

Cardiovascular Disease Mortality and Cancer Incidence in Vegetarians: A Meta-Analysis and Systematic Review

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Key Words

Vegetarians · Mortality · Cancer · Incidence · Meta-analysis

Abstract

Background: Prospective cohort studies have examined mortality and overall cancer incidence among vegetarians, but the results have been inconclusive. **Aims:** The objective of the present meta-analysis was to investigate cardiovascular disease mortality and cancer incidence among vegetarians and nonvegetarians. **Methods:** Medline, EMBASE and Web Of Science databases were searched for cohort studies published from inception to September 2011. Studies were included if they contained the relative risk (RR) and corresponding 95% CI. Participants were from the UK, Germany, California, USA, the Netherlands and Japan. **Results:** Seven studies with a total of 124,706 participants were included in this analysis. All-cause mortality in vegetarians was 9% lower than in nonvegetarians (RR = 0.91; 95% CI, 0.66–1.16). The mortality from ischemic heart disease was significantly lower in vegetarians than in nonvegetarians (RR = 0.71; 95% CI, 0.56–0.87). We observed a 16% lower mortality from circulatory diseases (RR = 0.84; 95% CI, 0.54–1.14) and a 12% lower mortality from cerebrovascular disease (RR = 0.88; 95% CI, 0.70–1.06) in vegetarians compared with nonvegetarians. Vegetarians had a significantly lower cancer incidence than

nonvegetarians (RR = 0.82; 95% CI, 0.67–0.97). **Conclusions:** Our results suggest that vegetarians have a significantly lower ischemic heart disease mortality (29%) and overall cancer incidence (18%) than nonvegetarians.

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Introduction

The number of vegetarians is increasing in many western countries [1]. Besides avoiding meat, vegetarians generally exhibit other healthy lifestyle habits such as abstinence from smoking and alcohol consumption [2]. Studies of risk factors for chronic disease have shown that vegetarians have lower serum cholesterol concentrations, lower body mass indices, lower incidence of diabetes and possibly lower blood pressure than comparable nonvegetarians [1, 3]. A repeatedly asked question is whether the avoidance of meat or other dietary components plays an important role in reducing mortality. There is some evidence suggesting that meat consumption increases the risk of cancers of the colorectum, breast and prostate [4, 5]. Particular dietary practices and lifestyles, therefore, have often provided instructive insight into the effect of diet and lifestyle factors on mortality from specific causes.

Five prospective cohort studies involving a large proportion of vegetarians and nonvegetarians with a shared interest in healthy living or a similar social/religious background have reported some evidence that infrequent meat consumption or vegetarianism was associated with a reduction in mortality from ischemic heart disease, but some of these individual results were not statistically significant or were not observed in both sexes [2]. However, an association of vegetarian diets with a lower risk of coronary heart disease has been well established across studies [3, 6, 7]. In addition, meat consumption was associated with an increased mortality rate from prostate cancer, bladder cancer and ovarian cancer but not with mortality from cancers of the colorectum and breast [1]. Results from the Adventist Health Study have suggested that vegetarians have a significantly lower risk of cancers of the colon and prostate than nonvegetarians, but the risk of breast cancer does not differ significantly between these dietary groups [8]. Results from the Oxford Vegetarian Study suggested no large difference in the incidence of colorectal cancer between vegetarians and nonvegetarians [9], whereas the UK Women's Cohort Study suggested that women who do not eat any meat have a lower risk of breast cancer than do meat eaters [10]. A pooled analysis of mortality rates in 5 prospective studies suggested no large differences in overall cancer mortality between vegetarians and nonvegetarians [11].

Therefore, the associations of a vegetarian diet with mortality from specific causes are not firmly established, although it is most certain for disease-specific mortality from cardiovascular diseases [12, 13] and certain cancers [14]. The current analysis sought to analyze previous vegetarian cohort studies together using, as far as possible, common definitions in order to provide an overall estimate of any association of a vegetarian diet with mortality and cancer incidence.

