

# Dietary Fiber Intake and Mortality from All Causes, Cardiovascular Disease, Cancer, Infectious Diseases and Others: A Meta-Analysis of 42 Prospective Cohort Studies with 1,752,848 Participants

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Results from observational studies on dietary fiber intake on total mortality and cause-specific mortality are inconsistent. The objective of the present meta-analysis was to investigate dietary fiber intake and mortality, and cause-specific mortality. Medline, EMBASE and web of science database was searched for cohort studies published from inception to February 2013. Studies were included if they provided a hazard ratio (HR) and corresponding 95% CI for mortality in relation to fiber consumption. A database was developed on the basis of 25 eligible studies and 42 cohorts, including 1,752,848 individuals with an average 12.4 years of follow-up. 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 cardiovascular diseases (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 68% for digestive diseases, by 58 % for infectious diseases, 43 % for inflammatory diseases. For each 10 g/d increase in fiber intake, the pooled HR was estimated to be 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 coronary heart disease (CHD) mortality, and 0.66 (95% CI, 0.40-0.92) for ischemic heart disease (IHD) mortality. Dietary fiber and CVD mortality showed a strong dose-response relation. For each 10 g/d 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). In conclusion, our meta-analysis results clearly show that high dietary fiber intake is associated with low all-cause mortality and mortality due to CVD, CHD, cancer, digestive disease, infectious diseases, and other inflammatory diseases.

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**Key Words:** fiber, mortality, cancer, cardiovascular disease, meta-analysis

## INTRODUCTION

Dietary fiber, which is a vast array of complex saccharide-based molecules, has been confirmed as a key dietary factor with beneficial effect on health.<sup>1</sup> The fiber has the potential capability to prevent the absorption of bind nutrients and nutrient precursors. The edible parts of plants or analogous carbohydrates is defined as dietary fiber which are unable to be digested or absorbed in the human small intestine, with complete or partial fermentation in the large intestine.<sup>2</sup>

High dietary fiber intake could promote overall health and be associated with lower mortality through several mechanisms

through prevention and mitigation of type 2 diabetes mellitus, cardiovascular disease and colon cancer.<sup>1</sup> A few observational studies have examined the effect of dietary fiber on mortality and reported inconsistent results. The Scottish Heart Health study found that dietary fiber intake was inversely related to total mortality in men but not in women.<sup>3</sup> The Zutphen Study in the Netherlands found a 9% lowered risk of total death per 10 g/d of dietary fiber intake.<sup>4</sup> On the other hand, the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study found no association between dietary fiber intake and total mortality.<sup>5</sup>

However, previous studies examining the association between dietary fiber and mortality were limited by small sample sizes, leading to decreased power. Furthermore, negative publication bias and residual confounding by other

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lifestyle factors remain possibilities. A thoroughly systematic and quantitative assessment of published findings is not available. Therefore, in the present meta-analysis and

systematic review, we investigated dietary fiber intake in relation to total and cause-specific mortality in large prospective cohorts.

