

## Original Article

# The association of tea consumption with bladder cancer risk: a meta-analysis

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The association between tea consumption and bladder cancer has been confirmed in several animal studies, but one epidemiological study in 2001 showed no association between them. In order to provide an accurate assessment of this, we conducted a meta-analysis on tea consumption and bladder cancer risk. Studies were identified by a literature search in PubMed from January 1980 to March 2012 and the reference lists of relevant studies. Random effect models were used to calculate summary relative risk estimates (RR) and their corresponding 95% confidence intervals (CI) based on high contrast to low intake values. Twenty-four publications (6 cohort studies and 18 case-control studies) based on consumption of overall tea, black tea, and green tea to bladder cancer risk were included in this analysis. For overall tea, the summary RR indicated no association between tea consumption and bladder cancer (RR= 1.09, 95%CI: 0.85-1.40). In subgroup analyses, we found a moderate increase of bladder cancer risk in smoking group (RR= 1.77, 95%CI: 1.04-3.01). In the black tea group, no statistically significant association was observed (RR= 0.84, 95%CI: 0.70-1.01). Interestingly, in the subgroup of sex, a protective effect was observed between tea consumption and bladder cancer risk in females (RR= 0.61, 95%CI: 0.38-0.98). For green tea group, there was no relationship associated with bladder cancer risk (RR= 1.03, 95%CI: 0.82-1.31). In conclusion, our data suggest that high overall tea intake in smokers increased the risk of bladder cancer, and high black tea intake in females may reduce the risk of bladder cancer.

**Key Words:** bladder cancer, overall tea, black tea, green tea, meta-analysis

## INTRODUCTION

Bladder cancer is the second most common genitourinary tumor and a significant cause of morbidity and mortality for both males and females globally.<sup>1</sup> At present, the majority of bladder cancers are superficial at the time of diagnosis and most of them (60-70%) have a propensity for recurrence after initial transurethral resection of bladder cancer. Some (15-25%) of patients are at high risk for progression to invasive bladder cancer.<sup>2</sup> Adjuvant chemotherapy and immunotherapy have been used to treat invasive bladder cancer but have failed to show an apparently survival advantage.<sup>3-5</sup>

Bladder cancer has the highest lifetime treatment cost of any cancer.<sup>6</sup> The direct exposure to carcinogens is implicated in bladder cancer development and many potentially protective compounds are concentrated in urine, making it an ideal target for preventive therapies.<sup>7</sup> Over the past three decades, a number of epidemiological studies have been conducted to investigate determinants of bladder cancer.<sup>8-9</sup> These studies suggested that bladder cancer is significantly influenced by environmental fac-

tors (eg cigarette smoking, fluid, chemicals and infections).

Tea is the most popular beverage in the world, second only to water, consumed by over two thirds of the world's population.<sup>10</sup> It is produced from the leaves of the plant *Camellia sinensis*, with differences in processing methods, of which green and black tea are the most consumed worldwide.<sup>11-13</sup> Animal studies strongly have suggested that tea or the active ingredient of tea, polyphenols, have cancer preventative or inhibitory effects in various tissues.<sup>14-15</sup> However, the effect of tea consumption on the risk of bladder cancer is poorly explored, only one meta-

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analysis article of association between tea consumption and bladder cancer risk has been published by Maurice PA Zeegers et al. in 2001.<sup>16</sup>

In order to clarify the role of different kind of tea in bladder cancer, we conducted a meta-analysis from cohort and case-control studies (until March 2012).

## METHODS

### Search strategy

We conducted a literature search in PubMed for all relevant papers published from January 1980 to March 2012 using the search terms “tea”, “green tea”, “black tea”, “catechin”, “theaflavin”, “thearubigin”, “water”, “beverage” or “fluid” combined with “bladder cancer”, “urothelial cancer”, “urinary tract cancer”, “bladder neoplasm” or “urothelial neoplasm”. Furthermore, we also reviewed the reference of those papers to make sure all relevant articles were collected.

### Study selection

The following criteria were used to select relevant studies: 1) original cohort or case-control study design; 2) overall, green tea, and black tea consumption; 3) bladder cancer as the outcome (or bladder cancer accounting for the majority); 4) the risks estimate [relative risk (RR) or odds ratio (OR)] with their corresponding 95% confidence intervals (CI) were reported or these data could be calculated.

The process of study selection is showed in Figure 1.

