



Meta-analyses

Dietary fiber intake and all-cause and cause-specific mortality: An updated systematic review and meta-analysis of prospective cohort studies

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SUMMARY

Background: Accumulating evidence supports the effects of dietary fiber on the risk of non-communicable diseases (NCDs). However, there is no updated systematic review and meta-analysis that compares and pools the effect of different types of fiber on mortality.

Methods: In this systematic review and meta-analysis, all prospective cohort studies that evaluated the relationship between dietary fiber intake and all-cause or cause-specific mortality were included. The PubMed, SCOPUS, and Web of Science databases were searched up to October 2022. Data extraction and quality assessment were performed by two researchers independently. Heterogeneity between studies was assessed using Chi-square based test. Random/fixed effect meta-analysis was used to pool the hazard ratios (HR) or relative risks (RR) and 95 % confidence intervals (CI) for the association between different types of fiber and mortality.

Results: This systematic review included 64 eligible studies, with a total sample size of 3512828 subjects, that investigated the association between dietary fiber intake and mortality from all-cause, cardiovascular disease (CVD), and cancer. Random-effect meta-analysis shows that higher consumption of total dietary fiber, significantly decreased the risk of all-cause mortality, CVD-related mortality, and cancer-related mortality by 23, 26 and 22 % (HR:0.77; 95%CI (0.73,0.82), HR:0.74; 95%CI (0.71,0.77) and HR:0.78; 95%CI (0.68,0.87)), respectively. The consumption of insoluble fiber tended to be more effective than soluble fiber intake in reducing the risk of total mortality and mortality due to CVD and cancer. Additionally, dietary fiber from whole grains, cereals, and vegetables was associated with a reduced risk of all-cause mortality, while dietary fiber from nuts and seeds reduced the risk of CVD-related death by 43 % (HR:0.57; 95 % CI (0.38,0.77)).

Conclusion: This comprehensive meta-analysis provides additional evidence supporting the protective association between fiber intake and all-cause and cause-specific mortality rates.

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1. Introduction

Non-communicable diseases (NCDs), such as cardiovascular disease (CVD), cancer, and type 2 diabetes (T2D), continue to be significant global public health issues as primary causes of death, accounting for nearly 70 % of mortality worldwide [1,2]. Because a substantial proportion of NCDs are preventable, the necessity for

effective preventative methods has long been emphasized [3]. One of the most promising approaches to prevent NCDs is a high-quality diet that incorporates functional foods or components [4]. According to a study by the Global Burden of Diseases (GBD) consortium, low consumption of whole grains and fruits is one of the main dietary risk factors for mortality worldwide [1]. The importance of dietary fiber as a healthy ingredient in high-quality diets has been widely acknowledged [5,6]. The term “dietary fiber” refers to a diverse group of substances with different structures and physicochemical properties (e.g., solubility, viscosity, and fermentability) [7]. The two basic categories of dietary fiber are soluble and insoluble [8,9]. Soluble fiber dissolves in water, and it is effective in decreasing cholesterol levels and blood sugar stabilization. Thus, increasing soluble fiber intake is important in reducing the risk of CVD and T2D [10–12]. In contrast, insoluble fibers, such as cellulose and lignin, have fecal-bulking characteristics that may promote regular bowel movements and avoid constipation [13,14].

Dietary fiber consumption is associated with reduced constipation and enhanced intestinal health [15]. Moreover, various favorable effects of fiber on serum cholesterol, blood pressure, insulin sensitivity, satiety, body weight, and chronic inflammation may reduce the risk of NCDs [10,16–18] and on longer term, it may play a role in the prevention of mortality [7,19].

The primary sources of dietary fiber, such as fruits, vegetables, and whole grains, provide different combinations of dietary fiber molecules with unique characteristics [7]. Consequently, in order to increase fiber consumption, it is essential to have information on effective fiber-rich dietary sources. Recent research has demonstrated that different fiber sources may have varying effects on specific health conditions. For instance, some studies suggest that fiber from whole grains may be especially beneficial for lowering the risk of CVD [14,20].

