OPEN ACCESS Freely available online

PLoS one

Association between Alcohol Consumption and Cancers in the Chinese Population—A Systematic Review and Meta-Analysis

Ying Li[1], Huan Yang[2], Jia Cao[2]*

1 Department of Social Medicine and Health Service Management, Third Military Medical University, Chongqing, China, **2** Department of Hygienic Toxicology, Key Lab of Medical Protection for Electromagnetic Radiation, Ministry of Education of China, Third Military Medical University, Chongqing, China

Abstract

Background: Alcohol consumption is increasing worldwide and is associated with numerous cancers. This systematic review examined the role of alcohol in the incidence of cancer in the Chinese population.

Methods: Medline/PubMed, EMBASE, CNKI and VIP were searched to identify relevant studies. Cohort and case-control studies on the effect of alcohol use on cancers in Chinese were included. Study quality was evaluated using the Newcastle-Ottawa Scale. Data were independently abstracted by two reviewers. Odds ratios (OR) or relative risks (RR) were pooled using RevMan 5.0. Heterogeneity was evaluated using the Q test and I-squared statistic. $P<.01$ was considered statistically significant.

Results: Pooled results from cohort studies indicated that alcohol consumption was not associated with gastric cancer, esophageal cancers (EC) or lung cancer. Meta-analysis of case-control studies showed that alcohol consumption was a significant risk factor for five cancers; the pooled ORs were 1.79 (99% CI, 1.47–2.17) EC, 1.40 (99% CI, 1.19–1.64) gastric cancer, 1.56 (99% CI, 1.16–2.09) hepatocellular carcinoma, 1.21 (99% CI, 1.00–1.46) nasopharyngeal cancer and 1.71 (99% CI, 1.20–2.44) oral cancer. Pooled ORs of the case-control studies showed that alcohol consumption was protective for female breast cancer and gallbladder cancer: OR 0.76 (99% CI, 0.60–0.97) and 0.70 (99% CI, 0.49–1.00) respectively. There was no significant correlation between alcohol consumption and lung cancer, colorectal cancer, pancreatic cancer, cancer of the ampulla of Vater, prostate cancer or extrahepatic cholangiocarcinoma. Combined results of case-control and cohort studies showed that alcohol consumption was associated with 1.78- and 1.40-fold higher risks of EC and gastric cancer but was not significantly associated with lung cancer.

Conclusions: Health programs focused on limiting alcohol intake may be important for cancer control in China. Further studies are needed to examine the interaction between alcohol consumption and other risk factors for cancers in Chinese and other populations.

Citation: Li Y, Yang H, Cao J (2011) Association between Alcohol Consumption and Cancers in the Chinese Population—A Systematic Review and Meta-Analysis. PLoS ONE 6(4): e18776. doi:10.1371/journal.pone.0018776

Editor: Lisa Hartling, Alberta Research Centre for Health Evidence, University of Alberta, Canada

Received July 1, 2010; **Accepted** March 18, 2011; **Published** April 15, 2011

Funding: This work was supported in part by Major International (Regional) Joint Research Projects (30320140461) and National Natural Science Foundation of China (NSFC) (No. 30630056, No. 30771841, No. 30700676, No. 30800933), and by a Grant-in-Aid for Scientific Research on Special Priority Areas of Cancer from the Ministry of Education, Culture, Sports, Science and Technology of Japan (12670383). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: caojia1962@126.com

Introduction

Alcohol has a long history of use and abuse in numerous cultures around the world, and alcohol consumption has been increasing rapidly in many countries [1]. In particular, there has been a rapid increase in the consumption of alcohol in China. According to the data from national surveys conducted in 1999, 2002 and 2007, alcohol consumption increased 12.8% for males (from 35.09% to 39.6%) and 73.1% for females (from 2.58% to 4.5%) between 1991 and 2002; alcohol consumption doubled for males (from 39.6% to 84.1%) and increased 6.5 times (from 4.5% to 29.3% for females) for females during the five years between 2002 and 2007 [2–3]. It is estimated that there are currently more than 500 million Chinese who regularly consume alcohol [3]. The WHO pointed out that the ''safe limit'' of ethanol consumption is less than 40 g for males and 20 g for females per day [4]. The current suggested alcohol limit in China is less than 25 g for males and 15 g for females [5]. However, the average Chinese subject who consumes alcohol drinks 41.04 g, which exceeds the international and national limits [3]. The overall heavy drinking rate of adults in China also increased rapidly, from 4.7% in 2002 to 37.04% in 2007, and 65.39% of drinkers have poor health [2–3]. With the purpose of addressing the social and medical challenges highlighted by these reports, in 2007, the Chinese government advocated ***limited drinking, scientific drinking and protection of personal health*** [2], but heavy drinking is still common. Moreover, it is clear that alcohol consumption has already become one of the most important

dietary habits linked with poor health in contemporary Chinese society.

Ethanol itself is not carcinogenic. However, its first metabolite (acetaldehyde) has recently been shown to be a local carcinogen in humans [6]. Moreover, alcohol consumption is an important risk factor for numerous cancers worldwide [7]. Due to hereditary differences/genetic polymorphisms [8–9], the incidence and causes of cancers and the responses to anti-cancer drugs vary substantially among different ethnic groups. Numerous researchers have studied the association between alcohol consumption and cancers in Chinese people [10–17]. The potential association between alcohol consumption and cancer risk for the Chinese population is currently being debated in the literature, and a clear consensus of opinion has not emerged.

Although there have been a few meta-analyses based on studies that investigated the association between alcohol and EC, gastric cancer, HCC or lung cancer in Chinese patients [18–21], few of these earlier studies systematically analyzed the association between alcohol and some common cancers in the Chinese population. With the aim of understanding the effect of alcohol consumption on the risk of developing various cancers in the Chinese population, we qualitatively and quantitatively reviewed all of the available literature published in English and Chinese regarding the association between alcohol and cancers in Chinese people. We conclude with a series of recommendations regarding future intervention programs and studies.

Materials and Methods

Search strategy

Electronic searches of databases and hand searches of other resources were conducted to identify published articles for review. We searched articles (published up to February 2010) from four main databases: Medline/PubMed, EMBASE, CNKI (China National Knowledge Infrastructure) and the VIP database (Chinese Journal of Science and Technology of VIP). These searches included a mixture of free text and index terms to maximize the retrieval of potentially relevant articles. In addition to reviewing the references cited in the retrieved articles, the bibliographies of retrieved papers were searched by hand.

Selection of studies

Cohort and case-control studies of Chinese subjects were included in the study. The risk factor examined in all of these studies was alcohol consumption. Numerous cancer types were included. The types of alcohol consumed included beer, yellow rice wine, red wine, and hard liquor. We also included studies that were designed with the purpose of analyzing risk factors for cancer in Chinese people other than alcohol but that included alcohol as one factor for which the data were collected and analyzed as a secondary aim. Studies that only provided odds ratios (OR) or relative risk (RR) values and did not provide sufficient original data to calculate the OR or RR; studies that used data reported by earlier studies; systematic reviews; and meta-analyses were excluded from the present meta-analysis.

Validity assessment

The quality of the primary studies was evaluated using the Newcastle-Ottawa Scale (NOS) [22]. This scale judges the study 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.

Data abstraction

All of the identified studies about alcohol consumption and cancer in Chinese subjects were examined in detail. The data from potentially relevant articles were independently abstracted by two reviewers. Differences were resolved by consensus. For case-control studies, information about the size of the case and control groups, including the number of cases and controls exposed and not exposed to alcohol, were abstracted from each study. For cohort studies, the number of subjects in the cohort and the number of incident cases of cancer in the alcohol-exposed and non-exposed groups were abstracted from each study. When the results of a study were published more than once, only the most complete data were included in the analysis.

Assessment of heterogeneity and data synthesis

The definitions of drinker and non-drinker were complex and varied widely between studies. In this review, we took participants described as drinking the smallest amount and those who said that they never drink as "non-drinkers", while the rest of the subjects were classified into the "drinker" category. A qualitative meta-analysis was conducted by summarizing, comparing and contrasting the abstracted data. We calculated the pooled ORs for case-control studies and the RRs for cohort studies separately using RevMan 5.0 software. Heterogeneity was evaluated using the Q test [23] and the I-squared statistic [24]. If the level of heterogeneity was acceptable ($p>0.10$, or $p\leq0.10$ but $I^2\leq50\%$), the meta-analysis was conducted using a fixed effects model. If significant heterogeneity was found ($p\leq0.10$, $I^2>50\%$), a random effects model was used for the meta-analysis. Subgroup analyses were also performed to explore the possible reasons for the heterogeneity. Additionally, sensitivity analyses were undertaken to evaluate the stability of the relationship between alcohol consumption and cancer.

For the studies with dose-response analysis, we considered to pool the effect of dose-response. We took the amount of alcohol consumed per week, the duration of drinking or the age at the start drinking as explanatory variables. Because for many studies exposure was reported as a categorical data with a range, we assigned the mid-point of the range as the average length of exposure. For the highest consumption category, we assigned a value equal to half of the width of the previous interval above the uppermost cut-off point. We analyzed dose-response relationship using the method described by Greenland and Longnecker [25]. $P<0.01$ was chosen as the level of statistical significance for all tests.

Results

Description of studies

A detailed diagram of the review process is presented in Figure 1. We identified a total of 796 potentially relevant articles. After reviewing the titles, abstracts and full text of the literature, 134 articles were indentified with analysis on the association between alcohol consumption and cancers in Chinese. However, 14 articles were excluded because they involved the same study subjects as other included articles. Finally, 120 studies, which included 181,300 study subjects (including 34,742 cancer patients) from 28 provinces, municipalities and regions, were included in this review. Among these studies, 4 were cohort studies, and 115 were case-control studies [10–17,26–135].