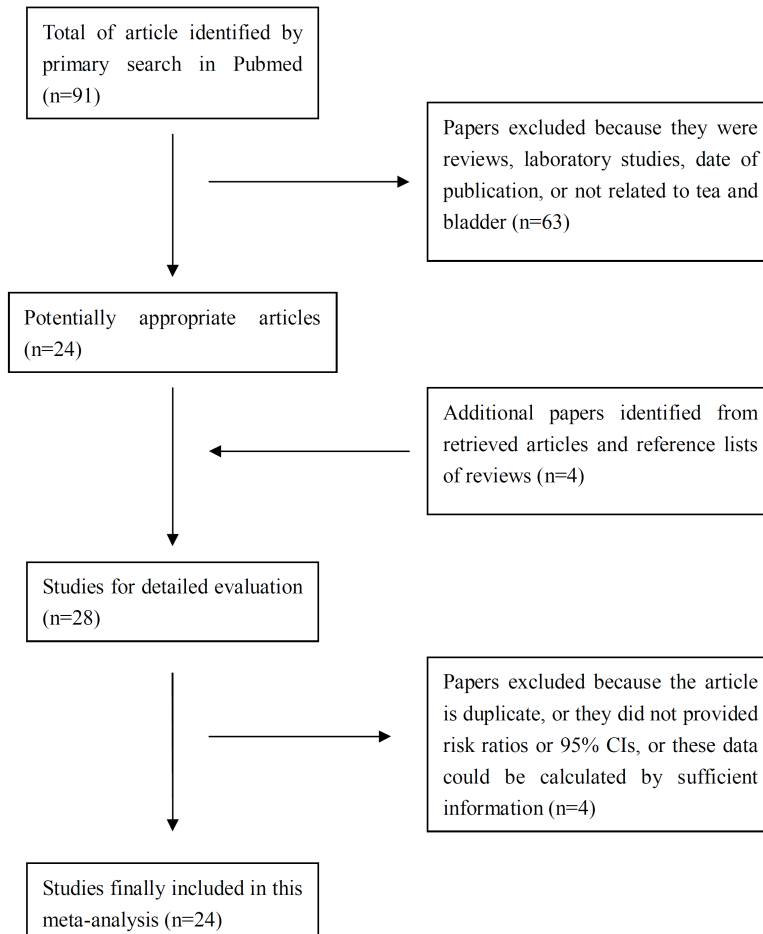
Twenty-four potentially relevant studies were identified by searching PubMed and references of retrieved articles or reviews. Four studies were excluded because of duplication, or if risk ratios or 95% CIs were not provided, or these data could not be calculated by sufficient information. Thus, a total of 24 studies were included in this meta-analysis.

### Date extraction

All date were extracted independently by two investigators (Zhang and Li) according to the pre-specified selection criteria. Discrepancies were resolved by discussion. We extracted the following data from each publication by using a standardized data form: study name (first author and publication year), study design (cohort or case-control studies), study location, sample size, study follow-up period, tea type, results of studies (adjusted RR or OR with their corresponding 95% CI) and the adjusted factors. We are considering that bladder cancer is a rare disease, so the RR was assumed to be approximately the same as the OR.<sup>17</sup> The most recent and complete study (adjusted by more factors in main multivariable model) was included if date were duplicated in more than one studies

### Statistical analyses

All statistical analyses were based on comparisons of the highest intake category with the lowest intake category (contained persons who did not consume tea). Heteroge-



**Figure 1.** Process of study selection for tea consumption and risk of bladder cancer

neity was measured by Q-test, and was considered statistical significance while  $p < 0.1$ . OR is the common measure instead of HR and RR in this study.<sup>18</sup> Fixed or Random effects models were used to calculate summary OR, 95% CI and corresponding  $p$ -values for heterogeneity.<sup>19</sup> Forest plots were applied to assess the relationship between tea consumption and bladder cancer. Subgroup analyses (study design, sex, geographic region, smoking status and publication year) were also carried out for establishing the effects of clinical heterogeneity between studies. Age, gender, BMI, smoking status, and energy intake were the most essential confounders to bladder cancer risk. To evaluate whether low-quality studies would affect the results, this analysis were stratified according to whether the effect sizes had been adjusted for at least 3 of these confounders.<sup>17</sup> A sensitivity analysis was conducted to test the impact of each study on the pooled estimates by removing each study in turn from the meta-analysis.<sup>7</sup> Egger's and Berg's tests were applied to assess the possible bias captured to investigate whether publication bias might affect the validity of the estimates. As the two tests above have limited ability to detect possible biases,<sup>17</sup> especially when the number of studies is small,<sup>20</sup> we set  $p = 0.1$  as our statistical penalty in these two tests ( $p < 0.1$  indicated possible publication bias). All statistical analyses were conducted with Stata (version 12.0, Stata Corp, College Station, TX, USA).

## RESULTS

Twenty-four studies are presented in Table 1. Studies were classified into 3 groups: overall tea group, green tea group and black tea group. Fifteen studies based on overall tea; whereas 5 reported data on green tea and 6 on black tea individually (some studies contained green tea or black tea besides overall tea). Among these studies, 8 were in Asia, 10 in the Americas, 5 in Europe and 1 in Oceania (Table 1). The primary outcomes of some studies were defined as urinary tract cancer.<sup>21-25</sup> Most cases in these studies were bladder cancer. Moreover the other studies contained bladder cancer only.

