Urologia Internationalis

Review Article

Urol Int 2023;107:723–733
DOI: 10.1159/000530435

Received: October 29, 2022
Accepted: February 21, 2023
Published online: June 21, 2023

Cruciferous Vegetable Intake and Risk of Prostate Cancer: A Systematic Review and Meta-Analysis

Jiaye Long[a] Zhaohui Liu[b] Shuai Liang[c] Baoxiang Chen[a]

[a]Department of Interventional Radiology, The Second Clinical Medical School of Inner Mongolia University for The Nationalities (Inner Mongolia Forestry General Hospital), Yakeshi, PR China; [b]Department of Urology, The Second Clinical Medical School of Inner Mongolia University for The Nationalities (Inner Mongolia Forestry General Hospital), Yakeshi, PR China; [c]Department of Cardiology, The Second Clinical Medical School of Inner Mongolia University for The Nationalities (Inner Mongolia Forestry General Hospital), Yakeshi, PR China

Keywords
Cruciferous vegetables intake · Prostate cancer · Meta-analysis · Dose-response analysis

Abstract

Introduction: The relationship between cruciferous vegetables and prostate cancer (PCa) risk remains contentious. This study aimed to assess the association between consuming cruciferous vegetables and PCa risk. ***Methods:*** We carried out a systematic search through PubMed, Embase, Web of Science, and the Cochrane Library until September 20, 2022. The results of the article will be analyzed using the Stata 14 software. This meta-analysis was reported as directed by the PRISMA guidance, and the study protocol was recorded in PROSPERO (CRD42022361556). ***Results:*** 7 case-control studies and 9 cohort studies were eventually included, including 70,201 PCa cases and 1,264,437 members. The higher the intake of cruciferous vegetables, the lower the risk of PCa. In comparison to the lowest dose of cruciferous vegetables, the overall relative risk (RR) of cruciferous vegetables having the highest dose was 0.87 (95% confidence interval [CI]: 0.80–0.95; I^2 = 59.2%). A significant linear trend (p = 0.002) was observed for the association, with a combined RR of 0.955 (95% CI: 0.928–0.982) for every 15 g of cruciferous vegetables per day. ***Conclusions:*** The study revealed that consumption of cruciferous vegetables may be linked to reduced PCa risk.

Introduction

Prostate cancer (PCa) is the second most prevalent type of cancer in men and the sixth significant cause of cancer-related fatality [1]. In 2018, it was predicted that there would be 359,000 cancer-related fatalities and 1,266,000 new cases worldwide [1]. Additionally, compared to Asian nations, PCa is substantially lower in non-Asian nations [2]. However, it has risen rapidly in recent decades with a longer average lifespan and a progressively westernized lifestyle [2]. PCa primary prevention is a significant public health concern worldwide.

There is mounting proof that consuming more fruits and vegetables can reduce the risk of some cancer sites

Jiaye Long and Zhaohui Liu contributed equally to this work.

Correspondence to:
Baoxiang Chen, 280496340@qq.com

karger@karger.com
www.karger.com/uin

Karger

[3]. Remarkably, the association involving cruciferous vegetables and the risk of developing cancer has been the subject of much heated discussion. Cruciferous vegetables are a type of vegetable that is also known as cruciferous flowers. People frequently consume cruciferous vegetables: cauliflower, cabbage, and Brussels sprouts [4]. Indole and isothiocyanate, two active components of cruciferous vegetables, are known to have anticancer characteristics [5, 6]. Numerous epidemiological studies have demonstrated reverse relationships between cruciferous vegetables and cancer risks, including endometrial, lung, gastric, colorectal, and other cancers [7]. Meanwhile, Liu et al. [8] found that consumption of cruciferous vegetables was associated with lower risk of PCa. Over the last 30 years, multiple epidemiological studies have looked into the connection between eating cruciferous vegetables and the risk of PCa. Most studies reported that cruciferous vegetables had a statistically insignificant negative correlation with PCa risk, whereas some reports showed that there was a statistically insignificant positive correlation among them. Hence, the ratio of cruciferous vegetable consumption to PCa risk is controversial. A meta-analysis is needed to ascertain their link to one another.

Methods

We systematically searched PubMed, Embase, the Cochrane Library, and Web of Science databases from start-up dates to September 20, 2022. The elementary search process for meta-analyses was as follows: (prostatic neoplasms) OR (prostate cancer) OR (prostate neoplasm) OR (prostatic cancer) OR (Cancer of the Prostate) AND (cruciferous vegetables). See online supplementary Material 1 (for all online suppl. material, see https://doi.org/10.1159/000530435) for detailed search strategy. This meta-analysis was performed in light of the PRISMA (registration number: CRD42022361556) statement [9].

Selection Criteria

The following criteria were used to select the studies: (1) study types included cohort and case-control studies, (2) the study centered on the connection between cruciferous vegetables and PCa risk, (3) the study provided information on the ingestion of cruciferous vegetables for exposure interest, (4) the study involved PCa as a measure of results. The diagnosis of PCa was confirmed through a medical diagnosis, pathology reports, medical records, self-report, or cancer registration form. (5) The study provided estimates of relative risk (RR) or odds ratio (OR) and associated confidence intervals (CIs) to evaluate the relationship between cruciferous vegetables and PCa. Provided that diverse estimates were supplied, multivariable-adjusted risk estimates were preferred. If identified studies were published in more than one publication, older reports or those containing less relevant information were excluded.

Two investigators (J.L. and Z.L.) independently screened all obtained articles for inclusion and exclusion criteria. Any differences in research and literature selection were solved by the third investigator (S.L.).

Data Extraction

Each study consisted of the following details: the leading author's name, study region, type of study, quality score, participant number, patient number, RRs along with 95% CIs, and the latent confounders considered or adjusted.

Quality Assessment

The potential for bias was assessed using the Newcastle-Ottawa Scale (NOS) [10], which considers the choice of research groups, verification of exposure and result, and comparability of groups. Studies that received 7–9 points were categorically identified as high quality, those that received 5–6 points as intermediate quality, and those that received less than 4 points as poor quality.