The NOS results showed that the median overall score was 7 (range 5 to 9), which indicated that the methodological quality was generally good. We defined studies that scored a 7 or above as having high methodological quality, and we judged that 10

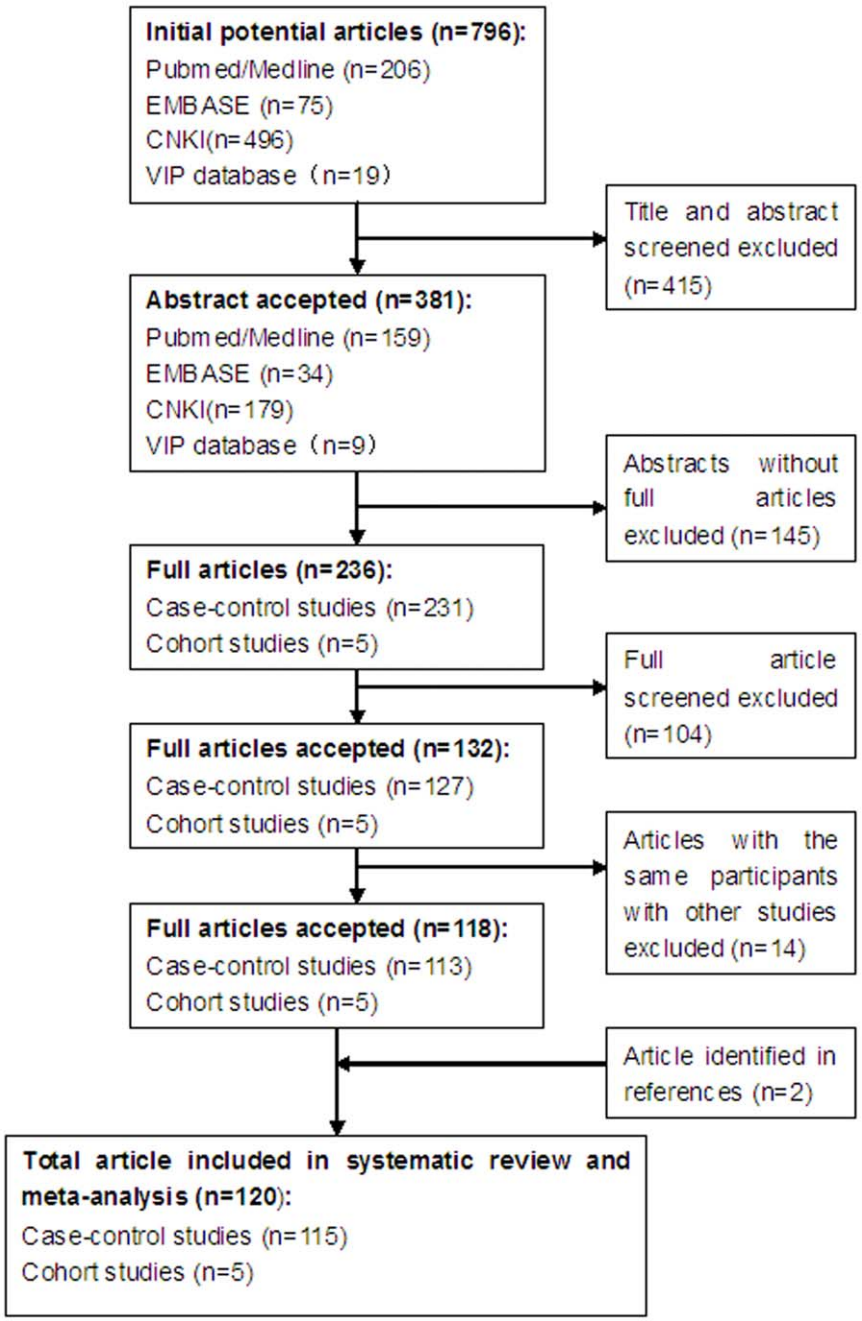

Figure 1. Results of literature search. This figure describes the whole process of searching for articles for inclusion in this systematic review and meta-analysis.
doi:10.1371/journal.pone.0018776.g001

out of the 120 studies to be of low quality (nine studies [49,56,66,71,82,97,112,132,135] and one study [46] scored 6 and 5, respectively) primarily due to either no description of the case selection, no definition of controls, a lack of adjusted analysis, or no description of the method of ascertainment for cases and controls.

Qualitative analysis

In total, the association between alcohol consumption and the incidence of 13 cancers was investigated (see Table 1). Four cancers, including EC, gastric cancer, lung cancer and colorectal cancer, were studied in both case-control studies and cohort studies, while the other cancers were investigated only in case-control studies. The association between alcohol and five cancers, EC, gastric cancer, HCC, pancreatic cancer and lung cancer, were analyzed separately in male patients and female patients in individual studies. In addition to prostate cancer, the effect of alcohol on five other cancers (EC, gastric cancer, HCC, colorectal cancer, and lung cancer) was only investigated in males in some studies. Participants in one study on HCC and all participants in studies on breast cancer were female.

Synergistic effects of alcohol and smoking were analyzed for four cancers in individual studies. Synergistic effects of alcohol and smoking were found for HCC [94]. In addition, a synergistic effect

Table 1. Studies on the association between alcohol and cancers in Chinese people.

Cancers	No. of studies and study design	Sample size (cases/control)	Participants
Esophageal cancers (EC) [10–11,27–59]	34 case-control studies 2 cohort studies	10189/60318	Male, Female Male and female
Gastric cancer [12–13,38,49–50,55,60–83]	29 case-control studies 2 cohort studies	8645/41580	Male, Female Male and female
Hepatocellular carcinoma (HCC) [14,49,55,84–98]	18 case-control studies	3812/10927	Male, Female Male and female
Colorectal cancer [15,99–108]	10 case-control studies 1 cohort studies	4311/6051	Male, Female Male and female
Lung cancer [16,109–113]	4 case-control studies 2 cohort studies	1104/14731	Male, Female Male and female
Breast cancer [17,114–116]	4 case-control studies	1655/2175	Female
Pancreatic cancer [117–121]	5 case-control studies	1612/3997	Male, Female Male and female
Prostate cancer (PCa) [122–125]	4 case-control studies	569/967	Male
Nasopharyngeal cancer(NPC) [126–129]	4 case-control studies	1698/1874	Male and female
Oral cancer [130–132]	3 case-control studies	347/539	Male, Female Male and female
Gallbladder cancer [133–134]	2 case-control studies	467/1315	Male and female
Ampulla of Vater cancer [133–134]	2 case-control studies	105/1331	Male and female
Extrahepatic cholangiocarcinoma (ECC) [134–135]	2 case-control studies	228/753	Male and female

doi:10.1371/journal.pone.0018776.t001

was found for EC in three studies [30,53–54], but another study reported no significant effect of the combination on EC [28]. No synergistic effects were found for gastric cancer [64,74] or pancreatic cancer [123].

Quantitative analysis

Heterogeneity tests indicated that studies analyzing the association between nine cancers (EC, gastric cancer, lung cancer, HCC, colorectal cancer, pancreatic cancer, female breast cancer, nasopharyngeal cancer, and cancer of the ampulla of Vater) and alcohol consumption had significant heterogeneity ($p<0.10$ and $I^2>50\%$). We therefore conducted meta-analyses using the random effects model. The case-control studies on prostate cancer, oral cancer, gallbladder cancer and ECC lacked heterogeneity ($p = 0.24$, 0.33, 0.27 and 0.81, respectively) (Table 2). The fixed effects model was used for the meta-analysis of these four cancers.

We performed meta-analyses of the study design and cancers separately (see Figures 2, 3, 4 and Table 2). The pooled RRs of the cohort studies were 1.08 (99% CI, 0.94–1.23, $p = 0.17$), 1.14 (99% CI, 0.99–1.32, $p = 0.02$) and 1.27 (99% CI, 0.85–1.91, $p = 0.25$) for EC, gastric cancer and lung cancer, respectively. These results indicate that alcohol consumption was not significantly associated with EC, gastric cancer or lung cancer. Meta-analysis of the case-control studies revealed that alcohol consumption was a significant risk factor for five cancers. The pooled ORs were 1.79 (99% CI, 1.47–2.17, $p<0.00001$) for EC, 1.40 (99% CI, 1.19–1.64, $p<0.00001$) for gastric cancer, 1.56 (99% CI, 1.16–2.09, $p = 0.0001$) for HCC, 1.21 (99% CI, 1.00–1.46, $p = 0.009$) for nasopharyngeal cancer, and 1.71 (99% CI, 1.20–2.44, $p<0.0001$) for oral cancer. The pooled ORs of the case-control studies showed that alcohol consumption was a protective factor for two cancers, female breast cancer, with an OR of 0.76 (99% CI, 0.60–0.97, $p = 0.004$) and gallbladder cancer, with an OR of 0.70 (99% CI, 0.49–1.00, $p = 0.009$) respectively. However, the effects of alcohol consumption on lung cancer, colorectal cancer, pancreatic cancer, cancer of the ampulla of Vater, prostate cancer and ECC were uncertain [pooled OR (99% CI): 1.59 (0.86–2.94), 1.58 (0.90–2.76), 1.15 (0.97–1.37), 0.68 (0.20–2.37), 1.17 (0.84–1.62) and 1.14 (0.75, 1.75), respectively].

We also pooled the results of both case-control and cohort studies for EC, gastric cancer and lung cancer. The overall estimates were 1.78 (99% CI, 1.38–2.30, $p<0.00001$) for EC, 1.40 (99% CI, 1.20–1.64, $p<0.00001$) for gastric cancer, and 1.39 (99% CI, 0.93–2.07, $p = 0.03$) for lung cancer. These results were consistent with pooled ORs for the case-control studies for these three cancers (alcohol consumption was a risk factor for EC and gastric cancer but had no significant association with lung cancer; see Figure 2 and Table 2).