Methods

Data Sources and Study Selection

We searched Medline, EMBASE and Web Of Science electronic databases from inception to September 2011 for the following terms: 'vegetarians', 'nonvegetarians', 'omnivore', 'all-cause mortality', 'ischemic heart disease', 'circulatory diseases', 'cancer incidence', 'mortality', 'Adventist', 'Zen priest' and 'vegetarianism'. Study selection and data extraction were undertaken independently by two investigators with discrepancies resolved by consensus. The search was restricted to studies published in English-language journals. We included cohort studies that evaluated associations of vegetarians/nonvegetarians with all-cause mortality, disease-specific mortality of cardiovascular diseases and cancer

incidence in humans. No restrictions were placed on the duration of follow-up or sample size. We excluded cross-sectional studies, letters and reviews. Studies were excluded from the pooled analysis if an outcome or data change was not obtainable.

Data Extraction

Data extraction was independently conducted by 2 authors (T.H. and B.Y.) blinded to the title, author and journal of publication. The data abstracted for each study were confirmed by reviewer consensus. The data that we collected included the first author's name, year of publication, duration of follow-up, number and age of participants, relative risk ratios (RRs) and standard errors (SEs) of these estimates, sample size, and cause of mortality. The study quality was assessed using the score method [15] in which the score ranged from 0 to 5. Criteria for assessment of the study quality included the method of the study, sample size or objective measurements and duration of follow-up.

Data Analyses and Statistical Methods

Extracted data were analyzed using Stata version 11 software (StataCorp, College Station, Tex., USA). A random-effects model was used to pool data. Effect sizes are presented as RR with 95% CI. Heterogeneity was assessed using the χ^2 method. Publication bias was assessed with the Egger test and the Begg-Mazumdar test [16, 17]. Sensitivity analyses were planned a priori and undertaken for the following variables: study design, number of subjects, country and length of follow-up.

Results

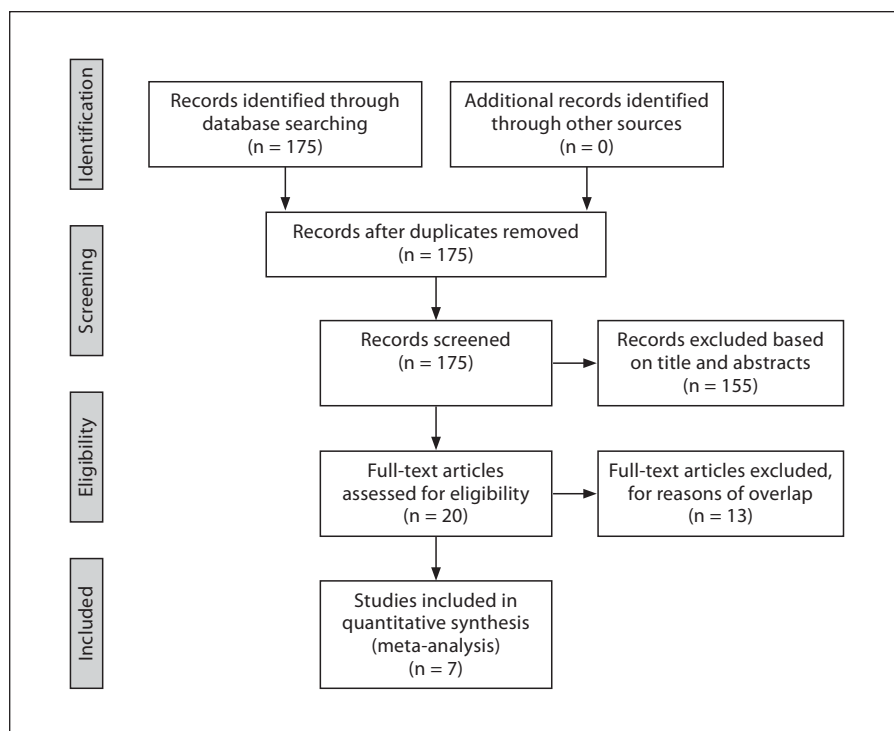
Study Selection

Our comprehensive search identified 175 citations using our search approach. These citations were sequentially screened independently by 2 authors (T.H. and B.Y.) for inclusion. Twenty citations were reviewed using the full articles. Repeated reports were excluded [12, 18–22]. Seven cohort studies met the inclusion criteria for the systematic review [2, 13, 18, 23–26] (fig. 1).

