RESEARCH ARTICLE

Tea Consumption, Alcohol Drinking and Physical Activity Associations with Breast Cancer Risk among Chinese Females: a Systematic Review and Meta-analysis

Ying Gao¹, Yu-Bei Huang², Xue-Ou Liu², Chuan Chen², Hong-Ji Dai², Feng-Ju Song², Jing Wang¹, Ke-Xin Chen²*, Yao-Gang Wang¹*

Abstract

Objective: To evaluate associations between tea consumption, alcohol drinking and physical activity and breast cancer risk among Chinese females. Methods: Three English databases (PubMed, ScienceDirect and Wiley) and three Chinese databases (CNKI, WanFang and VIP) were independently searched by 2 reviewers up to December 2012, complemented by manual searches. The quality of included studies was assessed with the Newcastle-Ottawa Scale items. Random-effects models were used to estimate the pooled odds ratios (ORs) and 95% confidence intervals (CIs). Potential publication bias was estimated through Egger’s and Begg’s tests. Heterogeneity between studies was evaluated with I² statistics. Results: Thirty-nine studies involving 13,204 breast cancer cases and 87,248 controls were identified. Compared with non-drinkers, regular tea drinkers had decreased risk (OR=0.79, 95% CIs: 0.65-0.95; I²=84.9%; N=16). An inverse association was also found between regular physical activity and breast cancer risk (OR=0.73, 95% CIs: 0.63-0.85; I²=77.3%; N=15). However, there was no significant association between alcohol drinking and breast cancer risk (OR=0.85, 95% CIs: 0.72-1.02; I²=63.8%; N=26). Most of the results from the subgroup analysis were consistent with the main results.

Conclusion: Tea consumption and physical activity are significantly associated with a decreased risk of breast cancer in Chinese females. However, alcohol drinking may not be associated with any elevation of risk.

Keywords: Breast cancer - tea consumption - alcohol drinking - physical activity - system review - meta-analysis

Introduction

Breast cancer is the most common cancer in women worldwide. In China, both the incidence and mortality of breast cancer have increased at a high speed during the past decades (Li et al., 2012) and would continue to climb in the following years (Zhang et al., 2008). Whereas the factors responsible for the increasing rate of breast cancer in China remain unknown. Hence, to explore effective preventive interventions is a main focus for the prevention and control of breast cancer. Smoking as an independent risk factor of breast cancer, we will independently expound the association between them in another systematic review. In addition, tea consumption, alcohol drinking and physical activity were the most closely modifiable risk factors for breast cancer except smoking, so this study focuses on the possible quantitative relationship between these three modifiable factors and breast cancer risk among Chinese female.

Historically, as part of traditional Chinese life, tea consumption can be traced to several thousand years ago. Compelling evidence suggested that tea is rich in polyphenols, including catechins and gallotannins, which have been reported to have antioxidant property and potential anti-tumor effect, especially for epigallocatechin-3-gallate (EGCG) (Landis-Piwowar et al., 2007; Shimizu et al., 2008). However, epidemiologic studies focused on the association between tea consumption and breast cancer risk have reported inconsistent results (Ewertz et al., 1990; La et al., 1992; Tao et al., 2002; Wu et al., 2003; Zhang et al., 2007; Shrubsole et al., 2009). Some Western studies reported no benefit (Ewertz et al., 1990; La et al., 1992), but most of Chinese studies suggested an inverse association (Tao et al., 2002; Wu et al., 2003; Zhang et al., 2007; Shrubsole et al., 2009). With high consumption of tea and increasing incidence of breast cancer in China, it’s very important to investigate the effect of tea on breast cancer.

In addition, alcohol drinking is also another traditional part of Chinese life. According to the national investigation, the prevalence rate of alcohol consumption in China has increased from 17.94% in 1991 (PRC, 1995) to 21.0%...
in 2002 (Ma et al., 2005). In parallel, there is a marked increase in the prevalence rate of alcohol dependence, which has moved from the ninth to the third most prevalent mental illness (Cochrane et al., 2003). Although alcohol drinking was considered as an important risk factor for breast cancer in Western countries (Key et al., 2006), this association was still unclear for Chinese female. A recent study reported that alcohol drinking was associated with an elevated risk of breast cancer (Odds Ratios = 1.86, 95% Confidence Intervals: 1.02-3.39) (Gao et al., 2013). However, one study showed an inverse association (OR = 0.63; 95%CI: 0.52-0.76) (Zhang et al., 2011), while another found no relationship between them (OR = 1.50; 95%CI: 0.74-1.02) (Wang et al., 2013). Hence, it is necessary to clarify the association between alcohol drinking and breast cancer risk among Chinese female.

