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Dietary intakes of fruits and vegetables and lung cancer risk in participants with different smoking status: a meta-analysis of prospective cohort studies

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ABSTRACT

Background and Objectives: The results from epidemiological studies are controversial between vegetable and fruit consumption and lung cancer risk in participants with different smoking status. The present meta-analysis aimed to investigate these associations with prospective cohort studies. Meanwhile, the potential dose-response relationship was evaluated. **Methods and Study Design:** Relevant studies were identified with PubMed and Scopus databases up to June 2019. Multivariate-adjusted relative risks for the highest versus the lowest category and 95% confidence intervals were calculated by using a random-effects model. The dose-response relationship was examined by using restricted cubic spline regression model. **Results:** Eight prospective studies were included for data synthesis. The summary estimates indicated that higher vegetable and fruit intake was significantly associated with lower risk of lung cancer in participants with current smokers (RR: 0.84, 95% CI: 0.73, 0.95; I^2=25.2%). No significant association was found in former smokers (RR: 0.97, 95% CI: 0.88, 1.07; I2=15.0%) and never smokers (RR: 0.90, 95% CI: 0.74, 1.11; I^2=6.6%). Dose-response analysis showed that 100 g/day increment of vegetable and fruit intake was associated with a 2% reduction in lung cancer risk among current smokers (95% CI: 0.97, 0.99). **Conclusions:** The present meta-analysis provides significant evidence of an inverse association between vegetable and fruit intake and lung cancer risk in current smokers.

Key Words: vegetable, fruit, smoking status, lung cancer, meta-analysis

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INTRODUCTION

As one of the most common malignant tumours, the incidence and the mortality of lung cancer has reached as high as 11.6% and 18.4% of the total cancer in 2018, respectively.[1] In terms of gender, lung cancer is the most frequent cancer and the leading cause of cancer death among men and second cause of cancer death among women. In addition, the 5-year survival rate of lung cancer is only 4-17%, since patients with lung cancer are diagnosed at an advanced disease stage because of poor diagnostic approach.[2]

A variety of risk factors have been well-established to be associated with lung cancer, including smoking, occupational exposure, air pollution and genetic factors.[3] Among these, smoking is the main factor affecting lung cancer incidence, no matter active smoking or passive smoking. Although quitting smoking is the most effective way to reduce the risk of lung cancer, it is difficult for smokers to give up smoking because of addiction. Therefore, there is an urgent need for a safe and effective way to reduce the risk of lung cancer among smokers. Nowadays, increasing attention has been paid to dietary and nutritional interventions to prevent cancer. A dietary pattern containing more fruits and vegetables has been recommended to prevent lung cancer in general population.[4,5] Considering fruits and vegetables are rich in a variety of antioxidant nutrients such as carotenoids, vitamin E, polyphenols and so on, which can scavenge free radicals to reduce oxidative damage.[6] Additionally, fruits and vegetables are also rich in bioactive phytochemicals that might provide desirable health benefits beyond basic nutrition to reduce the initiation and development of cancer.[7] Therefore, increasing intake of vegetables and fruits might be associated with lower risk of lung cancer.

Although the relationship of vegetable and fruit consumption with lung cancer risk was systematically analyzed using meta-analysis methodology,[8,9] no meta-analyses focused on the association between vegetable and fruit consumption and the risk of lung cancer in participants with different smoking status. Epidemiological studies have extensively investigated the relationship between vegetable and fruit consumption and risk of lung cancer in different smoking status; however, the findings are inconsistent. For example, the results from the European Prospective Investigation into Cancer and Nutrition suggested an inverse association between the intake of vegetable and fruit and lung cancer risk in current smokers, and no significant association was observed in former and never smokers.[10] Besides, in the National Institutes of Health (NIH)-AARP Diet and Health Study, vegetable and fruit consumption was not association with the risk of lung cancer among all smoking status.[11] Thus, we conducted the present meta-analysis to investigate the association of total fruit and vegetable intake with lung cancer risk in participants with different smoking status and also carried out a dose-response analysis for trend estimation.

MATERIALS AND METHODS

The meta-analysis was performed in according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[12]

Literature search

A systematic literature search was conducted for relevant articles up to June 2019 with PubMed and Scopus databases. The following search terms were used: (lung neoplasm OR lung tumour OR lung carcinoma OR lung cancer) AND (nutrition OR diet OR fruit OR vegetable). Additionally, manual search was also performed by screening the reference lists of

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original articles, published meta-analyses and recent reviews by using Google and Baidu Scholar.

Inclusive criteria

The inclusive criteria were as follows: 1) Prospective studies which included nested case-control, case-cohort and prospective cohort design; 2) The exposure variable of interest were total vegetable and fruit intake in different smoking status; 3) The outcome of interest was lung cancer incidence; 4) The estimated relative risks (RRs) and 95% confidence intervals (CIs) were reported. If the data were published more than one study on vegetable and fruit intake and the risk of lung cancer, the latest study or the study with the largest number of samples would be included.

Data extraction and quality assessment

Data extraction was conducted by two investigators (TY and CW) independently, and any discrepancies between two investigators about the eligibility data were resolved via discussion. The following information of the eligible study was extracted, such as surname of the first author, published year, country/region, duration of follow-up, gender, mean age of participants, number of cases, sample size, vegetable and fruit intake assessment method, RRs and 95% CIs and adjustment variable. The included studies used various measurements for fruit and vegetable consumption, such as gram per day and serving per week. We standardized all data into gram per day. First, we translated serving from per week to per day. Then, we converted serving per day to gram per day by multiplying 106, using a standard portion size of 106 grams.[13] A third investigator was consulted to resolve any discrepancy.

The quality of the included studies was assessed with Newcastle-Ottawa Scale.[14] The scoring system summarized nine aspects of each study, and a study with stars of 0-3, 4-6, and 7-9 was classified as low, medium and high quality, respectively.