Numerous epidemiological studies have examined the relationship between dietary fiber consumption and mortality from various non-communicable diseases (NCDs). While some systematic reviews have analyzed certain aspects of these studies, their inclusion of relevant research was limited in number [8,15,21–23]. A comprehensive and up-to-date systematic review comparing the effects of different forms of fiber on cause-specific mortality is currently lacking. Therefore, we performed a comprehensive systematic review and meta-analysis of prospective cohort studies to examine the associations between the consumption of different types of dietary fiber from diverse sources and the risk of all-cause mortality and mortality from CVD, stroke, and cancer.

2. Materials and methods

This systematic review and meta-analysis followed the established guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA statements) [24]. Current study registered in PROSPERO and the registration number was CRD42022372782.

2.1. Search strategy

A systematic literature search was conducted in PubMed, SCOPUS, and Web of Science databases up to October 2022 using the following search terms:

“Dietary fiber” OR “Dietary fibre” OR “Fibre” OR “Fiber” OR “Soluble fiber” OR “insoluble fiber” OR “Added Fiber” OR “Cellulose” OR “Hemicellulose” OR “Lignin” OR “Pectin” OR “Gums” OR “Mucilages” OR “resistant starch” OR “Non-starch polysaccharides” OR “resistant maltodextrin” OR beta-glucan*OR “glucomannan” OR “Galactomannan” OR Arabinan* OR “Polydextrose” OR “psyllium” OR

fructan*OR “inulin” OR oligosaccharide* OR fructooligosaccharide* OR galactooligosaccharide* OR galactan* OR xylooligosaccharide* OR “oligofructose” OR “Indigestible dextrins” OR “resistant dextrins” AND (“mortality” OR “Death” OR “Fatality”).

No restriction was set at the time of publication. Titles/abstracts were screened for relevant studies by two independent investigators (FR and MG) and any disagreement was resolved by discussion to reach a consensus. The reference lists of related review articles were hand-searched for additional relevant studies.

2.2. Selection of studies

2.2.1. Eligibility criteria

All identified articles were systematically evaluated against the inclusion and exclusion criteria, and any disagreement was resolved by mutual discussion and consensus. We retrieved all the studies that reported relative risks (RR) or hazard ratio (HR) for the association of dietary fiber intakes (Total fiber and fiber sourced from various groups, including cereals and whole grains (including cereal, bran, germ, and whole grain), legumes (including legumes and beans), soluble fiber, insoluble fiber (including insoluble fiber, cellulose, and lignin), vegetables, fruits, and non-starch polysaccharides (NCP)) and all-cause or cause-specific mortality (Cardiovascular diseases (CVD) including cerebrovascular diseases, coronary heart disease (CHD), and stroke, as well as different types of malignancy, including colorectal cancer) as the main outcomes of interest. So, the prospective cohort studies were included in this regard.

In the case of multiple published reports from the same study population, we included the one reporting the largest number of participants and outcomes for meta-analysis.

We excluded duplicate publications, reviews, meta-analyses, case reports, commentary, letters, editorials, studies not published in English, studies that did not report none of the parameters of (RR) or (HR) for the association of dietary fiber intakes and all-cause or cause-specific mortality. In general, papers were included if relative risks (RRs) or hazard ratio (HRs) and their corresponding 95 % confidence intervals (CI) of mortality relating to fiber consumption were reported.

Initially, duplicates were removed both automatically using EndNote software and manually. Then, the title and abstract of the documents were screened by two researchers independently. The full text was reviewed if any article seemed relevant or if the relevance was unclear. Any disagreement between the two researchers was resolved by discussing it with the corresponding authors.

2.3. Data extraction

Two investigators (FR and FP) independently reviewed each published study and extracted the relevant information. Discrepancies were resolved by the third party.

The collected data included the first author's last name, year of publication, type of study, country of origin, duration of follow-up, range or mean of participants' age at baseline, sample size, proportion of men, population health condition, number of deaths, cause of death, methods for measurement of dietary fiber, fiber types, category amount of fiber consumption, main outcome, covariates adjusted for in the analyses and RR or HR with the corresponding 95 % CI were extracted. Fiber intake has been considered in studies with different approaches, continuous or categorical. Regarding category-specific effect size, we extracted the highest category of RR or HR to the lowest category (the reference) from each study. In addition, we extracted RR or HR

estimates that reflected the greatest degree of adjustments for potential confounders.

