REVIEW

Fiber consumption and all-cause, cardiovascular, and cancer mortalities: A systematic review and meta-analysis of cohort studies

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The present meta-analysis aimed to investigate fiber consumption and all-cause mortality, and cause-specific mortality. MEDLINE and web of science database were searched for cohort studies published from inception to August 2014. Studies were included if they provided a hazard ratio (HR) and corresponding 95% CI for mortality in relation to fiber consumption. We found that, compared with those who consumed lowest fiber, for individuals who ate highest fiber, mortality rate was lower by 23% (HR, 0.77; 95% CI, 0.72–0.81) for CVD, by 17% (HR, 0.83; 95% CI, 0.74–0.91) for cancer, by 23% (HR, 0.77; 95% CI, 0.73–0.81) for all-cause mortality. For each 10 g/day increase in fiber intake, the pooled HR was estimated to be 0.89 (95% CI, 0.86–0.93) for all-cause mortality, 0.80 (95% CI, 0.72–0.88) for CHD mortality, and 0.66 (95% CI, 0.40–0.92) for IHD mortality, 0.91 (95% CI, 0.88–0.94) for cancer. Dietary fiber and CVD mortality showed a strong dose–response relation. Apparently, fiber consumption is inversely associated with all-cause mortality and CVD, IHD, cancer mortality.

Keywords:
All-cause mortality / Cancer / Cardiovascular disease / Fiber / Meta-analysis

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1 Introduction

Dietary fiber, a key component in healthy eating [1], is defined as the edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine, with complete or partial fermentation in the large intestine [2]. Compelling evidences demonstrated that high dietary fiber intake promotes overall health and associates with lower mortality through preventing and mitigating of type 2 diabetes mellitus, cardiovascular disease, and colon cancer [1]. Observational studies examining the effect of dietary fiber on mortality reported inconsistent results. For example, the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study did not observe association between dietary fiber intake and total mortality [3]. On the other hand, the Scottish Heart Health study found that dietary fiber intake was inversely related to total mortality in men but not in women [4]. The Zutphen Study in the Netherlands found a 9% lowered risk of total death per 10 g/day of dietary fiber intake [5]. Very recently, a meta-analysis mainly focusing on total mortality reported that high dietary fiber intake may reduce the risk of total mortality [6]. This study did not address the associations of fiber consumption and cardiovascular and cancer specific mortalities.

Previous studies examining the association between fiber consumption and mortality were limited by small sample sizes, leading to decreased power. Furthermore, negative publication bias and residual confounding by other lifestyle factors remain the possibilities. A thoroughly systematic and

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Abbreviations: **CHD**, coronary heart disease; **HR**, hazard ratio; **IHD**, ischemic heart disease; **RR**, relative risk

quantitative assessment of published findings is not available. Therefore, the present meta-analysis and systematic review aimed to investigate the association of fiber consumption and all-cause and cause-specific mortality in large prospective cohorts.

2 Methods

2.1 Data sources and study selection

All relevant observational studies were identified by searching MEDLINE and web of science database (from its inception to August 2014). Search terms included "fiber," "grain," "mortality," "death," "cancer," "cardiovascular disease," "fatal coronary heart disease" (CHD), and "fatal myocardial infarction." The search was restricted to prospective cohort studies in both healthy and diseased population, which were published in English language journals. We also used information of bibliographies from retrieved articles and recent reviews.

2.2 Data extraction

Two of our investigators independently reviewed each published paper and extracted relevant information. Discrepancies were resolved by group discussion. In general, papers were included if (i) relative risks (RRs) or hazard ratio (HRs) and their corresponding 95% CIs of mortality relating to each category of fiber consumption were reported; and (ii) frequency of fiber intake was provided, which permitted standardizing categorization of fiber consumption. We did not contact authors to request additional information. The data that we collected included the first author's name, year of publication, country of origin, duration of follow-up, range or mean of participants' age, sample size, proportion of men, number of events, category amount of fiber consumption, methods for measurement of dietary fiber, adjusted covariates, as well as HRs or RRs and 95% CIs of mortality for each category of fiber intake.