Subgroup analyses

Given the available data, we conducted subgroup analysis for EC, gastric cancer, HCC and pancreatic cancer after stratifying the participants by sex (male vs. female patients).

The heterogeneity test showed that studies on the effects of alcohol consumption on female EC and gastric cancer and on male pancreatic cancer lacked heterogeneity ($p = 0.88$, 0.34 and 0.93). Heterogeneity was still found among studies on female HCC and pancreatic cancer and on male EC, HCC and gastric cancer ($p = 0.001$, 0.10, <0.00001, 0.05 and 0.01, $I^2>50\%$).

For males, alcohol consumption was a risk factor for EC, HCC and pancreatic cancer but was not significantly associated with gastric cancer and lung cancer. The pooled ORs were 1.82 (99% CI, 1.49–2.22, $p<0.00001$), 1.56 (99% CI, 1.01–1.62, $p = 0.001$), 1.71 (99% CI, 1.32–2.20, $p<0.00001$), 1.12 (99% CI, 0.78–1.59, $p = 0.43$), and 1.19 (99% CI, 0.91–1.54, $p = 0.09$), respectively.

However, for females, alcohol consumption was only a risk factor for female gastric cancer and had no significant effect on the other three cancers. The pooled ORs were 1.97 (99% CI, 1.02–4.43, $p = 0.005$) for gastric cancer, 0.91 (99% CI, 0.47–1.77,

Table 2. Results of meta-analysis of the studies on association between alcohol and cancer in Chinese population.

Cancers	No. of cases (drinker/non-drinker)	No. of controls (drinker/non-drinker)	Variance between studies		Pooled OR/RR (99% CI)	Test for overall effect (p)
			Q(*p*)	I^2 (%)		
EC (*case-control*)	3764/4366	5343/9206	<0.00001	87	1.79 (1.47, 2.17)	<0.00001
EC (*cohort*)	519/1540	14058/31711	<0.00001	96	1.08 (0.94, 1.23)	0.17
EC(overall)	4283/5906	19401/40917	<0.00001	90	1.78 (1.38, 2.30)	<0.00001
Gastric cancer (*case-control*)	2839/4089	3686/7594	<0.00001	71	1.40 (1.19, 1.64)	<0.00001
Gastric cancer (*cohort*)	490/1227	7368/22932	0.008	86	1.14 (0.99, 1.32)	0.02
Gastric cancer (overall)	3329/5316	11054/30526	<0.00001	73	1.40 (1.20, 1.64)	<0.00001
Lung cancer (*case-control*)	370/333	1179/1071	0.003	79	1.59 (0.86, 2.94)	0.14
Lung cancer (*cohort*)	223/178	6325/6156	0.07	69	1.27 (0.85, 1.91)	0.25
Lung cancer (overall)	593/511	7503/7227	0.004	71	1.39 (0.93, 2.07)	0.03
HCC(*case-control*)	2050/1762	3671/7256	<0.00001	83	1.56 (1.16, 2.09)	0. 0001
Colorectal cancer (*case-control*)	1614/2697	1800/4251	<0.00001	95	1.58 (0.90, 2.76)	0.04
Breast cancer (*case-control*)	266/1379	359/1806	0.08	55	0.76 (0.60,0.97)	0.004
Pancreatic cancer (*case-control*)	452/1154	1005/2975	0.04	60	1.15 (0.97, 1.37)	0.04
Ampulla of Vater cancer (*case-control*)	28/77	467/965	0.04	77	0.68 (0.20, 2.37)	0.43
Prostate cancer (*case-control*)	262/307	415/552	0.24	29	1.17 (0.84, 1.62)	0.23
Nasopharyngeal cancer (*case-control*)	571/1127	536/1338	0.08	55	1.21 (1.00, 1.46)	0.009
Oral cancer (*case-control*)	172/170	243/388	0.33	9	1.71 (1.20, 2.44)	0.0001
Gallbladder cancer (*case-control*)	92/375	355/960	0.27	16	0.70 (0.49, 1.00)	0.009
ECC (*case-control*)	80/148	253/500	0.81	0	1.14 (0.75, 1.75)	0.41

doi:10.1371/journal.pone.0018776.t002

p = 0.72) for EC, 1.93 (99% CI, 0.81–4.57, p = 0.05) for HCC, and 1.16 (99% CI, 0.52–2.60, p = 0.63) for pancreatic cancer.

Sensitivity analysis

We carried out sensitivity analysis for EC, gastric cancer, HCC and lung cancer based on the year of publication and the quality of the study (according to the NOS score).

With regard to EC, gastric cancer and HCC, when six studies [28,37–38,39,54,57] on EC, three studies [38,69,83] on gastric cancer and one study [84] on HCC published before 2000 were excluded, the overall strength slightly changed, but the direction of results did not change significantly [the overall estimates were 1.89 (99% CI, 1.41–2.53, p<0.00001) for EC, 1.37 (99% CI, 1.16–1.62, p<0.00001) for gastric cancer, and 1.56 (99% CI, 1.14–2.21, p = 0.0002)for HCC, respectively, when these studies were excluded]. When three studies [46,49,56] on EC, three studies [66,71,82] on gastric cancer and one study [97] on HCC scoring 6.0 or below on the NOS were excluded, the overall strength slightly changed, but the direction of results did not change significantly [the overall estimates were 1.78 (99% CI, 1.37–2.31, p<0.00001) for EC, 1.40 (99% CI, 1.19–1.65, p<0.00001) for gastric cancer, and 1.55 (99% CI, 1.13–2.13, p = 0.0004) for HCC, respectively, when these studies were excluded]. Similarly, for lung cancer, the strength and direction of results did not changed significantly after excluding one study [112] that scored 6.0. Regarding pancreatic cancer, when two studies [120–121] published before 2000 were excluded, the strength increased [pooled OR (99% CI): 1.30 (1.04–1.63)].

Dose-response analysis

The dose-response relationship between alcohol consumption and four cancers were analyzed in some studies: there are 5 studies on alcohol consumption (g) per week/day/month and EC [11,39,49,54,57], 6 studies on duration of alcohol consumption (year) and EC [11,39–40,54,57,59], 5 studies on duration of alcohol consumption (year) and gastric cancer [61,64,69,74,83], 3 studies on initial age at starting alcohol consumption and gastric cancer [64,69,74], 4 studies on alcohol consumption (g) per week/day/month and gastric cancer [64,69,74,83], 4 studies on initial age at starting alcohol consumption and HCC [84,92,94–95], 3 studies on duration of alcohol consumption (year) and HCC [84,93–94], 6 studies on alcohol consumption (g) per week/day/month and HCC [84,92–95,97], and 2 studies on alcohol consumption (g) per week/day/month and pancreatic cancer [119–120]. We pooled study data before trend analysis using the "pool-first" method. But no data indicated a monotonic increasing function relating alcohol consumption with any cancer risk. There is no significant dose-response relationship between alcohol consumption and these cancers in Chinese. We therefore didn't pool the slopes of these studies.

Discussion

In China, alcohol consumption has an important place in many cultural celebrations, and there has been a drinking culture in China for at least 7000 years. In addition to consuming spirits during festive or happy occasions for celebration, it is also common to drink with business partners or would-be friends in order to solidify the partnership, especially in northern China. Thus, alcohol has played and is playing an increasingly common role in Chinese culture.

All of the previous meta-analyses based on international studies or studies in China consistently found alcohol to be a risk factor for EC (pooled RR = 4.2, pooled ORs = 2.30 and 2.16, respectively)