A moderate risk increase in smoking subgroup, but no significant association between overall tea consumption and bladder cancer were found in 15 studies on overall tea intake.<sup>21-23,26-37</sup> In random effects model, no significant association between overall tea consumption (high in contrast to low intake) and bladder cancer risk was observed (Table 2 and Figure 2a, RR = 1.09, 95% CI: 0.85-1.40,  $p$  for heterogeneity:  $< 0.01$ ). To explore the source of heterogeneity, we pooled the RR and 95% CI from the subgroups of study design (cohort or case-control), sex (male or female), geographical region, smoking, adjustments and publication years (before or after 2000). No significant association was observed in the subgroups stratified by study design (cohort: RR = 0.64, 95% CI: 0.40-1.04, case-control: RR = 1.22, 95% CI: 0.95-1.57). According to sex, both male (RR = 1.34, 95% CI: 0.62-2.88) and female (RR = 0.93, 95% CI: 0.56-1.53) showed no significant association between overall tea consumption and bladder cancer risk. When we stratified the studies by region, non-association was noted in the Americas (RR = 1.19, 95% CI: 0.86-1.64), Europe (RR = 0.91, 95% CI: 0.75-1.11) and other continents (China and Nether-

land) (RR = 1.26, 95% CI: 0.21-7.49). Interestingly, we found a moderate risk increase in the smoking group (RR = 1.77, 95% CI: 1.04-3.01), but no significance in the non-smoking group (RR = 1.35, 95% CI: 0.69-2.65). Both were not significant in the adjustments ( $\leq 3$  or  $> 3$ ) and publication years (before or after 2000) [(RR = 1.01, 95% CI: 0.80-1.29) and (RR = 1.00, 95% CI: 0.65-1.57)], [(RR = 1.22, 95% CI: 0.80-1.88) and (RR = 0.95, 95% CI: 0.73-1.23)]. The majority of them were not identified as a possible source of heterogeneity among all tea studies included (Table 2).

No publication bias was found among all studies either with Egger's ( $p = 0.88$ ) or Begg's test ( $p = 0.11$ ). We also performed sensitivity analysis by sequentially excluding each study in turn to examine the influence of individual studies on the overall estimate and found that none of the studies considerably affected the summary effects in this meta-analysis.

A risk decrease in females subgroup were found on black tea intake. The analysis of black tea and bladder cancer risk were based on 6 studies.<sup>24,25,38-41</sup> The summary RR and 95% CI of bladder cancer risk were 0.84 and 0.70-1.01 (Table 2 and Figure 2c). To explore the source of the borderline significance, we pooled the summary RR by sex (male and female). As shown in Table 2, a positive relationship between black tea consumption and bladder cancer risk was observed in women (RR = 0.61, 95% CI: 0.38-0.98), but not in men (RR = 0.91, 95% CI: 0.71-1.18). And there were no evidence of heterogeneity among all studies and subgroup (sex) studies. No publication bias was detected ( $p = 1.00$  by Egger's test and  $p = 0.89$  by Begg's test).

Green tea intake was not associated with bladder cancer risk. A limited number of 5 studies of green tea were included in our meta-analysis.<sup>21,38,39,42,43</sup> Green tea intake was not associated with bladder cancer risk (Table 2 and Figure 2b, RR = 1.03, 95% CI: 0.82-1.31). There was no evidence of heterogeneity and publication bias ( $p = 0.49$  by Egger's test and  $p = 0.81$  by Begg's test).

## DISCUSSION

Many studies had demonstrated that tea has cancer preventative or inhibitory effects in various tissues. However, no association had been found between tea consumption and bladder cancer in previous analysis.<sup>16</sup> Until now, 7 newly cohort or case-control studies on tea intake and bladder cancer have been published. Based on abundant literature, we completed this meta-analysis for more comprehensive results on the association between tea consumption and bladder cancer.

We evaluated the association between tea consumption and bladder cancer risk, and found no significant relationship between them. This result is similar to those found in 2001 by Maurice PA Zeegers *et al*<sup>16</sup> In order to examine the potential sources of heterogeneity, we conducted subgroup analysis by study design (cohort or case-control), sex (male or female), geographical region (the Americas, European, or other continents), smoking (ever or never), adjustments (at least 3 or not) and publication years (before or after 2000). However, the majority of them were not identified as a possible source of heterogeneity among all studies included. Interestingly, there was a moderate