2.4. Quality assessment

The quality of the included studies was appraised using the Newcastle-Ottawa Quality Assessment Scale (NOS) for cohort studies [25]. Two authors assessed the articles independently. Any disagreement between the two researchers was resolved by discussion until reaching a consensus. The NOS evaluates the methodological quality of the studies in eight items for cohort studies within three categories [1]: Selection of participants (maximum 4 scores) [2], Comparability of subjects (maximum 2 scores) [3], Assessment of outcome (maximum 3 scores) (See Appendix for included articles). The quality of each study is classified as follows:

Good quality: If a study gets 3 or 4 points in the selection part AND 1 or 2 points in the comparability part AND 2 or 3 points in the outcome part.

Fair quality: If a study gets 2 scores in the selection part AND 1 or 2 scores in the comparability part AND 2 or 3 points in the outcome part.

Poor quality: if a study scored 0 or 1 in the selection part OR 0 stars in the comparability part OR 0 or 1 star in the outcome part [25].

2.5. Statistical analysis

The I squared (I^2) and Cochran's Q tests were used to assess the heterogeneity between the studies and in cases of significant heterogeneity (P -value <0.1 or $I^2 > 50\%$), a random-effect model (DerSimonian and Laird model) was used for analyses; otherwise, a fixed-effect model was adapted [26]. Only the categorical HRs or RRs (for the highest category to the lowest category of fiber intake) of the included studies were pooled as an effect size for assessing the association of dietary fiber intake with mortality, and hazard ratios for continuous fiber intake were removed from the analysis. Meta-analysis was performed for outcomes with at least three observations within the studies. Sub-group analysis was performed for all-cause, CVD, and malignancy-related mortalities (stratified by sex, baseline general health status of study population, dietary assessment, and dietary fiber). Egger's test and funnel plots were used for publication bias assessment for each all-cause, CVD, and malignancy-related mortalities, and trim-fill analysis was performed if publication bias was present. To assess possible causes of heterogeneity among studies, Meta-Regression and sensitivity analysis were performed. STATA (Stata Corporation, College Station, Texas, USA) version 17 was used to analyze the data.

3. Results

3.1. Literature research

Electronic searches in three major databases (PubMed, Scopus, and Web of Science) retrieved 4285 papers, of which 1602 were duplicates. The remaining 2683 papers were screened on titles and abstracts. After excluding 2483 irrelevant papers, 200 full texts were reviewed, and 136 studies were further identified as ineligible. Finally, 64 articles were included in this systematic review (Fig. 1), as for the meta-analyses, 33 were pooled for the associations between dietary fiber usage and mortality, 47 were pooled for the associations between dietary fiber usage and CVD-related mortality, and 18 were pooled for the associations between dietary fiber usage and malignancy-related mortality (See Appendix for included articles).

3.2. Study characteristics

The included sixty-four studies and general characteristics are shown in Table 1. All the papers were prospective cohorts in study design and published between 1987 and 2022. Studies originated from 16 countries consisting of the USA (thirty studies), UK (four studies), China and Japan (six studies), Korea, Australia, Italy, France, Sweden (two studies from each country), Israel, Malaysia, Canada, Finland, Germany, Spain, Netherland (one study), also 7 studies conducted in multiple countries. Most of the studies were performed in the USA ($n = 30$). The sample size ranged from 148 to 452717, yielding a total sample of 3512828 subjects in our systematic review. The minimum age of participants was 15 years old. The range of follow-up was 3.75–40 years. Among all the 64 included studies, eleven studies were conducted only on female participants, and six studies only on male participants, also 13 studies were conducted on participants with baseline disease history (Such as CKD, type 2 diabetes, colorectal cancer, breast cancer, etc.). Data on fiber intake were collected mostly by a self-administered food frequency questionnaire (FFQ), Also some studies used 24-h to 7-day diet recall or in-person interviews or dietary history methods.

3.3. Quality assessments

The overall quality assessment of the included studies was good. Almost all of the studies had 8 to 9 points thus falling within the “good” subgroup. Only one study had poor quality which was due to not having good comparability. The quality assessment results are shown in Supplementary Table 1.