Since the first epidemiologic study on physical activity and breast cancer risk was published in 1985 (Frisch et al., 1985), more than 80 studies have been conducted to assess this association worldwide during the past 20 years (Friedenreich et al., 2008). The meta-analysis found that the risk of breast cancer had decreased approximately 50% among Asian women exercisers (Friedenreich et al., 2008). Another meta-analysis reported that this inverse association was only statistically significant among women in Western countries, but not in Asian countries (OR: 0.82; 95%CI: 0.62-1.08) (Wu et al., 2013). As another modifiable risk factor, numerous epidemiologic studies suggested physical activity has a protective role in breast cancer development in Western female, but it is unclear whether the empirical findings in Western countries will hold in Asian countries, especially in China. In order to increase statistical power and clarify these conflicting results, a large-scale population-based systematic review was conducted to determine the effects of these modifiable behavioral factors on breast cancer risk among Chinese female.

### Materials and Methods

This systematic review was conducted according to the MOOSE guidelines (Stroup et al., 2000).

#### Search strategy

Three English databases (ScienceDirect and Wiley) and three Chinese databases (WanFang and VIP) were independently searched by two reviewers up to December 2012, complemented by manual searching of reference. We used the following three groups of key words in the searching strategies: (1) case-control study, cohort study, prospective study, and randomized controlled trial; (2) breast cancer, breast carcinoma, breast tumor, breast neoplasm, mammary cancer, mammary carcinoma, mammary tumor, and mammary neoplasm; (3) risk factors, behavior factor, tea, drinking, alcohol drinking, physical activity, and exercise. Paper in English or Chinese was reviewed, and only studies on Chinese female were included.

#### Selection of Studies

Two reviewers independently determined the selection of studies. All included articles must provide a complete cross-table data of exposure with outcomes. Systematic reviews, meta-analysis, case-report, and studies with control selected from subjects with benign breast disease were excluded. For the different articles from the same study, only studies which had the largest sample size or most update data were included in the analysis.

#### Data Extraction and Quality Assessment

The data extraction and study quality assessment were independently performed by two reviewers. The following information was collected with standardized data extraction forms: the first author, publication year, region of China, type of study, original sample size, and sources of population. All data entry was double-checked. The Newcastle-Ottawa Scale (NOS) item (Wells et al., 2012) was used to assess the quality of included studies based on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively. Studies were classified into three levels: high quality with scores greater than 7, moderate quality with scores between 5-7, and low quality with scores less than 5.

Any disagreement on selection of studies, data collection, and quality assessment was adjudicated by a third reviewer.

#### Statistical Analysis

Pooled odds ratios (ORs) and 95% confidence intervals (95%CIs) were calculated with random effects model, and weighted with inverse of the variance. Statistical heterogeneity between studies was evaluated with I² statistic, and heterogeneity was considered significant when the two-tailed P value was less than 0.10 (Hedges et al., 2001).

Subgroup analysis were used to explore the heterogeneity source, including the type of study, the
Table 1. The Main Characteristics of Included Studies

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<th>Year</th>
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Note: NOS*: Newcastle-Ottawa Scale. A, NOS score = 8-9; B, NOS score = 5-7; C, NOS score ≤4; Included*: 1, included in the paper of green tea consumption; 2, included in the paper of alcohol drinking; 3, included in the paper of physical exercise

quality of articles, sample size (≥1000 vs. <1000), and publication year (After 2007 vs. before 2007). The potential publication bias was examined with Egger’s test (Egger et al., 1997) and Begg’s test (Begg et al., 1994) and represented by a funnel plot. The results were considered to indicate publication bias when any P value of these two tests was less than 0.05. All the analyses were performed using STATA version 12.0 software.