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

First Author [ref]	Year, Country, Follow-up, years	Participants /Events	Men, %; Age, years	Dietary dosages, g/d	Diet assessment	Outcomes
Khaw [9]	1987, USA,12	859/65	41; 50-79	6	24h dietary	IHD deaths
WHO [29]	1988, NR, 7	20076/42	NR; 50	20.3(m);19.2(w)	FFQ	MI
Fraser [10]	1992, USA,6	22642/90	40.6; 55	29.7 (m);19.9(w)	FFQ	CHD, MI
Knekt [11]	1994, Finland ,14	5193/195	53.5; 48	21.9(m);17.7(w)	Dietary history	Fatal CHD
Barefoot [12]	1995, Denmark, 27	3324/52	56; 50	17.1(m);14.3(w)	Dietary history	Acute MI and total deaths.
Pietine [13]	1996, Finland, 6.1	21141/534	100; 56	18.9	Dietary history	Nonfatal MI and CHD deaths
Rimm [14]	1996, USA,6	41574/421	100; 52	20.6	FFQ	Fatal and nonfatal MI
Kushi [15]	1996, USA,7	30180/294	0; 61	17.8	FFQ	CHD deaths
Folsom [16]	1997, USA,4-7	11721/68	NR; 53	17.1(m); 15.2(w)	FFQ	CHD deaths
Jansen [17]	1999, 7 countries study,25	12763/5974	100; 40-59	3.32	Record method	Cancer deaths
Wolk [18]	1999, USA,10	61706/208	0; 52	16.9	FFQ	CHD deaths
Todd [3]	1999, UK,9	11629/591	NR; 49	8.8(m);10.6(w)	FFQ	All-cause deaths
Liu [19]	2002, USA,6	37272/10	0; 52	16.9	FFQ	CVD and MI
Bazzano [5]	2003, USA,19	9776/ 2632 all-cause deaths, 233 stroke, 668 CHD, 1198 CVD	41; 25-74	11.2	24h diet recall	All-cause deaths, stroke, CHD, CVD
Mai [20]	2003, USA,8.5	45491/487	0; 62	11.3	FFQ	Breast Cancer
McEligot [21]	2006, USA,1	516/96	0; 65	Tertiles: lowest vs. upper 2	FFQ	Breast Cancer
Streppel [4]	2008, Netherlands, 40	1373/1130	100; 40-60	10	Dietary history	CHD, and all-cause deaths
Crowe [22]	2012, European, 11.5	306331/2381	38; 54	10	24h diet recall	IHD deaths
Eshak [23]	2010, Japan,15	58730/2080 CVD-deaths	0; 40-79	Never, 1-2/m, 1-2/w, 3-4/w, and every day.	FFQ	Strokes, CHD, and CVD
He [24]	2010, USA,26	7822/852 deaths and 295 CVD-deaths	0; 30-55	Quintiles: lowest (< 2.57) vs. upper 4	FFQ	CVD, and all-cause deaths
Park [2]	2011, USA,9	567169/31456	56; 50-71	Quintiles: lowest (12.6[m], 10.8[w]) vs. upper 4	FFQ	Cancer, CVD, and all-cause deaths
Burger [25]	2012, European, 9.2	6192/791 deaths; 306 CVD-deaths	54.2; 57	HR with 95% CI per SD of fiber (6.4)	FFQ	All-cause and CVD
Chuang [26]	2012, European, 12.7	452717/23582	29; 51	Quintiles: lowest (<16.4) vs. upper 4	FFQ	Cause-specific deaths
Krishnamurthy [27]	2012, USA, 8.4	14543/2141	0; 45	10	24h diet recall	All-cause deaths
Schoenaker [28]	2012, European,7.3	2108/46 deaths	0; 15-60	5	3-day record	CVD, and all-cause deaths

IHD, ischemic heart diseases, CVD, cardiovascular diseases, MI, myocardial infarction, CHD, coronary heart diseases, BMI, body mass index, HDL, high-density lipoprotein, LDL, low-density lipoprotein, PUFA, polyunsaturated fatty acid, SFA, saturated fatty acid, FFQ, food frequency questionnaire. NR, not reported.

## METHODS

### Data Sources and Study Selection

All relevant observational studies were identified by searching MEDLINE and EMBASE (from its inception to February 2013). Search terms included fiber, grain, mortality, death, cancer, cardio-vascular disease, fatal coronary heart disease, and fatal myocardial infarction. The search was restricted to studies using prospective cohort study design and published in English-language journals. We also used information of bibliographies from retrieved articles and recent reviews.

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 relative risks (RRs) or hazard ratio (HRs) and their corresponding 95% CIs of mortality relating to each category of fiber consumption were reported; and

frequency of fiber intake was provided, which permitted standardizing categorization of fiber consumption. When multiple published reports from the same study cohort were available, we included only the one with the most detailed information for HR estimation.

### Data Extraction

Data extraction was undertaken independently by two investigators with discrepancies resolved by consensus. When data were not available in a published report, 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% confidential intervals (CIs) of mortality for each category of fiber intake.

