Dietary patterns and endometrial cancer: a meta-analysis
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Previous studies have attempted to assess the relation between different dietary patterns and the risk of endometrial cancer (EC); however, a consistent perspective has not been established to date. Therefore, we carried out this meta-analysis to evaluate the associations between dietary patterns and the risk of EC. The most common dietary patterns with high loadings of foods and/or nutrients were selected. A total of 27 studies fulfilled the inclusion criteria and were included in the present meta-analysis. There was evidence of a decreased risk of EC in the highest compared with the lowest category of healthy dietary pattern [odds ratio (OR) = 0.74; confidence interval (CI): 0.62–0.88; \( P = 0.008 \)]. An increased risk of EC was shown for the highest compared with the lowest category of a western-style dietary pattern (OR = 1.37; CI: 1.15–1.64; \( P = 0.0005 \)). No significant association with the risk of EC was found in the highest compared with the lowest category of alcohol-drinking pattern (OR = 0.98; CI: 0.73–1.30; \( P = 0.87 \)). The results of this meta-analysis indicate that some dietary patterns may be associated with the risk of EC. European Journal of Cancer Prevention 00:000–000 Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

Keywords: dietary patterns, endometrial cancer, meta-analysis

Methods

Introduction

Endometrial cancer (EC) is the second most common gynecologic malignancy worldwide, with \( \sim 0.3 \) million new cases in 2012 (Gong \textit{et al.}, 2015). It is estimated that in China, EC has an incidence rate more than 10 times lower than that in developed countries (Parkin \textit{et al.}, 2003). In the USA, among women, EC is the fourth most common incident cancer, with an estimated 47,130 new cases in 2012 (Leitao \textit{et al.}, 2013). Known risk factors for EC include a history of hypertension and diabetes mellitus, obesity, late age at menopause, early menarche, and use of exogenous hormone replacement therapy (Yeh \textit{et al.}, 2009). In addition, dietary factors have also been considered to play an important role in the etiology of EC (Cook \textit{et al.}, 2006).

In the past few decades, information on the role of dietary patterns and the risk of EC has been limited. Many epidemiological studies of dietary influences on EC risk have largely focused on the investigations of specific foods or nutrients (Bravi \textit{et al.}, 2009; Kallianpur \textit{et al.}, 2010; Coleman \textit{et al.}, 2014). However, because of the complexity of diets and the potential interactions between food components (Lancaster \textit{et al.}, 2004), this analysis found limited impact of diets on chronic non-communicable diseases, including EC. In this context, dietary pattern analysis emerged as a more recognizable approach because it takes into account the combined effects of foods and potentially facilitates nutritional recommendations (Hu, 2002).

Recently, a number of studies have attempted to examine the association between dietary patterns and the risk of EC (Biel \textit{et al.}, 2011; Bravi \textit{et al.}, 2015; Canchola \textit{et al.}, 2015). Nevertheless, the results of an association between dietary patterns and the risk of EC were inconsistent. In the last report on EC by the World Cancer Research Fund and the American Institute for Cancer Research (Wiseman, 2008), there is limited evidence suggesting that red meat is a risk factor for EC. Therefore, we carried out a systematic meta-analysis of studies published from January 1990 up to May 2015 to further identify the role of different dietary patterns in the development of EC.