Statistical analysis

RR was regarded as the common risk estimate for the association between the vegetable and fruit intake and the risk of lung cancer. Multivariate-adjusted RRs with the corresponding 95% CIs for the highest versus lowest category were logarithm transformed, and the summary RR was calculated by using a random-effects model, as weighted by the inverse of their variance.[15] Heterogeneity among included studies was evaluated with I^2 statistic. The I^2 represented the proportion of total variation due to between-study heterogeneity with 25%,

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50% and 75% as the cut-off points, indicating low, medium and high degree of heterogeneity. To explore the source of heterogeneity, subgroup and meta-regression analyses were conducted based on the information of these studies, including mean age of participants, gender and duration of follow-up.

Two-stage random-effect dose-response meta-analysis was performed to estimate the potential curvilinear relation.16 We first adopted generalized least-square regression to estimate a restricted cubic spline model with three knots at the 25%, 50%, and 75% of the distribution regarding fruit and vegetable consumption. Then we conducted a meta-analysis of multivariate random effects using the limited maximum likelihood method.[17] The p value of the curvilinear association was calculated by testing the null hypothesis that the coefficient of the second spline was equal to zero. If the non-linear association was found to be non-significant, a linear dose response meta-analysis was carried out for trend estimation by using generalized least squares regression as proposed by Greenland and Longnecker to assess the associations between increment of vegetable and fruit intake and lung cancer risk.[18] The median or mean dose of vegetable and fruit consumption that was assigned in each category was extracted. If the median or mean dose was not reported in the category, we used the midpoint of the lower and upper categories as the quantile dose. If the highest quantile was open-ended, its dose was defined as 1.2-fold of the highest boundary.[19] The dose of the lowest quantile in each study was set to zero.[20] Of these, since there were two articles that did not report data directly, we took the average value for calculation.[10,21]

Publication bias was examined by Begg's test with a significant level at $p<0.1$.[22] If the result of Begg's test was significant, the potential publication bias was corrected by trim-and-fill method. Sensitivity analysis was to evaluate whether the result would be driven when a study was removed at a time. Statistical analysis was conducted using STATA version 11.0 software (Stata CORP, College station, TX). Two-tailed with p-value less than 0.05 was considered as statistically significant.

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RESULTS

Literature retrieval

The detailed steps of literature search are presented in the Figure 1. A total of 10,223 articles from PubMed and 12,789 articles from Scopus were screened. Additionally, two additional studies were identified by hand searching from the reference lists. Of these, 3981 duplicate articles were deleted, then 18,992 articles that including animal experiments, cell experiments, meta-analyses and systematic reviews were excluded by reviewing the titles and abstracts.

Finally, 41 articles were leaving for full-text examination. Among these, 33 papers were excluded because they were not eligible for inclusive criteria (25 articles did not report the associations of total vegetable and fruit with lung cancer risk in participants with different smoking status, seven articles reported the associations of fruit and vegetable intake with lung cancer mortality, and one article provided intakes of fruits and vegetables associated with total cancer risk, rather than lung cancer risk). Hence, eight cohort studies were included in this meta-analysis.[10,11,21,23-27]

Study characteristics

The basic characteristics of the eligible studies are presented in the Table 1. The article of Feskanich et al. included two cohort studies, the Nurses' Health Study and the Health Professionals' Follow-up Study.[25] Additionally, two articles were divided into men and women for analysis, respectively.[11,21] Overall, there were 11 independent cohort studies from 8 articles for data analysis. One article was carried out in European, two articles in Asia, four articles in North America and the other one article was a pooled analysis that including 8 cohorts. The period of follow-up ranged from 4 to 19 years. On the basis of Newcastle-Ottawa Scale (Table 2), five articles were classified as moderate quality study, and three articles were regarded as high quality study.

Vegetable and fruit intake and lung cancer risk in different smoking status

Six prospective cohort studies reported the association of vegetable and fruit intake with lung cancer risk in current smoking participants.[10,11,23-25,27] A higher intake of vegetables and fruits was associated with 16% (RR: 0.84, 95% CI: 0.73, 0.95; I^2=25.2%) lower risk of lung cancer. Seven studies in former smokers and seven studies in never smokers reported associations between vegetable and fruit intake and lung cancer risk, respectively.[10,11,21,23,25-27] No significant association were found in former (RR: 0.97, 95% CI: 0.88, 1.07; I^2=15.0%) and never smokers (RR: 0.90, 95% CI: 0.74, 1.11; I^2=6.6%). In addition, the pooled effect on all smoking status subjects showed an inverse association between vegetable and fruit consumption and lung cancer risk (RR: 0.91, 95% CI: 0.84, 0.98; I^2=18.8%) (Fig. 2).

Three prospective cohort studies among current smokers were eligible for dose-response analysis,[10,11,27] and non-significant curvilinear association was observed between vegetable and fruit intake and lung cancer risk (*p* for non-linearity=0.996) by using restricted cubic splines models. But linear dose-response analysis suggested that 100 g/day increment of vegetable and fruit intake was associated with 2% reduction in lung cancer risk among current

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smokers (95% CI: 0.97, 0.99; *p* for trend <0.001) (Figure 3). Four prospective cohort studies among former smokers and four prospective cohort studies among never smokers were eligible for dose-response analysis.[10,11,21,27] No significant curvilinear association and linear dose-response analysis were observed between vegetable and fruit intake and lung cancer risk in former (Figure 4) and never smokers (Figure 5).

Subgroup analysis and meta-regression

Then subgroup analyses were performed on the basis of demographic information (Table 3). Subgroup analysis stratified by average age for current smokers showed that the combined effect of vegetable and fruit intake was borderline related with lung cancer risk among participants with mean age >54 years (RR = 0.88, 95% CI: 0.73, 1.05; I^2=0.0%). Marginal association between vegetable and fruit intake with risk of lung cancer in current smokers were found in the women when stratified by gender (RR=0.88, 95% CI: 0.73, 1.05; I^2=0.0%). For duration of follow-up, subgroup analysis indicated that the combined effect of vegetable and fruit intake in current smokers was borderline associated with lung cancer risk among those participants with less than 10 years of follow-up (RR=0.88, 95% CI: 0.76, 1.01; I^2=4.5%). No significant association was observed between vegetable and fruit intake and the risk of lung cancer for former smokers and never smokers when stratified according to gender, mean age of participants and the duration of follow-up. Moderate heterogeneity was observed. Therefore, meta-regression was conducted with the covariates of gender, mean age of participants, the duration of follow-up in different smoking status to explore potential sources of the heterogeneity (Table 3). However, none of these covariates showed a significant impact on the between-study heterogeneity.