Results

Description of studies

A detailed diagram of the review process was presented in Figure 1. Totally 361 relevant articles were identified and reviewed in detail. Six studies were excluded because they involved the same study subjects included in other articles. After reviewing the full text of these studies in detail, a total of 39 articles, involving 100,452 participants from 14 provinces, municipalities and regions, were included in the final review (Appendix 1). Among these included studies, we identified 6 cohort studies (Li et al., 2005; Shannon et al., 2005; Wang et al., 2006; Dai et al., 2010; Pronk et al., 2011; Shrubsole et al., 2011;) and 33 case-control studies (Lu et al., 1992; Xu et al., 1997; Zhao et al., 1999; Tao et al., 2002; Zou et al., 2002; Zhang et al., 2003; Chow et al., 2005; Lee et al., 2005; Chou et al., 2006; Huang et al., 2006; Li et al., 2006; Jin, 2007; Ma, 2007; Zhang et al., 2007; Kallianpur et al., 2008; Ren, 2008; Wang et al., 2008; Gao et al., 2009; Gao et al., 2009; Shrubsole et al., 2009; Wang et al., 2009; Zhang et al., 2009; Qian et al., 2010; Shi et al., 2010; Bao et al., 2011; Dai et al., 2011; Leu et al., 2011; Zhang et al., 2011; Hou et al., 2012; Xu et al., 2012; Yu et al., 2012; Zhang et al., 2012; Wang et al., 2013). According to the NOS items, 11 studies were evaluated as high quality, 25 studies as modest quality, and 3 studies as low quality, respectively. The main characteristic of included studies was summarized in Table 1.
Table 2. The Results of Subgroup Analysis Included All Studies of Tea

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<th>Subgroup</th>
<th>N</th>
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<th>Exposure/Control</th>
<th>OR(95%CI)</th>
<th>I²</th>
<th>P values</th>
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<td>Case-control</td>
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<td>2317/6929</td>
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<td>0.71(0.58-0.87)</td>
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<td>High quality</td>
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Table 3. The Result of Subgroup Analysis Included All Studies of Alcohol Drinking

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<td>0.98(0.67-1.43)</td>
<td>51.9</td>
<td>0.101</td>
</tr>
<tr>
<td>Moderate quality</td>
<td>20</td>
<td>903/7516</td>
<td>1181/9040</td>
<td>0.89(0.72-1.10)</td>
<td>65.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low quality</td>
<td>2</td>
<td>31/684</td>
<td>100/1105</td>
<td>0.46(0.31-0.71)</td>
<td>0</td>
<td>0.658</td>
</tr>
<tr>
<td>Sample size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1000</td>
<td>10</td>
<td>951/9993</td>
<td>2893/3056</td>
<td>0.84(0.68-1.05)</td>
<td>76.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;1000</td>
<td>16</td>
<td>192/3121</td>
<td>279/4033</td>
<td>0.89(0.65-1.21)</td>
<td>51</td>
<td>0.01</td>
</tr>
<tr>
<td>Year of publication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 2007</td>
<td>15</td>
<td>786/10593</td>
<td>2798/84084</td>
<td>0.78(0.64-0.94)</td>
<td>59.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Before 2007</td>
<td>11</td>
<td>357/2521</td>
<td>374/3005</td>
<td>1.01(0.75-1.37)</td>
<td>53.5</td>
<td>0.018</td>
</tr>
</tbody>
</table>

Figure 2. Forest Chart Based on All Studies of Tea Consumption (Yes Vs. No) with Breast Cancer

**Tea consumption**

Three cohort studies and thirteen case-control studies on tea consumption were included, involving 28,737 cases and 60,936 controls. Overall, there was a marginally significant reduction in risk of breast cancer among tea drinkers when compared to nondrinkers (OR = 0.79, 95%CI: 0.65-0.95; I²=84.9%, P<0.001; N=16) (Figure 2). Visual inspection of funnel plot with Egger’s test (P=0.656) and Begg’s test (P=0.893) did not show publication bias (Appendix 2a).

Subgroup analysis had showed significant inverse association between tea consumption and breast cancer among case-control studies (OR = 0.71, 95%CI: 0.58-0.87), studies of moderate quality (OR = 0.69, 95%CI: 0.56-0.85), studies with sample size less than 1000 (OR = 0.77, 95%CI: 0.67-0.89), and studies published after 2007 (OR = 0.77, 95%CI: 0.61-0.96), but no significant associations observed in other subgroup studies.

**Alcohol drinking**

Two cohort studies and twenty-four case-control studies on alcohol drinking were included, involving 13,204 cases and 87,248 controls. No significant association between alcohol drinking and breast cancer was found (OR = 0.85, 95%CI: 0.72-1.02; I²=63.8%, P<0.001; N=26) (Figure 3). As showed in the funnel plot (Appendix 2b), combining with Egger’s test (P=0.092) and Begg’s test (P=0.290), there was no publication bias.