**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 for all mortality	42	1.00 (referent)	0.82 (0.79, 0.84)	0.72 (0.68, 0.76)
All-cause mortality				
All	9	1.00 (referent)	0.84 (0.80, 0.87)	0.77 (0.73, 0.81)
Men	4	1.00 (referent)	0.81 (0.73, 0.90)	0.73 (0.66, 0.79)
Women	2	1.00 (referent)	0.83 (0.81, 0.85)	0.79 (0.75, 0.83)
Both	3	1.00 (referent)	0.89 (0.78, 1.01)	0.84 (0.70, 0.99)
Cancer mortality				
All	5	1.00 (referent)	0.90 (0.88, 0.93)	0.83 (0.74, 0.91)
Men	2	1.00 (referent)	0.91 (0.88, 0.95)	0.82 (0.76, 0.89)
Women	2	1.00 (referent)	0.89 (0.86, 0.93)	0.88 (0.74, 1.02)
Both	1	1.00 (referent)	0.78 (0.38, 1.18)	0.48 (0.18, 0.77)
Total CVD mortality				
All	16	1.00 (referent)	0.86 (0.82, 0.91)	0.77 (0.72, 0.81)
Both	8	1.00 (referent)	0.87 (0.79, 0.95)	0.80 (0.72, 0.87)
Men	4	1.00 (referent)	0.89 (0.82, 0.95)	0.78 (0.71, 0.84)
Women	4	1.00 (referent)	0.83 (0.74, 0.93)	0.71 (0.63, 0.80)
Fiber type for CVD mortality				
Total dietary fiber	10	1.00 (referent)	0.87 (0.82, 0.93)	0.77 (0.72, 0.82)
Soluble dietary fiber	3	1.00 (referent)	0.84 (0.76, 0.93)	0.75 (0.59, 0.90)
Insoluble dietary fiber	3	1.00 (referent)	0.86 (0.72, 1.00)	0.76 (0.64, 0.88)
Digestive disease mortality	2	1.00 (referent)	0.58 (0.38, 0.77)	0.32 (0.20, 0.44)
Infectious disease mortality	2	1.00 (referent)	0.71 (0.49, 0.93)	0.42 (0.25, 0.59)
Inflammatory disease mortality	2	1.00 (referent)	0.64 (0.54, 0.74)	0.57 (0.46, 0.68)
Respiratory disease mortality	4	1.00 (referent)	0.71 (0.59, 0.83)	0.53 (0.41, 0.66)
Circulatory disease mortality	2	1.00 (referent)	0.81 (0.76, 0.87)	0.75 (0.59, 0.90)