The characteristics of the included studies are shown in table 1. Six of the cohort studies were conducted in European countries of dominant European ethnicity and one was undertaken in Japan among Zen Buddhist priests. The duration of the studies was from 10 to 23 years. The age of the participants ranged from 10 to 90 years. A total of 124,706 participants were included in the present meta-analysis. In these 7 studies, vegetarians included lacto-ovo vegetarians (who did not eat meat or fish or ate these foods less than once a week, but did eat eggs or dairy products, or both) or vegans (who did not eat meat, fish, eggs or dairy products).

Data Synthesis

Seven studies were included in the analysis of all-cause mortality [2, 13, 18, 23–26] (table 2). All-cause mortality

Fig. 1. Flowchart for selection of included cohort studies.**Table 1.** Characteristics of the 7 included cohort studies

Study	Study name	Country	Median year of recruitment	End of follow-up	Follow-up, years	Number of subjects	Adjusted covariables	Age years	Cause of mortality	Study quality
Beeson et al. [18], 1989	California Seventh-Day Adventists	California, USA	1976 (1976–1980)	1988	11.1	28,952	BMI, alcohol intake, education and exercise	20–89	All causes of death	3
Berkel and de Waard [24], 1983	Seventh-Day Adventists in the Netherlands	The Netherlands	1968 (1968–1977)	1977	10	3,217	BMI, alcohol intake, education and exercise	20–89	All causes of death	2
Chang-Claude et al. [2], 2005	The Heidelberg Study	Germany	1976 (1976–1978)	1999	21	1,904	Age, sex, smoking, alcohol intake, BMI, education and activity level	>10	All causes of death	4
Key et al. [26], 1996	Health Food Shoppers	UK	1973 (1973–1979)	1995	17	11,000	Age, sex, smoking, alcohol intake, BMI and education	16–89	All causes of death	5
Key et al. [13], 2009	The EPIC-Oxford cohort	UK	1993 (1993–1999)	2007	17	64,234	Age, sex, smoking and alcohol consumption	20–89	All causes of death	5
Ogata et al. [25], 1984	Japanese male Zen priests study	Japan	1955–1978	1978	23	4,352	BMI, alcohol intake, education and exercise	>20	All causes of death	1
Thorogood et al. [23], 1994	Oxford Vegetarian Study	UK	1981 (1980–1984)	1995	13.7	11,047	Smoking, BMI and social class	20–89	All causes of death	4

Table 2. All-cause mortality in vegetarians and nonvegetarians

Study	Vegetarians		Nonvegetarians	
	event	total	event	total
Chang-Claude et al. [2], 2005	380	1,225	155	679
Key et al. [13], 2009	654	16,081	2,311	31,173
Beeson et al. [18], 1989	3,564	8,003	10,480	20,949
Thorogood et al. [23], 1994	819	4,674	1,119	6,373
Berkel and deWaard [24], 1983	1,104	4,000	Dutch population	
Ogata et al. [25], 1984	1,396	4,352	General Japanese male population	
Key et al. [26], 1996	1,343	11,000	2,686	11,000

was 9% lower in vegetarians than in nonvegetarians after the follow-up. The RR and 95% CI for all-cause mortality are shown in figure 2. The pooled RR is 0.91 (95% CI, 0.66–1.16).