Figure 3. Forest Chart Based on All Studies of Alcohol Drinking (Yes Vs. No) with Breast Cancer
Figure 4. Forest Chart Based on All Studies of Physical Activity (Yes Vs. No) with Breast Cancer

Table 4. The Result of Subgroup Analysis Included All Studies of Physical Activity

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N</th>
<th>Exposure/Case</th>
<th>Exposure/Control</th>
<th>OR(95%CI)</th>
<th>F</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case-control</td>
<td>12</td>
<td>2440/9027</td>
<td>3467/10562</td>
<td>0.69(0.59-0.82)</td>
<td>77.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cohort</td>
<td>3</td>
<td>561/1179</td>
<td>26328/73671</td>
<td>0.89(0.72-1.11)</td>
<td>42.4</td>
<td>0.176</td>
</tr>
<tr>
<td>NOS level</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High quality</td>
<td>5</td>
<td>1965/5300</td>
<td>28005/77827</td>
<td>0.82(0.72-0.94)</td>
<td>53.6</td>
<td>0.072</td>
</tr>
<tr>
<td>Moderate quality</td>
<td>10</td>
<td>1036/4906</td>
<td>1790/6406</td>
<td>0.68(0.53-0.86)</td>
<td>81.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sample size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1000</td>
<td>7</td>
<td>2412/8596</td>
<td>28834/81870</td>
<td>0.75(0.65-0.87)</td>
<td>77.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;1000</td>
<td>8</td>
<td>589/1610</td>
<td>961/2363</td>
<td>0.71(0.51-0.99)</td>
<td>79.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Year of publication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 2007</td>
<td>114</td>
<td>2397/8021</td>
<td>28464/81108</td>
<td>0.73(0.60-0.87)</td>
<td>82.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Before 2007</td>
<td>4</td>
<td>604/2185</td>
<td>1331/3125</td>
<td>0.70(0.59-0.83)</td>
<td>45.5</td>
<td>0.139</td>
</tr>
</tbody>
</table>

Kaur et al., 2007). The population-based studies also found a protective effect of tea consumption against breast cancer (Tao et al., 2002; Wu et al., 2003). Our results were similar to a recently published systematic review, which found that green tea consumption significantly reduced the breast cancer risk by 19% (OR = 0.81; 95% CI: 0.68-0.99) (Ren et al., 2013). However, other four population-based systematic reviews showed inconsistent results. One meta-analysis found that green tea but not black tea consumption was associated with a weak reduction risk of breast cancer (OR = 0.78; 95% CI: 0.61-0.98) (Sun et al., 2006). Another meta-analysis of all studies reported no association between green tea and breast cancer, but case-control studies suggested the beneficial effect of green tea (OR = 0.81, 95% CI: 0.75-0.88) (Ogunleye et al., 2010). Another two systematic reviews also did not support the protective effect of green tea on breast cancer (Seely et al., 2005; Wu et al., 2013). After revising the previous five systematic reviews (Seely et al., 2005; Wu et al., 2003; Sun et al., 2006; Ogunleye et al., 2010; Ren et al., 2013), all of them included two Japanese cohort studies (Key et al., 1999; Suzuki et al., 2004) which reported no relationship between tea consumption and breast cancer. One study by Key et al reported that majority of subjects were atomic bomb survivors of Hiroshima and Nagasaki, Japan (Key et al., 1999), the other study by Suzuki et al reported that subjects with higher tea intake tended to be postmenopausal, slightly older and had a higher body mass index which may be confounding variables (Suzuki et al., 2004). Therefore, including these studies would inevitably incur bias in these previous systematic reviews. That might be the most important reasons for the differences between our study and previous studies. Besides, type of tea, dose of daily intake, years of drinking, might also contribute to the differences (Wu et al., 2013), though current systematic review could not provide the direct evidence of the differences.

Secondly, the results of our review on breast cancer in relation to alcohol drinking were in agreement with two Japanese cohort studies, which demonstrated that alcohol drinking had no effect on breast cancer risk (Chisato et al., 2007; Kawai et al., 2011). A meta-analysis showed drinking alcohol may slightly decrease the risk of breast cancer among Chinese female (Li et al., 2011), but it only included four articles and omitted 9 major important studies on this association, including a population-based prospective study from the Shanghai Women’s Health Study (Shrubsole et al., 2011), a large population-based case-control study from the Shanghai Breast Cancer Study (Bao et al., 2011), two
studies of high quality (Gao et al., 2009; Dao et al., 2011), and five studies with large sample size (Lu et al., 1992; Li et al., 2006; Wang et al., 2009; Qian et al., 2010; Xu et al., 2012). Omission of these studies would necessarily incur publication bias and finally biased the pooled results. Beside, previous Western studies indicated that alcohol drinking was associated with an elevated risk of breast cancer (Smith-Wamer et al., 1998; Hamajima et al., 2002). The differences between our study and Western studies probably were due to the prevalence of alcohol drinking, the daily dose of alcohol, the type of alcohol drinking and some unknown biologic effects. For example, the reported prevalence rate of alcohol drinking among Chinese female had increased from 2.58% in 1993 (PRC, 1995) to 4.5% in 2002 (Ma et al., 2005), while the prevalence is reported to be 59.9% in American women, 81.9% in British women, 89.6% in French women, respectively (WHO). In addition, the daily dose of distilled spirits among Chinese female was about 50-100 gram, which was less than those reported in the Europe and American. According to the alcohol consumption data provided by World Health Organization in 2003-2005, the pure alcohol consumption per capita was approximately 5.19 liters for Chinese females 15 years and older (WHO), which was much lower than average 10 liters for Western females, such as 8.45 liters for American women, 9.46 liters for British women, 8.79 for French women, 8.43 liters for Swedish women, 15.58 liters for Spanish women, 7.78 for German women, and 5.75 liters for Japanese women (WHO). Moreover, distilled spirits was the first choice for 50.3% current drinkers in China. But in Europe and American, beer and wine were more preferred for drinkers (WHO). Likewise, racial differences in the metabolism of alcohol (Yu et al., 1995) and estrogen (Taioli et al., 1996) had also been reported to affect the relationship between alcohol drinking and breast cancer in different ethnics. For example, 10398G allele in the mitochondrial genome was reported to influence the alcohol metabolism, which may also modify the association between alcohol drinking and breast cancer (Pezzotti et al., 2009).