Sensitivity analysis and publication bias

In sensitivity analysis, we sequentially excluded one study at a time and the rest of data were not substantially driven (Figure 6-8). The Begg's test indicated that no evidence of publication bias was found when analyzing the relationship between vegetable and fruit intake and lung cancer risk in current smokers (*p*=0.536), former smokers (*p*=0.721) and never smokers (*p*=0.858).

DISCUSSION

The meta-analysis indicated that higher vegetable and fruit intake was significantly associated with 16% lower risk of lung cancer in current smokers. Meanwhile, 100 g/day increment in

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vegetable and fruit intake was associated with 2% reduction in risk of lung cancer among current smokers.

Vegetables and fruits are generally consumed in our daily life, and they play an important role in health promotion and cancer prevention. The beneficial effects of fruits and vegetables on human health are attribute to the nutrients and biologically active compounds, such as phytochemicals, vitamins, minerals, and fibers.[28] A recent meta-analysis concluded that the consumption of apple has a protective effect against cancer in different anatomical sites, including lung cancer, breast cancer and so on.[29] Another meta-analysis showed that intake of dietary flavonoids was negatively correlated with smoking-related cancer risk and the association was only observed among smoker.[30] The potential mechanisms of fruits and vegetables for cancer suppression among smokers have been summarized as follows: Tobacco smoke contains thousands of vapor phase and particulate phase compounds, at least 60 of which have been classified as carcinogens.[31] Thus, chronic exposure of the lung epithelium to this mixture of compounds confers increased cancer susceptibility due to the formation of DNA adducts that produce oncogenic mutations.[32] Furthermore, smoking can cause chronic pulmonary inflammatory microenvironment, oxidative stress and cell structure changes, such as the increase of cell proliferation, angiogenesis and apoptosis arrest and other irreversible processes.[33] On the contrary, the nutrition and bioactive components from vegetables and fruits could inhibit DNA-carcinogen adduct formation and repair DNA which damaged by smoking.[34] Meanwhile, the nutrients provided by fruits and vegetables could elevate and maintain cellular antioxidant to reduce oxidative stress, such as vitamin A, vitamin C, polyphenols, carotenoids and so on.[35] Furthermore, isothiocyanates, indoles, flavonoids and other phytochemicals could also regulate anti-tumour pathways through different mechanisms, inhibit the invasion of cancer cells to normal tissues and the development of neovascularization required for rapid growth of tumours, thereby reducing the risk of lung cancer.[36] Besides, bioactive components in vegetables and fruits have shown anti-inflammatory, anti-infection, anti-viral and anti-bacterial effects contributing to the lung cancer prevention.[37]

Several strengths of this study should be highlighted. First, to the best of our knowledge, this is the first meta-analysis to explore associations between vegetable and fruit consumption and the risk of lung cancer in different smoking status. Second, the studies qualified for this meta-analysis were prospective cohort studies, which reduced the possibility of recall errors and selection biases compared to a retrospective design. Third, there were no significant publication bias, indicating that our results were stable. Meanwhile, sensitivity analysis

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showed that the result was not be significantly affected by one study at a time when a study was removed, indicating that the stability of the combined estimation. Simultaneously, there were several limitations in this meta-analysis. First, the studies included in this meta-analysis were published from 1993 to 2015 in Europe, Asia and North America. Incomparability of results between studies might occur due to the different categories of vegetables and fruits included in different populations, different regions and different periods. Second, dietary consumption of vegetable and fruit was assessed by a food frequency questionnaire (FFQ), so an inaccurate assessment or record was inevitable. Third, although confounding factors are adequately adjusted, qualified observational studies are inevitably affected by inherent or unmeasured biases. The different exposure measurement scale across included studies were not detailed enough to allow standardization of fruit and vegetable consumption, thus our analysis primarily considered the highest versus the lowest exposure category. In addition, lung cancer subtypes were not stratified, because few studies have focused on the association between vegetable and fruit consumption and risk of different lung cancer subtypes. Additional studies should focus on the relationship between vegetable and fruit subtypes and lung cancer risk.

Conclusion

The present study found an inverse association between fruit and vegetable intake and lung cancer risk in current smokers, but not in former or never smokers. These findings have important public health implications in the prevention of lung cancer risk. Further studies with large sample-size should be implemented to confirm these associations.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest. This study is supported by the National Basic Research Program of China (973 Program: 2015CB553604); by National Natural Science Foundation of China (NSFC: 81773433); by the Key scientific Research Projects in Shandong Provence China (2017YYSP007); and by the 2018 Chinese Nutrition Society (CNS) Nutrition Research Foundation-DSM Research Fund (CNS-DSM2018A30). The funders have no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Table 1. Characteristics of included studies