Statistical Analysis

The OR value is virtually consistent with the RR value when the low occurrence of PCa is taken into account [11]. Therefore, the effect of all included studies was evaluated using the RR value and its 95% confidence range. We aggregated RR estimates for distinct dosages of cruciferous vegetables relevant to the study. The ability to examine study heterogeneity is a feature of the I^2 statistic [12]. According to the results of the I^2, the fixed or random (DerSimonian-Laird) effect model was applied to analyze the article's heterogeneity [12]. If I^2 is below 50% ($I^2 < 50\%$), the heterogeneity between tests is weak or moderate. The RR estimates are therefore calculated using a fixed effect model. If I^2 is greater than or equal to 50% ($I^2 \geq 50\%$), there is moderate to significant heterogeneity between studies. Hence, a random effect model is applied to figure out the RR estimate. When the study is moderately heterogeneous (I^2 30–60%), the random effect model is selected as a more conservative approach [13, 14].

Subgroup analyses were stratified in line with study location, study type, year of publication, and adjustment for potential confounders, including a family history of PCa, body mass index (BMI), smoking status, and alcohol intake. We employed funnel plots [15, 16], the Egger linear regression test [17], and the Begg rank correlation asymmetry test [18] to look for evidence of publication bias. First, we visually evaluate whether the scatter points on the funnel plot are symmetrical. To the extent that the funnel chart is asymmetrical, there may be a likelihood of publishing bias. Second, publication bias was formally assessed through the Begg and Egger correlation test. If the p value was below 0.1, it was taken as a statistically significant publication bias. Should a publication bias occur, we will utilize the trim and fill method for analysis [19]. Sensitivity analyses were also conducted to determine if the exclusion from one research each time could have affected the aggregate results.

Furthermore, the probable dose-response link between eating cruciferous vegetables and PCa risk was looked into. In order to use the methodology recommended by Greenland and Longnecker [20], 95% of associated RRs and ICs were collected for dose-response analysis. In order to use this method, the intake of at least three groups was required, and the case number within each group and the participant number within each group/person per year could be provided. We then estimated the overall RR value in light

of the trend of each study. At the same time, we tested the linear and nonlinear connections between the consumption of cruciferous vegetables and PCa risk using a restricted quartic spline. Generalized least squares regression was used to estimate the restricted quartic spline, which was 4 knots at each fixed percentile (5%, 35%, 65%, and 95%) of the distribution [21]. We modified the consumption in grams per day, using 80 g as the roughly average portion, given that the included studies utilized various units to measure the intake of cruciferous vegetables. When the original study group provided an intake dose interval for cruciferous vegetables, in the closed interval, the midpoint of the upper and lower bounds of the interval was considered to be the mean intake dose; for the lower open interval, we divided the endpoint of the interval by 1.2; in the upper open interval, we multiply the endpoint of the interval by 1.2.

In all analyses, the p value below 0.05 was found to be statistically meaningful. Stata version 14 (StataCorp, College Station, TX, USA) was utilized for statistical analysis.

Results

Literature Search

703 records were obtained from a total of 4 databases. After removing 212 duplicate records, 491 records were still used in the selection of titles and abstracts, and 473 irrelevant records were ruled out following the selection of headlines and abstracts. Three studies were removed because they lacked relevant risk evaluations or 95% CIs after a thorough review of the remaining 18 trials. Fifteen studies were identified from the full-text screening. One additional study was acquired by examining the reference list of recovered articles. As a result, 16 studies were incorporated into the ultimate analysis (Fig. 1).

Study Characteristics

Of the 16 papers from the analysis, seven were case-control studies [22, 23, 24, 25, 26, 27, 28], and nine were cohort studies [29, 30, 31, 32, 33, 34, 35, 36, 37]. There were 1,264,437 people enrolled in the study, and 70,201 PCa cases were reported. There were 10 articles [22, 23, 24, 25, 26, 27, 29, 31, 33, 34] on data from North America, three from Europe [28, 30, 32], one from Australia [35], one from Asia [36], and one from Europe and Asia [37]. The characteristics of this investigation are outlined in Table 1. Articles analyzing the consumption of cruciferous vegetables from the dietary habit applied a questionnaire or a proven food frequency questionnaire to gather daily food consumption. In some studies, the food intake of participants was documented weekly or monthly and converted into a daily intake. The entire research reported employing risk estimates such as RR or OR. The quality of each item was evaluated using criteria from the Newcastle-Ottawa Case-Control and Cohort Scales. The mean scores for the case-control and cohort studies were 7.43 (SD = 0.5) and 7.89 (SD = 1.0), respectively.

Overall Analyses and Dose-Response Analyses

The association between eating cruciferous vegetables and PCa is depicted in Figure 2. The RR values for the initial study ranged from 1.30 (95% CI: 0.80–2.00) in Ambrosini's study [35] to 0.54 (95% CI: 0.38–0.78) in Joseph's study [26]. The highest intake of cruciferous vegetables decreased the incidence of PCa by 13% in comparison to the lowest intake (RR = 0.87; 95% CI: 0.80–0.95). Over the course of the research, moderate heterogeneity was identified ($p = 0.001$, $I^2 = 59.2\%$).

The outcome of the dose-response analysis is displayed in Figure 3. The findings suggest that consuming cruciferous vegetables may reduce the likelihood of developing PCa. With a daily increase of 15 g of cruciferous vegetables, the combination RR for PCa was 0.955 (95% CI: 0.928–0.982). In the funnel graph, no substantial publication bias was observed in the included studies. However, Egger's test ($p = 0.001$) and Begger's test ($p = 0.034$) both showed evidence of publication bias. Then the trim and fill method was applied to identify and rectify the deviation. Its result is illustrated in Figure 4. Finally, there was no missing document, which means there was no publication bias. The pooled RRs using fixed effect and random effect models were 0.96 (95% CI: 0.92–1.00) and 0.90 (95% CI: 0.83–0.97), respectively, which were consistent with the combined effects before using the trim and fill method.

