

# Dietary factors associated with bladder cancer

Chandrika Piyathilake

Department of Nutrition Sciences, University of Alabama at Birmingham (UAB), Birmingham, AL, USA

It is biologically plausible for dietary factors to influence bladder cancer risk considering that beneficial as well as harmful components of a diet are excreted through the urinary tract and in direct contact with the epithelium of the bladder. However, studies that investigated the association between dietary factors and bladder cancer (BC) risk have largely reported inconsistent results. The macronutrient intake and risk of BC could have yielded inconsistent results across studies because of lack of details on the type, source and the quantities of different dietary fatty acids consumed. There is evidence to suggest that consumption of processed meat may increase BC risk. Dietary carbohydrate intake does not appear to be directly associated with BC risk. Even though a large number of studies have investigated the association between fruit/vegetable consumption/micronutrients in those and BC risk, they have yielded inconsistent results. Gender-specific subgroup analysis, details of how fruits and vegetables are consumed (raw vs. cooked), adequate control for smoking status/aggressiveness of the cancer and consideration of genetic make-up may clarify these inconsistent results. There is no strong evidence to suggest that supplementation with any common micronutrient is effective in reducing BC risk. These limitations in published research however do not totally eclipse the observation that a diet rich in fruits and vegetables and low in processed meat along with especially smoking cessation may convey some protective effects against BC risk.

**Keywords:** Diet; Risk; Urinary bladder neoplasms

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## INTRODUCTION

Cancers in the bladder is the most common malignancy in the urinary tract and the age adjusted incidence rate is approximately nine per 10,000 for men and 2.2 for women globally [1,2]. Bladder cancer (BC) is the ninth most common cancer world-wide [2] and is the fifth most common cancer in the United States and represents 4.5% of all new cancer cases. In 2015, it is estimated that there will be 74,000 new cases of BC (56,320 in men and 17,680 in women) and an estimated 16,000 people will die of this disease (~11,510 men and 4,490 in women) [3].

Age, gender, cigarette smoking, exposures to aromatic amines, polycyclic aromatic hydrocarbons or arsenic, certain medications (phenacetin, cyclophosphamide, chlornaphazine), radiation and genetic factors are established risk factors for developing BC while there is suggestive evidence for several other factors, including diet [4]. Since BC is one of the most expensive diseases to treat because of the need for extended courses of treatment coupled with frequent follow-up examinations [5], examination of modifiable risk factors associated with this disease will aid in implementing preventive measures. Even though epidemiological evidence is inconsistent or controversial, diet is believed to be one

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**Corresponding Author:** Chandrika Piyathilake

Department of Nutrition Sciences, University of Alabama at Birmingham,  
UAB Wallace Tumor Institute 420 D, 1824 6th Avenue South, Birmingham, AL 35294-3300, USA  
TEL: +1-205-975-5398, FAX: +1-205-975-5398, E-mail: [piyathic@uab.edu](mailto:piyathic@uab.edu)

of the most important modifiable risk factors for cancer prevention [6]. The purpose of this article is to critically review the findings published thus far on the associations between dietary factors and BC focusing on several aspects of diet, including, specific dietary factors such as food groups, intake and circulating concentrations of specific micronutrients.

## INTAKE OF MACRONUTRIENTS OR MACRONUTRIENT CONTAINING FOOD ITEMS AND RISK OF BLADDER CANCER

Several case-control studies have documented that diets high in meat or fat is associated with higher risk of BC [7]. A limitation of these studies is that lack of detailed dietary data to examine the intake of different types of dietary fat or different sources of protein intake in relation to the risk of BC. A study that addressed these limitations showed that a 3% increase in the consumption of energy intake from animal protein was associated with a 15% higher risk of developing BC while a 2% increase in energy from plant protein intake was associated with a 23% lower risk of developing BC [8]. This study also documented that dietary intake of fat or carbohydrate was not associated with BC risk. However, other studies have documented statistically significant reduced odds of BC for high intakes of  $\alpha$ -linolenic acid and vegetable fat and borderline statistically significant reduced odds for polyunsaturated fat and linoleic acid, indicating the importance of investigating the type, source and the quantities of different dietary fatty acids consumed [9]. Brinkman et al. [10] reported a statistically significant inverse association between olive oil intake and BC consistent with a linear dose-response relationship.