Six studies were included in the analysis of ischemic heart disease mortality [2, 13, 18, 23, 24, 26]. We found that ischemic heart disease mortality was significantly lower (by 29%) in vegetarians than in nonvegetarians (RR = 0.71; 95% CI, 0.56–0.87) (fig. 3). We further analyzed the circulatory diseases (ischemic heart disease and cerebrovascular disease) in vegetarians and nonvegetarians. Five studies were included in this analysis [2, 13, 23, 24, 26]. The circulatory disease mortality was 16% lower in vegetarians than in nonvegetarians (RR = 0.84; 95%

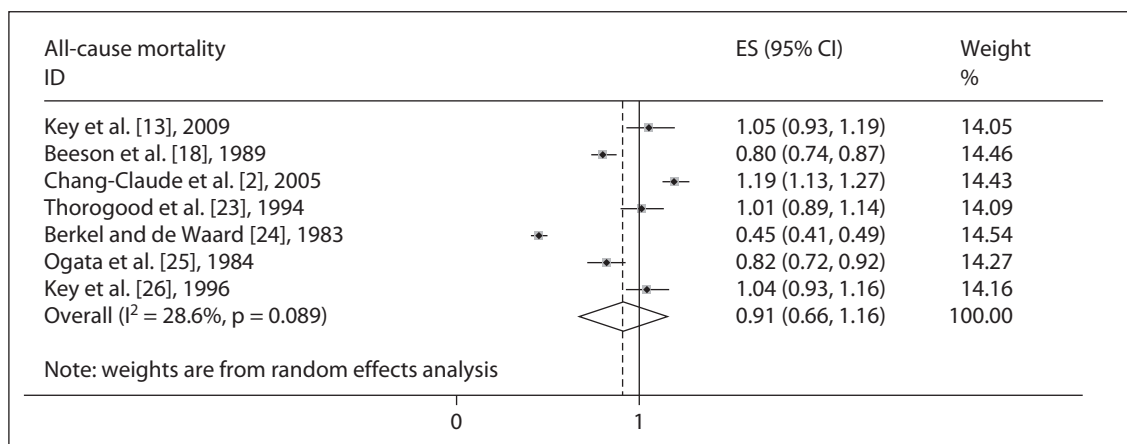


Fig. 2. Forest plot summary of all-cause mortality in 7 studies included in the meta-analysis. ID = Author name and year; ES = effect size.

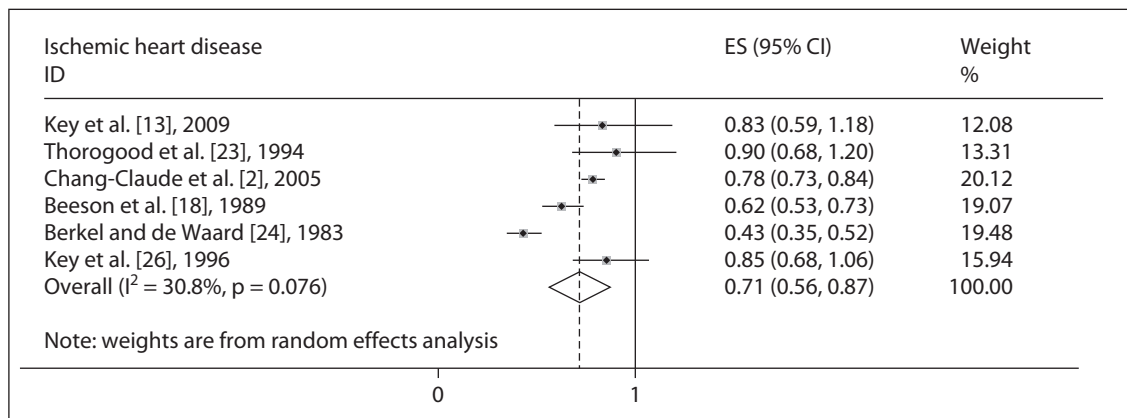


Fig. 3. Forest plot summary of ischemic heart disease mortality in 6 studies included in the meta-analysis. ID = Author name and year; ES = effect size.

CI, 0.54–1.14) with significant heterogeneity ($I^2 = 58\%$, $p = 0.046$) (fig. 4). In sensitivity analyses, we excluded the studies one by one to identify the source of heterogeneity. It was noted that when the study by Berkel and de Waard [24] was excluded no heterogeneity was observed ($I^2 = 0\%$, $p = 0.986$). However, no significant changes in the circulatory disease mortality were observed (RR = 0.91; 95% CI, 0.74–1.01). We also noted a 12% lower cerebrovascular disease rate in vegetarians than in nonvegetarians (RR = 0.88; 95% CI, 0.70–1.06) (fig. 5).