3.4. General findings of the included studies

HRs and 95 % CIs of all-cause mortality in relation to fiber consumption are shown in Table 2, in addition, Tables 3–4 show HR and 95 % CIs of cause-specific mortality related to fiber intake. The analysis encompassed the association between dietary fiber from various sources and mortality rates, considering both all-cause and cause-specific deaths. Studies that reported non-starch polysaccharide (NSP), NSP density, and fiber from nuts and seeds reached to enough numbers only for CVD-related mortality, however, there was an insufficient number of studies to draw conclusive findings for fiber obtained from potatoes and tubers in relation to mortality. Among the different types of cancer, only colorectal cancer had a sufficient number of studies to evaluate its association with dietary fiber.

3.5. Meta-analysis

3.5.1. Quantitative synthesis

Significant heterogeneity was detected among studies assessing all-cause and malignancy-related mortality (I^2 :76.46 %, P -value <0.001 ; I^2 :74.26 %, P -value <0.001 , respectively). There was no significant heterogeneity among studies assessing CVD-related mortality. The association between dietary fiber usage and mortalities are shown in Tables 2–4 Based on the random effect models meta-analyses, total dietary fiber usage significantly decreased the hazard of all-cause and cancer-related mortalities by 23 and 22 %, respectively (HR:0.77; 95%CI (0.73,0.82) and HR:0.78; 95%CI (0.68,0.87)). Based on the fixed effect model meta-analysis, total dietary fiber usage significantly decreased the hazard of CVD-related mortality by 26 % (HR:0.74; 95%CI (0.71,0.77)). Supplementary Fig. 1 (A, B, and C) illustrate the included studies and their reported associations with all-cause, CVD and malignancy-related mortalities, respectively.

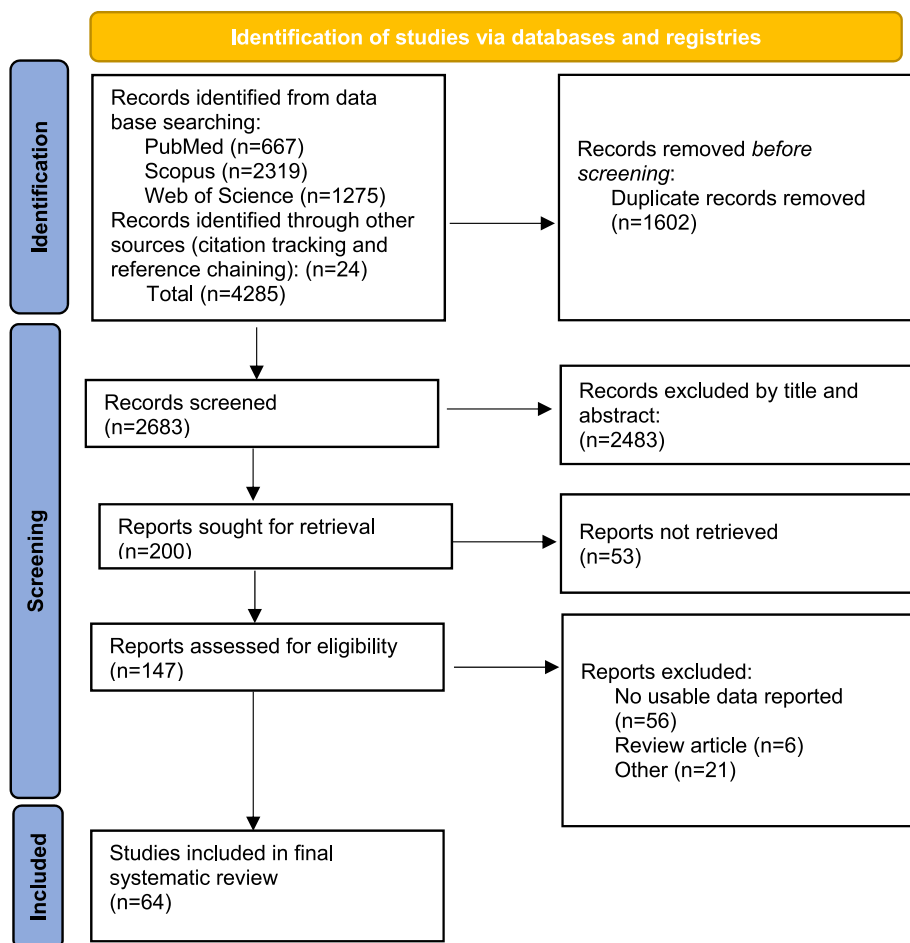


Fig. 1. Flow chart for study identification and selection. Based on PRISMA 2020.