Keywords: dietary patterns, endometrial cancer, meta-analysis

Methods

Literature search strategy

A literature search of MEDLINE and EBSCO databases was performed to identify relevant studies written in the English and Chinese languages published from January 1990 up to May 2015 with the following keywords or phrases: ‘dietary pattern’ OR ‘dietary patterns’ OR ‘eating pattern’ OR ‘eating patterns’ OR ‘food pattern’ OR ‘food patterns’ OR ‘diet’ OR ‘alcohol drinking’ OR ‘alcohol consumption’ AND ‘endometrial neoplasms’ OR ‘endometrial cancer’ OR ‘endometrial tumor’ OR ‘endometrial carcinoma’. In addition, we manually searched all references cited in original studies and reviews identified.
Inclusion criteria of studies
Two of the authors (C.J. Si and L. Shu) read the abstracts of articles retrieved in the initial search to identify studies that examined the associations between dietary patterns and risk of EC. When all the authors agreed (L. Shu, C.J. Si, and P.F. Zheng), the articles were reviewed against inclusion and exclusion criteria for this meta-analysis. To be eligible, the studies had to fulfill the following criteria: (i) the study was an original report investigating the association between food and/or dietary patterns and the risk of EC; (ii) full-length journal articles were reviewed to identify studies that examined food and/or food patterns by factor analysis and/or principal component analysis; (iii) odds ratios (ORs) and percentage of EC (or sufficient information to calculate them) had been listed; and (iv) EC was diagnosed on the basis of review of medical charts and available pathological slides.

To minimize error, the authors ensured that the selected dietary patterns were similar with respect to factor loadings of foods which are consumed within those dietary patterns. For example, the first pattern, named a healthy pattern, is characterized by high loadings of foods such as fresh vegetables and fruit, whole grains, fish, soy and antioxidants (e.g. vitamins C and E, flavonoids, and carotenoids), and low-fat dairy. The papers under consideration labeled it as ‘healthy’ (McCann et al., 2001), ‘fruit and vegetable’ (Tao et al., 2005; Terry et al., 2002), ‘plant-based’ (Zheng et al., 1995; Dalvi et al., 2007; Biel et al., 2011; Canchola et al., 2015), and ‘total vegetables’ (McCann et al., 2000; Yeh et al., 2009). The second pattern was named a ‘western-style’ dietary pattern, which is characterized by high consumption of red and/or processed meat, refined grains, sweets, high-fat dairy products, butter, potatoes, and high-fat gravy, and low intakes of fruits and vegetables. The articles labeled it as ‘red meat intake’ (Shu et al., 1993; McCann et al., 2000; Tavani et al., 2000; Genkinger et al., 2012; Arem et al., 2013), ‘meat/all meat’ (Potischman et al., 1993; Xu et al., 2006; van Lonkhuijzen et al., 2011; Biel et al., 2011; Terry et al., 2002), ‘Western-type/western’ (Dalvi et al., 2007; Bravi et al., 2015), ‘high-fat’ (McCann et al., 2001; Canchola et al., 2015), and ‘animal food’ (Zheng et al., 1995). The third pattern, called the ‘alcohol-drinking’ pattern, included high consumption of beers, wines, and white spirits. The articles labeled this as ‘alcohol drinking’ (Hosono et al., 2008; Fedirko et al., 2013; Parazzini et al., 1995), ‘alcohol consumption’ (Newcomb et al., 1997; Loerbroks et al., 2007), and ‘alcohol intake’ (Setiawan et al., 2008; Yang et al., 2011; Je et al., 2014). Finally, 27 studies relevant to the role of dietary patterns and/or food and the risk of EC were included in our analyses.

Data extraction
We extracted the following data from all included studies: the authors, the year of publication, geographic location, the study design, the sample size, percentage of EC, the number in each dietary pattern, the method of assessment of diet, identification of dietary patterns, and the factors that were adjusted for in the analysis.

Definition of ‘high intake’
Dietary patterns were identified by principal component analysis or factor analysis. Factor scores for each pattern were categorized into tertiles, quartiles, or quintiles (the lowest category and the highest category represented low and high intake, respectively, of each dietary pattern). The different forms of alcohol consumption were converted into grams of ethanol per day. Alcohol consumption of less than 12.5 g/day or 1 drink/day was defined as low consumption of alcohol and more than 25 g/day or 2 drinks/day was defined as high consumption of alcohol (Turati et al., 2010).

Assessment of heterogeneity
Heterogeneity of study results was measured by Cochran’s $Q$-statistic and the $I^2$-statistic. A $P$-value for the $Q$-test of more than 0.10 or $I^2$ less than 50% indicated an absence of heterogeneity between studies and a fixed-effects model was used to calculated the pooled ORs. If a $P$-value for the $Q$-test of up to 0.10 or $I^2$ of at least 50% indicated a high degree of heterogeneity among studies, then a random-effects model (DerSimonian and Laird method) was used (Higgins et al., 2003).