Seven studies were included in the further analysis of the cancer incidence among vegetarians and nonvegetarians [2, 9, 18, 24–28]. We found an 18% lower cancer incidence in vegetarians than in nonvegetarians. The RR

and 95% CI for cancer incidence are shown in figure 6. The pooled RR is 0.82 (95% CI, 0.67–0.97).

Begg's funnel plot and Begg's test showed a slight significant publication bias in all-cause mortality, cancer incidence, ischemic heart disease and circulatory disease. No publication bias was observed in cerebrovascular disease.

Discussion

In the present study we sought to extend these observations by combining the studies of vegetarians to give reasonable scope for detecting associations with mortal-

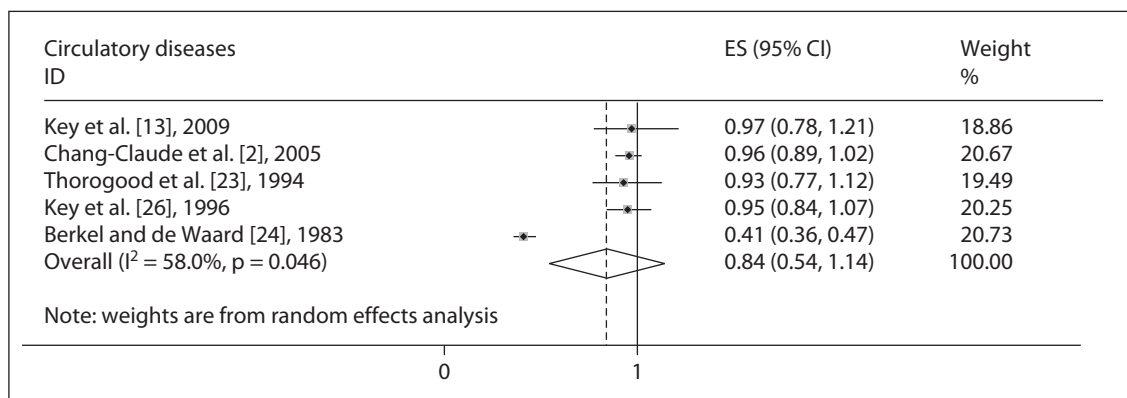


Fig. 4. Forest plot summary of circulatory disease mortality in 5 studies included in the meta-analysis. ID = Author name and year; ES = effect size.

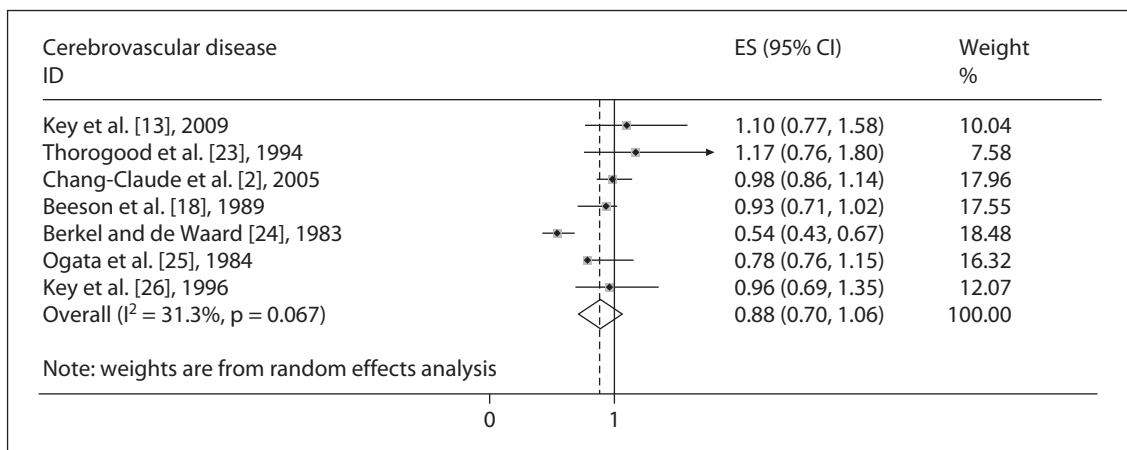


Fig. 5. Forest plot summary of cerebrovascular disease mortality in 7 studies included in the meta-analysis. ID = Author name and year; ES = effect size.