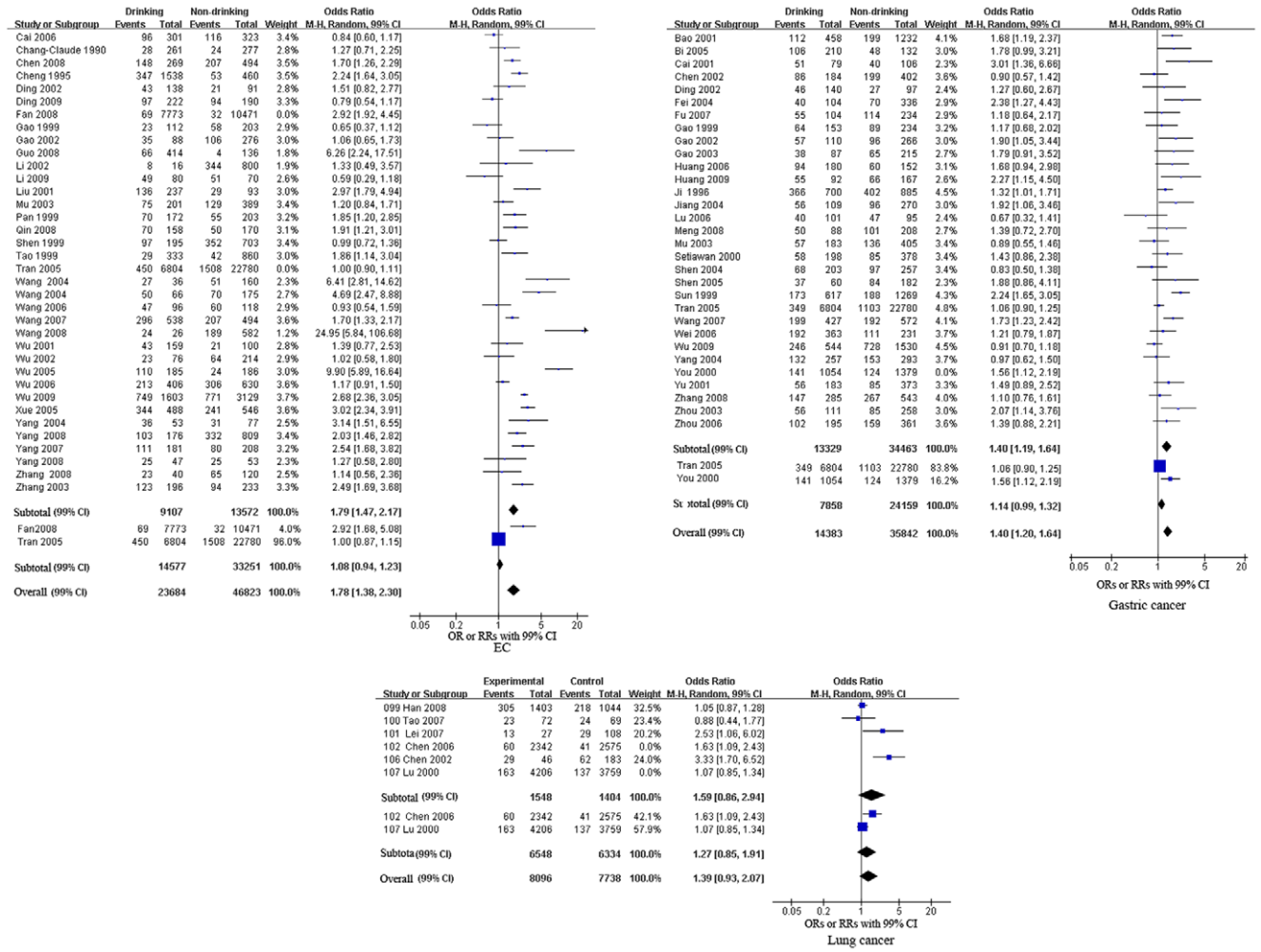

Figure 2. Forest plot of relative risk estimates of incident EC, gastric cancer, and lung cancer by alcohol consumption in Chinese. This figure shows forest plots for the meta-analysis of the association between alcohol consumption and the risk of EC, gastric cancer, and lung cancer. OR and the 99% CI for each cancer was given.
doi:10.1371/journal.pone.0018776.g002

[18,136–137], gastric cancer (pooled RR = 1.32, pooled ORs = 2.03 and 1.90, respectively) [19,136–138] and HCC (RR = 1.86 and OR = 1.872, respectively) [21,136]. Our meta-analysis provides further support that alcohol consumption is a significant risk factor for EC, gastric cancer, and HCC in the Chinese population. Our subgroup analysis found that the effect of alcohol on the development of gastric cancer and HCC likely depends on sex: alcohol consumption is a risk factor for EC and HCC in male Chinese subjects (pooled ORs = 1.82 and 1.56 respectively), but not for the females; however, it is a risk factor for gastric cancer in Chinese females (pooled OR: 1.97), but not Chinese males. Regarding colorectal cancer, earlier meta-analyses found that alcohol consumption was a risk factor for colorectal cancer (RR = 1.32 and 1.38) worldwide [136,139]. The present meta-analysis similarly found that alcohol is not a risk factor for colorectal cancer in the Chinese population ($p = 0.04$) based on a significance level of $p<0.01$.

One previous meta-analysis [135] found that alcohol consumption was not significantly associated with lung cancer or prostate cancer worldwide. We similarly found no significant association between alcohol consumption and the risk of lung and prostate cancers in the Chinese population. However, another meta-analysis of international studies found that consumption of beer and hard liquor was a risk factor for the development of lung cancer in males (pooled ORs = 1.46 and 1.34) [20]. Our subgroup analysis did not identify alcohol consumption as a risk factor for Chinese males ($p = 0.09$). It appears that the effect of alcohol consumption on lung cancer may vary based on the type of alcohol consumed, the ethnicity of the study subjects, or on other lifestyle factors of the participants.

International meta-analyses on the effect of alcohol consumption on pancreatic cancer have provided inconsistent results. Bagnardi et al. found no significant association between alcohol and pancreatic cancer [136], but Tramacere et al. found that heavy drinking was a risk factor for pancreatic cancer (pooled RR: 1.22, 95% CI: 1.12–1.34) [140]. Another meta-analysis of Chinese studies also found that heavy drinking was a risk factor for pancreatic cancer in males (OR = 1.58, 95% CI: 1.01–2.34) [141]. Our meta-analysis found no significant ($p = 0.04$) association between alcohol consumption and pancreatic cancer based on a significance level of $p<0.01$. Our subgroup analysis similarly revealed that alcohol consumption was a significant risk factor for pancreatic cancer among Chinese males (pooled OR = 1.71, $p<0.00001$).

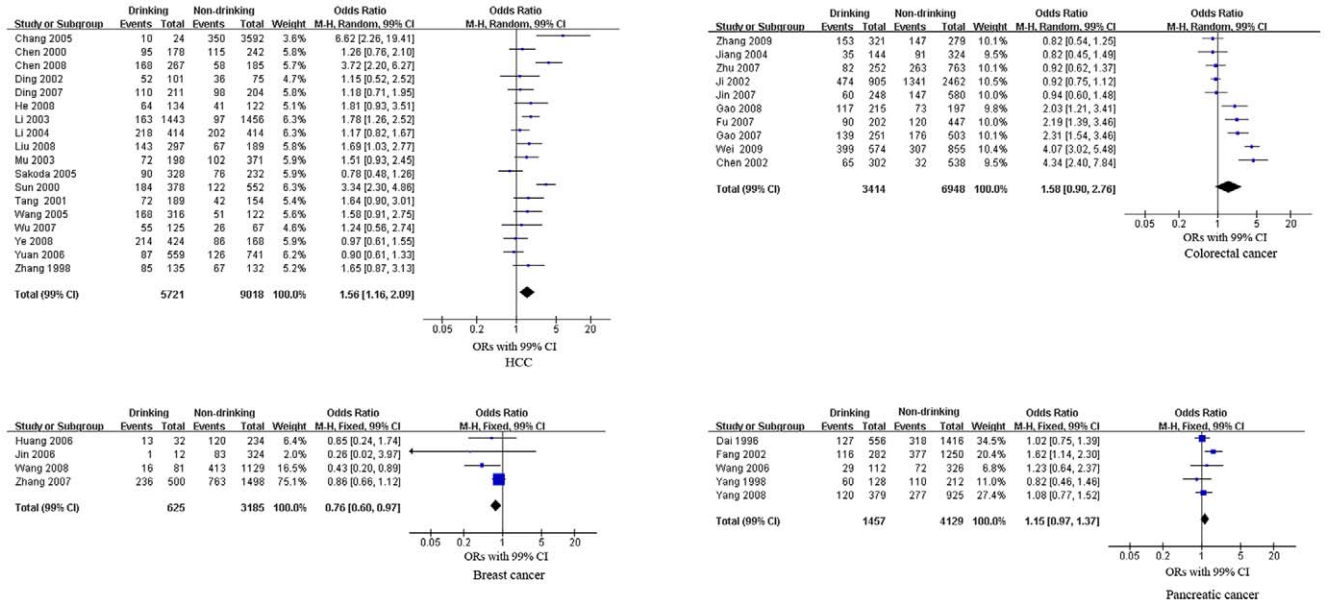

Figure 3. Forest plot of relative risk estimates of incident HCC, colorectal cancer, breast cancer and pancreatic cancer by alcohol consumption in Chinese. This figure shows forest plots for the meta-analysis of the association between alcohol consumption and the risk of HCC, colorectal cancer, breast cancer and pancreatic cancer. OR and the 99% CI for each cancer was given.
doi:10.1371/journal.pone.0018776.g003

There are few studies on the association between alcohol drinking and breast cancer among Chinese people. Interestingly, our meta-analysis of four studies found that alcohol consumption is a protective factor for female breast cancer (pooled OR = 0.76) in the Chinese population. Previous meta-analyses of international studies on non-Chinese populations) reported a positive association between alcohol consumption and breast cancer [136,142–143]. One study reported that the risk factors for breast cancer varied among different ethnic groups [144]. These findings suggest that alcohol may play different roles in the development of breast cancer in different ethnic groups or people with different lifestyle, environmental, behavioral and genetic factors. Further studies are

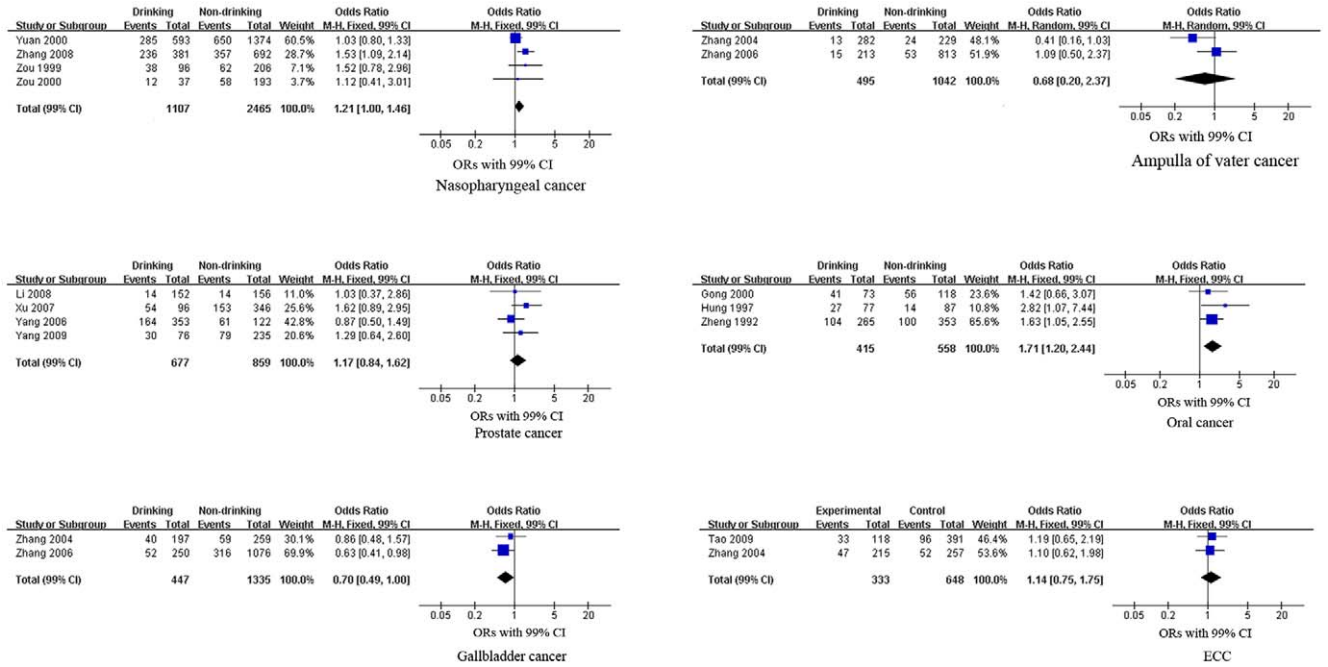

Figure 4. Forest plot of relative risk estimates of incident nasopharyngeal cancer, cancer of the ampulla of Vater, prostate cancer, oral cancer, gallbladder cancer and ECC by alcohol consumption in Chinese. This figure shows the forest plots for the meta-analysis of the association between alcohol consumption and the risk of nasopharyngeal cancer, cancer of the ampulla of Vater, prostate cancer, oral cancer, gallbladder cancer and ECC. OR and the 99% CI for each cancer was given.
doi:10.1371/journal.pone.0018776.g004

needed to determine which of these differences are responsible for the differences in risk.