**Table 1.** Study characteristics of published cohort and case-control studies on tea intake and bladder cancer

First author and year	Study design	Tea types	Anatomical site of urinary tract	Study location	Study period	Cases/Subjects	Tea consumption levels (lowest vs highest)	Pooled RR (95% CI)	Adjustments
Ohno <i>et al</i> , 1985 <sup>40</sup>	case-control	black tea	Bladder	Japan	1976-1978	292/589	ever vs not (men) ever vs not (women)	0.95 (0.68, 1.32) (men) 0.55 (0.29, 1.03) (women)	age, smoking
Jensen <i>et al</i> , 1986 <sup>31</sup>	case-control	tea	Bladder	Denmark	1979-1981	371/771	0 ml/day vs (1000-1499) ml/day (men) 0 ml/day vs (1000-1499) ml/day (women)	1.50 (0.70, 3.20) (men) 1.0 (0.40, 2.50) (women)	smoking
Heilbrun <i>et al</i> , 1986 <sup>50</sup>	cohort	black tea	Bladder	Japan	1965-1985	57/7833	never vs once/day	0.71 (0.24, 1.74)	age and smoking
Slattery <i>et al</i> , 1988 <sup>27</sup>	case-control	tea	Bladder	America	1977-1982	419/889	0 cup/day vs ≥4 cups/day (never smoker) 0 cup/day vs ≥4 cups/day (ever smoker)	2.25 (1.25, 3.91) (never smoker) 3.04 (1.92, 4.84) (ever smoker)	age, sex, diabetes, bladder infection
Abraham <i>et al</i> , 1991 <sup>25</sup>	case-control	black tea	urinary tract	America	1977-1986	259/520	0 cup-years vs >10 cups-years* (men) 0 cup-years vs >10 cups-years* (women)	0.70 (0.4, 1.20) (men) 0.7 (0.30, 1.70) (women)	pack-years, cigarette smoking
Kunze <i>et al</i> , 1992 <sup>24</sup>	case-control	black tea	urinary tract	Germany	1977-1985	283/486	0 cup/day vs ≥5 cups/day (men) 0 cup/day vs >5cups/day (women)	1.40 (0.70, 3.10) (men) 0.70 (0.20, 2.30) (women)	smoking
La Vecchia <i>et al</i> , 1992 <sup>32</sup>	case-control	tea	Bladder	Italy	1983-1990	365/6147	never vs ≥1 cup/day	0.80 (0.50, 1.10)	age, sex, area of residence, education, smoking, coffee consumption
D'Avanzo <i>et al</i> , 1992 <sup>33</sup>	case-control	tea	Bladder	Italy	1985-1990	555/855	never vs ever	0.90 (0.60, 1.20)	age, sex, education, smoking, alcohol and exposure to occupation at risk(chemical industry, dyestuff, painting, pharmaceutical and coal/gas)
Lynne <i>et al</i> , 1996 <sup>21</sup>	case-control	tea and green tea	urinary tract	America	1979-1986	/	never vs frequency (men of tea) never vs frequency (women of tea) never vs frequency (men of green tea) never vs frequency (women of green tea)	0.70 (0.40, 1.30) (men of tea) 0.90 (0.40, 2.20) (women of tea) 1.10 (0.60, 2.30) (men of green tea) 0.90 (0.30, 2.60) (women of green tea)	age, smoking, occupation and, dark green vegetables in men and total vitamin C consumption in women

\*: Cup-years indicate number of cups/day×years. For example: 10cups-years could equal 10cups/day for one year

**Table 1.** Study characteristics of published cohort and case-control studies on tea intake and bladder cancer (cont.)

First author and year	Study design	Tea types	Anatomical site of urinary tract	Study location	Study period	Cases/Subjects	Tea consumption levels (lowest vs highest)	Pooled RR (95% CI)	Adjustments
Bates <i>et al</i> , 2007 <sup>35</sup>	case-control	mate	Bladder	Argentina	1996-2000	114/114	≤0.09 L/day vs >0.9 L/day (Mate con bombilla) never vs ≥ 2.25L/day (Mate cocido)	1.16 (0.46, 2.93) (Mate con bombilla) 1.30 (0.65, 2.60) (Mate cocido)	sex, age, county of residence, level of education, cigarettes smoked per day, and an indicator variable for whether or not the other type of mate was consumed at that time
De Stefani <i>et al</i> , 2007 <sup>29</sup>	case-control	tea	Bladder	Uruguay	1996-2000	221/462	Never vs ≥7 cups/week	1.50 (0.80, 2.80)	age, sex, residence, urban/rural status, education, family history of bladder cancer among first-degree relatives, body mass index, occupation, smoking status, years since quitting, number of cigarettes smoked per day, mate drinking, soft drink intake, milk intake
Demirel <i>et al</i> , 2008 <sup>41</sup>	case-control	black tea	Bladder	Japan	2001-2006	/	/	0.74 (0.38, 1.43)	/
Jiang <i>et al</i> , 2008 <sup>36</sup>	case-control	tea	Bladder	America	1987-1999	1586/1586	0 cup/day vs ≥5 cups/day	0.88 (0.54, 1.45)	education, NSAIDs, intake of carotenoids, number of years as a hairdresser/barber, smoking
Kurahashi <i>et al</i> , 2009 <sup>39</sup>	cohort	green tea	Bladder	Japan	1990-2005	206/104440	<1 cup/day vs ≥5 cups/day (men) <3 cup/day vs ≥5 cups/day (women)	0.9 (0.56, 1.45) (men) 2.29 (1.06, 4.92) (women)	age, area, smoking status, alcohol, coffee
Hemelt <i>et al</i> , 2010 <sup>42</sup>	case-control	green and black tea	Bladder	China	2005-2008	432/392	Never vs ≥4 cups/day (green tea) Never vs ≥4 cups/day (black tea)	0.83 (0.53, 1.28) (green tea) 0.88 (0.57, 1.38) (black tea)	age, sex, smoking status, smoking frequency, smoking duration
Ros <i>et al</i> , 2011 <sup>34</sup>	cohort	tea	Bladder	European	not mentioned	513/233236	<12 ml/day (men) or 16 ml/day (women) vs <200 ml/day (men) or 264 ml/day (women)	0.91 (0.64, 1.30)	age and sex and centre