First author	Publication year and region	Age gender	Subjects (cases)	Follow-up period	Exposure measure	Outcome measure	Exposure	Covariates adjusted
Feskanich	2000, America	50.94 y W	77,283 (519)	12 y	FFQ	medical record, death certificates, FFQ	Fruits and vegetables	age, follow-up cycle, smoking status, years since quitting among past smokers, cigarettes smoked/day among current smokers, age at start of smoking, total energy intake, and availability of diet data after baseline measure
Feskanich	2000, America	54.44 y M	47,778 (274)	10 y	FFQ	medical record, death certificates, FFQ	Fruits and vegetables	age, follow-up cycle, smoking status, years since quitting among past smokers, cigarettes smoked/day among current smokers, age at start of smoking, total energy intake, and availability of diet data after baseline measure
Linseisen	2007, Europe	51.16 y W/M	478,590 (1126)	6.4 y	FFQ, 14-day dietary record	active follow-up, next-to-kin information, health insurance records, cancer and pathology registries, mortality registries	Fruits and vegetables	tobacco smoking (status and duration), education (5 categories), physical activity at work (5 categories), intake of red meat, intake of processed meat, height, weight, nonfat energy intake, energy intake from fat, ethanol intake at baseline
Liu Cohort 1	2004, Japan	49.53 y W/M	42,224 (177)	10 y	self-administered questionnaire, FFQ	histological examination of specimens from surgery or autopsy, biopsy or cytology, clinical findings or unspecified evidence	Fruits and vegetables	age, gender, areas, sports, frequency of alcohol intake, body mass index, vitamin supplement use, salted fish and meat, pickled vegetables, smoking status, smoking duration, and number of cigarettes per day
Liu, Cohort 2	2004, Japan	53.87 y W/M	51,114 (251)	7 y	Self-administered questionnaire, FFQ	histological examination of specimens from surgery or autopsy, biopsy or cytology, clinical findings or unspecified evidence	Fruits and vegetables	age, gender, areas, sports, frequency of alcohol intake, body mass index, vitamin supplement use, salted fish and meat, pickled vegetables, smoking status, smoking duration, and number of cigarettes per day
Smith Warner	2003	NR W/M	430,281 (3206)	6-16 y	self-administered questionnaire FFQ	follow-up questionnaires, medical record, cancer registry, mortality registries or death certificates	Fruits and vegetables	education (<high school, high school, >high school), body mass index (<23, 23 to<25, 25 to<30, ≥30 kg/m^2), alcohol intake (0, >0 to<5, 5 to<15, 15 to<30, ≥30 g/day) and calories (continuous), smoking status (never, past, current), smoking duration for past smokers (continuous), smoking duration for current smokers (continuous), amount smoked for current smokers (continuous).

W: woman; M: man; FFQ: food-frequency questionnaire; NR: not report.

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Table 1. Characteristics of included studies (cont.)

First author	Publication year and region	Age gender	Subjects (cases)	Follow-up period	Exposure measure	Outcome measure	Exposure	Covariates adjusted
Steinmetz	1993, America Iowa	57 y W	2,952 (138)	4 y	self-administered questionnaire, FFQ	Health Registry, Surveillance, Epidemiology, and End Results program of the National Cancer Institute	Fruits and vegetables	age, energy intake, and pack-years of smoking
Wakai	2015, Japan	54.5 y W/M	190,940 (1742)	10.5-15.3 y	self-administered FFQ, dietary records	Cancer registries, death certificates	Fruits and vegetables	age, area, smoking and intake of total energy
Wright	2008, America	62 y W/M	472,081 (6035)	8 y	FFQ	cancer registries, self-reports and medical records	Fruits and vegetables	age, energy intake, race, education, body mass index, smoking status, smoking dose, time since quitting smoking, alcohol intake, physical activity, and family history of any cancer.
Yong	1997, America	49.5 y W/M	10,068 (248)	19 y	In-person interviews with FFQ, non-quantitative food frequency questionnaire, dietary interview	hospital records, death certificates. follow-up interviews	Fruits and vegetables	sex, race, educational attainment, non recreational activity level, body mass index, family history, smoking status/pack-years of smoking, total calorie intake, and alcohol intake

W: woman; M: man; FFQ: food-frequency questionnaire; NR: not report.

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Table 2. Quality assessment of each included study according to Newcastle-Ottawa Scale

Study	Representativeness of the exposed cohort	Selection of the unexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest at start of study	Comparability of cohorts on the basis of the design or analysis	Outcome assessment
Feskanich		☆		☆	☆☆	☆
Linseisen		☆		☆	☆	☆
Liu		☆		☆	☆☆	☆
Smith-Warner		☆		☆	☆	☆
Steinmetz		☆		☆	☆☆	☆
Wakai	☆	☆		☆	☆☆	☆
Wright		☆		☆	☆☆	☆
Yong		☆		☆	☆	☆

Study	Follow-up long enough for the outcomes to occur	Adequacy of follow-up of cohorts	Total quality scores
Feskanich	☆	☆	☆☆☆☆☆☆☆
Linseisen	☆		☆☆☆☆☆
Liu	☆	☆	☆☆☆☆☆☆☆
Smith-Warner	☆		☆☆☆☆☆
Steinmetz			☆☆☆☆☆
Wakai	☆		☆☆☆☆☆☆☆
Wright	☆		☆☆☆☆☆☆
Yong	☆	☆	☆☆☆☆☆☆

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Table 3. Subgroup and meta-regression analyses for smoking status

Factors stratified	Current smoker					Former smoker				
	No.[†]	Pooled effect (95% CI)	Heterogeneity		p**	No.[†]	Pooled effect (95% CI)	Heterogeneity		p**
			I^2 (%)	p*				I^2 (%)	p*	
Mean age, year					0.832					0.698
≤54	4	0.779 (0.548, 1.11)	61.	0.051		5	0.992 (0.896, 1.10)	0.0	0.463	
>54	3	0.875 (0.731, 1.05)	0.0	0.497		4	0.856 (0.588, 1.25)	44.	0.148	
Sex					0.123					0.652
Men	2	1.01 (0.795, 1.30)	0.0	0.745		3	0.997 (0.858, 1.16)	31	0.231	
Women	3	0.875 (0.731, 1.05)	0.0	0.497		4	0.856 (0.588, 1.25)	44	0.148	
Follow-up, year					0.625					0.944
≤10 year	5	0.875 (0.759, 1.01)	4.5	0.381		6	0.961 (0.856, 1.08)	5.1	0.384	
>10 year	3	0.760 (0.510, 1.13)	56	0.098		4	0.965 (0.779, 1.20)	43	0.154	

Factors stratified	Never smoker				
	No.[†]	Pooled effect (95% CI)	Heterogeneity		p**
			I^2 (%)	p*	
Mean age, year					0.592
≤54	5	0.863 (0.611, 1.22)	9.8%	0.350	
>54	4	0.996 (0.744, 1.33)	9.4%	0.346	
Sex					0.489
Men	3	0.729 (0.491, 1.08)	0%	0.952	
Women	4	0.996 (0.744, 1.33)	9.4%	0.346	
Follow-up, year					0.958
≤10 year	6	0.886 (0.660, 1.19)	4.4%	0.388	
>10 year	4	0.874 (0.618, 1.24)	30%	0.229	