We also identified studies of the effect of alcohol consumption on the risk of developing cancer of the ampulla of Vater cancer, nasopharyngeal cancer, oral cancer, gallbladder cancer and ECC. Our meta-analyses found that alcohol was a significant risk factor for nasopharyngeal and oral cancers in Chinese people (pooled ORs = 1.21 and 1.71 respectively), that it was a protective factor for gallbladder cancer, and that no significant association existed between alcohol consumption and the other two cancers. However, these results need to be confirmed in further studies because the sample size and the number of studies on these cancers covered in this review were relatively small (see Table 1).

The interaction of alcohol consumption and other risk factors was not studied in sufficient detail, and the results are inconsistent in the present study. There is some evidence to suggest that alcohol and smoking have a greater relative (even synergistic) effect together than alone [6]. It seems that alcohol drinkers are more likely to be smokers, so it is valuable to clarify whether the two habits interact with each other with regard to the incidence of various cancers.

The strengths and limitations of this review include the following. First, bias may have been introduced because non-published data and papers published in languages other than English and Chinese were not included and because some studies without sufficient data to calculate the OR or RR were excluded. Second, the strengths of our review include the large number of subjects investigated and the comprehensive picture provided. However, the lack of uniformity among the definitions of drinking and the inconsistent classification of ethanol doses and the duration or frequency of alcohol consumption are serious weaknesses in the primary studies. Third, although we conducted a subgroup analysis, there was still heterogeneity between the studies, possibly due to the differences among the definitions of alcohol consumption. The sensitivity analysis indicated the results of our meta-analysis were relatively consistent even when some studies were excluded. Last, this present review primarily involved case-control studies published in the existing literature, and the results should be interpreted cautiously due to the recall bias of case-control studies. Therefore, further prospective studies based on intensive designs are needed.

Implications for future practice and study: A previous study found that there was a clear decrease in risk with longer periods of abstention from alcohol consumption [39]. Given that alcohol consumption, and even heavy drinking, is so common and is an inveterate habit in China, public health programs and national policy responses including legislation, education, and the organization of alcohol control activities are important for cancer prevention in the Chinese population. We would like to emphasize the importance of adopting a consistent definition of current, former, ever, and never drinking and the need to be explicit when presenting the data. Uniformity is also important if a study reports the drinking dose, duration, and frequency; uniformity facilitates making comparisons between studies of different populations and regions. Furthermore, future studies need to focus on the interaction of alcohol consumption with other common risk factors, such as tobacco use.

In conclusion, the effect of alcohol consumption on the risk of some cancers might vary with ethnicity, the type of alcohol consumed, the drinking dose, or the lifestyle of the participants. For the Chinese population, alcohol consumption increased the risk for EC, gastric cancer, HCC, colorectal cancer, pancreatic cancer and NPC.

Public health programs and national policy responses to limit alcohol intake are needed to reduce the incidence of cancer in China. Further intensive studies based on well-designed schemes must focus on the interaction between alcohol consumption and common lifestyles, as well as the possible interaction with other risk factors, such as tobacco use.

Acknowledgments

The authors thank the library of the Third Military Medical University for literature searches. We are grateful to Dr. Ruiwen Zhang (University of Alabama, Birmingham, USA) and Professor Jinlin Tang (Chinese Cochrane Centre, Hong Kong Branch) for their revision and comments on the manuscript.

Author Contributions

Conceived and designed the experiments: JC. Performed the experiments: YL HY. Analyzed the data: YL HY. Wrote the paper: YL. Polished the manuscript: JC.

References

1. World Health Organization (1999) Global status report on alcohol. Geneva: World Health Organization.
2. Ma GS, Du SM, Hao LN, Li YP, Hu XQ, et al. (2009) The prevalence of heavy drinking among adults in China. Acta Nutrimenta Sinica 3: 213–217.
3. Health drinking activity committee (2007) Survey on alcohol drinking and health of Chinese people in 2007. .
4. World health organization (2000) International Guide for Monitoring Alcohol Consumption and Related Harm. Geneva. Available: http://whqlibdoc.who.int/HQ/2000/WHO_MSD_MSB_00.4.pdf. [Accessed 30 March 2010.].
5. Chinese nutrition society (2008) Dietary Guidelines for Chinese People. 2007 ed. Lhasa: Tibet Peoples Publishing press. pp 90–95.
6. Salaspuro MP (2003) Alcohol consumption and cancer of the gastrointestinal tract. Best Pract Res Clin Gastroenterol 17(4): 679–94.
7. Boffetta P, Hashibe M (2006) Alcohol and cancer. Lancet Oncol 7(2): 149–56.
8. Ragin CC, Langevin S, Rubin S, Taioli E (2010) Review of studies on metabolic genes and cancer in populations of African descent. Genet Med 12(1): 12–8.
9. Alberti C (2010) Hereditary/familial versus sporadic prostate cancer: few indisputable genetic differences and many similar clinicopathological features. Eur Rev Med Pharmacol Sci 14(1): 31–41.
10. Wang Z, Tang L, Sun G, Tang Y, Xie Y, et al. (2006) Etiological study of esophageal squamous cell carcinoma in an endemic region: a population-based case control study in Huaian, China. BMC Cancer 6: 287.
11. Guo YM, Wang Q, Liu YZ, Chen HM, Qi Z, et al. (2008) Genetic polymorphisms in cytochrome P4502E1, alcohol and aldehyde dehydrogenases and the risk of esophageal squamous cell carcinoma in Gansu Chinese males. World J Gastroenterol 14(9): 1444–9.
12. Zhang P, Di JZ, Zhu ZZ, Wu HM, Wang Y, et al. (2008) Association of transforming growth factor-beta 1 polymorphisms with genetic susceptibility to TNM stage I or II gastric cancer. Jpn J Clin Oncol 38(12): 861–6.
13. Wu J, Lu Y, Xu YC (2009) Relationship between IL-12B Gene Polymorphism and the Susceptibility of Gastric Cancer. China Cancer 4: 322–324.
14. Liu TT, Fang Y, Xiong H, Chen TY, Ni ZP, et al. (2008) A case-control study of the relationship between hepatitis B virus DNA level and risk of hepatocellular carcinoma in Qidong, China. World J Gastroenterol 14(19): 3059–63.
15. Wei YS, Lu JC, Wang L, Lan P, Zhao HJ, et al. (2009) Risk factors for sporadic colorectal cancer in southern Chinese. World J Gastroenterol 15(20): 2526–30.
16. Han RQ, Zhao JK, Liu AM, Wu M, Wang PH, et al. (2008) The effect of green tea and its possible interactions with relevant factors on lung cancer in Dafeng county, Jiangsu province, China. Acta Universitatis Medicinalis Nanjing(Natural Science) 3: 354–359.
17. Zhang M, Holman CD, Huang JP, Xie X (2007) Green tea and the prevention of breast cancer: a case-control study in Southeast China. Carcinogenesis 5: 1074–8.
18. Wang B, Zhang Y, Xu DZ, ZhangLei, Wang AH, et al. (2004) Meta-analysis of risk factors of esophageal cancer in Xi'an. Journal of The Fourth Military Medical University 51: 1952–1954.
19. Lu CD, Zhang SH (2007) Meta Meta-analysis of the relationship between alcohol drinking and gastric cancer in Chinese people. Journal of Xin Xiang medical college 1: 66–68.
20. Fan L H, Cai L (2009) Meta-analysis on the relationship between alcohol consumption and lung cancer risk. Journal of Hygiene Research 1: 85–89.