Subgroup and Sensitivity Analyses

A subgroup analysis was conducted in order to minimize heterogeneity. Table 2 lists the findings of the subgroup analysis of cruciferous vegetable consumption and PCa risk. Consuming cruciferous vegetables reduced PCa risk among participants from North America (RR = 0.85, 95% CI: 0.75–0.94) and Australia (RR = 0.56, 95% CI: 0.20–0.92), but there was no statistically significant difference among participants from Europe (RR = 0.91, 95% CI: 0.79–1.04) and Asia (RR = 0.92, 95% CI: 0.60–1.24). Analysis of subgroups in relation to the type of study found that consuming cruciferous vegetables considerably reduced the PCa risk in the case-control study (RR = 0.79, 95% CI: 0.70–0.87) but not in the cohort study (RR = 0.98, 95% CI: 0.93–1.02). In addition, with the exception of marital status and alcohol consumption, significant negative correlations were found in other confounding correction subgroups.

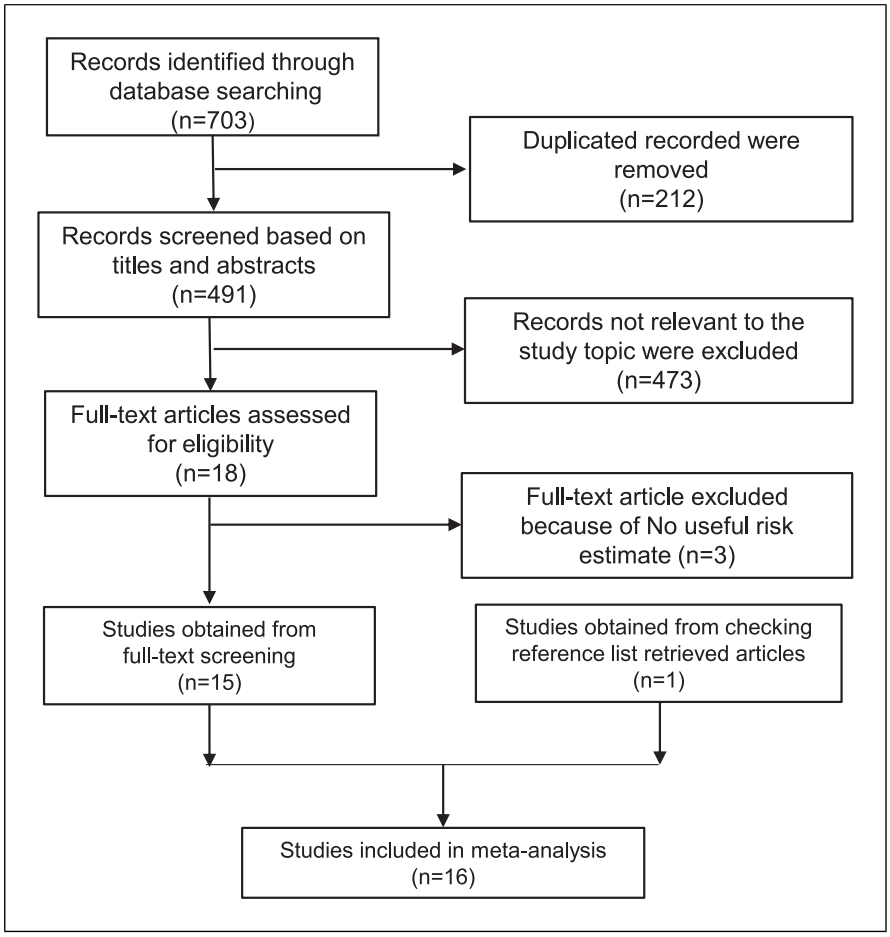

Fig. 1. Literature search and screening process.

The combined RR values for the remaining studies are recalculated after excluding a study in the sequence of sensitivity analysis. The total RR from 0.85 (95% CI: 0.77–0.93) to 0.89 (95% CI: 0.82–0.96) has not changed considerably overall.

Discussion

According to this meta-analysis, consuming cruciferous vegetables is related to the reducing risk of PCa. Liu et al. [8] conducted the first meta-analysis of this topic. We have made a further analysis on this basis.

When analyzing subgroups by geographical region, studies from North America (RR 0.85, 95% CI: 0.75–0.94) and Australia (RR 0.56, 95% CI: 0.20–0.92) are more relevant than those from Europe (RR 0.91, 95% CI: 0.79–1.04) and Asia (RR 0.92, 95% CI: 0.60–1.24), indicating that regional differences may bring about the heterogeneity of observations. Meanwhile, among the 10 studies [22, 23, 24, 25, 26, 27, 29, 31, 33, 34] in North America, there are 6 case-control studies [22, 23, 24, 25, 26, 27], which may be the reason for the internal heterogeneity. Synthetic analysis of case-control studies revealed that eating cruciferous vegetables reduced the PCa risk when subgroups were analyzed by research type. The pooled estimate of the cohort studies was insignificant, indicating that our findings were based primarily on case-control studies. It is worth mentioning that 2 of the included studies were case-control studies from the USA and Australia, where the dietary pattern has grown beyond Europe and focuses on food processing. Furthermore, due to the dietary differences between the USA and Europe, it is necessary to conduct a prospective study to explore this difference. We also studied some essential confounders, including the family-related history of PCa, smoking, drinking as well as obesity.