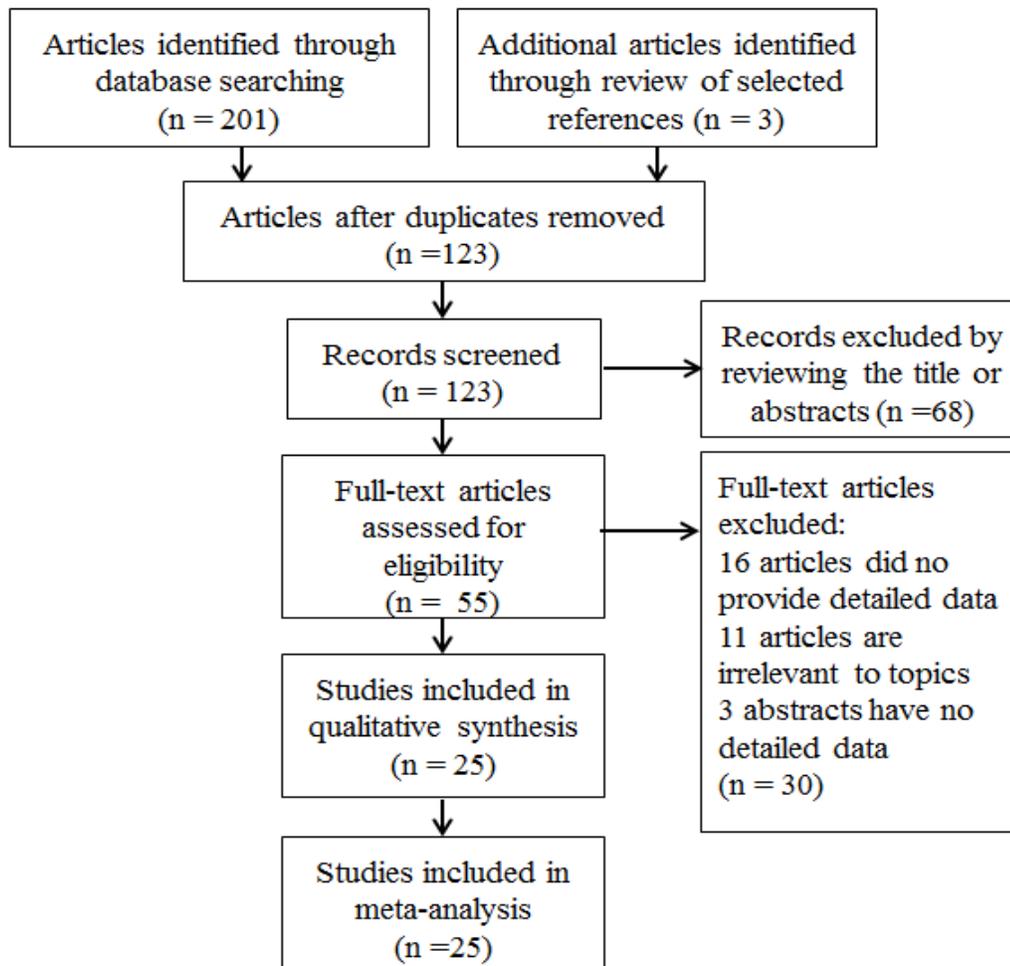
CVD: Cardiovascular disease

### Data Synthesis

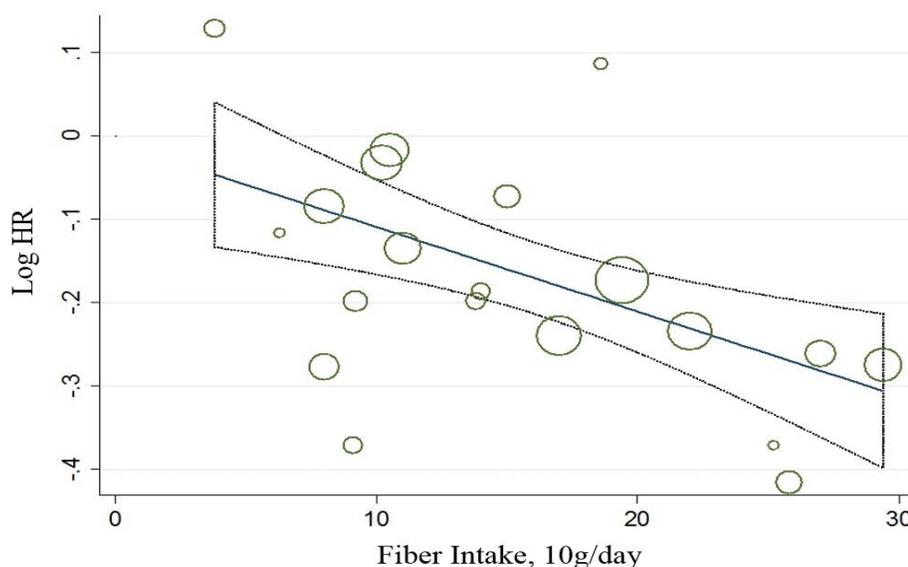
We standardized and categorized fiber consumption into 3 intervals: “lowest,” “moderate,” and “highest.” According to the range or average amount of fiber intake in each category, we then assigned each HR reported from each individual study into its corresponding fiber intake intervals. If more than one HRs were reported in a single study for the same standardized category, then the pooled HR by using random-effects model were used to represent this individual study for the overall meta-analysis. The pooled HRs and 95% CIs of mortality for fiber intake were estimated by using fixed-effects or random-effects models weighted by the inverses of their variances<sup>6,7</sup> depending on the heterogeneity between studies. 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  $\chi^2$  statistic. A weighted linear regression was used to model the HR for mortality as a linear function of fiber intake. The

median intake of fiber for each category was used. The common regression slope and 95% CI were calculated by combining the individual HR of each category from individual studies using the inverse of the variance as the study weights. We conducted subgroup analyses to examine potential sources of heterogeneity according to: (1) gender; (2) diseases; and (3) type of fiber.