Quality assessment
The Newcastle–Ottawa Quality Assessment scale was used for quality assessment (Stang, 2010). Eight questions were assessed and each satisfactory answer received one point (they may receive two points in comparability categories), resulting in a maximum score of 9. Only those studies in which most of the questions were deemed satisfactory (i.e. with a score of 6 or higher) were considered to be of high methodological quality.

Statistical analysis
Statistical analyses were carried out using Review Manager, version 5.0 (Nordic Cochrane Centre, Copenhagen, Denmark) and STATA, version 12 (Stata Corp., College Station, Texas, USA). All statistical tests were two sided and $P$ values less than 0.05 were considered significant. The original papers reported the results of dietary patterns in terms of tertiles, quartiles, and quintiles of dietary factor scores and the risk of EC. We used meta-analysis to evaluate the risk of EC in the highest versus the lowest categories of healthy, western-style, and alcohol-drinking patterns. Random-effects models were used to calculate the pooled OR for dietary patterns in the highest categories compared with the lowest categories. ORs and 95% confidence intervals (CIs) from individual studies were combined to produce an overall OR. Publication bias was assessed by inspection of the funnel plot and by formal testing for ‘funnel plot’ asymmetry using Begg’s test and Egger’s test (Begg et al., 1994).
Sensitivity analysis was carried out to determine whether differences in study design, sample size, age, and races affected study conclusions.

**Results**

**Overview of included studies for the systematic review**

An electronic literature search in the database of MEDLINE and EBSCO identified 417 studies, 390 of which were excluded on the basis of the reasons listed in Fig. 1. Twenty-seven articles (Potischman et al., 1993; Shu et al., 1993; Parazzini et al., 1995; Zheng et al., 1995; Newcomb et al., 1997; McCann et al., 2000; Tavani et al., 2000; Kasum et al., 2001; McCann et al., 2001; Terry et al., 2002; Tao et al., 2005; Xu et al., 2006; Dalvi et al., 2007; Loerbroks et al., 2007; McCullough et al., 2007; Hosono et al., 2008; Setiawan et al., 2008; Yeh et al., 2009; Biel et al., 2011; van Lonkhuijzen et al., 2011; Yang et al., 2011; Genkinger et al., 2012; Arem et al., 2013; Fedirko et al., 2013; Je et al., 2014; Bravi et al., 2015; Canchola et al., 2015) fulfilled the inclusion criteria and were included in this meta-analysis, including 12 (Zheng et al., 1995; Kasum et al., 2001; Loerbroks et al., 2007; McCullough et al., 2007; Setiawan et al., 2008; van Lonkhuijzen et al., 2011; Yang et al., 2011; Genkinger et al., 2012; Arem et al., 2013; Fedirko et al., 2013; Je et al., 2014; Canchola et al., 2015) cohort studies and 15 (Potischman et al., 1993; Shu et al., 1993; Parazzini et al., 1995; Newcomb et al., 1997; McCann et al., 2000; Tavani et al., 2000; McCann et al., 2001; Terry et al., 2002; Tao et al., 2005; Xu et al., 2006; Dalvi et al., 2007; Hosono et al., 2008; Yeh et al., 2009; Biel et al., 2011; Bravi et al., 2015) case–control studies. Study characteristics are presented in Table 1.

**Healthy dietary pattern**

The healthy dietary pattern is characterized by high intake of vegetables, fruits, whole grains, olive oil, fish, soy, poultry, and low-fat dairy. Figure 2 shows obvious evidence of a decreased risk of EC in the highest compared with the lowest category of a healthy dietary pattern (OR = 0.74; CI: 0.62–0.88; P = 0.0008). A random-effects model was used to assess the data included in our analyses. The heterogeneity was apparent in all the studies (P < 0.00001; I² = 72%).