PCa is a highly hereditary cancer [38]. Epidemiological and family studies have confirmed the apparent family aggregation of PCa [39]. Smoking [40, 41], alcohol, and fat [42–44] have all been related to an increased risk of PCa in recent epidemiological and follow-up studies. Eating more cruciferous vegetables is often accompanied

Table 1. Characteristics of included studies

Author	Region	Study type	Case/ subjects	Intake measurement	RR (95% CI)	Adjustments	Quality score
Hsing et al. [29] (1990)	USA	Cohort	149/ 17,633	<1.2 times/month 1.2–2.2 times/ month 2.3–4.5 times/ month >4.5 times/month	1.00 1.10 (0.70–1.80) 1.20 (0.80–2.00) 1.30 (0.80–2.00)	Age and SS	6
Schuurman et al. [30] (1998)	The Netherlands	Cohort	642/ 58,279	25 g/day 50 g/day 75 g/day 100 g/day 125 g/day	1.00 0.98 (0.72–1.32) 0.81 (0.59–1.12) 0.87 (0.64–1.18) 0.82 (0.59–1.12)	Age, AFHPC, socio-economic status, FC, and VC	9
Jain et al. [22] (1999)	Canada	Case-control	617/ 1,253	<8.7 g/day 8.7–24.0 g/day 24.1–44.6 g/day >44.6 g/day	1.00 0.95 (0.73–1.24) 0.69 (0.52–0.91) 0.85 (0.64–1.13)	Age, total energy intake, SS, MS, study area, BMI, ES, dietary fiber, VSU, total grains, FC, and VC	7
Villeneuve et al. [23] (1999)	Canada	Case-control	1,623/ 3,246	<1 servings/week 1–<2 servings/ week 2–<4 servings/ week ≥4 servings/week	1.00 0.80 (0.70–1.10) 0.90 (0.70–1.10) 0.90 (0.70–1.10)	Age, AC, coffee and tea consumption, ES, MS, household income, meat, fish, VC, FC, race and AFHPC	8
Cohen et al. [24] (2000)	USA	Case-control	628/ 1,230	<1 servings/week 1–2.9 servings/ week ≥3 servings/week	1.00 0.84 (0.61–1.14) 0.59 (0.39–0.90)	Age, race, AFHPC, ES, BMI, PSA tests, FC, VC, energy, fat, vitamin C, and carotenoid intakes	7
Kolonel et al. [25] (2000)	Canada	Case-control	1,619/ 3,237	≤8.8 g/day 8.9–21.23 g/day 21.3–36.6 g/day 36.7–72.9 g/day >72.9 g/day	1.00 1.10 (0.88–1.37) 0.90 (0.72–1.13) 1.04 (0.83–1.31) 0.78 (0.61–1.00)	Age, race, ES, BMI, calories intake, geographic location	7
Giovannucci et al. [31] (2003)	USA	Cohort	2,969/ 47,365	≤0.5 servings/week 0.55–1 servings/ week 1.05–1.5 servings/ week 1.55–2.5 servings/ week >2.5 servings/week	1.00 0.99 (0.88–1.12) 0.93 (0.82–1.06) 0.94 (0.83–1.06) 0.91 (0.79–1.04)	BMI, height, SS, AFHPC, diabetes, race, PA, calorie intake, red meat, processed meat, fish, α-linolenic acid, calcium, and tomato sauce	8

Table 1 (continued)

Author	Region	Study type	Case/ subjects	Intake measurement	RR (95% CI)	Adjustments	Quality score
Joseph et al. [35] (2004)	USA	Case-control	428/965	<680 g/month 681–1,081 g/month 1,082–1,892 g/month ≥1,893 g/month	1.00 0.54 (0.38–0.78) 0.78 (0.54–1.12) 0.58 (0.38–0.89)	Age, SS, BMI, height and weight, and AFHPC	7
Key et al. [32] (2004)	Europe	Cohort	1,104/ 130,544	9.7 g/day 13.2 g/day 18.8 g/day 23.7 g/day 29.2 g/day	1.00 1.10 (0.87–1.39) 1.29 (1.04–1.60) 1.07 (0.87–1.32) 1.01 (0.83–1.23)	ES, SS, PA, height, weight, and energy intake	7
Stram et al. [33] (2006)	USA	Cohort	3,922/ 78,564	Q1 Q2 Q3 Q4 Q5	1.00 1.10 (0.99–1.22) 1.06 (0.95–1.18) 1.09 (0.98–1.21) 1.03 (0.92–1.14)	Age, race, ES, BMI, SS, and AFHPC	8
Darlington et al. [27] (2007)	Canada	Case-control	752/ 2,365	<1.0 times/month 1.0 times/month 1.1–3.0 times/month >3.0 times/month	1.00 0.80 (0.60–1.10) 1.00 (0.70–1.20) 0.80 (0.60–1.10)	Age, AFHPC, BMI, ES, and type of occupation	8
Krish et al. [34] (2007)	USA	Cohort	1,338/ 29,361	0.1 servings/day 0.2 servings/day 0.4 servings/day 0.6 servings/day 1.1 servings/day	1.00 0.98 (0.83–1.17) 0.92 (0.77–1.09) 0.95 (0.80–1.13) 0.85 (0.71–1.02)	Age, race, ES, height, weight, adult occupation, SS, AFHPC, PA, BMI, SS, total energy, study center, supplemental vitamin E intake, total fat intake, red meat intake, diabetes, and aspirin use	9
Ambrosini et al. [28] (2008)	Australia	Cohort	97/2,183	0–0.3 servings/week >0.3–1.5 servings/week >1.5 servings/week	1.00 0.80 (0.50–1.26) 0.56 (0.31–1.02)	Age, BMI, source of asbestos exposure, and SS	8
Takachi et al. [29] (2010)	Japan	Cohort	339/ 43,475	16 g/day 35 g/day 55 g/day 95 g/day	1.00 1.25 (0.89–1.75) 1.07 (0.76–1.51) 0.92 (0.66–1.30)	Age, BMI, study area, SS, VSU, MS, consumption of the dairy product and of soy products, green tea consumption, and AC	7

Table 1 (continued)

Author	Region	Study type	Case/ subjects	Intake measurement	RR (95% CI)	Adjustments	Quality score
Turati et al. [28] (2015)	Italy and Switzerland	Case-control	1,294/ 2,588	<1 servings/week >1 servings/week	1.00 0.87 (0.70–1.09)	SS, AC, dietary habits, and AFHPC	8
Petimar et al. [30] (2017)	Europe and Japan	Cohort	52,680/ 842,149	<10 g/day 10–<30 g/day 30–<50 g/day 50–<70 g/day ≥70 g/day	1.00 1.03 (1.01–1.06) 1.01 (0.97–1.05) 1.00 (0.96–1.04) 1.02 (0.96–1.09)	Age, AFHPC, BMI, height, weight, SS, PA, ES, race, MS, VSU, and history of diabetes	9

RR, relative risk; CI, confidence interval; BMI, body mass index; AFHPC, a family history of prostate cancer; SS, smoking status; ES, education status; MS, marital status; AC, alcohol consumption; PA, physical activity; FC, fruit consumption; VC, vegetable consumption; VSU, vitamin supplement use.