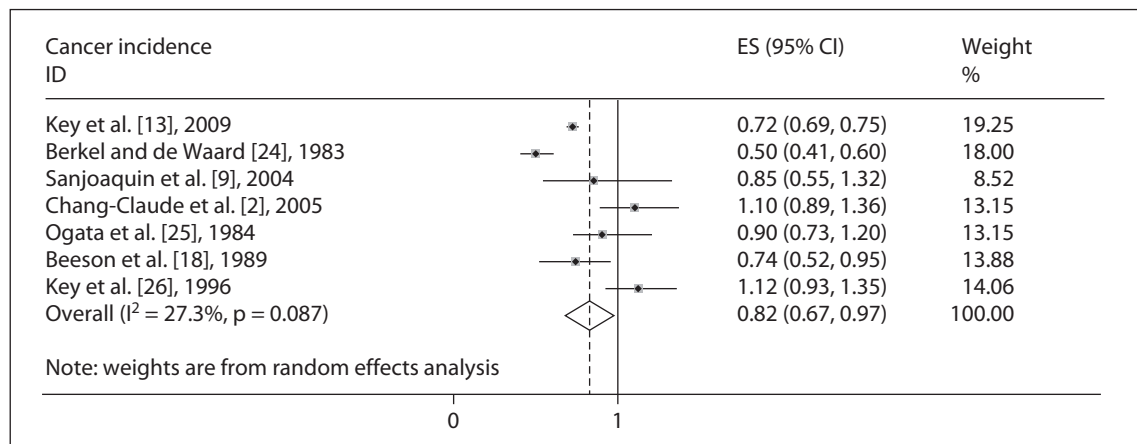


Fig. 6. Forest plot summary of cancer incidence in 7 studies included in the meta-analysis. ID = Author name and year; ES = effect size.

ity from all-cause mortality and cancer incidence. We believe that the studies analyzed here are the only prospective studies that included a large number of subjects. Therefore, the results presented here represent most of the information available on comparisons of mortality between vegetarians and nonvegetarians with broadly similar lifestyles. The exception in the present meta-analysis is the inclusion of the Japanese Zen Buddhist study where the principles of vegetarianism are somewhat different to those encountered among those of European ancestry.

The overall cancer incidence rates and mortality from ischemic heart disease were significantly lower in vegetarians than in nonvegetarians, and all-cause mortality and mortality from circulatory disease were 9 and 16% lower in vegetarians than in nonvegetarians.

We observed a 9% lower all-cause mortality in vegetarians than in nonvegetarians. Our results are consistent with previous studies [13, 29]. In the EPIC-Oxford study, for all causes of death combined, the rate of mortality in vegetarians was similar to that in meat eaters, and the rate of mortality in fish eaters was nonsignificantly lower than in meat eaters [13]. Moreover, in the previous collaborative analysis of 5 prospective studies, the rate of all-cause mortality was nonsignificantly lower among vegetarians than among nonvegetarians [11]. However, data from a prospective cohort study of adults in North America and Europe raise the possibility that a lifestyle pattern that includes a very low meat intake is associated with greater longevity [30]. In the subgroup analysis we found that ischemic heart disease mortality was 22% lower in vegetarians than in nonvegetarians. Previous studies also re-

ported similar results [31–34]. In addition, mortality from ischemic heart disease was 24% (95% CI: 0.06, 0.38) lower among vegetarians than among nonvegetarians in the collaborative reanalysis of 5 prospective studies [11]. The lower mortality from ischemic heart disease among vegetarians was greater in those of a younger age and was restricted to those who had followed their current diet for more than 5 years [11]. The highly significant association suggests that the lower mortality from ischemic heart disease was due to the dietary differences between vegetarians and nonvegetarians. The relatively low prevalence of smoking in these cohorts [11] and the lower serum total cholesterol concentrations in vegetarians also contributed to the lower mortality from ischemic heart disease among the vegetarians [35–37]. Other factors such as reduced oxidation of LDL cholesterol or changes in blood clotting also help explain the lower mortality rate in vegetarians [11].