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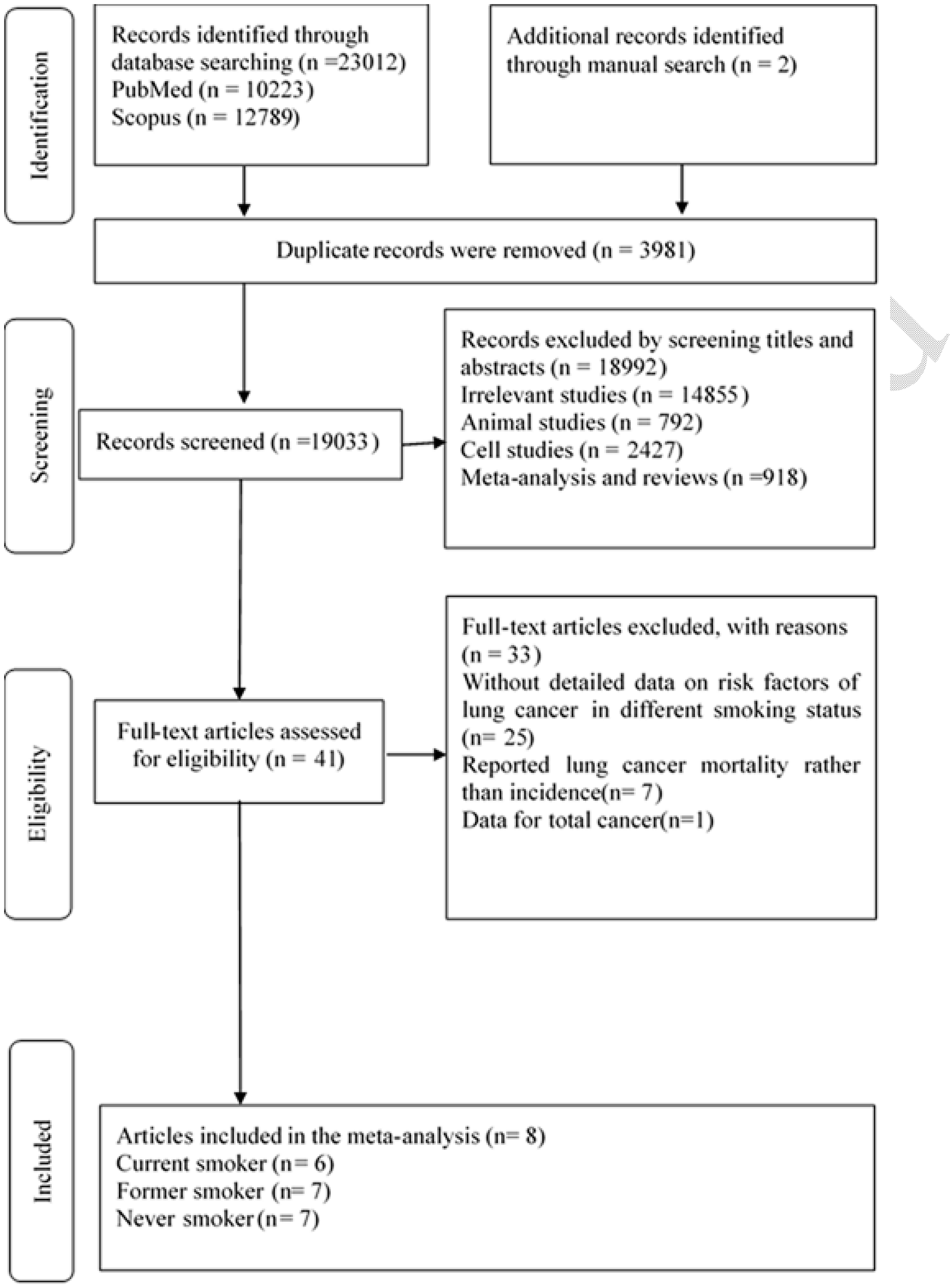

Figure 1. Flow chart of the study selection procedure showing the number of eligible cohorts included in the meta-analysis.