21. Pei GJ, Fu L, Cui YL, Lu WQ (2008) Meta-analysis on the association of hepatocellular carcinoma with alcohol drinking among drinking Chinese people. Modern Preventive Medicine 14: 2626–2627.
22. Wells GA, Shea B, O'Connell D, Petersen J, Welch V, et al. (2010) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. [http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm]. Accessed 2 March, 2010.
23. Cochran BG (1954) The combination of estimates from different experiments. Biometrics 10: 101–129.
24. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21: 1539–1558.
25. Greenland S, Longnecker MP (1992) Methods for trend estimation from summarized dose–response data, with applications to meta-analysis. Am J Epidemiol 135: 1301–1309.
26. Wu CF, Wu DC, Hsu HK, Kao EL, Lee JM, et al. (2005) Relationship between genetic polymorphisms of alcohol and aldehyde dehydrogenases and esophageal squamous cell carcinoma risk in males. World J Gastroenterol 11(33): 5103–8.
27. Fan Y, Yuan JM, Wang R, Gao YT, Yu MC (2008) Alcohol, tobacco, and diet in relation to esophageal cancer: the Shanghai Cohort Study. Nutr Cancer 60(3): 354–63.
28. Chang-Claude JC, Wahrendorf J, Liang QS, Rei YG, Muñoz N, et al. (1990) An epidemiological study of precursor lesions of esophageal cancer among young persons in a high-risk population in Huixian, China. Cancer Res 50(8): 2268–74.
29. Wu M, Zhao JK, Hu XS, Wang PH, Qin Y, Lu YC, et al. (2006) Association of smoking, alcohol drinking and dietary factors with esophageal cancer in high- and low-risk areas of Jiangsu Province, China. World J Gastroenterol 12(11): 1686–93.
30. Ke L, Yu P, Zhang ZX, Huang SS, Huang G, et al. (2002) Congou tea drinking and oesophageal cancer in South China. Br J Cancer 86(3): 346–7.
31. Qin JM, Yang L, Chen B, Wang XM, Li F, et al. (2008) Interaction of methylenetetrahydrofolate reductase C677T, cytochrome P4502E1 polymorphism and environment factors in esophageal cancer in Kazakh population. World J Gastroenterol 14(45): 6986–92.
32. Ding JH, Li SP, Cao HX, Wu JZ, Gao CM, Su P, et al. (2009) Polymorphisms of alcohol dehydrogenase-2 and aldehyde dehydrogenase-2 and esophageal cancer risk in Southeast Chinese males. World J Gastroenterol 15(19): 2395–400.
33. Yang SJ, Wang HY, Li XQ, Du HZ, Zheng CJ, et al. (2007) Genetic polymorphisms of ADH2 and ALDH2 association with esophageal cancer risk in southwest China. World J Gastroenterol 13(43): 5760–4.
34. Yang YF, Li H, Xu XQ, Diao YT, Fang XQ, et al. (2008) An expression of squamous cell carcinoma antigen 2 in peripheral blood within the different stages of esophageal carcinogenesis. Dis Esophagus 21(5): 395–401.
35. Wang AH, Sun CS, Li LS, Huang JY, Chen QS, et al. (2004) Genetic susceptibility and environmental factors of esophageal cancer in Xi'an. World J Gastroenterol 10(7): 940–4.
36. Wu M, Liu AM, Kampman E, Zhang ZF, Van't Veer P, et al. (2009) Green tea drinking, high tea temperature and esophageal cancer in high- and low-risk areas of Jiangsu Province, China: a population-based case-control study. Int J Cancer 124(8): 1907–13.
37. Tao X, Zhu H, Matanoski GM (1999) Mutagenic drinking water and risk of male esophageal cancer: a population-based case-control study. Am J Epidemiol 150(5): 443–52.
38. Gao CM, Takezaki T, Ding JH, Li MS, Tajima K (1999) Protective effect of allium vegetables against both esophageal and stomach cancer: a simultaneous case-referent study of a high-epidemic area in Jiangsu Province, China. Jpn J Cancer Res 90(6): 614–21.
39. Cheng KK, Duffy SW, Day NE, Lam TH, Chung SF, et al. (1995) Stopping drinking and risk of oesophageal cancer. BMJ 310(6987): 1094–7.
40. Cai L, You NC, Lu H, Mu LN, Lu QY, et al. (2006) Dietary selenium intake, aldehyde dehydrogenase-2 and X-ray repair cross-complementing 1 genetic polymorphisms, and the risk of esophageal squamous cell carcinoma. Cancer 106(11): 2345–54.
41. Yang W, Zhang Y, Tian X, Ning T, Ke Y (2008) p53 Codon 72 polymorphism and the risk of esophageal squamous cell carcinoma. Mol Carcinog 2: 100–4.
42. Zhang LW, IlyarSheyhidin, Wu MB, Wang YP, Zhang Z (2008) Study on relationship between genetic polymorphisms in methylenetetrahy drofolate reductase and risk of Kazakh's esophageal cancer in Xinjiang. Chinese Journal of Cancer Prevention and Treatment 17: 1294–1297.
43. Chen MR, Wang JN, Guo GP, Hua SL, Zhou Q, et al. (2008) Polymorphism of DNA repair gene XPD and XRCC1 and its relationship with esophageal squamous cell carcinoma. Fudan University Journal of Medical Sciences 2: 273–277.
44. Wang RD, Huai Y, Li QW (2008) Interaction of Risk Factors for Esophageal Cancer in Dongping County. Chinese Journal of Prevention and Control of Chronic Non-Communicable Diseases 1: 27–28.
45. Xue JH, Pan Q, Li XW, Luo R, Chen DR, et al. (2005) The correlation between risk factor of EC and Bcl-2 P-(53). Zhejiang Clinical Medical Journal 12: 1249–1250.
46. Wang W, Shi RH, Zhao ZQ (2004) Impact of CYP2E1 Polymorphisms on the Risk of Esophageal Cancer. Acta Academiae Medicinae Nanjing 4: 344–347.
47. Yang J, Yang RS, Li HQ, Wen PE, Jin SK (2004) Study of a CYP1A1 genotype associated with susceptibility to esophageal cancer. Chinese Journal of Clinical Oncology and Rehabilitation 1: 9–11.
48. Zhao DL, Yang YD, Chen MH, Hu MX, Zhang QH, et al. (2003) Study on Risk Factors of Esophageal Cancer in Feicheng City. Journal of Qilu Oncology 1: 27–30.
49. Ding JH, Wu JZ, Li SP, Gao CM, Zhou JN, et al. (2002) Polymorphisms of Aldehyde Dehydrogenase-2 Genotypes and Alcohol Consumption for the Susceptibility of the Liver Cancer,Stomach Cancer and Esophageal Cancer. Bulletin of Chinese Cancer 8: 450–452.
50. Gao CM, Takezaki T, Wu JZ, Li ZY, Ding JH, et al. (2002) Effects of GSTT1 and GSTM1 Genotypes,Lifestyle Factors and Their Interactions on Risk of Esophageal and Stomach Cancers. Journal of Qilu Oncology 2: 113–117.
51. Wu JZ, Gao CM, Ding JH, Liu YT, Zang Y, et al. (2002) Polymorphisms of methylenetetrahy drofolate reductase C677T and the risk of esophageal cancer. Tumor 4: 268–270.
52. Wu JZ, Ding JH, Li SP, Gao CM, Zang Y, et al. (2001) Polymorphisms of Aldehyde Dehydrogenase-2 Genotypes and the Risk of Esophageal Cancer. Bulletin of Chinese Cancer 12: 705–707.
53. Liu XM, Wang QS, Zhang YL, Meng ZH (2001) Etiological fraction and interactions analysis of risk factors in male esophageal cancer in Tianjin. Modern Preventive Medicine 3: 257–259.
54. Shen YP, Dai Q, Hu X, Xu TL, Xiang YB, et al. (1999) A case-control study on esophageal cancer in Huai An city, Jiangsu province (I): role of the cigarette smoking and alcohol drinking. TUMOR 6: 363–367.
55. Mu LN, Zhou XF, Ding BG, Wang RH, Zhang ZF, et al. (2003) A case-control study on drinking green tea and decreasing risk of cancers in the alimentary canal among cigarette smokers and alcohol drinkers. Chinese Journal of Epidemiology 24(3): 192–195.
56. Li H, Diao TY, Zhou ZY, Yang FY, Ma Q, et al. (2009) Relationship between the expression of hTERT and EYA4 mRNA in peripheral blood mononuclear cells with the progressive stages of carcinogenesis of the esophagus. Journal of Experimental and Clinical Cancer Research 28: 145.
57. Pan G, Takahashi K, Feng Y, Liu L, Liu T, et al. (1999) Nested case-control study of esophageal cancer in relation to occupational exposure to silica and other dusts. American Journal of Industrial Medicine 35(3): 272–280.
58. Tran GD, Sun XD, Abnet CC, Fan JH, Dawsey SM, et al. (2005) Prospective study of risk factors for esophageal and gastric cancers in the Linxian General Population Trial cohort in China. International Journal of Cancer 113(3): 456–463.
59. Wang JM, Xu B, Rao JY, Shen HB, Xue HC, et al. (2007) Diet habits, alcohol drinking, tobacco smoking, green tea drinking, and the risk of esophageal squamous cell carcinoma in the Chinese population. European Journal of Gastroenterology and Hepatology 19(2): 171–176.
60. Shen J, Wang RT, Wang LW, Xu YC, Wang XR (2004) A novel genetic polymorphism of inducible nitric oxide synthase is associated with an increased risk of gastric cancer. World J Gastroenterol 10(22): 3278–83.
61. Cai L, Yu SZ, Zhan ZF (2001) Cytochrome P450 2E1 genetic polymorphism and gastric cancer in Changle, Fujian Province. World J Gastroenterol 7(6): 792–5.
62. You WC, Zhang L, Gail MH, Chang YS, Liu WD, et al. (2000) Gastric dysplasia and gastric cancer: Helicobacter pylori, serum vitamin C, and other risk factors. J Natl Cancer Inst 92(19): 1607–12.
63. Setiawan VW, Zhang ZF, Yu GP, Li YL, Lu ML, et al. (2000) GSTT1 and GSTM1 null genotypes and the risk of gastric cancer: a case-control study in a Chinese population. Cancer Epidemiol Biomarkers Prev 9(1): 73–80.
64. Bao PP, Tao MH, Liu DK, Gao LF, Jin F (2001) A case-control study of smoking, alcohol consumption and stomach cancer. TUMOR 21(5): 334–338.
65. Huang GP, Zheng ZL, Cai L (2006) DNA repair gene XRCC3 Thr241Met polymorphism and susceptibility to cardia and non-cardia gastric cancer:a case-control study. Chinese Journal of Epidemiology 27(5): 420–425.
66. Lu Y, Xu YC, Shen J, Yu RB, Liu JY, et al. (2006) Relationship between polymorphism of E-cadherin gene and genetic susceptibility of non-cardia gastric cancer. Chinese Journal of Public Health 22(12): 1419–1420.
67. Meng QL, Huang S, Ji GZ, Fan ZN (2008) The associations between the Klotho gene G-395A and C1818T polymorphisms and the risk of gastric cancer. Acta Universitatis Medicinalis Nanjing (Natural Science) 28(10): 1258–1262, 1278.
68. Zhou Y, Jin GF, Jiang GJ, Wang HM, Tan YF, et al. (2007) Correlations of Polymorphisms of TGFB1 and TGFBR2 Genes to Genetic Susceptibility to Gastric Cancer. Chinese Journal of Cancer 26(6): 581–585.
69. Sun XW, Dai XD, Lin YJ, Shi YB, Jiang JS (1999) Study on the association between diet and gastric cancer. Journal of Practical Oncology 17(5): 220–221.
70. Chen JS, Chen ZC, Chen XZ, Chen LC, Wu JP (2002) Dietary and Other Living Habits and the Risk of Gastric Cancer in Changle, a High - Risk Area in China. Chinese Journal of Natural Medicine 4(3): 131–134.
71. Huang X, Lu YF, Xie NC, Zhang HT, Ning Z, et al. (2009) A case-control study on the association between genetic polymorphism of GSTM1 and gastric cancer susceptibility in population from Guangxi province of China. Chinese Journal of Gastroenterology and Hepatology 18(2): 97–99.
72. Fei SJ, Xiao SD (2004) Non-dietary factors and gastric cancer: a case-control study. Acta Academiae Medicinae Xuzhou 24(5): 379–383.
73. Shen XB, Pu YP, Zhang J, Zhu LJ (2005) Influence of GSTM1 and GSTT1 Genotypes and Smoking, Alcohol Exposure on the Occurrence of Gastric