Publication bias was assessed by using a Begg’s modified funnel plot, in which the HR was plotted on a logarithmic scale against its corresponding 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.<sup>8</sup> Extracted data was analyzed using the Stata, version 11 software (Stata Corp, College Station, TX, USA). A two-tailed  $P < 0.05$  was considered statistically significant.



**Figure 1.** Flowchart of the study selection process.



**Figure 2.** Dose-response relation of HR of CVD mortality in relation to fiber consumption. Scatterplots represent HRs for each category of fiber intake reported by studies included; smooth, solid line shows weighted HR on all scatterplots, with two dashed lines region representing its 95% CIs around the regression line. Circles indicate HR in each study. The circle size is proportional to the precision of the HR (inverse of variance).

## RESULTS

**Table 1** lists the 25 eligible studies and selected characteristics. A database was developed on the basis of 25 eligible studies and 42 cohorts,<sup>2,5,9-29</sup> including 1,752,848 individuals with an average 12.4 years of follow-up. Thirteen cohorts were from the United States, 10 from Europe, and 1 from Japanese. The number of participants ranged from 516 in the study by McEligot et al to 567169 in the study by Park et al. Of the 25 studies, 4 included only male participants, 9 included only female participants. The range of follow-up period was from 1 to 40 years. Data on fiber consumption were collected by using self-administered food frequency questionnaire (FFQ) or 24-h diet recall or dietary history methods. All studies reported multivariate adjusted HRs and 95% CIs.

**Table 2** presents pooled HRs and 95% CIs of mortality in relation to fiber consumption. Compared with those who consumed lowest fiber, individuals who ate moderate fiber had significantly lower All-cause mortality (HR, 0.84; 95% CIs, 0.80-0.87), cancer mortality (HR, 0.90; 95% CIs, 0.88-0.93), total CVD mortality (HR, 0.86; 95% CIs, 0.82-0.91), digestive diseases, infectious diseases, inflammatory diseases, respiratory diseases, circulatory diseases mortality. Beneficial effects on mortality gradually increased as a function of fiber consumption. For individuals who ate highest fiber, 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 68% for digestive diseases, by 58 %

for infectious diseases, 43% for inflammatory diseases, 47% for respiratory diseases, 25% for circulatory diseases.

**Table 3** presents pooled HRs and 95% CIs of mortality in relation to an increment of 10 g/d fiber consumption. For each 10 g/d 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) for 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, both Begg's adjusted rank correlation test and Egger's regression asymmetry test indicated no evidence of substantial publication bias. The estimated overall dose-response relation is shown in **Figure 2**. For each 10 g/d 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).

A Begg's test and funnel plot were applied for accessing the potential publication bias. The Begg's funnel plot in **Figure 3** showed slightly more data points below the horizontal line (representing the pooled estimate of log HR), indicating a possible minor publication bias in favor of the null association. In addition, both Begg's adjusted rank correlation test and Egger's regression asymmetry test indicated no evidence of substantial publication bias (P=0.19 for Begg's test; P = 0.18 for Egger's test).