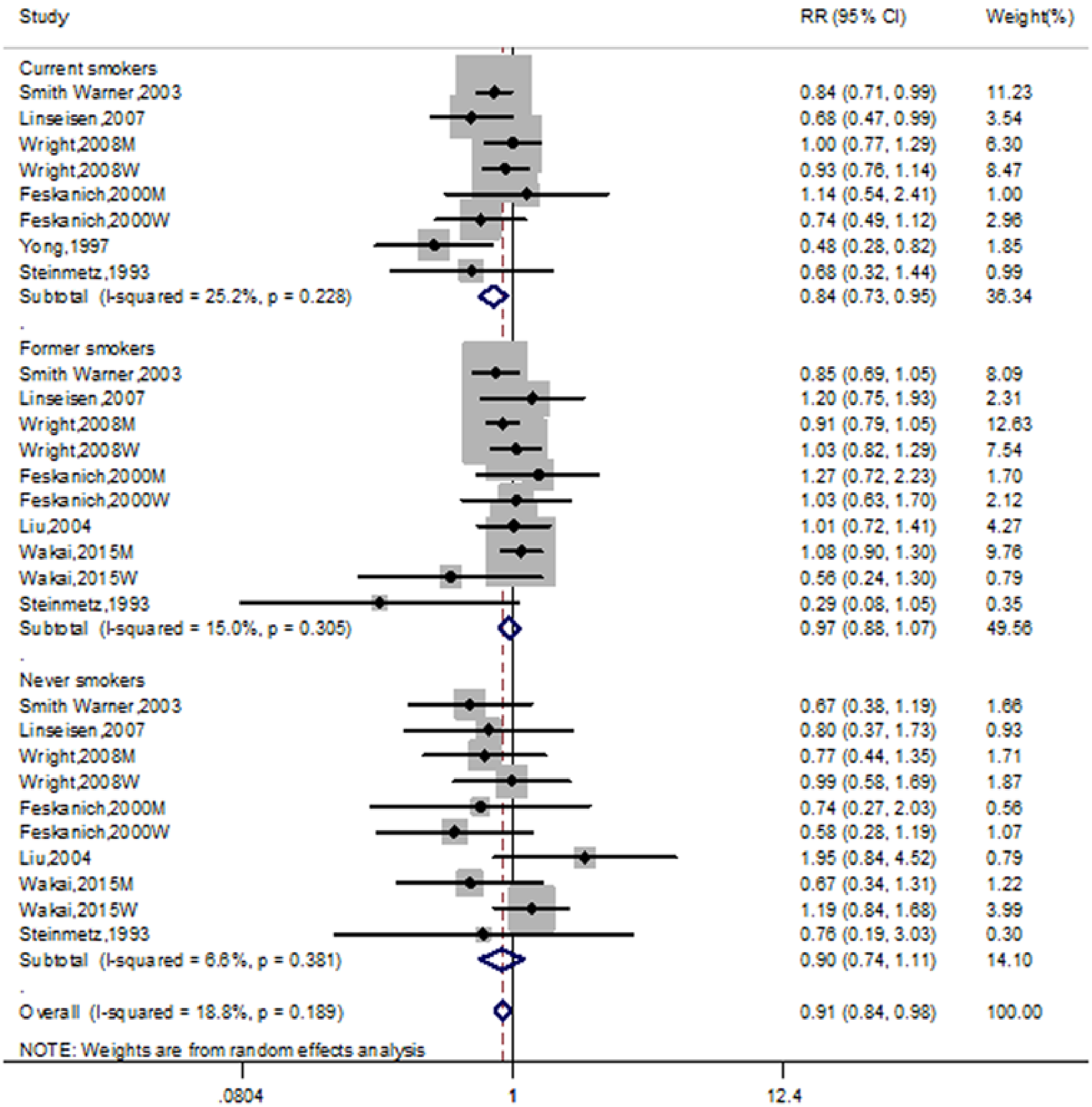

Figure 2. Forest plot of fruit and vegetable consumption with risk of lung cancer in different smoking status. The pooled effect was calculated by using a random-effects model. The diamonds denote summary risk estimate, and horizontal lines represent 95% CI. M, man; W, woman; RR, relative risk

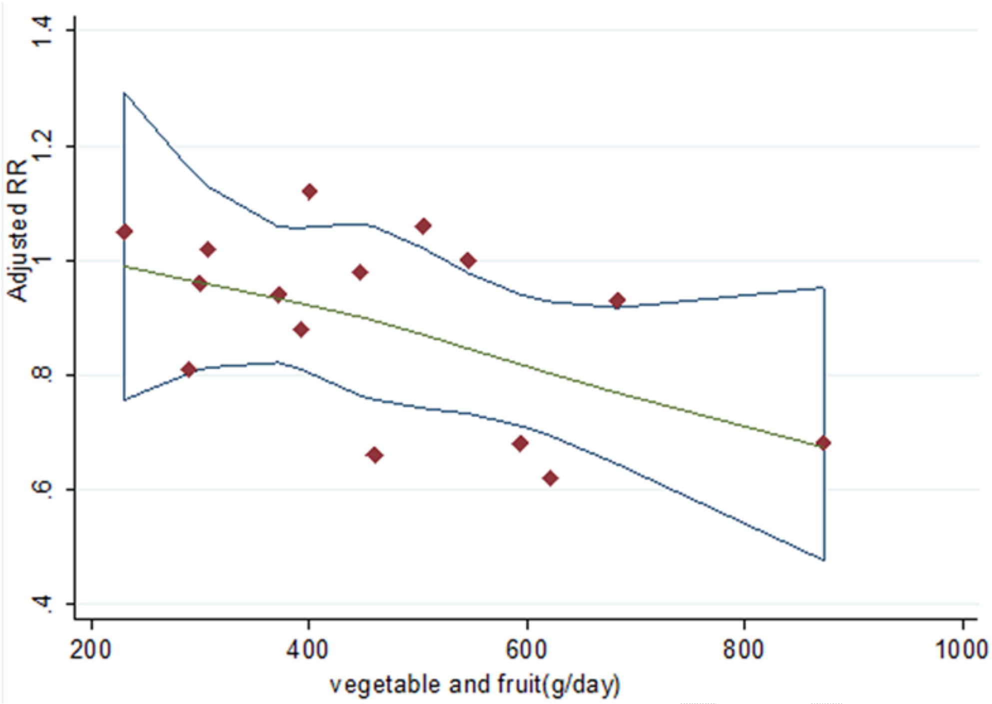

Figure 3. Forest plot of fruit and vegetable consumption with risk of lung cancer in different smoking status. The pooled effect was calculated by using a random-effects model

