.83
Ever drinking (%)	3.0	3.7	2.9	2.2	0.34
Ever smoking (%)	3.2	1.8	2.3	1.2	0.02
BMI at survey (kg/m <sup>2</sup> )	24.6 ± 3.8	24.5 ± 3.5	24.2 ± 3.5	24.0 ± 3.3	0.001
Physical activity at survey (MET-h/wk)	11.0 ± 14.0	12.8 ± 14.7	13.1 ± 14.4	14.6 ± 14.8	<0.001
Comorbidity at 6-month survey (%) <sup>e</sup>	28.7	19.2	16.7	14.3	<0.001

Abbreviations: BMI, body mass index; CHFP-2007, Chinese Food Pagoda 2007; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.

<sup>a</sup>Mean ± SD (all such values).

<sup>b</sup>The range may overlap across adjacent quartiles due to rounding to one digit.

<sup>c</sup>Defined as having a high school education or more.

<sup>d</sup>Defined as a monthly personal income >1,000 yuan.

<sup>e</sup>Comorbidity was assessed using Charlson Comorbidity Index, with a score of zero indicating no comorbidity at time of cancer diagnosis.

The Iowa Women's Health Study (IWHS; ref. 30), also showed that postdiagnosis adherence to dietary recommendations (according to the 2007 World Cancer Research Fund/American Institute for Cancer Research report; WCRF/AICR) was not significantly associated with breast cancer-specific mortality (HR, 0.88; 95% CI, 0.41–1.91). However, this study included only 938 breast cancer survivors who were

elderly women with an average age of 78.9 years at high competing risk of death (median comorbidity was two at dietary assessment; ref. 30).

The CHFP-2016 reflects more advanced knowledge in nutrition and recent evidence in the general population and may be relevant for current and future long-term breast cancer survivors. On the other hand, the dietary survey for our study participants was conducted

**Table 2.** HRs (95% CI) for total mortality by dietary recommendation adherence scores.

Dietary recommendations	Quartile of dietary recommendation adherence scores				By 5-point increase <sup>a</sup>	P <sub>trend</sub>
	1 (low)	2	3	4		
<b>CHFP-2007 score</b>	14.5-31.6	31.6-35.6	35.6-39.2	39.2-45.0	14.5-45.0	
No. of participants	870	872	843	865	3,450	
No. of events	136	87	84	67	374	
Age- and energy-adjusted HR <sup>b</sup>	1.00 (Ref.)	0.68 (0.52-0.89)	0.71 (0.54-0.93)	0.58 (0.43-0.78)	0.83 (0.76-0.91)	<0.001
Multivariable-adjusted HR <sup>c</sup>	1.00 (Ref.)	0.72 (0.55-0.95)	0.78 (0.59-1.04)	0.66 (0.48-0.89)	0.87 (0.79-0.96)	0.01
<b>CHFP-2016 score</b>	13.2-27.9	27.9-31.7	31.7-35.7	35.7-44.6	13.2-44.6	
No. of participants	874	846	880	850	3,450	
No. of events	133	95	76	70	374	
Age- and energy-adjusted HR <sup>b</sup>	1.00 (Ref.)	0.81 (0.62-1.06)	0.68 (0.51-0.91)	0.66 (0.49-0.89)	0.84 (0.76-0.92)	<0.001
Multivariable-adjusted HR <sup>c</sup>	1.00 (Ref.)	0.87 (0.67-1.14)	0.76 (0.57-1.02)	0.75 (0.55-1.01)	0.87 (0.79-0.96)	0.01
<b>DASH score</b>	8.3-38.2	38.2-44.1	44.1-49.3	49.3-67.7	8.3-67.7	
No. of participants	869	855	856	870	3,450	
No. of events	119	94	96	65	374	
Age- and energy-adjusted HR <sup>b</sup>	1.00 (Ref.)	0.86 (0.66-1.13)	0.90 (0.68-1.18)	0.62 (0.45-0.84)	0.91 (0.86-0.96)	0.001
Multivariable-adjusted HR <sup>c</sup>	1.00 (Ref.)	0.92 (0.70-1.21)	0.99 (0.75-1.30)	0.66 (0.49-0.91)	0.93 (0.87-0.98)	0.01
<b>HEI-2015 score</b>	38.0-58.7	58.7-61.9	61.9-65.8	65.8-78.5	38.0-78.5	
No. of participants	876	862	836	876	3,450	
No. of events	121	105	85	63	374	
Age- and energy-adjusted HR <sup>b</sup>	1.00 (Ref.)	1.09 (0.84-1.42)	0.98 (0.73-1.30)	0.74 (0.53-1.02)	0.90 (0.83-1.00)	0.05
Multivariable-adjusted HR <sup>c</sup>	1.00 (Ref.)	1.08 (0.82-1.42)	1.01 (0.76-1.36)	0.79 (0.57-1.10)	0.94 (0.85-1.03)	0.19