**Western-style dietary pattern**

The western-style dietary pattern is characterized by high consumption of red and/or processed meat, refined grains, sweets, high-fat dairy products, butter, potatoes and high-fat gravy, and low intakes of fruits and vegetables. The association between a western-style dietary pattern and the risk of EC is shown in Fig. 3. There was evidence of an increased risk of EC in the highest compared with the lowest category of a western-style dietary pattern (OR = 1.37; CI: 1.15–1.64; P = 0.0005) where all studies were combined in the random-effects model. There was significant heterogeneity (I² = 81%; P < 0.00001).

**Alcohol-drinking pattern**

The alcohol-drinking pattern is characterized by high consumption of alcohol-containing beers, wines, and white spirits. Eight articles were identified that referred to (or included the) alcohol-drinking pattern in this meta-analysis (Fig. 4). No significant association with the risk of EC was found in the highest compared with the lowest category of alcohol-drinking pattern (OR = 0.98; CI: 0.73–1.30; P = 0.87). Data from these studies were assessed using a random-effects model and there was obvious evidence of heterogeneity (P = 0.0001; I² = 76%).

**Publication bias**

Inspection of funnel plots did not show evidence of asymmetry. Begg’s tests for publication bias were not statistically significant (highest compared with lowest category: healthy dietary pattern, P = 0.891; Western-style dietary pattern, P = 0.656; and alcohol-drinking pattern, P = 0.835).

**Quality assessment**

The quality of each study in terms of population and sampling methods, description of exposure and outcomes, and statistical adjustment of data is summarized in Appendix 1, Supplemental digital content 1, http://links.lww.com/EJCP/A66. All studies received a score of 6 or higher on the Newcastle–Ottawa Quality Assessment scale and were considered to be of high methodological quality (Shu et al., 1993; Parazzini et al., 1995; Zheng et al., 1995; McCann et al., 2000; Kasum et al., 2001; McCann et al., 2001; Terry et al., 2002; Tao et al., 2005; Xu et al., 2006; Dalvi et al., 2007; Hosono et al., 2008; Yeh et al., 2009; Biel et al., 2011; Bravi et al., 2015) case–control studies. Study characteristics are presented in Table 1.

**Sensitivity analysis**

The sensitivity analysis showed that differences in age, sample size, race, and study design had an impact on the associations between dietary patterns and the risk of EC. When the highest category was compared with the lowest category of a healthy dietary pattern, the healthy dietary pattern/EC association was obvious when patients were white. In addition, the positive association was obvious for those in the highest compared with the lowest category of a western-style dietary pattern in studies with a small sample size. As these variables have a strong effect on the association between different dietary patterns and the risk of EC; their differences may partially explain the heterogeneity between studies (Table 2).

**Discussion**

Limited studies have shown the associations between dietary patterns and the risk of EC in the Chinese population. To the best of our knowledge, this is the first
meta-analysis of dietary patterns and the risk of EC. The results from the present study show that a healthy dietary pattern may decrease the risk of EC, whereas a western-style dietary pattern may increase the risk of EC. Data from 27 studies involving 1,492,718 participants were included in the present meta-analysis. Our findings have added to the existing literature by supporting the associations between dietary patterns and the risk of EC.

In our analyses, the healthy dietary pattern was associated with a decreased risk of EC. Our results are consistent with previous studies reporting the favorable effect of a healthy/prudent dietary pattern on the prevention of EC (Yeh et al., 2009; Biel et al., 2011). One possible mechanism of their apparently protective effect against EC is that they are good sources of antioxidants (e.g., vitamins A, C, and E, and other carotenoid compounds) and dietary fiber. Antioxidants such as vitamin E and carotenoids can neutralize reactive oxygen species and protect against free radical damage involved in carcinogenesis (Young and Lowe, 2001; Schneider, 2005). In addition, several studies found that higher dietary fiber consumption could modify plasma sex hormone concentrations, including lower serum estrone and 17β estradiol concentrations (Bagga et al., 1995; Frische et al., 2003). Furthermore, vegetables and fruits contain large amounts of folate. Previous studies have also shown that folate is a necessary component for the synthesis and methylation of DNA, which plays an important role in maintaining normal cellular functions (Davis and Uthus, 2004).
Table 1  Characteristics of 27 studies included in the meta-analysis (1990–2015)