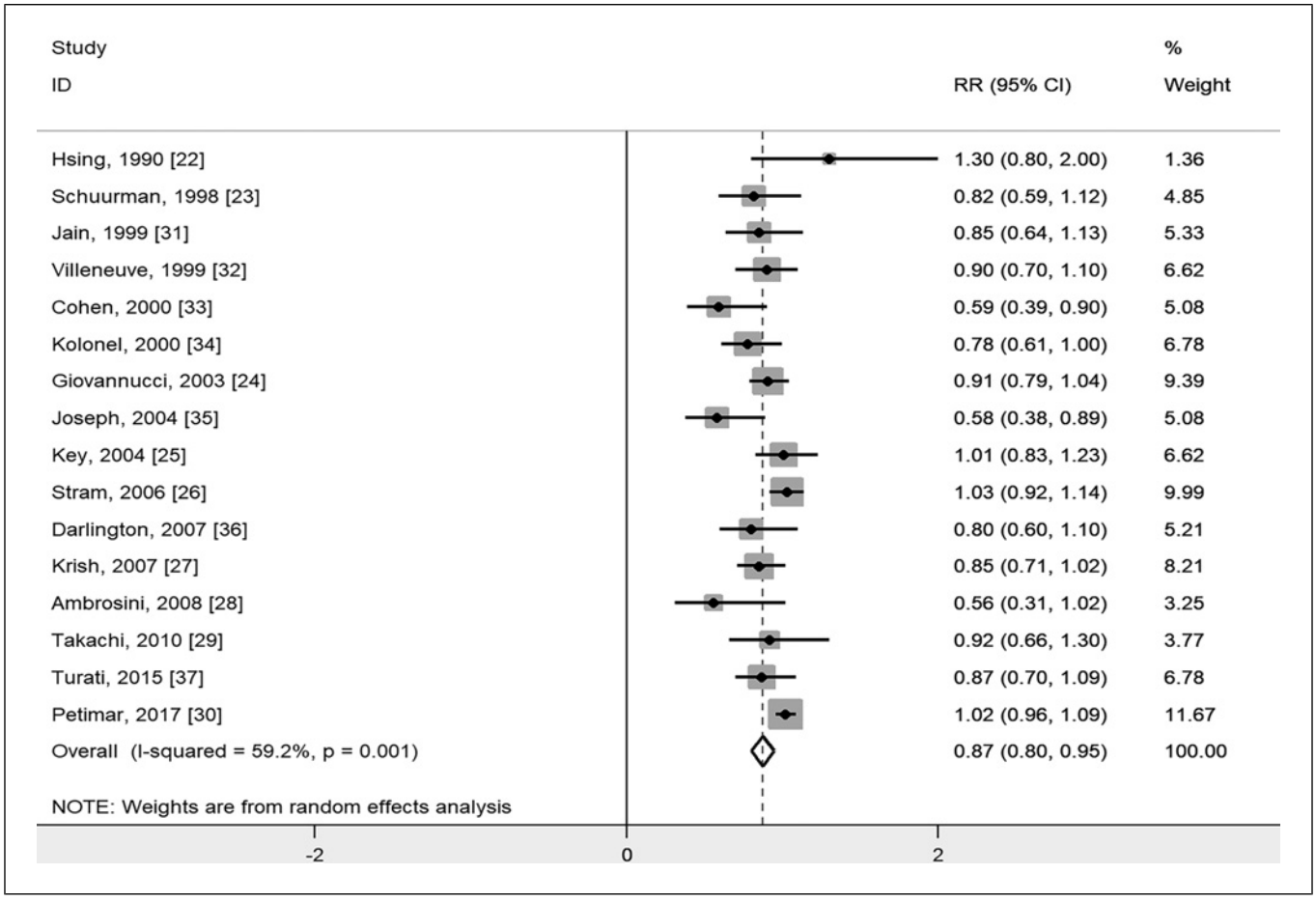

Fig. 2. Forest plots of the association between PCa and cruciferous vegetable consumption.

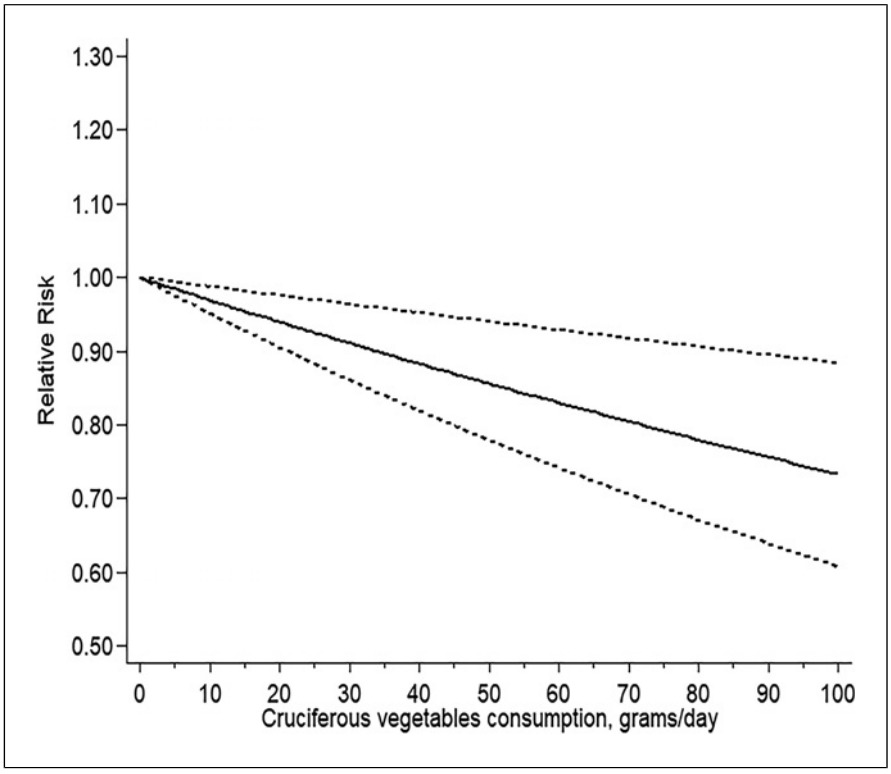

Fig. 3. RR for PCa by doses of cruciferous vegetable consumption in light of the results of the dose-response meta-analyses. The solid line represents the estimated RRs. The dotted lines represent the 95% CIs.