2.3 Data synthesis

We categorized fiber consumption into three intervals: "lowest," "moderate," and "highest" in each cohort. According to the range or average amount of fiber intake in each category, we then assigned each HR or RR reported from each individual study into its corresponding intervals. If the average fiber intake from more than one category in a single study fell into the same category of fiber intake in our meta-analysis, we then pooled this HR with inverse variance weight and used the combined estimate for that group. As compared with the lowest category, the pooled HRs and 95% CIs of mortality for all other categories of fiber intake were estimated using fixed-effects or random-effects models. The pooled HR was obtained by averaging the HRs weighted by the inverses of their variances [7]. We used DerSimonian and Laird's random-effects model to incorporate the between-study variability [8]. If a significant heterogeneity was present, we reported the pooled estimate from the random-effect models. Formal tests of between-study heterogeneity were based on a χ^2 statistic. A weighted linear regression was used to model the HR for mortality as a linear function of fiber intake. We conducted subgroup analyses to examine potential sources of heterogeneity according to (i) gender, (ii) diseases, and (iii) type of fiber. In addition, we carried out a dose–response analysis for the trend estimation using generalized least squares regression (two-stage GLST in Stata).

Publication bias was assessed using Begg's modified funnel plot and Egger's regression asymmetry test. In Begg's modified funnel plot, the HR was plotted on a logarithmic scale against its corresponding std error (SE) for each study. In the absence of publication bias, one would expect studies of all sizes to be scattered equally above and below the line showing the pooled estimate of HR [9]. Extracted data were analyzed using the Stata, version 11 software (StataCorp, College Station, TX, USA).

3 Results

The 25 eligible studies and selected characteristics are listed in Table 1. A database was developed based on these 25 eligible studies and 42 cohorts [3–5, 10–31], including 1 752 848 individuals with an average 12.4 years of follow-up (Supporting Information Fig. 1). Thirteen cohorts were from the United States, ten from Europe, and one from Japanese. Of the 25 studies, four included only male participants, nine included only female participants. Data on fiber consumption were collected using self-administered food frequency questionnaire (FFQ) or 24-h diet recall or dietary history methods. The range of follow-up period was from 1 to 40 years.

Table 2 presents pooled HRs and 95% CIs of mortality in relation to fiber consumption. Individuals with moderate fiber consumption had significantly lower all-cause mortality (HR, 0.84; 95% CIs, 0.80–0.87), total CVD mortality (HR, 0.86; 95% CIs, 0.82–0.91), cancer mortality (HR, 0.90; 95% CIs, 0.88–0.93), and circulatory diseases mortality, when compared with those who consumed lowest fiber. For individuals with highest fiber consumption, mortality rate was lower by 23% (HR, 0.77; 95% CI, 0.72–0.81) for CVD, by 23% (HR, 0.77; 95% CI, 0.73–0.81) for all-cause mortality, by 17% (HR, 0.83; 95% CI, 0.74- 0.91) for cancer, by 25% for circulatory diseases.

Table 3 presents pooled HRs and 95% CIs of mortality in relation to an increment of 10 g/day fiber consumption. In dose–response analysis, for each 10 g/day increase in fiber intake, the pooled HR was estimated to be 0.83 (95% CI, 0.80–0.87) for CVD, 0.89 (95% CI, 0.86–0.93) for all-cause mortality, 0.91 (95% CI, 0.88–0.94) for cancer, 0.80 (95% CI, 0.72–0.88) for CHD mortality, and 0.66 (95% CI, 0.40–0.92)

Table 1. Characteristics of 42 included cohorts (from 25 studies) of dietary fiber and mortality