<table>
<thead>
<tr>
<th>References</th>
<th>Locations</th>
<th>Study designs</th>
<th>Total number of patients</th>
<th>Age (years)</th>
<th>Diet-assessment methods</th>
<th>Factors adjusted for in analysis</th>
<th>Dietary patterns identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeh et al. (2009)</td>
<td>USA</td>
<td>Case–control</td>
<td>541 Cases</td>
<td>27–96</td>
<td>FFQ</td>
<td>Age, BMI (continuous variable), exogenous estrogen use, smoking, total menstrual months, and total energy</td>
<td>Total vegetables, total fruit</td>
</tr>
<tr>
<td>Canchola et al. (2015)</td>
<td>USA</td>
<td>Cohort</td>
<td>75 093 Cases</td>
<td>&lt;85</td>
<td>FFQ</td>
<td>Race and its interaction with time-dependent age, age at menarche, gravidity and age at last pregnancy and its interaction with time-dependent age, oral contraceptive use, physical activity, smoking status, height, caloric intake, the other four dietary patterns, BMI, and the following time-dependent exposures menstropausal status/hormone therapy use, and their interaction; age was the time metric, and the model was stratified by age at baseline</td>
<td>Plant-based, salad and wine, high protein/fat, high carbohydrate</td>
</tr>
<tr>
<td>Bravi et al. (2015)</td>
<td>Italy</td>
<td>Case–control</td>
<td>454 Cases</td>
<td>18–79</td>
<td>FFQ</td>
<td>Age, study center, period of interview, education, BMI, history of diabetes, age at menarche, menopausal status, parity, oral contraceptive use, hormone replacement therapy use, and all the five factors simultaneously</td>
<td>Western-type, vitamins and fiber, starch-rich, animal-derived nutrients and PUFAs, other fats</td>
</tr>
<tr>
<td>Biel et al. (2011)</td>
<td>Canada</td>
<td>Case–control</td>
<td>549 Cases</td>
<td>30–79</td>
<td>FFQ</td>
<td>Age, total energy intake, BMI, age at menarche, parity, hypertension history, hormone contraception use, alcohol intake</td>
<td>Sweets, meat, plants</td>
</tr>
<tr>
<td>Tao et al. (2005)</td>
<td>China</td>
<td>Case–control</td>
<td>832 Cases</td>
<td>30–69</td>
<td>FFQ</td>
<td>Age, education, menopausal status, years of menstruation, first-degree family history of breast, colorectal, endometrial cancer, OC use, number of pregnancies, history of diabetes, BMI, total meat and fish intake and caloric intake</td>
<td>Fruit and vegetable</td>
</tr>
<tr>
<td>Xu et al. (2006)</td>
<td>China</td>
<td>Case–control</td>
<td>1204 Cases</td>
<td>30–69</td>
<td>FFQ</td>
<td>Age, menopausal status, diagnosis of diabetes, alcohol consumption, BMI, physical activity, and total energy intake</td>
<td>Total meat intake</td>
</tr>
<tr>
<td>McCullough et al. (2007)</td>
<td>USA</td>
<td>Cohort</td>
<td>97 786</td>
<td>50–74</td>
<td>FFQ</td>
<td>Age, age at menarche, age at menopause, number of live births and age at first birth, hormone replacement therapy, current combined replacement therapy, cigarette smoking, recreational physical activity in quintiles, total energy intake, and BMI</td>
<td>Fruit intake, vegetable intake</td>
</tr>
<tr>
<td>Shu et al. (1993)</td>
<td>China</td>
<td>Case–control</td>
<td>268 Cases</td>
<td>18–74</td>
<td>FFQ</td>