Even though some case-control studies have reported that a higher red meat intake was associated with BC risk [11], a meta-analysis published in 2014 based on 1,558,848 participants documented that red meat intake was not associated with BC, but suggested that high consumption of processed meat was correlated with rising risk of BC, especially in United States [12]. Similar results were observed in a study conducted in the New England region of the United States [13]. These studies indicate the importance of separating red meat and processed meat in evaluating BC risk in relation to meat consumption. Dietary carbohydrate intake does not appear to be associated with BC risk [9], but only limited data is available on this aspect. Two meta-analysis studies published in 2013, however, reported a positive association between diabetes mellitus and risk of BC, indirectly suggesting that control of carbohydrate

intake may lower the BC risk [14,15]. The studies associating macronutrients or macronutrient containing foods and risk of BC have been summarized in Table 1.

## CONSUMPTION OF FRUITS AND VEGETABLES OR MICRONUTRIENTS IN THOSE AND RISK OF BLADDER CANCER

Even though a large number of studies have investigated the association between fruit and vegetable consumption and BC risk, they have yielded inconsistent results, especially with regard to the types of fruits and vegetables consumed. A male prospective cohort study documented that high cruciferous vegetable consumption may reduce BC risk, but other vegetables and fruits may not confer appreciable benefits against this disease [16]. A cohort of atomic-bomb survivors in Japan reported that consumption of green-yellow vegetables and fruits were protective against the development of BC [17]. A prospective cohort study of male smokers reported that consumption of fruits and vegetables, groups of fruits or vegetables (berries and cruciferous vegetables), specific fruits and vegetables or intakes of alpha-carotene, beta-carotene, lycopene, lutein/zeaxanthin, beta-cryptoxanthin, vitamins A, E, and C, and folate were not related to the risk of BC [18]. In contrast, a population-based case-control study conducted in non-Asians of Los Angeles, California showed a strong inverse associations between smoking-related BC risk and intake of dark-green vegetables, yellow-orange vegetables, citrus fruits/juices, tomato products, total carotenoids and vitamin C [19]. A similar inverse association between fruits and vegetables and risk of BC was observed in a meta-analysis [7]. However, a prospective population-based cohort study of Swedish women and men reported no statistically significant association between intakes of total fruits and vegetables, total fruits, total vegetables, citrus fruits, cruciferous vegetables, or green leafy vegetables and BC risk and these associations did not differ by sex or by smoking status [20]. A population-based case-control study performed in the Belgian province of Limburg showed that total fruit consumption, but not total vegetable intake reduces the effect of smoking on BC risk [21]. The European Prospective Investigation into Cancer and Nutrition (EPIC) study did not support an effect of fruit and vegetable consumption, combined or separately, on BC [22]. The EPIC study also documented that a variety in vegetable and fruit consumption also was not significantly associated with BC risk further providing evidence for the absence of any strong association between fruit and vegetable consumption and aggressive or nonaggressive BC risk [23,24].

Table 1. Summary of the studies associating macronutrient and macronutrient containing foods and risk of bladder cancer

Study	Dietary factor	Publication year	No. of patients	Study method	Recruitment/ follow-up period	Main findings
Steinmaus et al. [7]	Fat	2000	38 Articles, 4,578 cases	Meta-analysis	1980–1999	37% Elevated risk of BC with high intakes of fat
Allen et al. [8]	Protein	2013	469,339 Participants, 1,416 cases	Multicenter, prospective	1992–2000	3% Increase in the consumption of energy intake from animal protein was associated with a 15% higher risk of developing BC while a 2% increase in energy from plant protein intake was associated with a 23% lower risk of developing BC
Brinkman et al. [9]	Fat	2011	322 Cases and 239 controls	Case-control	1998–2001	73% Reduced odds of BC with high intakes of $\alpha$ -linolenic acid 61% Reduced odds of BC with high intakes of vegetable fat. Borderline statistically significant reduced odds were detected for polyunsaturated fat and linoleic acid
Brinkman et al. [10]	Olive oil	2011	200 Cases and 386 controls	Case-control	1999–2004	Higher intake of olive oil was associated with 53% reduced risk of BC
Lin et al. [11]	Red meat	2012	884 Cases and 878 controls	Case-control	1999	A significant dose response trend of elevated risk of developing BC with high intakes of red meat
Li et al. [12]	Red and Processed meat	2014	1,558,848, 7,562 Cases	Meta-analysis	1980–2012	High consumption of processed meat but not red meat was correlated with rising risk of BC
Wu et al. [13]	Processed meat	2012	1,068 Cases and 1,266 controls	Case-control (New England Bladder Cancer Study)	2001–2004	High intakes of processed meat and processed red meat were associated with 28% and 41% increased risk of BC

BC, bladder cancer.