Author	Year	Country	Follow-up (years)	Participants	Events	Men (%)	Age	Dietary categories (g/day)
Khaw et al. [10]	1987	United States	12	859	65 IHD	41	50–79	6
WHO [31]	1988	NA	7	9521 (M); 10 555 (W)	38 (M); 4 (W)	\	50 (39–70)	20.3 (M); 19.2 (W)
Fraser et al. [11]	1992	United States	6	9212 (M); 13 430 (W)	49 (M); 41 (W)	40.6	54 (M); 56 (W)	29.7 (M); 19.9 (W)
Knekt et al. [12]	1994	Finland	14	2712 (M); 2481 (W)	147 (M); 48 (W)	53.5	47 (M); 49 (W)	21.9 (M); 17.7 (W)
Barefoot et al. [13]	1995	Denmark	27	1658 (M); 1666 (W)	38 (M); 14 (W)	56	50	17.1 (M); 14.3 (W)
Pietinen et al. [14]	1996	Finland	6.1	21 141	534	100	56 (49–70)	18.9
Rimm et al. [15]	1996	United States	6	41 574	421	100	52 (39–77)	20.6
Kushi et al. [16]	1996	United States	7	30 180	294	0	61 (52–71)	17.8
Folsom et al. [17]	1997	United States	4–7	5240 (M); 6481 (W)	51 (M); 17 (W)	\	54 (M); 53 (W)	17.1 (M); 15.2 (W)
Jansen et al. [18]	1999	Seven country study	25	12 763	5974	100	40–59	3.32, 10% of mean intake
Wolk et al. [19]	1999	United States	10	61 706	208	0	52 (39–66)	16.9
Todd et al. [4]	1999	Scotland, United Kingdom	9	11 629	591 deaths	\	49.7 (M); 49.4 (W)	8.8 (M); 10.6 (W)
Liu et al. [20]	2002	United States	6	37 272	10	0	52 (38–89)	16.9
Bazzano et al. [3]	2003	United States	19	9776	2632 all-cause mortality, 233 stroke, 668 CHD, 1198 CVD	41	25–74	11.2
Mai et al. [21]	2003	United States	8.5	45 491	487	0	62	11.3
McEligot et al. [22]	2006	United States	1	516	96	0	64.78 (9.25)	Tertiles
Streppel et al. [5]	2008	Netherlands	40	1373	1130	100	40–60	10
Crowe et al. [23]	2012	Eight European countries	11.5	306 331	2381	38	53.8 (8.0)	10
Eshak et al. [24]	2010	Japan	15	58 730	2080 CVD deaths (983 strokes, 422 CHD, and 675 other CVD)	0	40–79	Never, once or twice/month, once or twice/wk, 3–4 times/wk, and almost every day
He et al. [25]	2010	United States	26	7822	852 all-cause deaths and 295 CVD-deaths	0	30–55	1.9 (<2.57), 2.99 (2.57–3.40), 3.80 (3.41–4.22), 4.70 (4.23–5.30), 6.29 (5.31–22.50)
Park et al. [2]	2011	United States	9	567 169	20 126 (M); 11 330 (W)	56	50–71	12.6, 16.4, 19.4, 22.9, 29.4
Burger et al. [27]	2012	European	9.2	6192	791 deaths; 306 due to CVD	54.2	57.4 (6.7)	HR with 95% CI per SD of fiber (6.4)
Chuang et al. [28]	2012	Ten European countries	12.7	452 717	23 582	29	50.8 (9.8)	16.4, 16.4–20.1, 20.1- 23.6, 23.6 -28.5
Krishnamurthy et al. [29]	2012	United States	8.4	14 543	2141	0	45.0 (15.8)	10
Schoenaker et al. [30]	2012	European	7.3	2108	46 all-cause deaths	0	15–60	5