Additionally, consistent J-shaped curve of alcohol drinking on the risk of diseases was found in many cardiovascular diseases (White et al., 1999; Gmel et al., 2001). Whether the J-shaped curve also existed in the incidence of breast cancer, it really deserved further studies. And whether the type of alcohol drinking could bring different effect on the risk of breast cancer, it also needed more representative studies. In a word, though small drinking of alcohol might bring health benefits, especially for preventing cardiovascular disease, it was not suggested as a strategy for the prevention of breast cancer, because of more potential health harms against benefits. In fact, stay away from alcohol may be one of the healthiest lifestyle.

Lastly, the protective effect of regular physical activity on the risk of breast cancer was also consistent with a previous meta-analysis, which found that a decreased breast cancer risk of approximately 50% in Asian women (Friedenreich et al., 2008). Another meta-analysis, however, reported that this protective effect was not statistically significant among Asian women (OR = 0.82; 95%CI: 0.62-1.08) (Wu et al., 2013). Although the latter meta-analysis had included three prospective studies on Asian women, an important large population-based cohort study from Shanghai Breast Self-Examination study has been omitted (Shannon et al., 2011). Moreover, it included some articles which only provided the multivariate-adjusted relative risk (RR) with 95% confidence intervals (CIs). Due to different confounding variables were adjusted in different studies, pooling these results from different calculation methods might bring more confounding rather than get a clearer result. Furthermore, Chinese National Nutrition and Health Survey in 2002 reported that the current prevalence of exercise was only 15.1% for Chinese residents in urban, which was great lower than 50.6% for American female (WHO). Along with the low rate of exercise and increasing incidence of breast cancer, it is beneficial and meaningful to initiates health promotion campaigns for Chinese female. In addition, some studies also reported that common daily activities also could slightly reduce the risk of women breast cancer, when comparing to sedentary lifestyle (McTieman et al., 2003; Friedenreich et al., 2008). Hence, mild exercise was also suggested for Chinese female who were mainly responsible for daily housework. Besides, Tai Chi, a Chinese martial art, was also thought to promote health through slow moving exercise and breathing techniques. In overall, the results of the current study show that physical activity is an important protective factor for Chinese female. National physical activity promotion programs should be developed and tailored to the needs for women as a public health recommendation.

There were several potential limitations to be considered in this meta-analysis. Primarily, due to lack of enough information, results from our studies could not provide more detailed information of dose-response relationship between three lifestyles and risk of breast cancer, though we made great efforts to get relative information. Secondly, our results were likely to be affected by heterogeneity, because the tests for heterogeneity between different studies suggested that there was a strong heterogeneity. In order to explore the potential sources of heterogeneity, a lot of subgroup analyses were conducted according to the majors attributes of primary studies. And the results of different subgroups were relatively consistent with the major results, which meant that our results were relatively credible. Finally, it is possible that an observed association might suffer from publication bias in a meta-analysis, because studies with null results tend not to be published. However, no significant publication bias was detected most of results.

In conclusion, tea consumption and physical activity are significantly associated with a decreased risk of breast cancer for Chinese female. However, alcohol drinking may not be related with the risk of breast cancer. It’s very necessary to promote tea consumption and physical activity for the purpose of preventing breast cancer, but it’s not recommended to prevent breast cancer with alcohol drinking among Chinese female.

Acknowledgements

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