\*: Cup-years indicate number of cups/day×years. For example: 10cups-years could equal 10cups/day for one year

**Table 2.** Summary of pooled risk ratios of bladder cancer for the highest versus lowest category of tea intake by study design, sex, geographic region, smoking, publication years

Analysis specifications	Number of studies	Pooled RR (95% CI)	<i>p</i> -values for interaction or moderation effect between the stratified factor and tea consumption
Overall tea	15	1.09 (0.85-1.40)	<0.01
Study design			
Cohort	3	0.64 (0.40-1.04)	0.05
Case-control	12	1.22 (0.95-1.57)	<0.01
Sex			
Men	3	1.34 (0.62-2.88)	0.03
Women	3	0.93 (0.56-1.53)	0.98
Geographical region			
The Americas	9	1.19 (0.86-1.64)	<0.01
European	4	0.91 (0.75-1.11)	0.64
Other continents	2	1.26 (0.21-7.49)	<0.01
Smoking			
Ever	3	1.77 (1.04-3.01)	0.02
Never	3	1.35 (0.69-2.65)	0.08
Adjustments*			
≥3	7	1.01 (0.80-1.29)	0.06
<3	8	1.00 (0.65-1.57)	<0.01
Publication years			
Before 2000	8	1.22 (0.80-1.88)	<0.01
After 2000	7	0.95 (0.73-1.23)	<0.01
Black tea	6	0.84 (0.70-1.01)	0.88
Sex			
Male	4	0.91 (0.71-1.18)	0.48
Female	3	0.61 (0.38-0.98)	0.88
Green tea	5	1.03 (0.82-1.31)	0.83

\*: adjusted for at least three of the following factors: age, gender, BMI, smoking, and energy intake.

positive and higher association of tea consumption with risk of bladder cancer in smokers. We found that generally, smokers had higher tea consumption compared to non-smokers, and that the persons of no smoking and no drinking tea had a 2-fold increased risk compared to the persons of no smoking and drinking tea in a previous analysis,<sup>44</sup> and smoking was a specific risk factor to bladder cancer. So in smokers, tea consumption may increase risk of bladder cancer, and the mechanism of this is unclear.

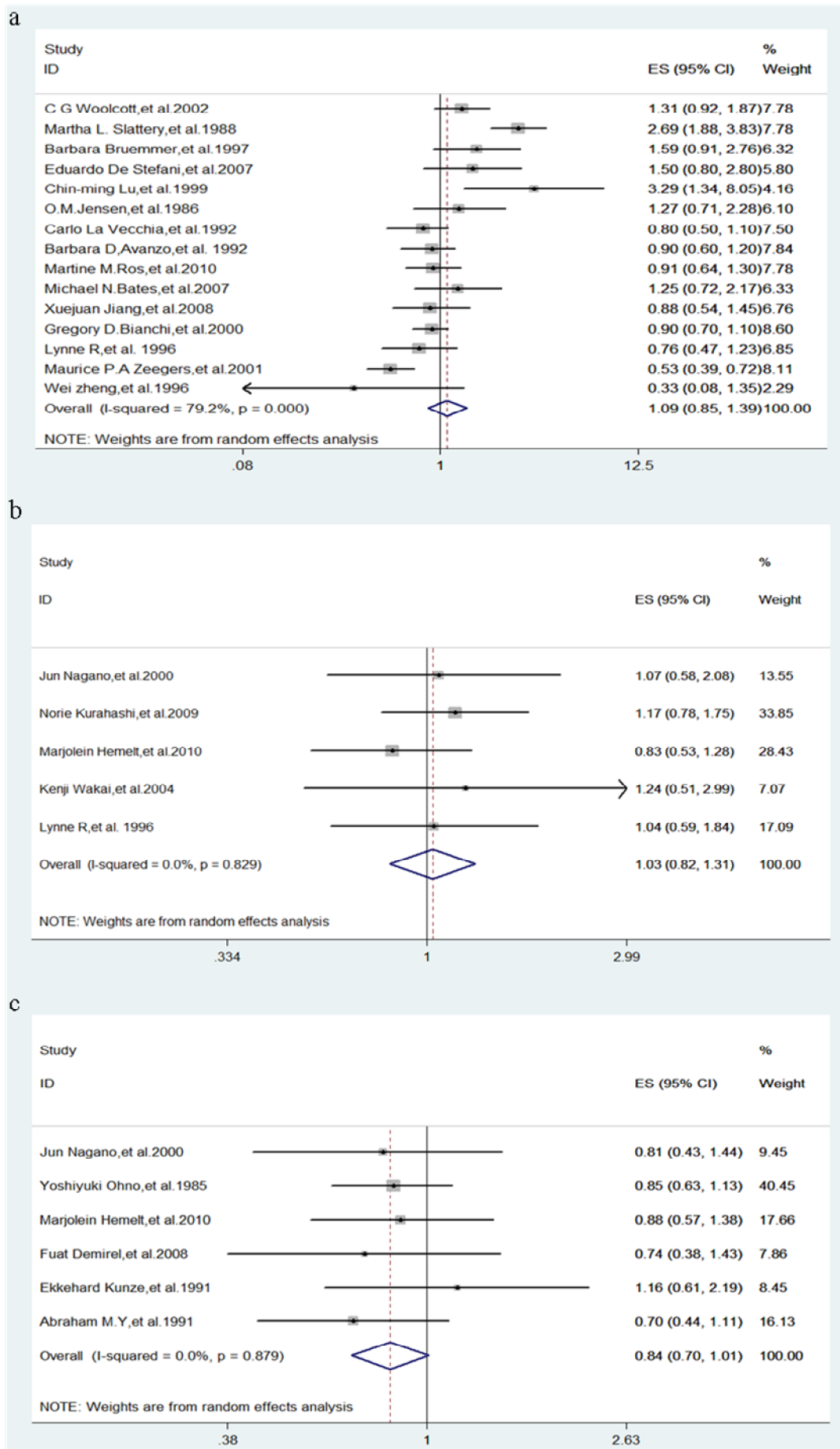
A completely novel finding of the present study compared with the previous meta-analysis was that high intake of black tea in females was associated with a statistically marginal reduced risk of bladder cancer, but the same association was not found with in green tea. Black tea (78%) is the most commonly consumed tea worldwide. Many *in vitro* and animals studies suggest that thearubigins and theaflavins that exist in black tea, specifically theaflavin-3,3'-digallate, have strong antioxidant activity and could reduce tumor formation, tumor size and cellular proliferation.<sup>45-47</sup> In females, the androgen is much more lower than in male, and the androgen deprivation (androgen inhibitor) is a novel finding in bladder cancer treatment. In addition to these, less smoking and alcohol consumption could be found in females compared to males. So the anti-tumor effect on bladder cancer of black tea was reasonably better in females than in males. However, the total phenol content and antioxidant capacity of green tea have been shown to be much higher than that of black tea,<sup>48,49</sup> but no association between green tea consumption and bladder cancer risk were found in this meta-analysis. Although this finding was very interesting