Abbreviations: CHFP-2007, Chinese Food Pagoda 2007; CHFP-2016, Chinese Food Pagoda 2016; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2015, Healthy Eating Index 2015; HR, hazard ratio; No., number.

<sup>a</sup>Linearity of associations between dietary scores and total mortality was tested using restricted cubic spline function. The *P* for linearity values for CHFP-2007, CHFP-2016, DASH, and HEI-2015 scores were 0.38, 0.35, 0.96, and 0.63, respectively.

<sup>b</sup>Cox regression model was adjusted for age at 60-month survey, intervals between diagnosis and 60-month survey, and total energy intake.

<sup>c</sup>Cox regression model was additionally adjusted for income, education, marriage, menopausal status at diagnosis, BMI at 60-month survey, physical activity at 60-month survey, ER, PR, HER2, TNM stages, comorbidity, chemotherapy, radiotherapy, and immunotherapy.

**Table 3.** HRs (95% CI) for breast cancer-specific events by dietary recommendation adherence scores.<sup>a</sup>

Dietary recommendations	Quartile of dietary recommendation adherence scores				By 5-point increase <sup>b</sup>	P <sub>trend</sub>
	1 (low)	2	3	4		
<b>CHFP-2007 score</b>						
No. of participants	14.5–31.6	31.6–35.6	35.6–39.2	39.2–45.0	14.5–45.0	
No. of events	769	768	758	793	3,088	
Age- and energy-adjusted HR <sup>c</sup>	1.00 (Ref.)	0.71 (0.51–1.00)	0.53 (0.37–0.78)	0.59 (0.41–0.85)	0.83 (0.73–0.93)	0.002
Multivariable-adjusted HR <sup>d</sup>	1.00 (Ref.)	0.77 (0.54–1.08)	0.55 (0.38–0.81)	0.64 (0.44–0.93)	0.84 (0.74–0.95)	0.01
<b>CHFP-2016 score</b>						
No. of participants	14.0–27.9	27.9–31.7	31.7–35.7	35.7–44.6	14.0–44.6	
No. of events	773	759	779	777	3,088	
Age- and energy-adjusted HR <sup>c</sup>	1.00 (Ref.)	0.93 (0.67–1.29)	0.55 (0.37–0.82)	0.62 (0.43–0.91)	0.82 (0.73–0.93)	0.001
Multivariable-adjusted HR <sup>d</sup>	1.00 (Ref.)	0.98 (0.70–1.37)	0.58 (0.39–0.87)	0.67 (0.45–0.99)	0.84 (0.74–0.95)	0.01
<b>DASH score</b>						
No. of participants	10.0–38.2	38.2–44.1	44.1–49.3	49.3–67.7	10.0–67.7	
No. of events	700	717	701	742	3,088	
Age- and energy-adjusted HR <sup>c</sup>	1.00 (Ref.)	0.92 (0.65–1.29)	0.83 (0.58–1.18)	0.57 (0.38–0.84)	0.90 (0.84–0.98)	0.01
Multivariable-adjusted HR <sup>d</sup>	1.00 (Ref.)	0.96 (0.68–1.36)	0.88 (0.61–1.26)	0.60 (0.40–0.90)	0.92 (0.85–0.99)	0.03
<b>HEI-2015 score</b>						
No. of participants	38.0–58.7	58.7–61.9	61.9–65.8	65.8–78.5	38.0–78.5	
No. of events	780	766	757	785	3,088	
Age- and energy-adjusted HR <sup>c</sup>	1.00 (Ref.)	1.05 (0.74–1.49)	0.88 (0.61–1.28)	0.82 (0.55–1.21)	0.91 (0.80–1.03)	0.12
Multivariable-adjusted HR <sup>d</sup>	1.00 (Ref.)	1.06 (0.74–1.52)	0.90 (0.61–1.32)	0.89 (0.59–1.33)	0.92 (0.81–1.05)	0.23