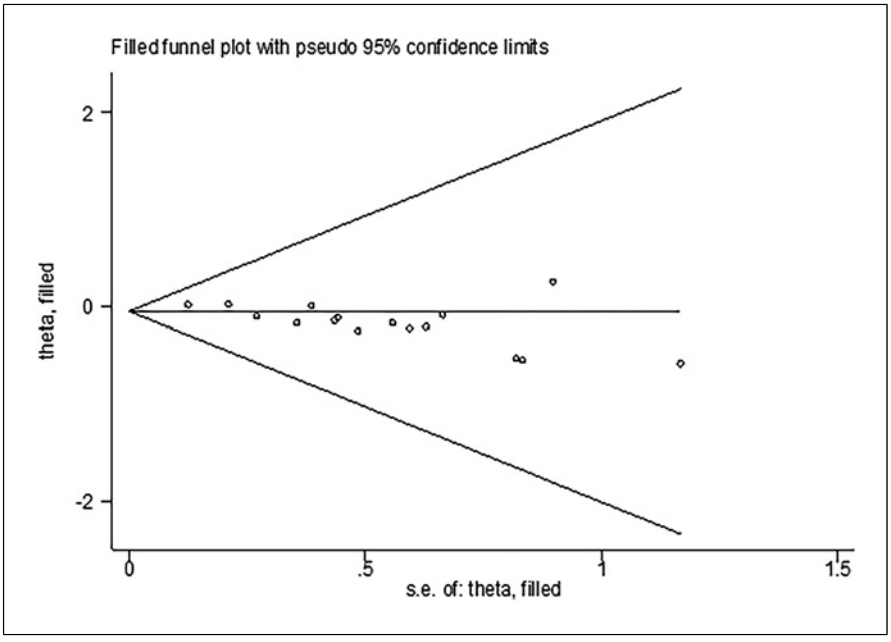

Fig. 4. Trim and fill analysis for RR of the relationship of cruciferous vegetables and PCa.

by a good lifestyle. As a result, healthy habits are linked to lower smoking rates, alcohol use, and BMI. However, after extensive investigation of the confounding factors of smoking, alcohol consumption, and BMI, the inverse relationship between cruciferous vegetables and PCa remains. It also confirms the accuracy and reliability of our research findings, namely that consuming cruciferous vegetables may be a protective factor for PCa.

Table 2. Subgroup analysis of cruciferous vegetables with the risk of PCa

	Number of studies	Summary RR	95% CI	I^2 (%)	*p* value
Overall	16	0.87	(0.80–0.95)	59.2	0.001
Study location					
North America	10	0.85	(0.75–0.94)	57.5	0.012
Europe	3	0.91	(0.79–1.04)	0.0	0.458
Oceania	1	0.56	(0.20–0.92)	–	–
Asia	1	0.92	(0.60–1.24)	–	–
Europe and Asia	1	1.02	(0.96–1.08)	–	–
Study type					
Cohort	9	0.98	(0.93–1.02)	43.8	0.076
Case-control	7	0.79	(0.70–0.87)	14.5	0.319
Adjustment for confounders					
Family of PCa					
Yes	9	0.87	(0.77–0.96)	70.6	0.001
No	7	0.88	(0.76–0.99)	23.0	0.254
Smoking status					
Yes	11	0.91	(0.89–0.99)	58.2	0.008
No	5	0.79	(0.69–0.89)	0.0	0.464
Alcohol consumption					
Yes	3	0.89	(0.76–1.02)	0.0	<0.001
No	13	0.86	(0.78–0.95)	66.8	0.959
BMI					
Yes	11	0.85	(0.75–0.94)	70.2	<0.001
No	5	0.92	(0.82–1.02)	0.0	0.532

Cruciferous vegetables have been known for their medicinal value since ancient times [45]. Over the last few decades, the anticancer impact of cruciferous vegetables has attracted extensive attention. Numerous scientists have sought to investigate the relationship between cruciferous veggies and the tumor. However, the preventative effect of cruciferous vegetables on cancer can involve various convoluted mechanisms that have not yet been fully acknowledged. So far, most research has attended to the ability of cruciferous vegetable components to modify the expression and liveness of biotransformation enzymes. Glucosinolates are natural phytochemicals that produce bioactive species in cruciferous vegetables. When broken down by the endogenous plant enzyme myrosinase, they produce two bioactive substances: sulforaphane and indole-3-carbinol. Sulforaphane can induce phase II enzyme [46] and then inhibit Akt signal transduction from inducing apoptosis of PCa cells [47]. The cell cycle inhibitors p21 and p27 are downregulated by indole-3-carbinol, and CDK6 activity is inhibited as a result [48], and then, the growth of PCa is curbed. Additionally, studies have demonstrated that vitamin K is negatively correlated with PCa [49, 50]. As one of the two forms of vitamin K, the intake of menaquinones (vitamin K2) is negatively related to PCa risk, rather than phylloquinone (vitamin K1) [49]. As a product of cruciferous vegetables, phylloquinone is converted to menaquinones in the vitamin K cycle [50].

The strength of our study lies in the dose-response analysis we performed to back up the research hypothesis that a larger consumption of cruciferous vegetables is related with a linear reduction in PCa risk. A thorough subgroup analysis was also performed to identify underlying factors of moderate heterogeneity.