and novel, it should be interpreted with caution because the subgroup analysis (black tea and green tea) included data from only 6 and 5 studies.

Five studies on urinary tract cancer were included in the present meta-analysis.<sup>21-25</sup> Because the overwhelming majority of urinary tract tumors occurred in the bladder and, since the renal pelvis and urethra are covered by the same urothelium as the urinary bladder, no biologically plausible difference would be expected.<sup>16</sup>

Our meta-analysis has several important limitations which should be taken into account when interpreting our results. Firstly, analytic comparisons varied a great deal across studies in this analysis. Different units (times/d, cups/d, cups/wk, ml/d, frequency/wk, cups/y) were found in each study with regard to tea consumption data. Secondly, only few studies were included in each subgroup (sex, smoking, geographical region). Thirdly, loss of follow-up in cohort study and recall bias in case-control study maybe exist. These differences may have contributed to the heterogeneity among studies (overall tea, green tea, black tea and some other subgroups). Lastly, we were prone to collect published studies, and the language of such publications was limited to English, so the publication bias maybe inevitable, even though no significant evidence of publication bias was observed.

In conclusion, our meta-analysis suggests that there was an absence of an association between tea intake and the risk of bladder cancer; however, high intake of overall tea in smokers and low intake of black tea in women may increased the risk of bladder cancer according to the results found in theses limited number studies. Further studies are needed to confirm these findings.



**Figure 2.** Pooled relative risks (highest in contrast to lowest category) for 15 studies of overall tea intake (a), 5 studies of green tea intake (b), 6 studies of black tea intake (c) and bladder cancer risk.

**AUTHOR DISCLOSURES**

The authors have declared that no competing interests exist.