<td>Age, number of pregnancies, BMI, and total calories</td>
<td>Red meat intake</td>
</tr>
<tr>
<td>Genkinger et al. (2012)</td>
<td>Sweden</td>
<td>Case–control</td>
<td>232 Cases</td>
<td>40–76</td>
<td>FFQ</td>
<td>Age, energy, BMI, parity, and education</td>
<td>Red meat intake</td>
</tr>
<tr>
<td>McCann et al. (2001)</td>
<td>USA</td>
<td>Cohort</td>
<td>639 Controls</td>
<td>40–85</td>
<td>FFQ</td>
<td>Energy, age, education, BMI, diabetes, hypertension, pack-years cigarette smoking, age at menarche, menopause status, parity, oral contraceptive use, and menopausal estrogen use</td>
<td>Healthy; high-fat</td>
</tr>
<tr>
<td>Arem et al. (2013)</td>
<td>USA</td>
<td>Cohort</td>
<td>566 398</td>
<td>50–71</td>
<td>FFQ</td>
<td>Age, BMI, smoking status, continuous total energy intake and was mutually adjusted for other meat intake, age at menarche, age at first child’s birth, parity, age at menopause, HT use, oral contraceptive use, diabetes and physical activity</td>
<td>Red meat intake</td>
</tr>
<tr>
<td>McCann et al. (2000)</td>
<td>USA</td>
<td>Case–control</td>
<td>232 Cases</td>
<td>40–85</td>
<td>FFQ</td>
<td>Age, education, BMI, diabetes, hypertension, pack-years cigarette smoking, age at menarche, parity, oral contraceptive use, menopause status, and postmenopausal estrogen use</td>
<td>Total vegetable, red meat</td>
</tr>
<tr>
<td>Potischman et al. (1993)</td>
<td>USA</td>
<td>Case–control</td>
<td>399 Cases</td>
<td>20–74</td>
<td>FFQ</td>
<td>Age-group, BMI, ever estrogen usage, current smoking, ever oral-contraceptive usage, number of births, education, total calories</td>
<td>All meat intake</td>
</tr>
<tr>
<td>Terry et al. (2002)</td>
<td>Sweden</td>
<td>Case–control</td>
<td>709 Cases</td>
<td>50–74</td>
<td>FFQ</td>
<td>Age, BMI, smoking, physical activity, prevalence of diabetes, fatty fish consumption, and quintiles of total food consumption</td>
<td>Total fruit and vegetables, meat</td>
</tr>
<tr>
<td>Zheng et al. (1995)</td>
<td>Germany</td>
<td>Cohort</td>
<td>23 070</td>
<td>55–69</td>
<td>FFQ</td>
<td>Age, age at menopause, parity, postmenopausal hormone use, and energy from animal foods</td>
<td>Animal foods, plant foods</td>
</tr>
<tr>
<td>Dalvi et al. (2007)</td>
<td>USA</td>
<td>Case–control</td>
<td>488 Cases</td>
<td>30–79</td>
<td>FFQ</td>
<td>Age, race/ethnicity, age at menarche, OC use, parity, average daily caloric intake, average weekly physical activity, and the joint effects of menopausal status, HT use, and BMI</td>
<td>Plant-based; western, ethnic, phytoestrogen-rich</td>
</tr>
<tr>
<td>van Lonkhuizen et al. (2011)</td>
<td>Canada</td>
<td>Case–cohort</td>
<td>26 024</td>
<td>Mean: 58.9</td>
<td>FFQ</td>
<td>Age, BMI, age at menarche, number of live births, breastfeeding, number of years of oral contraceptive use, average exercise per week expressed as hours of exercise per week multiplied by metabolic ratio as compared with resting from the exercise, average kcal intake per day and average consumption of cruciferous vegetables, and for postmenopausal status at baseline and hormone replacement therapy</td>
<td>Meat consumption</td>
</tr>
</tbody>
</table>