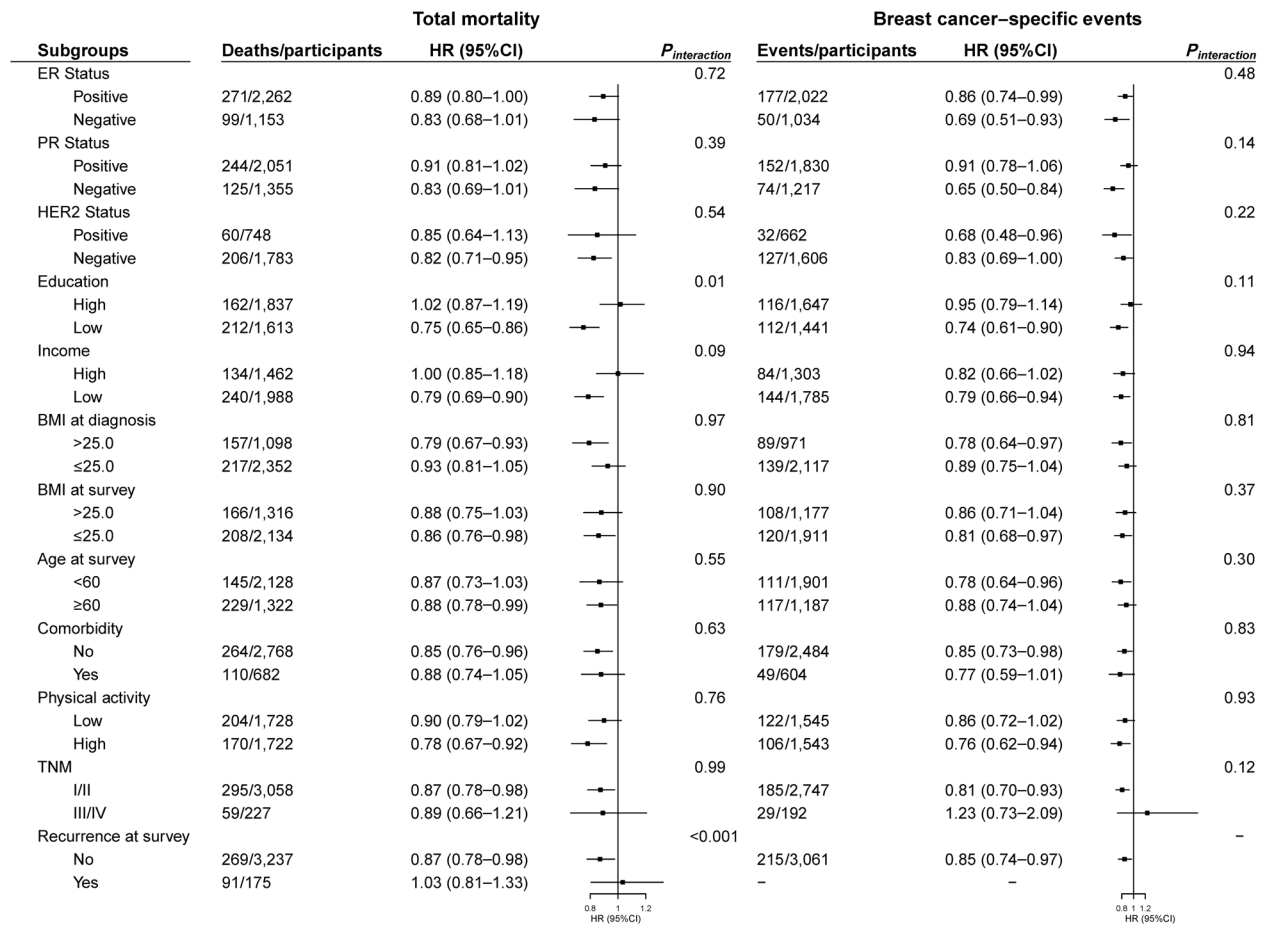
Abbreviations: CHFP-2007, Chinese Food Pagoda 2007; CHFP-2016, Chinese Food Pagoda 2016; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2015, Healthy Eating Index 2015; HR, hazard ratio; No., number.