**REFERENCES**

- Hussain SA, James ND. The systemic treatment of advanced and metastatic bladder cancer. *Lancet Oncol.* 2003; 4:489-97.
- Hu Z, Tan W, Zhang L, Liang Z, Xu C, Su H, Lu J, Gao J. A novel immunotherapy for superficial bladder cancer by intravesical immobilization of GM-CSF. *J Cell Mol Med.* 2010; 14:1836-44.
- Herr HW, Morales A. History of bacillus Calmette-Guerin and bladder cancer: an immunotherapy success story. *J Urol.* 2008;179:53-6.
- Whitmore WF Jr. Management of invasive bladder neoplasms. *Semin Urol.* 1983;1:34-41.
- Zhang X, Shi X, Li J, Hu Z, Zhou D, Gao J, Tan W. A novel therapeutic vaccine of mGM-CSF surface-modified MB49 cells against the metastatic bladder cancer. *J Urol.* 2012;187:1071-9.
- Busby JE, Kamat AM. Chemoprevention for bladder cancer. *J Urol.* 2006;176:1914-20.
- Li Z, Yu J, Miao Q, Sun S, Yang H, Hou L. The association of fish consumption with bladder cancer risk: A meta-analysis. *World J Surg Oncol.* 2011;9:107.
- Johansson SL, Cohen SM. Epidemiology and etiology of bladder cancer. *Semin Surg Oncol.* 1997;13:291-98.
- Ross RK, Jones PA, Yu MC. Bladder cancer epidemiology and pathogenesis. *Semin Oncol.* 1996;23:536-45.
- Sing MF, Yang WS, Gao S, Gao J, Xiang YB. Epidemiological studies of the association between tea drinking and primary liver cancer: a meta-analysis. *Eur J Cancer Prev.* 2011;20:157-65.
- Bushman JL. Green tea and cancer in humans: a review of the literature. *Nutr Cancer.* 1998;31:151-9.
- Kuroda Y, Hara Y. Antimutagenic and anticarcinogenic activity of tea polyphenols. *Mutat Res.* 1999;436:69-97.
- Tang N, Wu Y, Zhou B, Wang B, Yu R. Green tea, black tea consumption and risk of lung cancer: A meta-analysis. *Lung Cancer.* 2009;65:274-83.
- Yang CS, Wang X, Lu G, Picinich SC. Cancer prevention by tea: animal studies, molecular mechanisms and human relevance. *Nat Rev Cancer.* 2009;9:429-39.
- Chung FL, Schwartz J, Herzog CR, Yang YM. Tea and cancer prevention: studies in animals and humans. *J Nutr.* 2003; 133:3268S-74S.
- Zeegers MP, Tan FE, Goldbohm RA. Are coffee and tea consumption associated with urinary tract cancer risk? A systematic review and meta-analysis. *Int J Epidemiol.* 2001; 30:353-62.
- Li F, An SL, Zhou Y. Milk and Dairy consumption and risk of bladder cancer: A meta-analysis. *Urology.* 2011;78:1298-305.
- Zheng J, Yang B, Huang T, Yu Y, Yang J, Li D. Green tea and black tea consumption and prostate cancer risk: an exploratory meta-analysis of observational studies. *Nutr Cancer.* 2011;63:663-72.
- Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;357:557-60.
- Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. *J Clin Epidemiol.* 2000;53:1119-29.
- Wilkens LR, Kadir MM, Kolonel LN, Nomura AM, Hankin JH. Risk factors for lower urinary tract cancer: the role of total fluid consumption, nitrites and nitrosamines, and selected foods. *Cancer Epidemiol Biomarkers Prev.* 1996; 5:161-6.
- Zeegers MP, Dorant E, Goldbohm RA, Van den Brandt PA. Are coffee, tea, and total fluid consumption associated with bladder cancer risk? Results from the Netherlands Cohort Study. *Cancer Causes Control.* 2001;12:231-8.
- Zheng W, Doyle TJ, Kushi LH, Sellers TA, Hong CP, Folsom AR. Tea consumption and cancer incidence in a prospective cohort study of postmenopausal women. *Am J Epidemiol.* 1996;144:175-82.
- Kunze E, Chang-Claude J, Frentzel-Beyme R. Life style and occupational risk factors for bladder cancer in Germany. A case-control study. *Cancer.* 1992;69:1776-90.
- Nomura AM, Kolonel LN, Hankin JH, Yoshizawa CN. Dietary factors in cancer of the lower urinary tract. *Int J Cancer.* 1991;48:199-205.
- Woolcott CG, King WD, Marrett LD. Coffee and tea consumption and cancers of the bladder, colon and rectum. *Eur J Cancer Prev.* 2002;11:137-45.
- Slattery ML, West DW, Robison LM. Fluid intake and bladder cancer in Utah. *Int J Cancer.* 1988;42:17-22.
- Bruemmer B, White E, Vaughan TL, Cheney CL. Fluid intake and the incidence of bladder cancer among middle-aged men and women in a three-county area of western Washington. *Nutr Cancer.* 1997;29:163-8.
- De Stefani E, Boffetta P, Deneo-Pellegrini H, Correa P, Ronco AL, Brennan P, Ferro G, Acosta G, Mendilaharsu M. Non-alcoholic beverages and risk of bladder cancer in Uruguay. *BMC Cancer.* 2007;7:57.
- Lu CM, Lan SJ, Lee YH, Huang JK, Huang CH, Hsieh CC. Tea consumption: fluid intake and bladder cancer risk in Southern Taiwan. *Urology.* 1999;54:823-8.
- Jensen OM, Wahrendorf J, Knudsen JB, Sorensen BL. The Copenhagen case-control study of bladder cancer. II. Effect of coffee and other beverages. *Int J Cancer.* 1986;37:651-7.
- La Vecchia C, Negri E, Franceschi S, D'Avanzo B, Boyle P. Tea consumption and cancer risk. *Nutr Cancer.* 1992;17:27-31.
- D'Avanzo B, La Vecchia C, Franceschi S, Negri E, Talamini R, Buttino I. Coffee consumption and bladder cancer risk. *Eur J Cancer.* 1992;28:1480-4.
- Ros MM, Bas Bueno-de-Mesquita HB, Buchner FL, Aben KK, Kampman E, Egevad L, et al. Fluid intake and the risk of urothelial cell carcinomas in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Int J Cancer.* 2011;128:2695-708.
- Bates MN, Hopenhayn C, Rey OA, Moore LE. Bladder cancer and mate consumption in Argentina: a case-control study. *Cancer Lett.* 2007;246:268-73.
- Jiang X, Castelao JE, Groshen S, Cortessis VK, Shibata DK, Conti DV, Gago-Dominguez M. Water intake and bladder cancer risk in Los Angeles County. *Int J Cancer.* 2008;123:1649-56.
- Bianchi GD, Cerhan JR, Parker AS, Putnam SD, See WA, Lynch CF, Cantor KP. Tea consumption and risk of bladder and kidney cancers in a population-based case-control study. *Am J Epidemiol.* 2000;151:377-83.
- Nagano J, Kono S, Preston DL, Moriwaki H, Sharp GB, Koyama K, Mabuchi K. Bladder-cancer incidence in relation to vegetable and fruit consumption: a prospective study of atomic-bomb survivors. *Int J Cancer.* 2000;86:132-8.
- Kurahashi N, Inoue M, Iwasaki M, Sasazuki S, Tsugane S. Coffee, green tea, and caffeine consumption and subsequent risk of bladder cancer in relation to smoking status: a prospective study in Japan. *Cancer Sci.* 2009;100:294-91.
- Ohno Y, Aoki K, Obata K, Morrison AS. Case-control study of urinary bladder cancer in metropolitan Nagoya. *Natl Cancer Inst Monogr.* 1985;69:229-34.
- Demirel F, Cakan M, Yalcinkaya F, Topcuoglu M, Altug U. The association between personal habits and bladder cancer in Turkey. *Int Urol Nephrol.* 2008;40:643-7.