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<table>
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<th>Diet-assessment methods</th>
<th>Factors adjusted for in analysis</th>
<th>Dietary patterns identified</th>
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</thead>
<tbody>
<tr>
<td>Tavani et al. (2000)</td>
<td>Italy</td>
<td>Case–control</td>
<td>750 Cases 4770 Controls</td>
<td>&lt;75</td>
<td>FFQ</td>
<td>Age, year of recruitment, sex, education, smoking habits and alcohol, fat, fruit and vegetable intakes</td>
<td>Consumption of red meat</td>
</tr>
<tr>
<td>Kasum et al. (2001)</td>
<td>USA</td>
<td>Cohort</td>
<td>23 014</td>
<td>55–69</td>
<td>FFQ</td>
<td>Age, kilocalories, education, BMI, smoking, vitamin use, fruit and vegetable intake, red meat intake, whole grain intake, total fat, saturated fat, age at menarche, age at menopause, number of live births, and hormone use</td>
<td>Whole grain intake</td>
</tr>
<tr>
<td>Loerbroks et al. (2007)</td>
<td>The Netherlands</td>
<td>Cohort</td>
<td>62 573</td>
<td>55–69</td>
<td>FFQ</td>
<td>Age, BMI, parity, use of oral contraceptives, nonoccupational physical activity, hypertension, age at first child birth, age at menopause, and current cigarette smoking</td>
<td>Alcohol consumption</td>
</tr>
<tr>
<td>Parazzini et al. (1995)</td>
<td>Italy</td>
<td>Case–control</td>
<td>726 Cases 2123 Controls</td>
<td>28–74</td>
<td>FFQ</td>
<td>Age, education, quetelet index, parity, menopausal status, smoking, oral contraceptive and estrogen replacement therapy use, diabetes, and hypertension</td>
<td>Alcohol drinking</td>
</tr>
<tr>
<td>Fedirko et al. (2013)</td>
<td>Europe</td>
<td>Cohort</td>
<td>301 051</td>
<td>20–85</td>
<td>FFQ</td>
<td>Age at recruitment, BMI, physical activity level, smoking status and intensity, menopause and menopausal status, age at first menses, number of full-term pregnancies, hormone replacement therapy use, and oral contraceptive use</td>
<td>Alcohol drinking</td>
</tr>
<tr>
<td>Newcomb et al. (1997)</td>
<td>USA</td>
<td>Case–control</td>
<td>739 Cases 2313 Controls</td>
<td>40–79</td>
<td>Telephone interview</td>
<td>Age, smoking status, education, relative weight, use of hormone replacement therapy, and parity</td>
<td>Alcohol consumption</td>
</tr>
<tr>
<td>Je et al. (2014)</td>
<td>USA</td>
<td>Cohort</td>
<td>68 067</td>
<td>34–59</td>
<td>FFQ</td>
<td>BMI, age at menopause, age at menarche, parity and age at last birth, duration of oral contraceptive use, smoking status, postmenopausal hormone use, physical activity, history of hypertension, cumulative average intakes of total energy, coffee intake, and glycemic load</td>
<td>Alcohol intake</td>
</tr>
<tr>
<td>Setiawan et al. (2008)</td>
<td>USA</td>
<td>Cohort</td>
<td>41 574</td>
<td>45–75</td>
<td>Questionnaire</td>
<td>Age at recruitment, year of recruitment, race/ethnicity and study center, education, BMI, age at menarche, age at menopause, duration and type of hormone therapy use, duration of oral contraceptive use, parity, smoking history, diabetes, hypertension and vigorous physical activity</td>
<td>Alcohol intake</td>
</tr>
<tr>
<td>Yang et al. (2011)</td>
<td>USA</td>
<td>Cohort</td>
<td>114 414</td>
<td>&gt;55</td>
<td>FFQ</td>
<td>Age, BMI, smoking status, race/ethnicity, parity, oral contraceptive use, oral menopausal hormone use, and age at menopause</td>
<td>Alcohol intake</td>
</tr>
<tr>
<td>Hosono et al. (2008)</td>
<td>Japan</td>
<td>Case–control</td>
<td>148 Cases 1478 Controls</td>
<td>20–79</td>
<td>FFQ</td>
<td>Age, smoking, BMI, regular exercise, menstrual status, age at menarche, duration of menstruation, parity, diabetes history, hypertension history, contraceptive use</td>
<td>Alcohol drinking</td>
</tr>
</tbody>
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FFQ, food frequency questionnaire; HT, hormone replacement therapy; OC, oral contraceptives; PUFAs, polyunsaturated fatty acids.
The western-style dietary pattern was associated with an increased risk of EC in our analyses. Our results were consistent with previous studies (van Lonkhuijzen et al., 2011; Bravi et al., 2015) suggesting that diets rich in meat (especially red meat and processed meat) or fat were significantly associated with a higher risk. A recent meta-analysis of meat intake and the risk of EC concluded that high consumption of meat was associated with a 44% increased risk of EC in five ‘robust’ case–control studies (Bandera et al., 2007). There are several plausible explanations for the positive associations between a western-style dietary pattern and the risk of EC. First, cooking temperatures and methods for animal food may be associated with an increased risk of EC. In particular,
frying, broiling, and grilling can produce large amounts of heterocyclic amines or polycyclic aromatic hydrocarbons, which are potent experimental mutagens or carcinogens (Wong et al., 2005). Second, high red meat intake may result in higher pro-oxidant load from the consumption of readily absorbed heme iron, resulting in greater oxidative stress and potential for DNA damage (McCord, 1998). Besides, dietary fat may influence estrogen metabolism and enhance estrogen reabsorption in the bowel, although the association of dietary fat and the risk of EC remains controversial (Holmes et al., 2000). Finally, processed meat often contains high concentrations of N-nitroso compounds and heterocyclic amines, which are considered to be carcinogenic (Sinha and Rothman, 1999; Sinha and Norat, 2002).