Moreover, mortality from circulatory diseases (ischemic heart disease and cerebrovascular disease) in the present study is 16% lower in vegetarians than in nonvegetarians. The possible reason for this result is that there were no significant differences between vegetarians and nonvegetarians in mortality from cerebrovascular disease which is one component of circulatory diseases [1, 11]. High-fat diets are implicated in the onset of cardiovascular disease, cancer and obesity. Large intakes of saturated and trans-fatty acids, therefore, together with low levels of polyunsaturated fatty acids, particularly n-3 polyunsaturated fatty acids, appear to have the greatest impact on the development of cardiovascular disease [38]. Hence, lower platelet/plasma concentrations of n-3

polyunsaturated fatty acids in vegetarians may contribute to the nonsignificant difference in mortality from circulatory diseases in these two groups [39–40]. We also thought that the marginal association of mortality rate with vegetarians might have been due to residual confounding among former smokers or to a recent change in diet in an attempt to alleviate ill health. For example, smoking and both low and high BMI increased mortality, and moderate alcohol consumption decreased mortality from circulatory diseases, ischemic heart disease, and all causes combined [13, 41].

We found that the overall cancer incidence in vegetarians was 18% lower than in nonvegetarians. This reduction in risk associated with vegetarianism might be due to changes in diet during the long-term follow-up of the study. Some large studies have found a significant correlation between red meat consumption and the incidence of colon cancer [42], but large prospective studies do not confirm this observation [11, 27, 43, 44]. The difference in total cancer between meat eaters and nonmeat eaters could not be ascribed to any one of the major cancer sites examined. This difference might be partly due to dietary differences between the groups. Furthermore, the results may be influenced by residual confounding because of measurement error in the assessment of confounding factors and by confounding by unknown factors. However, among vegetarians who had followed their current diet for less than 5 years, mortality was significantly higher than in nonvegetarians from lung cancer, other causes, and all causes [11]. The cause of this small difference is not known. More data are needed to further our understanding of this observation which, if confirmed, is likely to be due to differences for specific cancer sites.

Our study is the first meta-analysis to date which has pooled all the data available to investigate the associations between vegetarians and all-cause mortality and cancer incidence. We, therefore, included more cohort studies than any previous relevant studies and provided more sufficient data for this issue. Some limitations are also presented here. First, cohort studies could not avoid

the residual confounding or bias despite their relatively longer duration period and larger sample size. Second, we have pooled the data from different ethnicities together, leading to some unavoidable bias. Finally, exclusion of studies which did not provide adequate information might contribute to the tested publication bias.

A potential weakness of the type of cohort studies we have compiled is the accuracy of the assessment of vegetarian status [27, 45]. Vegetarian diets can differ in many ways from nonvegetarian diets, and vegetarian diets themselves vary between different vegetarian groups as in the case of Buddhist vegetarianism [1]. In comparison to the mortality from all-cause mortality among vegetarians, there was also heterogeneity between studies. Moreover, the vegetarians were compared with all nonvegetarians or with meat eaters. Some heterogeneity between studies is to be expected because the dietary differences between vegetarians and nonvegetarians vary between different populations, but we did not have sufficient dietary data from these studies to evaluate this fully. Therefore, it is impossible to draw any conclusions as to which aspects of the diet are protective [1].

In conclusion, the overall cancer incidence and mortality from ischemic heart disease were significantly lower, but there were no associations of a vegetarian diet with all-cause mortality and mortality from circulatory and cerebrovascular diseases.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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