Certain constraints in this meta-analysis cannot be neglected. To begin with, as we all know, Asia is a high-consumption area of cruciferous vegetables, making it an ideal object of research. Nevertheless, only one such study was carried out in Japan. Another study was carried out jointly in Japan and Europe. Because of the scarcity of relevant literature, we also considered controlled trials and cohort studies. There may be an erroneous negative connection between eating cruciferous vegetables and the likelihood of developing PCa due to recall bias in the case-control model. Simultaneously, case-control studies may be flawed due to selection bias, which could skew the results of any association between a cruciferous vegetable diet and the risk of PCa. Therefore, the result of case-control studies should be carefully explained. Moreover, asymmetry in funnels was identified using Begg's and Egger's tests. The trim and fill method allowed us to virtually eliminate publication bias, but it also reflected

that the publications we included might have disparities in study quality, research heterogeneity, chance, and artefactual effects. Finally, the majority of research is conducted in North America and Europe because of the comparatively high frequency of PCa in those regions. As a result, we should be cautious when extending results to other regions with relatively low impacts.

Conclusion

In summary, meta-analysis results from case-control and published cohort studies reveal that greater consumption of cruciferous vegetables may be linked to a lower PCa risk. However, there are relatively few studies included in the meta-analysis, and the results from the cohort studies are not significant. At present, no clear conclusion can be drawn.

Statement of Ethics

An ethics statement is not applicable because this study is based exclusively on published literature.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

All authors announced that they had not received any fund support.

Author Contributions

J.Y.L. wrote the manuscript. Z.H.L. and S.L. revised the manuscript. J.Y.L. and Z.H.L. sought out and selected studies of relevance. S.L. extracted the data. Z.H.L. contributed to the data analysis. B.X.C. performed manuscript editing and review. A final manuscript was read and approved by all authors.

Data Availability Statement

All the data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

References

1 Culp MBB, Soerjomataram I, Efstathiou JA, Bray F, Jemal A. Recent global patterns in prostate cancer incidence and mortality rates. Eur Urol. 2020 Jan;77(1):38–52.
2 Zhu Y, Mo M, Wei Y, Wu J, Pan J, Freedland SJ, et al. Epidemiology and genomics of prostate cancer in Asian men. Nat Rev Urol. 2021 Mar;18(5):282–301.
3 Yan H, Cui X, Zhang P, Li R. Fruit and vegetable consumption and the risk of prostate cancer: a systematic review and meta-analysis. Nutr Cancer. 2022 Jul;74(4):1235–42.
4 Murillo G, Mehta RG. Cruciferous vegetables and cancer prevention. Nutr Cancer. 2001 Sep;41(1–2):17–28.
5 Keck A-S, Finley JW. Cruciferous vegetables: cancer protective mechanisms of glucosinolate hydrolysis products and selenium. Integr Cancer Ther. 2004 Mar;3(1):5–12.
6 Fujioka N, Fritz V, Upadhyaya P, Kassie F, Hecht SS. Research on cruciferous vegetables, indole-3-carbinol, and cancer prevention: a tribute to Lee W. Wattenberg. Mol Nutr Food Res. 2016 May;60(6):1228–38.
7 Kim MK, Park JH. Conference on "Multidisciplinary approaches to nutritional problems." Symposium on "Nutrition and health." Cruciferous vegetable intake and the risk of human cancer: epidemiological evidence. Proc Nutr Soc. 2009 Feb;68(1):103–10.
8 Liu B, Mao Q, Cao M, Xie L. Cruciferous vegetables intake and risk of prostate cancer: a meta-analysis. Int J Urol. 2012 Feb;19(2):134–41.
9 Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. J Clin Epidemiol. 2009 Jul;339(339):b2700.
10 Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010 Jul;25(9):603–5.
11 Egger M, Smith GD, Phillips AN. Meta-analysis: principles and procedures. BMJ. 1997 Dec;315(7121):1533–7.
12 Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002 May;21(11):1539–58.
13 Jackson D, White IR, Thompson SG. Extending DerSimonian and Laird's methodology to perform multivariate random effects meta-analyses. Stat Med. 2009 Apr;29(12):1282–97.
14 Chen H, Manning AK, Dupuis J. A method of moments estimator for random effect multivariate meta-analysis. Biometrics. 2012 May;68(4):1278–84.
15 Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. J Clin Epidemiol. 2008 Oct;61(10):991–6.
16 Sterne JAC, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. J Clin Epidemiol. 2001 Oct;54(10):1046–55.
17 Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997 Sep;315(7109):629–34.
18 Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994 Dec;50(4):1088–101.
19 Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics. 2000 Jun;56(2):455–63.
20 Greenland S, Longnecker MP. Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. Am J Epidemiol. 1992 Jun;135(11):1301–9.
21 Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med. 1989 May;8(5):551–61.
22 Jain MG, Hislop GT, Howe GR, Ghadirian P. Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in Canada. Nutr Cancer. 1999 Jul;34(2):173–84.