No significant association was observed for alcohol-drinking pattern and the risk of EC in this meta-analysis. However, to our knowledge, two meta-analyses of alcohol consumption and the risk of EC concluded that alcohol drinking was not associated with a risk of EC (Turati et al., 2010; Sun et al., 2011). Moreover, a recent meta-analysis also found a possible J-shaped relationship between alcohol intake and the risk of EC (Friberg et al., 2010). In fact, the lack of an association between alcohol consumption and the risk of EC could be related to the amount of alcohol. On the one hand, alcohol may increase estrogen levels, which in turn has been shown to increase risk by stimulating the proliferation of endometrial cells (Rinaldi et al., 2006). On the other, Davies et al. (2002) have found that alcohol intake of 30 g/day may improve insulin sensitivity and reduce fasting insulin concentrations, thereby potentially decreasing the risk of EC. To our knowledge, hyperinsulinemia and diabetes are suspected or established risk factors for EC (Friberg et al., 2007). Besides, cancer patients are commonly advised to avoid or lower alcohol consumption following clinicians’ suggestions to improve prognosis. Thus, the change in alcohol consumption would probably lead to an underestimation of the relationship of alcohol intake with the risk of EC.

**Strengths and limitations**

This meta-analysis has its own strengths. First, the diagnosis of EC was confirmed by review of medical charts and available pathological slides, avoiding mis-diagnosis bias. Second, this is the first meta-analysis reporting the associations between dietary patterns and
the risk of EC. Our findings provide a more definitive conclusion on the associations between dietary patterns and the risk of EC. Alternatively, we also further evaluated the associations between alcohol-drinking pattern and the risk of EC in women. Third, no signs of publication bias were evident in the funnel plot, and the statistical test for publication bias was nonsignificant. However, a number of limitations should also be mentioned in this meta-analysis. First, the principal limitation of this study was the use of potentially biased evidence. There was an inconsistent adjustment for potential confounders among the studies included. As a consequence, the data included in our analyses may have differing degrees of completeness and accuracy. Second, 15 of 27 studies used a case-control design, which is more susceptible to recall and selection bias, especially dietary recall bias, than a cohort design.

Conclusion
This meta-analysis suggests that a healthy dietary pattern is associated with a decreased risk of EC, whereas a western-style dietary pattern is associated with an increased risk of EC. Our findings provide evidence of the role of dietary pattern in the development of EC. Therefore, public health implications of our findings highlight the importance of a diet of high vegetable and fruit intake, and low red meat intake to decrease the risk of EC in women.

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Conflicts of interest
There are no conflicts of interest.

References