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

Mortality	n	HR, CI 95%		
		Low	Moderate	High
All cohorts for all mortality	42	1.00 (referent)	0.82 (0.79, 0.84)	0.72 (0.68, 0.76)
All-cause mortality				
All	9	1.00 (referent)	0.84 (0.80, 0.87)	0.77 (0.73, 0.81)
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Cancer mortality				
All	5	1.00 (referent)	0.90 (0.88, 0.93)	0.83 (0.74, 0.91)
Men	2	1.00 (referent)	0.91 (0.88, 0.95)	0.82 (0.76, 0.89)
Women	2	1.00 (referent)	0.89 (0.86, 0.93)	0.88 (0.74, 1.02)
Both	1	1.00 (referent)	0.78 (0.38, 1.18)	0.48 (0.18, 0.77)
Total CVD mortality				
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Men	4	1.00 (referent)	0.89 (0.82, 0.95)	0.78 (0.71, 0.84)
Women	4	1.00 (referent)	0.83 (0.74, 0.93)	0.71 (0.63, 0.80)
Fiber type for CVD mortality				
Total dietary fiber	10	1.00 (referent)	0.87 (0.82, 0.93)	0.77 (0.72, 0.82)
Soluble dietary fiber	3	1.00 (referent)	0.84 (0.76, 0.93)	0.75 (0.59, 0.90)
Insoluble dietary fiber	3	1.00 (referent)	0.86 (0.72, 1.00)	0.76 (0.64, 0.88)
Digestive disease mortality	2	1.00 (referent)	0.58 (0.38, 0.77)	0.32 (0.20, 0.44)
Infectious disease mortality	2	1.00 (referent)	0.71 (0.49, 0.93)	0.42 (0.25, 0.59)
Inflammatory disease mortality	2	1.00 (referent)	0.64 (0.54, 0.74)	0.57 (0.46, 0.68)
Respiratory disease mortality	4	1.00 (referent)	0.71 (0.59, 0.83)	0.53 (0.41, 0.66)
Circulatory disease mortality	2	1.00 (referent)	0.81 (0.76, 0.87)	0.75 (0.59, 0.90)

CVD: Cardiovascular disease

## DISCUSSION

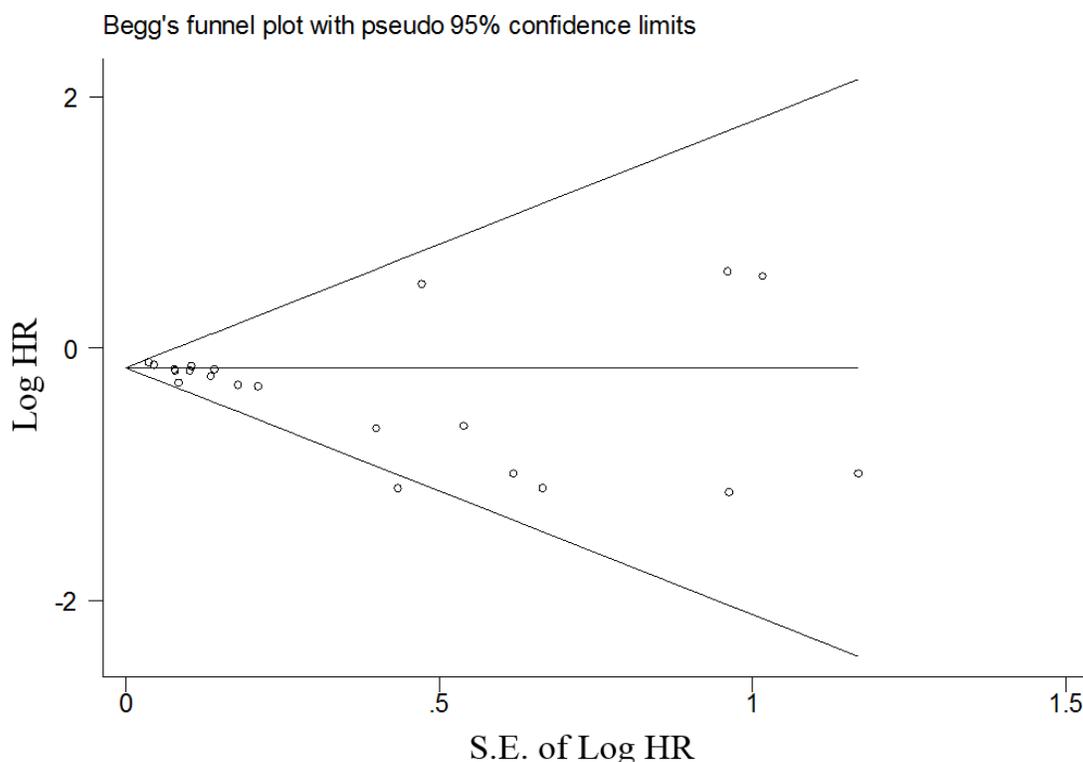
In the present study, we sought to extend these observations by combining the studies of dietary fiber to give reasonable power for detecting associations with all-cause mortality and cause-specific mortality. We believe that the results presented represent most of the information available on dietary fiber and mortality. We found 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, by 11% for all-cause mortality, by 9% for cancer, by 20% for CHD mortality, and by 34% for IHD mortality for each 10 g/d increment of total fiber.<sup>3</sup>