Cancer: Case-control Study from Nanjing. China Journal of Labour Medicine 22(4): 325–329, 382.
74. Wei YH, Lu H, Ni JF, Ye DQ, Zang TH (2006) Conditional logistic analysis of smoking, alcohol consumption and gastric cancer. Chinese Journal of Disease Control & Prevention 10(2): 116–119.
75. Zhou JN, Gao CM, Takezaki T, Li ZY, Wu JZ, et al. (2003) Interaction between Polymorphisms in CYP2E1 Rsa I Genotypes and Lifestyle with Risk of Stomach Cancer. Journal of Oncology 9(5): 285–288.
76. Gao CM, Wu JZ, Liu YT, Ding JH, Li SP, et al. (2003) Interactions between lifestyle, methylanetetrahydrofolate reductase gene and polymorphisms in thymidylate synthase gene with risk of stomach cancer. Chinese Journal of Epidemiology 24(7): 599–603.
77. Wang LN, Ke Q, Chen WS, Zhou Y, Tang YF, et al. (2007) Study on the association between total plasma homocysteine levels, dietary habits and the risk of gastric cancer. Chinese Journal of Epidemiology 28(6): 528–531.
78. Fu G, Yang YF, Shen XB, Pu YP, Zhang J (2007) Relationship between the Methylenetetrahydrofolate Reductase A1298C Genetic Polymorphisms and Susceptibility to Gastric Cancer. Journal of Environmental & Occupational Medicine 1: 32–35.
79. Jiang AR, Wu JZ, Gao CM, Ding JH, Liu YT, et al. (2004) Relationship between polymorphisms of methylenetetrahydrofolate reductase A1298C and the susceptibility of gastric cancer. Hebei Medical Journal 26(11): 851–853.
80. Bi JP, Cai L, Zheng ZL (2005) Study on C667T gene polymorphism and susceptibility to gastric cancer. China Public Health 26(1): 661–663.
81. Zhou Y, Wang LN, Jiang GJ, Wang HM, Tan YF, et al. (2006) Molecular epidemiological study on the relationship between polymorphism of reduced folate carrier gene RFC1-G80A and susceptibility of gastric cancer. Tumor 26(12): 1081–1084.
82. Yu SZ, Zhang ZF, Yu GP, Zhu WD, Li YL, et al. (2001) Epidemiological study of the influence of drinking green tea on gastric cancer and chronic gastritis incidence. China Oncology 11(1): 41–45.
83. Ji BT, Chow WH, Yang G, McLaughlin JK, Gao RN, et al. (1996) The influence of cigarette smoking, alcohol, and green tea consumption on the risk of carcinoma of the cardia and distal stomach in Shanghai, China. Cancer 77(12): 2449–2457.
84. Zhang JY, Wang X, Han SG, Zhuang H (1998) A case-control study of risk factors for hepatocellular carcinoma in Henan, China. Am J Trop Med Hyg 59(6): 947–51.
85. Wu Y, Lin JS (2007) DNA methyltransferase 3B promoter polymorphism and its susceptibility to primary hepatocellular carcinoma in the Chinese Han nationality population: a case-control study. World J Gastroenterol 13(45): 6082–6.
86. Yuan JM, Gao YT, Ong CN, Ross RK, Yu MC (2006) Prediagnostic level of serum retinol in relation to reduced risk of hepatocellular carcinoma. J Natl Cancer Inst 98(7): 482–90.
87. Chang CK, Astrakianakis G, Thomas DB, Seixas NS, Ray RM, et al. (2006) Occupational exposures and risks of liver cancer among Shanghai female textile workers–a case-cohort study. Int J Epidemiol 35(2): 361–9.
88. Ding JH, Li SP, Wu JZ, Gao CM, Zhou JN, et al. (2007) Relationship among ADH2 and ALDH2 genotypes, alcohol drinking and risk of primary hepatocellular carcinoma. Chinese Journal of Cancer Prevention and Treatment 14(7): 500–504.
89. Huang GY, Ma XG, Wang CC (2005) Heavy alcohol consumption can enhance risk of hepatocellular carcinom a associated with hepatitis B virus infection. Journal of Qilu Oncology 12(5): 405–408.
90. Ye XP, Pen T, Liu TW, Xiao KY, Su ZX, et al. (2008) The effect of interaction between alcohol drinking and polymorphisms of cytochrome P450 2E1 on the susceptibility of hepatocellular carcinoma in Guang XI region. Journal of Guangxi Medical University 25(4): 493–495.
91. He SJ, Gu YY, Lin WZ, Zeng XY, Liao ZH (2008) Polymorphism of microsomal epoxide hydrolase and susceptibility to primary hepatocellular carcinoma. Tumor 28(2): 125–128.
92. Li SP, Wu JZ, Ding JH, Gao CM, Cao HX, et al. (2004) Impact of Genetic Polymorphisms of Glutathione S-transferaseT1,M1 on the Risk of Primary Hepatocellular Carcinoma in Alcohol Drinkers. The Practical Journal of Cancer 19(3): 229–232.
93. Chen JS, Chen ZC, Chen LC, Gao Z, Chen XC, et al. (2000) A Case control Study on Risk Factors of Primary Liver Cancer in Changle City, Fujian. Strail journal of preventive medicince 6(3): 6–8.
94. Sun XW, Dai XD, Shi YB (2000) Case-control study on risk factors for Liver cancer in Haerbin city. Journal of Practical Oncology 14(3): 181–184.
95. Chen FM, Zhou XQ, Du ZH, Chen J (2008) A Case-Control Study for Detecting Risk Factors of Primary Hepatocellular Carcinoma in Nanchong City. West China Medical Journal 23(6): 1345–1347.
96. Tang Y, Zhang RH, Lou XM, Meng J (2001) Survey on the association between alcohol drinking, smoking and liver cancer. Zhejiang Journal of Preventive Medicine 13(12): 11–12.
97. Li Y, Gao G, Wang JB, Wang LY, Wang XY, et al. (2003) To investigate the relationship of alcohol intake and primary hepatocellular carcinoma (The etiologic factor of 1057 PHC in JILIN province). Chinese Journal of Clinical Hepatology 3: 140–142.
98. Sakoda LC, Graubard BI, Evans AA, London WT, Lin WY, et al. (2005) Toenail selenium and risk of hepatocellular carcinoma mortality in Haimen City, China. International Journal of Cancer 115(4): 618–624.
99. Gao CM, Takezaki T, Wu JZ, Zhang XM, Cao HX, et al. (2008) Polymorphisms of alcohol dehydrogenase 2 and aldehyde dehydrogenase 2 and colorectal cancer risk in Chinese males. World J Gastroenterol 14(32): 5078–83.
100. Zhu ZZ, Wang AZ, Jia HR, Jin XX, He XL, et al. (2007) Association of the TP53 codon 72 polymorphism with colorectal cancer in a Chinese population. Jpn J Clin Oncol 37(5): 385–90.
101. Gao CM, Takezaki T, Wu JZ, Chen MB, Liu YT, et al. (2007) CYP2E1 Rsa I polymorphism impacts on risk of colorectal cancer association with smoking and alcohol drinking. World J Gastroenterol 13(43): 5725–30.
102. Jiang XT, Chen K, Yu WP, Li LY, Zhu YM, et al. (2004) Case–control study on the polymorphisms of methylenetetrahydrofolate reductases, drinking interaction and susceptibility in colorectal cancer. Chinese Journal of Epidemiology 25(7): 612–616.
103. Chen J, Li J, Xu SP, Song J (2002) Study on the correlation between living habits and colorectal cancer in HuBei. World Chinese Journal of Digestology 10(1): 105–107.
104. Zhang YL, Yuan XY, Zhang Z, Yang H, Zhou YH, et al. (2009) Relationship of genetic polymorphisms in thymidylate synthase and alcohol drinking with risk of colorectal cancer. Chinese Journal of Cancer Prevention and Treatment 16(8): 568–572.
105. Fu QH, Gao CM, Wu JZ, Cao J, TajimaKazuo, et al. (2007) Polymorphisms of GSTM1, GSTT1 and GSTP1 and susceptibility of rectal cancer. Acta Universitatis Medicinalis Nanjing 27(2): 196–201.
106. Jin MJ, Chen K, Zhang Y, Zhang W, Liu B, et al. (2007) Correlations of Single Nucleotide Polymorphisms of DNA Repair Gene XRCC1 to Risk of Colorectal Cancer. Chinese Journal of Cancer 26(3): 274–279.
107. Chen K, Jian Q, Ma X, Li Q, Yao K, et al. (2005) Alcohol drinking and colorectal cancer: A population-based prospective cohort study in China. European Journal of Epidemiology 20(2): 149–154.
108. Ji BT, Dai Q, Gao YT, Hsing AW, McLaughlin JK, et al. (2002) Cigarette and alcohol consumption and the risk of colorectal cancer in Shanghai, China. European Journal of Cancer Prevention 11(3): 237–244.
109. Tao WH, Jin YT, Yu ZC, Xue SL, Xu YC, et al. (2007) The effects of p16 gene methylation on the risk of non-small cell lung cancer. Oncology Progress 5(4): 393–403.
110. Lei FM, Li SF, Zhou WD, Luo WH, He JY, et al. (2007) A case-control study of the impact of glutathione S-transferase M1 polymonrphism on the risk of lung cancer. Modern Preventive Medicine 34(4): 724–726.
111. Chen JC, Wu XG, Duan XF, Yu HX, Zheng YP, et al. (2006) A Prospective Study of the Effect of Smoking and Body Mass Index on the Risk of Lung Cancer in Male Workers of Beijing Steel Industry. Chinese Journal of Prevention and Control of Chronic Non-Communicable Diseases 14(5): 311–313.
112. Chen SD, Yu SY, Chen Q, Wang BG, Chen MX, et al. (2002) A case-control study of the impact of CYP2E1 RsaI polymorphism on the risk of lung cancer. Academic Journal of Guangdong College of Pharmacy 18(3): 220–224.
113. Lu QJ, Yao SY, Huang CY, Lan YJ, Jiang Y, et al. (2000) The Cohort Study on Intake of Alcohol and Lung Cancer Risk in the Yunnan Tin Corporation (YTC) Miners. China public health 16(8): 707.
114. Jin MJ, Chen K, Zhang SS, Zhang YJ, Ren YJ, et al. (2006) Association of single nucleotide polymorphisms and haplotypes in DNA repair gene XRCC1 with susceptibility of breast cancer. Journal of Zhejiang University(Medical Sciences 35(4): 370–369, 376.
115. Huang XM, Wang CX, Zhou YS, Ceng Y (2006) An elementary study on risk factors of breast cancer of women in Shenzhen Baoan area. Central Plains Medical Journal 33(22): 37–39.
116. Wang LY, Liu L, Tao F, Qin LP, Ding H (2008) Survey on the association between dietary habits and female breast cancer. Maternal and Child Health Care of China 23(32): 4630–4631.
117. Yang M, Sun T, Wang L, Yu D, Zhang X, et al. (2008) Functional variants in cell death pathway genes and risk of pancreatic cancer. Clin Cancer Res 14(10): 3230–6.
118. Wang L, Lin DX, Lu XH, Mu XP (2006) Polymorphisms of the DNA repair genes XRCC1 and XPC: relationship to pancreatic cancer risk. Journal of Hygiene Research 35(5): 534–536.
119. Fang YQ, Zhou GZ, Li ZS, Yu ZL, Zou XP, et al. (2002) Study on the relationship between pancreatic caner and lifestyle and diet habits. Medical Journal of Chinese People's Liberation Army 4: 289–291.
120. Dai Q, Ji BT, Jin F, Xu M, Gao YT (1996) Tobacco, alcohol and greent tea comsumption and pancreatic cancer: a population based case-control study in urban Shanghai, China. TUMOR 16(1): 5–10.
121. Yang X, Yu ZL (1998) The assoiation between smoking, alcohol comsumption, cholelithiasis, diabet and pancreatic cancer. Chinese Journal of Medicine 4: 5–7.
122. Li XM, Li J, Tsuji I, Nakaya N, Nishino Y, et al. (2008) Mass screening-based case-control study of diet and prostate cancer in Changchun, China. Asian J Androl 4: 551–60.
123. Yang J, Qian LX, Wu HF, Xu ZQ, Sui YG, et al. (2006) Genetic polymorphisms in the cytochrome P450 1A1 and 2E1 genes, smoking, drinking and prostate cancer susceptibility: a case-control study in a Han nationality population in Southern China. Int J Urol 6: 773–80.
124. Yang J, Gu M, Song NH, Feng NH, Hua LX, et al. (2009) Correlation of Prostate Cancer Susceptibility with Genetic Polymorphism of Cytochrome