Table 1. Continued

Author	Year	Diet assessment	Outcomes	Adjusted variables
Khaw et al. [10]	1987	24-h dietary	IHD mortality	Age, systolic blood pressure, plasma cholesterol, plasma glucose, obesity, and cigarette smoking
WHO [31]	1988	FFQ	MI	\
Fraser et al. [11]	1992	FFQ	CHD, MI	Age, sex, smoking, exercise, relative weight, and high blood pressure
Knekt et al. [12]	1994	Dietary history	Fatal CHD	Age, sex, blood pressure, total cholesterol level, BMI, drinking, energy intake
Barefoot et al. [13]	1995	Dietary history	Acute MI and total mortality.	Systolic blood pressure, smoking, triglycerides
Pietinen et al. [14]	1996	Dietary history	Nonfatal MI and CHD mortality	\
Rimm et al. [15]	1996	FFQ	Fatal and nonfatal MI	Saturated fat, vitamin E, age, body mass index, physical activity, smoking, hypertension, hypercholesterolemia, family history of MI, and profession
Kushi et al. [16]	1996	FFQ	CHD mortality	Age, total energy intake, BMI, waist-to-hip ratio, smoking, hypertension, diabetes mellitus, oral-contraceptive use, estrogen-replacement therapy, physical activity, alcohol, marital status, education
Folsom et al. [17]	1997	FFQ	CHD mortality	Age, race
Jansen et al. [18]	1999	Record method	Cancer mortality	Energy intake
Wolk et al. [19]	1999	FFQ	CHD mortality	Age, smoking, MBI, menopausal hormone use, multivitamin and vitamin E supplement use
Todd et al. [4]	1999	FFQ	All-cause mortality	Age, serum total cholesterol, systolic blood pressure, carbon monoxide, energy, diabetes, BMI, triglycerides, HDL, activity in leisure, and alcohol
Liu et al. [20]	2002	FFQ	CVD and MI	Age, smoking, exercise, alcohol, use of postmenopausal hormone, BMI, multivitamin supplements, hypertension, high cholesterol, diabetes, MI, dietary folate, fat, protein, and total energy intake
Bazzano et al. [3]	2003	24-h diet recall	All-cause mortality, stroke, CHD, CVD	Age, sex, race, education, blood pressure, total cholesterol level, diabetes status, physical activity, BMI, drinking, smoking, total fat intake
Mai et al. [21]	2003	FFQ	Breast Cancer	Nonsteroidal anti-inflammatory drugs, smoking, alcohol, calcium, vitamin D, red meat, height, body mass index, education
McEligot et al. [22]	2006	FFQ	Breast Cancer	\
Streppel et al. [5]	2008	Dietary history	CHD, and all-cause mortality	Total energy, SFA, trans-SFA, and cis-PUFA intakes; alcohol intake; wine use; fish intake; prescribed diet; smoking; BMI; and socioeconomic status
Crowe et al. [23]	2012	24-h diet recall	IHD mortality	Age, alcohol intake, BMI, physical activity, marital status, highest education level, current employment, hypertension, hyperlipidaemia, angina pectoris, diabetes mellitus, PUFA-to-SFA ratio and total energy intake
Eshak et al. [24]	2010	FFQ	Strokes, CHD, and CVD	Age, BMI, hypertension, diabetes, alcohol, smoking, education, exercise, walking, mental stress, sleep fish, SFA, (*n*-3) fatty acids, sodium, folate, and vitamin E
He et al. [25]	2010	FFQ	CVD, and all-cause mortality	Age; whole grain, bran, and germ; total energy; intakes of PUFA, SFA and trans-fat, magnesium, and folate
Park et al. [2]	2011	FFQ	Cancer, CVD, and all-cause mortality	Age; race/ethnicity; education; marital status; health status; BMI; physical activity; smoking; alcohol consumption; menopausal hormone therapy; red meat, total fruits and vegetables; and total energy
Burger et al. [27]	2012	FFQ	All-cause and CVD	\
Chuang et al. [28]	2012	FFQ	Cause-specific mortality	Education, smoking; former quit
Krishnamurthy et al. [29]	2012	24-h diet recall	All-cause mortality	Age, gender, race, smoking, alcohol, physical inactivity, calorie and protein intake, MI, congestive heart failure, stroke, cancer, diabetes, blood pressure, triglycerides, HDL, LDL, waist circumference, and serum CRP
Schoenaker et al. [30]	2012	3-day record	CVD, and all-cause mortality	Age, sex and energy intake, diabetes duration, HbA1c, smoking status, physical activity and alcohol intake, SFA intake

IHD, ischemic heart diseases; CVD, cardiovascular diseases; MI, myocardial infarction; CHD, coronary heart diseases; SFA, saturated fatty acid; FFQ, food frequency questionnaire; M, men; W, women; NA, not applicable.