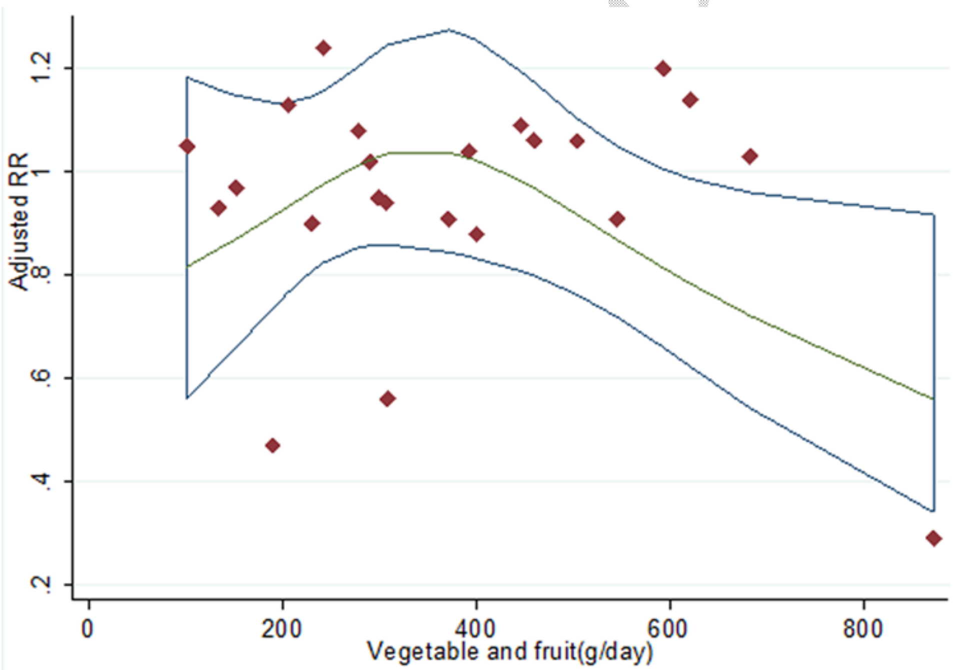

Figure 4. Dose-response analysis for the curvilinear association between vegetable and fruit intakes and the risk of lung cancer in former smokers. RR, relative risk

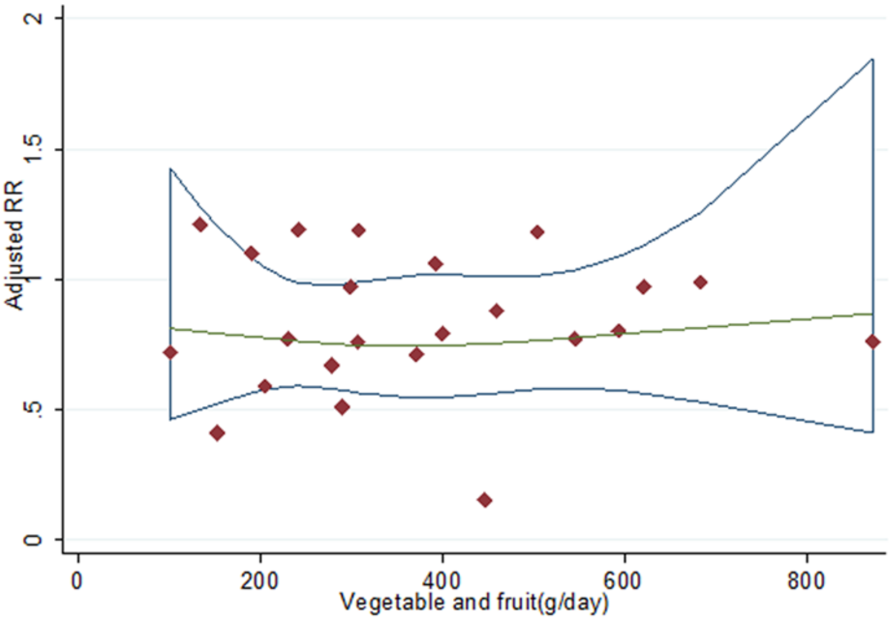

Figure 5. Dose-response analysis for the curvilinear association between vegetable and fruit intakes and the risk of lung cancer in never smokers. RR, relative risk

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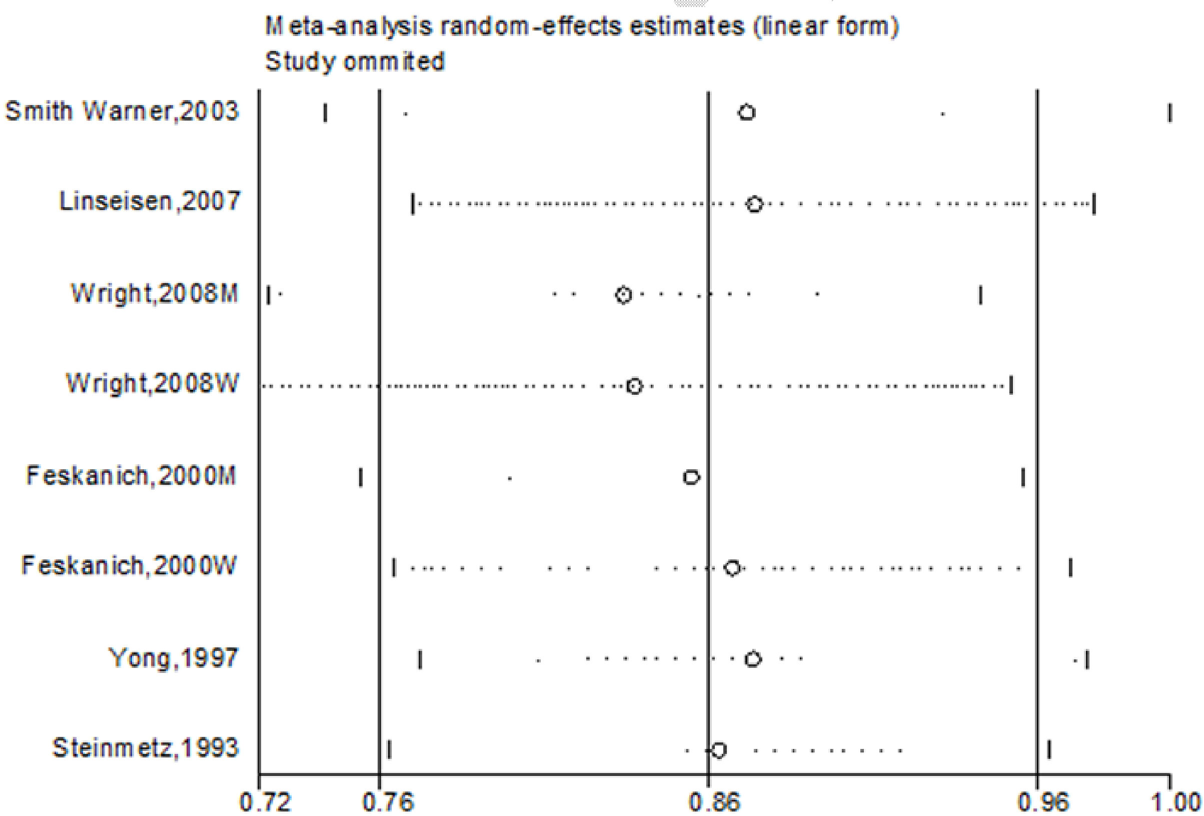