<sup>a</sup>Breast cancer-specific events were defined as recurrence or metastasis of breast cancer and deaths from breast cancer. Participants who had recurrence or metastasis of breast cancer before dietary survey (N = 175) or participants who were lost to follow-up at 10-year in-person follow-up and did not die from breast cancer (N = 189) were excluded from the analyses, resulting in 3,088 participants and 228 events.

<sup>b</sup>Linearity of associations between dietary scores and breast cancer-specific events was tested using restricted cubic spline function. The P<sub>linearity</sub> values for CHFP-2007, CHFP-2016, DASH, and HEI-2015 scores were 0.54, 0.75, 0.42, and 0.10, respectively.

<sup>c</sup>Cox regression model was adjusted for age at 60-month survey, intervals between diagnosis and 60-month survey, and total energy intake.

<sup>d</sup>Cox regression model was additionally adjusted for income, education, marriage, menopausal status at diagnosis, BMI at 60-month survey, physical activity at 60-month survey, ER, PR, HER2, TNM stages, comorbidity, chemotherapy, radiotherapy, and immunotherapy.



**Figure 2.** HRs (95% CI) for total mortality and breast cancer-specific events by CHFP-2007 score in stratified analyses. Breast cancer-specific events were defined as new recurrence or metastasis of breast cancer and deaths from breast cancer. Participants who reported breast cancer recurrence/metastasis before dietary survey (*n* = 175) or participants who were lost to follow-up at 10-year postdiagnosis in-person follow-up survey and did not die from breast cancer (*n* = 189) were excluded from breast cancer-specific events analyses. Cox regression model was adjusted for age at 60-month survey, intervals between diagnosis and 60-month survey, total energy intake, income, education, marriage, menopausal status at diagnosis, BMI at 60-month survey, physical activity at 60-month survey, ER, PR, HER2, TNM stages, comorbidity, chemotherapy, radiotherapy, and immunotherapy. HR was shown for every 5-point increase. BMI, body mass index; CI, confidence interval; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; PR, progesterone receptor.

between 2007 and 2011, during which the CHFP-2007 was the official dietary recommendation. Therefore, both dietary scores were included in the current study. We found significant associations only for the CHFP-2007, but not for the CHFP-2016 score. Both guidelines include the same food components, but the CHFP-2016 includes ranges of recommended intakes for many food groups. We applied the upper limits of recommended ranges in our scoring, which resulted in lower overall CHFP-2016 scores than CHFP-2007 and may have introduced misclassifications in the CHEF-2016 score, resulting lower statistical power. Therefore, our findings based on the 2016 guidelines should be interpreted with caution.

Few studies have investigated dietary patterns—breast cancer outcome associations by cancer subtypes. We found that association patterns did not differ across ER, PR, or HER2 subgroups. This is consistent with the WHI Study, which showed no significant interactions between HEI-2005 score and ER status (*P* = 0.45; ref. 12). In our study, known/suspected prognostic factors such as BMI and physical activity also did not modify the associations. The latter was consistent with findings from both HEAL and LACE studies (14, 28),

indicating that the benefit from better-quality dietary habits may be independent from other lifestyle factors.