Table 2. Pooled hazard risk (HR) and 95% CI of studies assessing the association between fiber consumption and mortality

Mortality	*n*	HR, CI 95%		
		Low	Moderate	High
All cohorts	42	1	0.82 (0.79, 0.84)	0.72 (0.68, 0.76)
All-cause mortality				
All	9	1	0.84 (0.80, 0.87)	0.77 (0.73, 0.81)
Men	4	1	0.81 (0.73, 0.90)	0.73 (0.66, 0.79)
Women	2	1	0.83 (0.81, 0.85)	0.79 (0.75, 0.83)
Cancer mortality				
All	5	1	0.90 (0.88, 0.93)	0.83 (0.74, 0.91)
Men	2	1	0.91 (0.88, 0.95)	0.82 (0.76, 0.89)
Women	2	1	0.89 (0.86, 0.93)	0.88 (0.74, 1.02)
Total CVD mortality				
All	16	1	0.86 (0.82, 0.91)	0.77 (0.72, 0.81)
TDF	10	1	0.87 (0.82, 0.93)	0.77 (0.72, 0.82)
SDF	3	1	0.84 (0.76, 0.93)	0.75 (0.59, 0.90)
IDF	3	1	0.86 (0.72, 1.00)	0.76 (0.64, 0.88)
Circulatory diseases mortality	2	1	0.81 (0.76, 0.87)	0.75 (0.59, 0.90)

CVD, cardiovascular diseases; IDF, insoluble dietary fiber; SDF, soluble dietary fiber; TDF, total dietary fiber.

for ischemic heart disease (IHD) mortality. In stratified analyses, gender and type of fiber did not appear to materially modify the inverse association between fiber intake and mortality. In addition, the estimated overall dose–response relation is shown in Fig. 1. For each 10 g/day increase in fiber intake, the pooled HR of CVD mortality was estimated to be 0.83 (95% CI, 0.80–0.87; p for trend = 0.001).

Begg's funnel plot showed slightly more data points below the horizontal line (representing the pooled estimate of logHR), indicating a possible minor publication bias in favor of the null association (Supporting Information Fig. 2). Both Egger's regression asymmetry test and Begg's adjusted rank correlation test did not observe evidence of substantial publication bias ($p > 0.05$ for Begg's test; $p > 0.05$ for Egger's test).

4 Discussion

The present study showed that high dietary fiber intake is associated with low all-cause mortality and CVD, cancer, IHD mortality. The mortality rate was lower by 17% for CVD, 11% for all-cause mortality, 9% for cancer, 20% for CHD mortality, and 34% for IHD mortality for each 10 g/day increment of total fiber [4]. We believe that the results presented represent most of the information available on dietary fiber and mortality.

Compelling evidences showed that dietary fiber intake provides many health benefits [32, 33], and inversely associates with risk of CHD [34], total death and death from CVD, infectious diseases, and respiratory diseases [2], and death from cancer [2]. Previous European Prospective Investigation into Cancer and Nutrition (EPIC) analyses showed that plant-based diets rich in fiber were related to increased survival in the elderly [35], and reduced colorectal cancer risk [36] and gastric cancer risk [37]. While, in a meta-analysis by Pereira et al., no such associations were observed for vegetable fiber, although cereal and fruit fiber had strong inverse associations with CHD risk [34]. The present meta-analysis found that beneficial effects on mortality gradually increased as a function of fiber consumption. Interestingly, most included studies were conducted in the United States. Unfortunately, most persons in the United States consume less than half of the recommended levels of dietary fiber daily [38]. Findings

Table 3. Pooled hazard risk (HR) and 95% CI of studies assessing the association between an increment of 10 g/day fiber consumption and mortality

Mortality Groups	*n*	HR, CI 95%		I^2	*p*
		Random model	Fixed model		
All mortality	38	0.87 (0.84, 0.90)		56.30	<0.001
All-cause mortality	11	0.89 (0.86, 0.93)		69.60	<0.001
Cancer mortality	3		0.91 (0.88, 0.94)	0.00	0.69
Total CVD mortality	24		0.83 (0.80, 0.87)	24.90	0.13
CHD mortality	14		0.80 (0.72, 0.88)	0.00	0.89
IHD mortality	4	0.66 (0.40, 0.92)	75.30	0.01	

CHD, coronary heart diseases; CVD, cardiovascular disease; IHD, ischemic heart disease.