Figure 6. Sensitivity analysis with respect to vegetable and fruit consumption in current smokers. M, man; W, woman

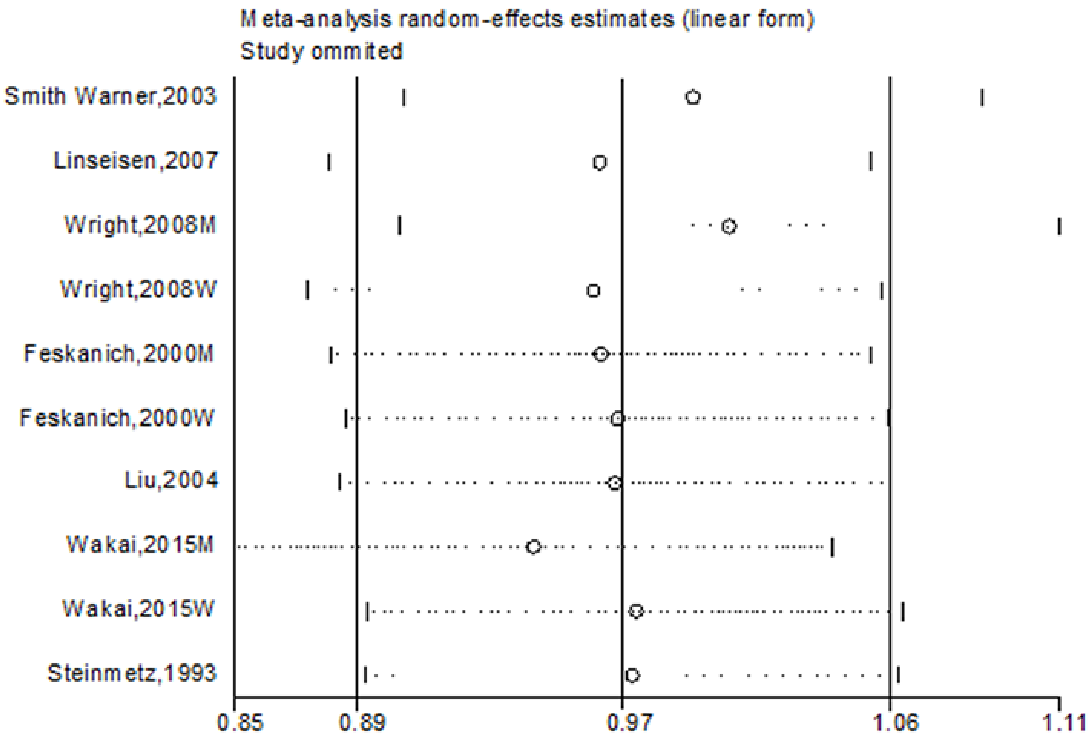

Figure 7. Sensitivity analysis with respect to vegetable and fruit consumption in former smokers. M, man; W, woman

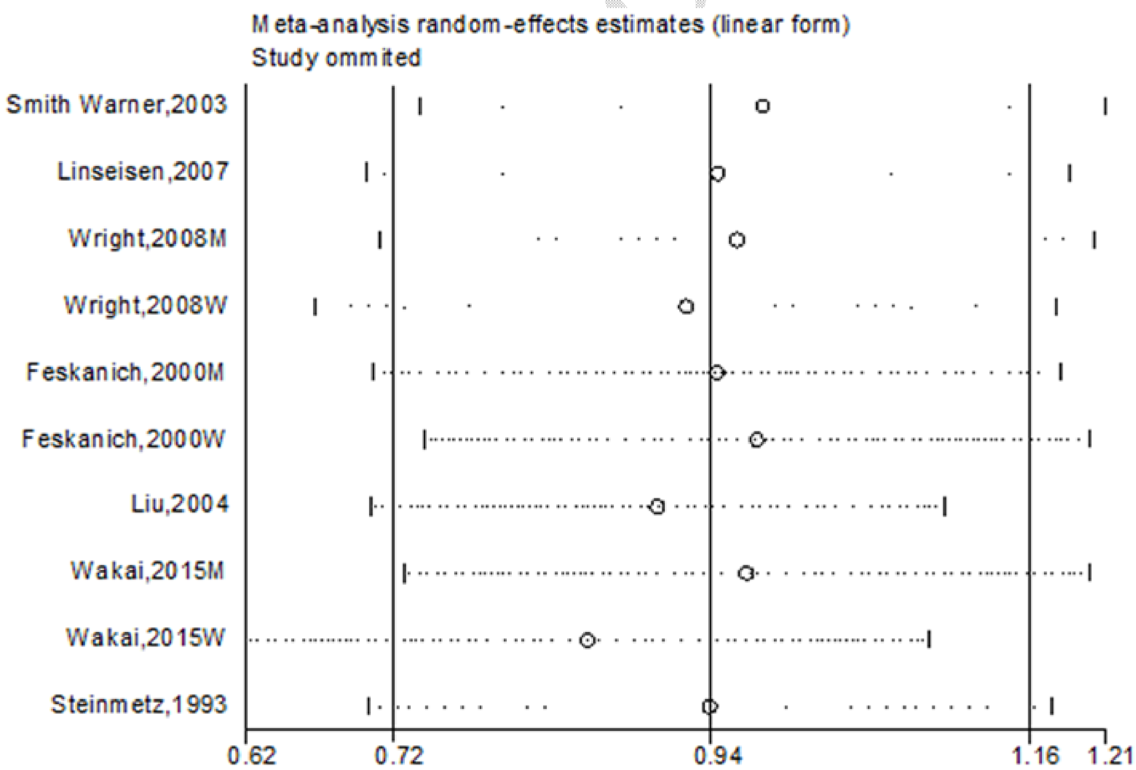

Figure 8. Sensitivity analysis with respect to vegetable and fruit consumption in never smokers. M, man; W, woman