We found little evidence to support that individual dietary components were significantly associated with breast cancer outcomes. The WHI Study (12), as well as the study by Beasley and colleagues (31), which included 4,441 female breast cancer survivors within 5 years of diagnosis, with follow-up periods of 5 and 9.6 years, also did not find significant associations of individual dietary item intake with breast cancer outcome. According to the WCRF/AICR report (11), there is still not enough strong evidence to make specific dietary recommendations for breast cancer survivors. These results indicate that overall dietary patterns, rather than individual dietary components, should be promoted among breast cancer survivors.

The biologic mechanisms for dietary adherence and cancer outcome associations are not entirely understood. Research has shown that breast cancer survivors with higher HEI-2005 or HEI-2010 scores had lower serum proinflammatory cytokines (32, 33), which are believed to be related to breast cancer growth (34). Nonetheless, because our study was an observational cohort study, this association should be



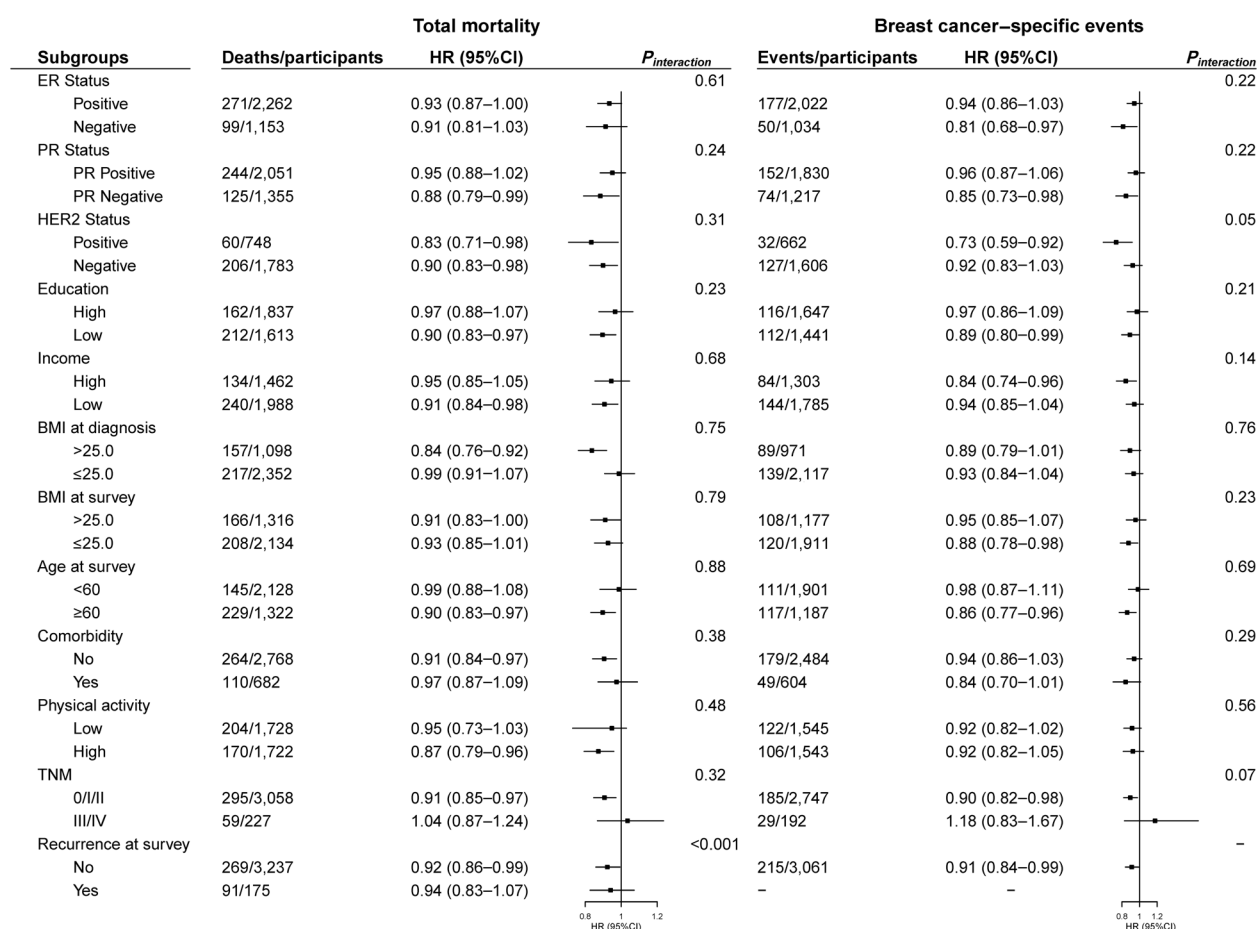


Figure 3.