P450 2E1, Smoking and Drinking:A Case-Control Study in the Population of Nanjing Area. National Journal of Andrology 1: 7–11.
125. Xu Z, Qian LX, Hua LX, Wang XR, Yang J, et al. (2007) Relationship Between DNA Repair Gene XRCC1 Arg399Gln Polymorphism and Susceptibility to Prostate Cancer in the Han Population in Jiangsu and Anhui. National Journal of Andrology 4: 327–331.
126. Zou J, Sun Q, Akiba S, Yuan Y, Zha Y, et al. (2000) A case-control study of nasopharyngeal carcinoma in the high background radiation areas of Yangjiang, China. J Radiat Res (Tokyo) 41 Suppl: 53–62.
127. Zou JM, Sun QF, Yuan YL, Qiu YDB, Cha YR, et al. (1999) A case control study of nasopharyngeal carcinoma among inhabitants in high background radiation areas of Yangjiang,China. Chinese journal of radiation mediation mediation and protection 19(2): 90–94.
128. Zhang XA, Zhou GQ, Cui Y, Xie WM, Zhuo T, et al. (2008) Lack of association between the polymorphism of-9C→G of PTEN gene and hereditary susceptibility to nasopharyngeal carcinoma in Chinese population. Medical Journal of Chinese People's Liberation Army 8: 943–946.
129. Yuan JM, Wang XL, Xiang YB, Gao YT, Ross RK, et al. (2000) Non-dietary risk factors for nasopharyngeal carcinoma in Shanghai, China. International Journal of Cancer 85(3): 364–369.
130. Hung HC, Chuang J, Chien YC, Chern HD, Chiang CP, et al. (1997) Genetic polymorphisms of CYP2E1, GSTM1, and GSTT1; environmental factors and risk of oral cancer. Cancer Epidemiol Biomarkers Prev 6(11): 901–5.
131. Zheng W, Blot WJ, Shu XO, Diamond EL, Gao YT, et al. (1992) Risk factors for oral and pharyngeal cancer in Shanghai, with emphasis on diet. Cancer Epidemiol Biomarkers Prev 1(6): 441–8.
132. Gong Y, Wang XF, Sun QS, Zhang ZL (2000) Study on the risk of smoking and alcohol drinking for tonque cancer. Chinese Primary Health Care 5: 54–55.
133. Zhang XH, Andreotti G, Gao YT, Deng J, Liu E, et al. (2006) Tea drinking and the risk of biliary tract cancers and biliary stones: a population-based case-control study in Shanghai. China. Int J Cancer 12: 3089–94.
134. Zhang XF, Gao YT, Asif R, Deng J, Liu EJ, et al. (2004) Cigarette Smoking,Alcohol Consumption and Risk of Biliary Tract Cancers:A Population-based Case-control Study in Shanghai,China. Cancer Research On Prevention and Treatment 31(10): 597–600.
135. Tao LY, He XD, Qu Q, Cai L, Liu W, et al. (2009) Risk factors for intrahepatic and extrahepatic cholangiocarcinoma: a case-control study in China. Liver Int 31(10): 759–63.
136. Bagnardi V, Blangiardo M, La Vecchia C, Corrao G (2001) A meta-analysis of alcohol drinking and cancer risk. Br J Cancer 85(11): 1700–5.
137. Zhang XF, Pei GJ, Xu ZY, Yao W, Feng LY, et al. (2009) Meta-analysis on the risk factors of esophageal cancer in China. Modern Preventive Medicine 5: 819–822.
138. Gao YM, Hu YL, Xin ZC, Chi BF (2005) Meta-analysis of the relationship between psychological factors, living habits and gastric cancer in Chinese people. Acta Academiae Medicinae Neimongol 27(4): 284–286.
139. Longnecker MP, Orza MJ, Adams ME, Vioque J, Chalmers TC (1990) A meta-analysis of alcoholic beverage consumption in relation to risk of colorectal cancer. Cancer Causes Control 1(1): 59–68.
140. Tramacere I, Scotti L, Jenab M, Bagnardi V, Bellocco R, et al. (2010) Alcohol drinking and pancreatic cancer risk: a meta-analysis of the dose-risk relation. Int J Cancer 126(6): 1474–86.
141. Shi J, Wu C, Liu S, Xie WF (2004) Meta analyses of risk factors for pancreatic cancer in China. Chinese Journal of Pancreatology 3: 154–158.
142. Smith-Warner SA, Spiegelman D, Yaun SS, van den Brandt PA, Folsom AR, et al. (1998) Alcohol and breast cancer in women: a pooled analysis of cohort studies. JAMA 18; 279(7): 535–40.
143. Key J, Hodgson S, Omar RZ, Jensen TK, Thompson SG, et al. (2006) Meta-analysis of studies of alcohol and breast cancer with consideration of the methodological issues. Cancer Causes Control 17(6): 759–70.
144. Nichols HB, Trentham-Dietz A, Love RR, Hampton JM, Hoang Anh PT, et al. (2005) Differences in breast cancer risk factors by tumor marker subtypes among premenopausal Vietnamese and Chinese women. Cancer Epidemiol Biomarkers Prev 14(1): 41–7.