Dietary fiber intake provides many health benefits which indicated that supplement of fiber might play an adjunctive role in offer a health benefits.<sup>30,31</sup> Few studies suggested that

dietary fiber is inversely associated with risk of CHD in both men and women.<sup>32</sup> Each 10g/d increment in total dietary fiber will induce a 27% reduction in risk for coronary mortality which was stronger than for all events (14% reduction in risk).<sup>32</sup> A prospective study of 7,822 women with type 2 diabetes observed that intakes of whole grain, cereal fiber and bran were inversely associated with all-cause and CVD-specific mortality during 26-year follow-up.<sup>24</sup> Dietary fiber intake was significantly inversely associated with the risk of total death and death from CVD, infectious diseases, and respiratory diseases in both men and women.<sup>2</sup> Also, a lower risk of death from cancer was observed among men with higher dietary fiber intake but not observed in women.<sup>2</sup> Current evidence indicated that a high dietary fiber intake through regular consumption of whole-grain cereals,

legumes, fruit, and vegetables has potential health benefits, particularly for preventing diabetes, CVD, and some cancers.<sup>26</sup> Among specific sources of dietary fiber, fiber from grains showed the most consistent inverse association with risk of total and cause-specific deaths.<sup>2</sup> 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.<sup>32</sup> In the present meta-analysis, we found that beneficial effects on mortality gradually increased as a function of fiber consumption. Compared with those who consumed lowest fiber, for individuals who ate highest fiber, mortality rate was lower by 23% for CVD, by 23% for all-cause mortality. Interestingly, most included studies were conducted in USA. Unfortunately, most persons in the United States consume less than half of

the recommended levels of dietary fiber daily.<sup>33</sup> Previous EPIC analyses showed that plant-based diets rich in fiber were related to increased survival in the elderly,<sup>34</sup> total dietary fiber intake was associated with reduced colorectal cancer risk,<sup>35</sup> and cereal fiber was associated with decreased gastric cancer risk.<sup>36</sup> Our results from meta-analysis on all-cause mortality are consistent with previous reports.<sup>3,4</sup> We pooled HRs and 95% CIs of mortality in relation to an increment of 10 g/d fiber consumption. For each 10 g/d increase in fiber intake, the pooled mortality rate was lower by 11% for all-cause mortality, compared with a 10% lower risk in the European Prospective Investigation into Cancer and Nutrition cohort,<sup>26</sup> and 9% lower risk observed in the Zutphen study<sup>4</sup> and a 12% and 15% lower risk among men and women, respectively, in the NIH-AARP cohort.<sup>2</sup>



**Figure 3.** Begg's funnel plot with pseudo 95% confidence limits for testing publication bias in the association of fiber intake and CVD mortality. S.E., standard error and Log HR, natural logarithm of hazard ratio.