The latest publication from the EPIC study confirmed these observations [25]. A prospective analysis of older adults participating in the US Multiethnic Cohort Study reported that in women, total fruits and vegetables, total vegetables, yellow-orange vegetables, total fruits and citrus fruits were inversely associated with the risk of invasive BC. In addition, this study also reported that women with the highest intakes of vitamins A, C, and E; the carotenoids  $\alpha$ -carotene,  $\beta$ -carotene, and  $\beta$ -cryptoxanthin; and folate had a lower risk of BC and for men, no associations for fruits, vegetables, or nutrients were found overall, although inverse associations were observed for vegetable intake among current smokers, and in ethnic-specific analyses, for fruit and vegetable intake among Latinos specifically. These findings suggest that higher consumption of fruits and vegetables may lower the risk of invasive BC among women and highlight the need for gender-specific subgroup analyses in future studies [27].

A hospital-based case-control study reported that consumption of raw, but not cooked cruciferous vegetables was inversely associated with bladder cancer risk [28]. A strong and significant inverse association was also observed between BC mortality and broccoli intake, in particular raw broccoli intake [29]. These studies suggest that cooking may alter the beneficial effects of protective nutrients and this may explain inconsistent results among different studies. In a population-based case-control study of bladder cancer in Maine, New Hampshire, and Vermont no association between fruits and vegetable consumption and risk of bladder cancer was observed [13]. Another US case-control study reported significant inverse associations between intakes of total vegetables, cruciferous vegetables, orange vegetables, dark green vegetables but not intakes of total fruits or citrus fruits and BC risk. Interestingly, this study also showed that the protective effect of vegetable consumption, especially cruciferous vegetables may be modified by genetic variants of *GSTM1* and *NAT2*, suggesting that genetic makeup of individuals may also contribute to inconsistent results reported by different studies [27].

A dose-response meta-analysis of observational studies supported the hypothesis that intakes of fruit and vegetables may reduce the risk of BC [29]. An updated meta-analysis of observational studies published in 2015 also suggested that intake of vegetables and fruits may significantly reduce the risk of BC [30]. A systematic review and meta-analysis published in 2015 as part of the World Cancer Research/American Institute for Cancer Research Continuous Update Project, however, documented that current evidence from

cohort studies is not consistent with a role for fruits and vegetables in preventing BC [31]. A preferred reporting items for systematic reviews and meta-analyses (PRISMA Compliant) study that included relevant prospective studies up to 2014 also documented that there is little evidence to support a beneficial effect for total fruits, vegetables or both together and citrus intake against BC [32]. The studies associating fruits and vegetables or micronutrients and risk of BC have been summarized in Table 2.

## CIRCULATING CONCENTRATIONS OF MICRONUTRIENTS AND RISK OF BLADDER CANCER

Studies have suggested a protective role of serum concentrations of selenium on BC risk, but not serum concentrations of retinol or beta-carotene [33]. However, a meta-analysis of epidemiological studies published in 2014 reported that higher serum or plasma concentrations of vitamin A, total carotenoids,  $\alpha$ -carotene,  $\beta$ -carotene, lutein and zeaxanthin were associated with lower risk of BC [34]. A case-control study conducted by Liang et al. [35] suggested potential protective effect of plasma concentrations of alpha-tocopherol and retinol on BC risk. A large prospective study conducted among Japanese-American men documented that cigarette smoking, which is a strong risk factor for BC, may explain the apparent protective effect of individual and total carotenoids against this disease [36]. Other studies that investigated joint effect of plasma carotenoids and tobacco smoking suggested that BC may be a preventable disease through nutritional intervention, especially in smokers [37].