23 Villeneuve PJ, Johnson KC, Kreiger N, Mao Y. Risk factors for prostate cancer: results from the Canadian national enhanced cancer surveillance system. The Canadian cancer registries epidemiology research group. Cancer Cause Control. 1999 May;10(5):355–67.
24 Cohen JH, Kristal AR, Stanford JL. Fruit and vegetable intakes and prostate cancer risk. J Natl Cancer Inst. 2000 Jan;92(1):61–8.
25 Kolonel LN, Hankin JH, Whittemore AS, Wu AH, Gallagher RP, Wilkens LR, et al. Vegetables, fruits, legumes and prostate cancer: a multiethnic case-control study. Cancer Epidem Biomar. 2000 Aug;9(8):795–804.
26 Joseph MA, Moysich KB, Freudenheim JL, Shields PG, Bowman ED, Zhang Y, et al. Cruciferous vegetables, genetic polymorphisms in glutathione S-transferases M1 and T1, and prostate cancer risk. Nutr Cancer. 2004;50(2):206–13.
27 Darlington GA, Kreiger N, Lightfoot N, Purdham J, Sass-Kortsak A. Prostate cancer risk and diet, recreational physical activity and cigarette smoking. Chronic Dis Can. 2007;27(4):145–53.
28 Turati F, Rossi M, Pelucchi C, Levi F, La Vecchia C. Fruit and vegetables and cancer risk: a review of southern European studies. Br J Nutr. 2015 Apr;113(Suppl 2):S102–10.
29 Hsing AW, McLaughlin JK, Schuman LM, Bjelke E, Gridley G, Wacholder S, et al. Diet, tobacco use, and fatal prostate cancer: results from the Lutheran Brotherhood Cohort Study. Cancer Res. 1990 Nov;50(21):6836–40.
30 Schuurman AG, Goldbohm RA, Dorant E, van den Brandt PA. Vegetable and fruit consumption and prostate cancer risk: a cohort study in The Netherlands. Cancer Epidem Biomar. 1998 Aug;7(8):673–80.
31 Giovannucci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC. A prospective study of cruciferous vegetables and prostate cancer. Cancer Epidem Biomar. 2003 Dec;12(12):1403–9.
32 Key TJ, Allen N, Appleby P, Overvad K, Tjønneland A, Miller A, et al. Fruits and vegetables and prostate cancer: no association among 1,104 cases in a prospective study of 130,544 men in the European Prospective Investigation into Cancer and Nutrition (EPIC). Int J Cancer. 2004 Dec;109(1):119–24.
33 Stram DO, Hankin JH, Wilkens LR, Park S, Henderson BE, Nomura AM, et al. Prostate cancer incidence and intake of fruits, vegetables and related micronutrients: the multiethnic cohort study* (United States). Cancer Cause Control. 2006 Nov;17(9):1193–207.
34 Kirsh VA, Peters U, Mayne ST, Subar AF, Chatterjee N, Johnson CC, et al. Prospective study of fruit and vegetable intake and risk of prostate cancer. J Natl Cancer Inst. 2007 Aug;99(15):1200–9.
35 Ambrosini GL, de Klerk NH, Fritschi L, Mackerras D, Musk B. Fruit, vegetable, vitamin A intakes, and prostate cancer risk. Prostate Cancer Prostatic Dis. 2008;11(1):61–6.
36 Takachi R, Inoue M, Sawada N, Iwasaki M, Sasazuki S, Ishihara J, et al. Fruits and vegetables in relation to prostate cancer in Japanese men: the Japan public health center-based prospective study. Nutr Cancer. 2010;62(1):30–9.
37 Petimar J, Wilson KM, Wu K, Wang M, Albanes D, van den Brandt PA, et al. A pooled analysis of 15 prospective cohort studies on the association between fruit, vegetable, and mature bean consumption and risk of prostate cancer. Cancer Epidem Biomar. 2017 Aug;26(8):1276–87.
38 Mucci LA, Hjelmborg JB, Harris JR, Czene K, Havelick DJ, Scheike T, et al. Familial risk and heritability of cancer among twins in nordic countries. JAMA. 2016 Jan;315(1):68–76.
39 Xu J, Labbate CV, Isaacs WB, Helfand BT. Inherited risk assessment of prostate cancer: it takes three to do it right. Prostate Cancer Prostatic Dis. 2020;23(1):59–61.
40 Hickey K, Do KA, Green A. Smoking and prostate cancer. Epidemiol Rev. 2001 Jan;23(1):115–25.
41 Ordóñez-Mena JM, Schöttker B, Mons U, Jenab M, Freisling H, Bueno-de-Mesquita B, et al. Quantification of the smoking-associated cancer risk with rate advancement periods: meta-analysis of individual participant data from cohorts of the CHANCES consortium. BMC Med. 2016 Apr;14(1):62–15.
42 Vartolomei MD, Kimura S, Ferro M, Foerster B, Abufaraj M, Briganti A, et al. The impact of moderate wine consumption on the risk of developing prostate cancer. Clin Epidemiol. 2018 Apr;10:431–44.
43 Michael J, Howard LE, Markt SC, De Hoedt A, Bailey C, Mucci LA, et al. Early-life alcohol intake and high-grade prostate cancer: results from an equal-access, racially diverse biopsy cohort. Cancer Prev Res. 2018 Aug;11(10):621–8.
44 Zadra G, Photopoulos C, Loda M. The fat side of prostate cancer. Biochim Biophys Acta. 2013 Oct;1831(10):1518–32.
45 Fenwick GR, Heaney RK, Mullin WJ, VanEtten CH. Glucosinolates and their breakdown products in food and food plants. Crit Rev Food Sci Nutr. 1983 Jan;18(2):123–201.
46 Brooks JD, Paton VG, Vidanes G. Potent induction of phase 2 enzymes in human prostate cells by sulforaphane. Cancer Epidem Biomar. 2001 Sep;10(9):949–54.
47 Kinkade CW, Castillo-Martin M, Puzio-Kuter A, Yan J, Foster TH, Gao H, et al. Targeting AKT/mTOR and ERK MAPK signaling inhibits hormone-refractory prostate cancer in a preclinical mouse model. J Clin Invest. 2008 Aug;118(9):3051–64.
48 W Watson G, M Beaver L, E Williams D, H Dashwood R, Ho E. Phytochemicals from cruciferous vegetables, epigenetics, and prostate cancer prevention. AAPS J. 2013 Jun;15(4):951–61.
49 Nimptsch K, Rohrmann S, Linseisen J. Dietary intake of vitamin K and risk of prostate cancer in the heidelberg cohort of the European prospective investigation into cancer and nutrition (EPIC-Heidelberg). Am J Clin Nutr. 2008 Apr 11;87(4):985–92.
50 Nimptsch K, Rohrmann S, Nieters A, Linseisen J. Serum undercarboxylated osteocalcin as biomarker of vitamin K intake and risk of prostate cancer: a nested case-control study in the heidelberg cohort of the European prospective investigation into cancer and nutrition. Cancer Epidemiol Biomarkers Prev. 2009 Jan 7;18(1):49–56.