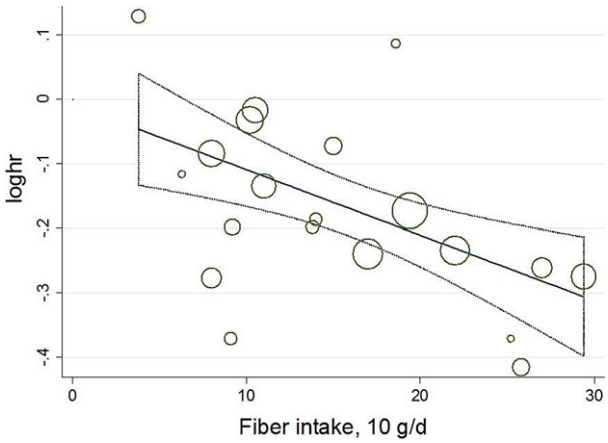

Figure 1. Dose–response relation of HR of CVD mortality in relation to fiber consumption. Scatterplots represent logHRs for each category of fiber intake reported by studies included; smooth, solid line shows weighted logHR on all scatterplots with two dashed lines representing its lower and uppers CIs.

from the present meta-analysis on all-cause mortality are consistent with previous reports [4, 5]. The present pooled data showed that the pooled mortality rate was lower by 11% for all-cause mortality for each 10 g/day increase in fiber intake, compared with a 10% lower risk in the European Prospective Investigation into Cancer and Nutrition cohort [28], and 9% lower risk observed in the Zutphen study [5], and a 12 and 15% lower risk among men and women, respectively, in the NIH-AARP cohort [2].

The potential mechanisms for our findings are biologically plausible. High fiber intake is known to improve serum lipid concentrations [39] and immune function [40], and slow glucose absorption and improve insulin sensitivity [41]. Dietary fiber may lower glycemic load of rapidly digestible and absorbable dietary carbohydrates [42], and associate with lower serum interleukin-6 and tumor necrosis factor-alpha receptor-2 in postmenopausal women [43]. High-fiber diet has been associated with higher plasma levels of anti-inflammatory adiponectin [44]. In addition, these effects of fiber have been shown to lower total and LDL-cholesterol levels [45] and improve insulin sensitivity [45]. Furthermore, high fiber consumption may lower the risk of type 2 diabetes [46, 47], which may partly explain the associations with CVD and all-cause mortality [25]. Soluble fiber-containing foods such as fruit and vegetables may slow down or reduce glucose absorption in the intestine due to a reduction in the glycemic index [48]. However, further study on the potential mechanism is required.

There are several advantages in the present study: first, this meta-analysis has greater sample size and statistical power than previous meta-analyses. Second, no evidence of publication bias on testing was observed. Lastly, we have disaggregated by gender, the findings may not be the same for men and women; this is particularly relevant to all-cause mortality, which includes cancer, since it is known that nutrient supplements may increase the risk of breast cancer in women. However, several limitations need to be considered. First, our meta-analysis combined participants with different health status and pooled data for different ethnicities to increase statistical power; genetic heterogeneity among ethnically diverse populations can lead to unavoidable bias. Second, differences in sampling protocols and measurement errors may contribute to study variation. Third, we acknowledge the limitation of categories of fiber consumption; the definition of the categorical fiber may be different in each study. Finally, we excluded the studies that did not provide adequate information. The exclusion might contribute to the tested publication bias. The exclusion of non-English language publications cannot be excluded.

In summary, our findings suggest that fiber consumption inversely associates with all-cause mortality and CVD, cancer, IHD mortality. However, further studies are warranted to further explore the possible mechanisms through which fiber may reduce the risk of all-cause mortality.

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The authors have declared no conflict of interest.

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