Some studies have reported that vitamin D status, as measured by serum 25-hydroxyvitamin D (25(OH) D) concentration, when it is low in male smokers had a nearly two-fold increased risk of BC compared to men with higher levels [38]. In contrast to this earlier report, the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Study observed no association between serum vitamin D status and risk of BC. It is possible that these differences between the 2 studies could be due to the inclusion of women and nonsmokers in the latter study population or due to the differences in the distribution of vitamin D concentrations between the two study populations [39]. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study provided additional support for an etiologic role for vitamin D in BC and suggested that free, rather than total, circulating vitamin D may be a more relevant exposure when examining BC risk in relation to vitamin D [40]. Other studies reported that individuals with low

Table 2. Summary of studies associating fruit and vegetable consumption and risk of bladder cancer

Study	Dietary factor	Publication year	No. of patients	Study method	Recruitment/follow-up period	Main findings
Michaud et al. [16]	Fruits and vegetables	1999	51,529 Participants, 252 cases	Prospective cohort study (Health Professionals Follow-Up Study)	1986–1996	High cruciferous vegetable consumption associated with reduce risk of BC, but other vegetables and fruits were not associated with risk of BC
Nagano et al. [17]	Fruits and vegetables	2000	38,540 Participants	Prospective follow up study (Life Span Study Cohort)	1979–1981	Consumption of fruits and vegetables 2–4 times per week and almost every day was associated with 50% and 48% reduced risk of BC respectively
Michaud et al. [18]	Fruits and vegetables and micronutrients	2002	27,111 Participants with complete information, 344 cases	Prospective cohort study (ATBC study)	1985–1988	Consumption of fruits and vegetables was not associated with the risk of BC Dietary intakes of alpha-carotene, beta-carotene, lycopene, lutein/zeaxanthin, beta-cryptoxanthin, vitamins A, E, and C, and folate were not related to the risk of BC
Castelao et al. [19]	Fruits, vegetables and micronutrients	2004	1,592 Cases and 1,592 controls	Population based case-control study	1987–1996	Inverse associations between smoking-related BC risk and intake of dark-green vegetables, yellow-orange vegetables, citrus fruits/juices, tomato products, total carotenoids and vitamin C
Larsson et al. [20]	Fruits and vegetables	2008	82,002 Participants, 485 cases	Prospective- population based cohort study	1987–1990	No statistically significant association between intakes of total fruits and vegetables, total fruits, or total vegetables and BC
Kellen et al. [21]	Fruits and vegetables	2005	200 Cases and 385 controls	Population-based case-control study	1999–2004	Total fruit consumption, but not total vegetable intake reduced the effect of smoking on BC risk by 39%
Buchner et al. [22]	Fruits and vegetables	2009	478,533 Participants, 1,015 cases	EPIC study	1991–2000	Fruit and vegetable consumption combined or separately were not associated with BC
Buchner et al. [23]	Fruits and vegetables	2011	452,185 Participants, 874 cases	EPIC study	1991–2000	Weak association was observed between fruit and vegetable consumption and risk of BC
Ros et al. [24]	Fruits and vegetables	2012	468,656,421 Aggressive and 433 nonaggressive cases	EPIC study	1991–2000	Total consumption of fruits and vegetables was not associated with neither aggressive BC nor with nonaggressive BC
Bradbury et al. [25]	Fruits and vegetables	2014	~470,000 Participants, 1,015 cases	EPIC study	1992–2000	No association between fruit and vegetable intake and risk of BC
Park et al. [26]	Fruits and vegetables	2013	185,885 Participants, 581 cases	Multiethnic cohort study	1991–2000	In women, total fruits and vegetables, total vegetables, yellow-orange vegetables and citrus fruits were inversely associated with the risk of invasive BC. Women with the highest intakes of vitamins A, C, and E; the carotenoids $\alpha$ -carotene, $\beta$ -carotene, and $\beta$ -cryptoxanthin; and folate had a lower risk of BC. No associations between fruit and vegetable intake and risk of BC were observed in men

Table 2. Continued

Study	Dietary factor	Publication year	No. of patients	Study method	Recruitment/ follow-up period	Main findings
Lin et al. [28]	Fruits and vegetables	2009	884 Cases and 878 controls	Case-control study	1999–2009	Highest vegetable consumption was protective against BC
Wu et al. [13]	Fruits and vegetables	2012	1,068 Cases and 1,266 controls	Case-control (New England Bladder Cancer Study)	2001–2004	No association between fruit and vegetable consumption and risk of BC
Steinmaus et al. [7]	Fruits and vegetables and carotenoids	2000	38 Articles, 5,174 cases	Meta-analysis	1980–1999	Low intake of fruits and vegetables separately was associated with 40% and 16% elevated risk of BC, respectively No association between low carotene/ retinol diet and risk of BC
Yao et al. [29]	Fruits and vegetables	2014	1,121,649 Participants, 12,610 cases	Meta-analysis	1989–2013	Intake of fruits and vegetables reduces the risk of developing BC by 17%
Liu et al. [30]	Fruits and vegetables	2015	27 Studies	Meta-analysis	1984–2014	the relative risk of BC decreased by 8% and 9% for every 200 g/day increment in vegetable and fruit consumption, respectively
Vieira et al. [31]	Fruits and vegetables	2013	15 Studies, 2,000–5,000 cases	Meta-analysis	1988–2013	No strong evidence of an association between fruits and vegetables and risk of BC
Xu et al. [32]	Fruits and vegetables	2015	17 Studies, 9,447 cases	Meta-analysis	1988–2014	No evidence of nonlinear association was examined between fruits and vegetable intake and risk of BC

BC, bladder cancer.