42. Hemelt M, Hu Z, Zhong Z, Xie LP, Wong YC, Tam PC, et al. Fluid intake and the risk of bladder cancer: results from the South and East China case-control study on bladder cancer. *Int J Cancer*. 2010;127:638-45.
43. Wakai K, Hirose K, Takezaki T, Hamajima N, Ogura Y, Nakamura S, Hayashi N, Tajima K. Foods and beverages in relation to urothelial cancer: case-control study in Japan. *Int J Urol*. 2004;11:11-9.
44. Slattery ML, Schumacher MC, West DW, Robison LM. Smoking and bladder cancer. The modifying effect of cigarettes on other factors. *Cancer*. 1988;51:402-8.
45. Ahmad N, Mukhtar H. Green tea polyphenols and cancer: biologic mechanisms and practical implications. *Nutr Rev*. 1999;57:78-83.
46. Yang CS, Wang ZY. Tea and cancer. *J Natl Cancer Inst*. 1993;85:1038-49.
47. Gardner EJ, Ruxton CH, Leeds AR. Black tea-helpful or harmful? A review of the evidence. *Eur J Clin Nutr*. 2007; 61:3-18.
48. Nagle CM, Olsen CM, Bain CJ, Whiteman DC, Green AC, Webb PM. Tea consumption and risk of ovarian cancer. *Cancer Causes Control*. 2010;21:1485-91.
49. Lee KW, Lee HJ, Lee CY. Antioxidant activity of black tea vs. green tea. *J Nutr*. 2002;132:785.
50. Heilbrun LK, Nomura A, Stemmermann GN. Black tea consumption and cancer risk: a prospective study. *Br J Cancer*. 1986;54:677-83.

## Original Article

## The association of tea consumption with bladder cancer risk: a meta-analysis

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### 喝茶与膀胱癌发生的整合分析

目前有关喝茶与膀胱癌的关系在动物实验中已经得以证实，但在 2001 年一篇研究却表明，喝茶与人类膀胱癌的发生无相关性。时至今日，为了能更精确的证明二者的相关性，我们对此进行整合分析。通过 Pubmed 检索工具收集 1980 年 1 月至 2012 年 3 月的所有关于喝茶与人类膀胱癌发生的前瞻性和回顾性研究，并且基于喝茶量的极值（最大值和最小值），利用随机效应模型计算 RR 和 CI。最终纳入 24 篇相关文献（6 篇为队列研究，18 篇为病例-对照研究）进行整合分析。研究结果表明，对于未分类的茶而言，喝茶与膀胱癌发生无相关性(RR= 1.09, 95%CI: 0.85-1.40)。但在亚组分析中，却发现抽烟人群喝茶反而轻度增加膀胱癌的发生率(RR= 1.77, 95%CI: 1.04-3.01)。喝红茶与膀胱癌的发生无相关性(RR= 0.84, CI: 0.70-1.01)；但女性喝红茶可略减低膀胱癌发生的风险(RR= 0.61, 95%CI: 0.38-0.98)；喝绿茶与膀胱癌的发生无相关性(RR= 1.03, 95% CI: 0.82-1.31)。因此，由整合分析的结论为，抽烟人群喝茶可增加膀胱癌的发生，女性喝红茶则可降低膀胱癌的发生。

**关键词：**膀胱癌、未分类茶、红茶、绿茶、整合分析