The beneficial effects from dietary fiber might not be limited to CVD and cancer. A higher intake of whole grains, a source of fiber and other potential beneficial nutrients, was found to be associated with a reduced risk of developing non-CVD, non-cancer inflammatory diseases in the Iowa Women's Health Study,<sup>37</sup> and a high dietary fiber intake was associated with a reduced risk of death from respiratory and infectious diseases, in addition to CVD and cancer, in the NIH-AARP cohort.<sup>2</sup> In the present meta-analysis, compared with those who consumed lowest fiber, for individuals who ate highest fiber, mortality rate was lower by 68% for digestive diseases, by 58% for infectious diseases, 43% for inflammatory diseases, 47% for respiratory diseases, and 25% for circulatory diseases.

Several mechanisms have been suggested to underlie the protective effects of fiber intake and its components on health. It has been hypothesized to lower the risk of coronary heart disease,<sup>38</sup> hypertension,<sup>39</sup> stroke,<sup>40</sup> diabetes,<sup>41</sup> obesity,<sup>42</sup> because it is known to improve serum lipid concentrations,<sup>43</sup> improve immune function,<sup>44</sup> improve laxation by increasing bulk and reducing transit time of feces through the bowel,<sup>30,31</sup> slow glucose absorption and improve insulin sensitivity.<sup>45</sup> Some dietary fiber is fermentable, and the gastrointestinal tract catabolism generates various bioactive materials that can markedly augment the gastrointestinal tract biomass and change the composition of the gastrointestinal tract flora.<sup>1</sup> Higher dietary fiber also has anti-inflammatory properties. Dietary fiber may inhibit

inflammation by lowering glycemic load of rapidly digestible and absorbable dietary carbohydrates.<sup>46</sup> It was showed that dietary fiber was associated with lower serum interleukin-6 and tumor necrosis factor-alpha receptor-2 in postmenopausal women in the Women's Health Initiative Study.<sup>47</sup> Dietary fiber intake was associated with lower serum CRP in cross-sectional and longitudinal analyses.<sup>48-50</sup> High-fiber diet has been associated with higher plasma levels of anti-inflammatory adiponectin.<sup>51</sup> In addition, soluble fiber might be able to delay the absorption of nutrients and bind bile acids in the small intestine, which may increase bile acid, estrogen, and fecal procarcinogens and carcinogens excretion.<sup>52</sup> These effects have been shown to lower total and LDL-cholesterol levels<sup>53</sup> and improve insulin sensitivity.<sup>31</sup> This in turn is associated with reductions in blood pressure. Furthermore, increased dietary fiber may lower the risk of type 2 diabetes,<sup>54,55</sup> which may partly explain the associations with CVD and all-cause mortality.<sup>24</sup> Soluble fiber-containing foods such as fruit and vegetables have been shown to slow down or reduce glucose absorption in the intestine due to a reduction in the glycemic index.<sup>56</sup> Results from the EURODIAB PCS show that total dietary fiber was significantly inversely associated with HbA1c levels, independently of other lifestyle and nutritional factors.<sup>57</sup>

As with all meta-analyses, there are limitations to ours. First, in order to increase statistical power, our meta-analysis combined participants with different health status and pooled data for different ethnicities, albeit mostly USA and European; genetic heterogeneity among ethnically diverse populations can lead to unavoidable bias. Second differences in sampling protocols and methods of dietary fiber measurement may have contributed to variation between studies. Finally, exclusion of studies which did not provide adequate information might contribute to the tested publication bias. We also cannot exclude the possibility of bias related to the exclusion of non-English language publications. However, the present study has advantages: a) this meta-analysis which has included five current studies has greater sample size and statistical power than previous meta-analyses. b) No evidence of publication bias on testing was observed. c) 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.

In conclusion, our results suggest that high dietary fiber intake is inversely associated with low all-cause mortality and CVD, cancer, IHD mortality. The mortality rate was lower by 17% for CVD, by 11% for all-cause mortality, by 9% for cancer, by 20% for CHD mortality, and by 34% for IHD mortality for each 10 g/d increment of total fiber. These results provide strong confirmation of the findings from previously published cohort studies. However, experimental studies are warranted to further explore the possible biological mechanisms through which fiber may reduce the risk of all-cause mortality.

#### CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

#### ETHICAL APPROVAL

This work meets all the ethical guidelines.

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