Table 3. Summary of studies associating circulating concentrations of micronutrients and risk of bladder cancer

Study	Dietary factor	Publication year	No. of patients	Study method	Recruitment/ follow-up period	Main findings
Helzlsouer et al. [33]	Retinol and carotenoids	1989	35 Cases and 70 matched controls	Case-control study	1975–1986	No association between circulating concentrations of retinol, retinol binding protein, or $\beta$ -carotene and risk of BC The risk of BC increased with decreasing levels of lycopene, $\alpha$ -tocopherol, and selenium
Tang et al. [34]	Vitamin A	2014	25 Studies, 11,580 cases	Meta-analysis	1988–2013	Higher circulating concentrations of vitamin A, total carotenoids carotene, $\beta$ -carotene, lutein and zeaxanthin were associated with lower risk of BC
Liang et al. [35]	Vitamin E and A	2008	386 Cases and 389 controls	Case-control study	1999	13% and 43% reduction in BC risk with increasing plasma $\alpha$ -tocopherol level and retinol levels respectively
Nomura et al. [36]	Carotenoids	2003	109 Cases and 110 controls	Nested Case-control study	1971–1977	No statistically significant association between carotenoids and risk of BC after adjusting for smoking
Hung et al. [37]	Carotenoids	2006	84 Cases and 173 controls	Case-control	1993–1997	Protective association between the circulating carotenoids and BC, Lower circulating concentrations of lutein and zeaxanthin were 5–6 times likely to increase risk of BC in smokers
Mondul et al. [38]	Vitamin D	2010	250 Cases and 250 controls (males)	Nested case-control (ATBC study)	1985–1988	Lower serum vitamin D was associated with increased risk of BC
Mondul et al. [39]	Vitamin D	2012	375 Cases and 375 controls	Nested Case-control study (PLCO study)	1993–2006	No statistically significant association between serum 25-hydroxyvitamin D and BC risk
Mondul et al. [40]	Vitamin D	2012	250 Cases and 250 controls (males)	Nested Case-control (ATBC study)	1985–1988	Free vitamin D rather than total circulating vitamin D has a protective effect on risk of BC
Amara et al. [41]	Vitamin D	2012	1,125 Cases and 1,028 control	Case-control	1998–2001	Low levels of plasma 25(OH)D(3) may be at high risk of more aggressive forms of BC
Liao et al. [43]	Vitamin D	2015	5 Eligible studies, 89,610 participants and 2,238 cases	Case-control	1999–2008	Inverse association between serum 25-hydroxyvitamin D level and risk of BC

BC, bladder cancer.

levels of plasma 25(OH)D(3) may be at high risk of more aggressive forms of BC, suggesting the importance of investigating the association by the aggressiveness of the disease [41]. A retrospective analysis of data in the Veterans Integrated Service Network-9 (southeastern US) suggested that adequate serum vitamin D levels early in the course of the disease provide the best opportunity to improve outcomes of BC [42]. Finally, a systemic review and meta-analysis published in 2015 documented that serum 25-hydroxyvitamin D concentrations were significantly associated with lower risk of BC [43]. The studies associating circulating concentrations of micronutrients and risk of BC have been summarized in Table 3.

### MICRONUTRIENT SUPPLEMENTS AND RISK OF BLADDER CANCER

US adults in the Cancer Prevention Study II cohort documented that regular use of vitamin E supplements (for ≥10 years), but not vitamin C was associated with a reduced risk of BC mortality [44]. The prospective Health Professionals Follow-Up Study, however, observed a significant dose-response relation not only for vitamin E but also for vitamin C supplement use and BC risk among US men [45]. In contrast, another study reported that the long-term use of commonly consumed supplemental vitamins (multivitamins, beta-carotene, retinol, folic acid, and vitamins B1, B3, B6, B12, C, D and E) have no significant effect on reducing BC risk [46]. The studies associating micronutrient supplements and risk of BC have been summarized in Table 4.