HRs (95% CI) for total mortality and breast cancer-specific events by DASH score in stratified analyses. Breast cancer-specific events were defined recurrence or metastasis of breast cancer after dietary survey and deaths from breast cancer. Participants who reported breast cancer recurrence/metastasis before dietary survey ( $n = 175$ ) or participants who were lost to follow-up at 10-year postdiagnosis in-person follow-up survey and did not die from breast cancer ( $n = 189$ ) were excluded from breast cancer-specific events analyses. Cox regression model was adjusted for age at 60-month survey, intervals between diagnosis and 60-month survey, total energy intake, income, education, marriage, menopausal status at diagnosis, BMI at 60-month survey, physical activity at 60-month survey, ER, PR, HER2, TNM stages, comorbidity, chemotherapy, radiotherapy, and immunotherapy. HR was shown for every 5-point increase. BMI, body mass index; CI, confidence interval; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; PR, progesterone receptor.

interpreted with caution, and future mechanical research and possible interventional studies are needed.

One of the most important advantages of our study is the employment of multidimensional dietary recommendations, which enabled us to investigate multiple dietary components as a whole. Further strengths of our study include a large sample size of long-term breast cancer survivors, a narrow window of dietary assessment ( $5.3 \pm 0.2$  years post-cancer diagnosis), a population-based prospective study design, and long-term and complete mortality follow-up, as well as comprehensive information on cancer characteristics, treatments and postdiagnosis activity, which provided us adequate statistical power, even in our stratified analyses. Our study also has some limitations. First, although FFQs used in our study were validated and administered by in-person interviewers, dietary measurement errors are inevitable. Second, miscalculation of dietary scores could not be ruled out, especially for the CHFP-2016, in which ranges of intakes are recommended for several food groups. Third, some dietary components originally proposed in the HEI-2015 were not included in our questionnaires because of low consumption in our study area (e.g., refined grains and whole grains;

ref. 35). In addition, consumption of some items was estimated by converting the amount in grams to serving sizes in cups, following food pattern guidelines, which may underestimate predictive values for DASH and HEI-2015. Fourth, we cannot completely rule out the possible misclassification of self-reported recurrence/metastasis due to lack of adjudication. However, the in-person survey rate for our study population was high (93.8%), and because recurrence/metastasis are serious outcomes, cancer survivors are less likely to make that mistake. Last but not the least, there is a potential over-attribution of breast cancer-specific death among breast cancer survivors.

In summary, in this large prospective cohort study including 3,450 5-year breast cancer survivors, we found that higher adherence to dietary guidelines was associated with reduced risk of both overall deaths, and breast cancer-specific recurrence or/and death. Our findings support that long-term breast cancer survivors would benefit from adherence to either Chinese or US dietary guidelines directed toward the general population for chronic disease prevention, and healthy dietary patterns should be included in health promotion and management for long-term breast cancer survivors.

## Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

## Authors' Contributions

**Conception and design:** D. Yu, P. Bao, X.-O. Shu

**Development of methodology:** D. Yu, Y. Zheng, X.-O. Shu

**Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.):** K. Gu, L. Shi, D. Yu, M. Zhang, W. Zheng, Y. Zheng, P. Bao, X.-O. Shu

**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** F. Wang, H. Cai, D. Yu

**Writing, review, and/or revision of the manuscript:** F. Wang, H. Cai, D. Yu, W. Zheng, X.-O. Shu

**Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases):** H. Cai, P. Bao, X.-O. Shu

**Study supervision:** Y. Zheng, X.-O. Shu

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