### OTHER FOOD ITEMS AND RISK OF BLADDER CANCER

A limited number of studies have investigated other food components in relation to BC such as dairy, tea, egg and fish. A study conducted among Swedish men and women reported that the total dairy intake, intake of milk or cheese were not significantly associated with risk of BC, but a statistically significant inverse association was observed for the intake of cultured milk (sour milk and yogurt) [47]. However, The Netherlands Cohort Study on Diet and Cancer only provided weak evidence that BC risk is inversely associated with lower intake of fermented dairy products [48]. With regard to tea, Wang et al. [49] reported that green tea may have a protective effect on BC in Asians while Zhang et al. [50] observed that in Western countries, an increase in tea consumption in general may reduce the

Table 4. Summary of studies associating micronutrient supplements and risk of BC

Study	Dietary factor	Publication year	No. of patients	Study method	Recruitment/ follow-up period	Main findings
Jacobs et al. [44]	Vitamin C and vitamin E	2002	991,522 Participants	Cancer prevention study II	1982–1998	Regular use of vitamin E supplements (for ≥10 years), but not vitamin C was associated with a reduced risk of BC mortality
Michaud et al. [45]	Vitamin C, A and E	2000	51,529 Participants	Health professionals follow-up study	1986–1998	Duration of vitamin E supplement intake was inversely associated with risk of BC; men with 10 or more years of vitamin E had a multivariate relative risk of 0.68 compared with never users. Nonstatistically significant inverse associations were observed for supplemental dose of vitamins C and E among United States men
Hotaling et al. [46]	Vitamin and mineral supplements	2011	77,050 Participants, 330 incident cases	Prospective follow-up study (VITAL cohort study)	2000–2007 (6-year follow-up)	Long-term use of the vitamin, mineral supplements (multivitamins, beta-carotene, retinol, folic acid, and vitamins B1, B3, B6, B12, C, D and E) supplements not significantly associated with BC

BC, bladder cancer.



Table 5. Summary of studies associating other food items and risk of BC

Study	Dietary factor	Publication year	No. of patients	Study method	Recruitment/ follow-up period	Main findings
Larsson et al. [47]	Cultured milk, Yoghurt and dairy intake	2008	82,002 Participants, 485 cases	Prospective follow-up study (Swedish Mammography Cohort and the Cohort of Swedish Men)	1998–2007	Women and men who consumed $\geq 2$ servings of cultured milk per day had a 38% lower risk of bladder cancer than did those who never consumed cultured milk
Keszei et al. [48]	Dairy intake	2010	1,549 Cases, 4,232 controls	Nested case-control study (Netherlands Cohort Study on Diet and Cancer)	1986–2002	Weak association between lower intake of fermented dairy products and risk of BC
Wang et al. [49]	Tea	2013	17 Studies, 8,225 cases	Meta-analysis	1980–2012	No association between tea consumption and risk of BC However, green tea consumption had a protective effect on BC
Zhang et al. [50]	Tea	2015	57 Articles, 49,812 cases	Meta-analysis	1980–2013	No association between tea consumption and risk of BC
Li et al. [51]	Egg	2013	13 Articles, 184,727 participants, 2,715 cases	Meta-analysis	1988–2012	No significant association was observed between egg consumption and BC Egg consumption was associated with 40% elevated risk of BC in North and South America
Li et al. [52]	Fish	2011	14 Studies, 320,264 participants, 4,947 cases	Meta-analysis	1986–2011	Consumption of fried eggs increased relative risk of BC by 2 times No significant association between fish consumption and risk of BC

BC, bladder cancer.

risk of BC. A meta-analysis published in 2013 reported that overall, there was no significant association between egg consumption and BC but, increased risk of bladder cancer was detected in North/South America and fried egg intake positively associated with BC risk [51]. The overall current literature on fish consumption and the risk of BC suggested no association. The studies associating other food items and risk of BC have been summarized in Table 5 [52].

In summary, studies that investigated the association between dietary factors and BC risk have largely reported inconsistent results. There is no strong evidence to suggest that specific dietary factors or supplementation with any common micronutrient present in food is effective in reducing BC risk. These limitations in published research however do not totally eclipse the observation that a diet rich in fruits and vegetables and low in processed meat along with especially smoking cessation may convey some protective effects against BC risk.

**CONFLICTS OF INTEREST**

The author has nothing to disclose.

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