3.5.2. Stratified meta-analysis

The pooled effect size of association between dietary fiber intake and all-cause and cause-specific mortality were summarized in Tables 2–4. Based on the random effect model, the hazard of all-cause mortality sub-grouped by sex in males, females, and both sexes were HR:0.81; 95%CI (0.75,0.87), HR:0.76; 95%CI (0.67,0.85) and HR:0.77; 95%CI (0.71,0.83) respectively (Table 2); and for malignancy-related mortality, the pooled hazard ratios were HR:0.80; 95%CI (0.68,0.92), HR:0.97; 95%CI (0.89,1.06) and HR:0.70; 95%CI (0.54,0.87) (Table 4).

The pooled hazard of all-cause mortality showed total dietary fiber is more protective in individuals with underlying disease than the general population without underlying disease (33 % prevention of all-cause mortality compared to 18 % prevention respectively). Similar results were reported for CVD and malignancy-related mortality; in fact, our analysis showed that total dietary fiber intake has a negative relationship with all-cause and CVD and malignancy-related mortality (Tables 2–4).

The hazard of all-cause mortality sub-grouped by dietary assessment method showed no significant difference between various methods (FFQ, and 24-h recall: HR:0.78; 95%CI (0.72,0.84), HR:0.79; 95%CI (0.67,0.90) respectively). For malignancy-related mortality, the pooled hazards were HR:0.79; 95%CI (0.65,0.93) and HR:0.65; 95%CI (0.29,1.01), respectively.

Different types of fiber demonstrated different amounts of protective effects on all-cause and malignancy and CVD-related mortality. It is worth noting that most of the fiber types were

significantly protective against all-cause and CVD-related mortality (Tables 2–3), on the other hand just two groups of fiber types showed significant protection for the malignancy-related mortality (Insoluble fiber: HR:0.80; 95 % CI (0.73,0.88) and Cereal (Whole grain) fiber: HR:0.85; 95 % CI (0.82,0.88)). Insoluble fiber showed the highest protection among all fiber types for all-cause mortality (HR:0.77; 95 % CI (0.72,0.82)). However, all fiber types except fruits demonstrated a significant inverse relationship with all-cause mortality. In addition, our data showed nuts and seeds consumption have the highest protective effect on CVD-related mortality, to the extent that intake of nuts and seeds can lower the risk of CVD mortality by about half (HR:0.57; 95%CI (0.38,0.77)), and insoluble fiber showed the second highest protection in this category (HR: 0.74; 95%CI (0.68,0.79)).

Also, the hazard of malignancy-related mortality was categorized based on the type of cancer. Unfortunately, the data were just enough to analyze the risk of colorectal cancer. Pooling results of 4 studies showed that total dietary fiber intake can reduce 18 % of the hazard for colorectal cancer (HR:0.82; 95%CI (0.67,0.96)) (Table 4).

The pooled association was calculated based on the fixed effect model for CVD mortality. Analysis showed that fiber intake has slightly more benefit in females than males and in both sexes' fiber intake reported a significant protective effect against CVD mortality (male: HR:0.76; 95%CI (0.71,0.80), female HR:0.72; 95%CI (0.67,0.77) and in both sexes: HR:0.74; 95%CI (0.68,0.79)). Fiber intake showed a more beneficial effect on stroke than CHD, although it was significantly protective for both of them (Stroke:

Table 1
Main characteristics of cohort studies examined the association of fiber intake with mortalities.

No	First Author/year	Study type	Country	Cohort name	F/U (Year)	Age range/mean age (at base line)	Sample size (n) Men (%)	Population	Outcomes (Causes and Number of death)	Dietary assessment method	Fiber types	Dietary fiber categories (g/day)	Quality score
1	Akbaraly/2011	Cohort	United kingdom	Whitehall II cohort study	18	39–63 Mean = 49.5	7319/(69.7 % men)	Nationally representative	All cause = 534 Cancer = 259 CVD = 141 (CHD = 74/stroke = 28) Non-cancer non-CVD = 127 Missing deaths = 7	Semi-quantitative FFQ	Total fiber	with each increase of 1 SD of component score.	Good
2	Baer/2010	Prospective Cohort	United States	the Nurses' Health Study (NHS)	18	30–55 Mean = 52.5	50112/(0 % Men)	Female nurses, No CVD - No cancer (Healthy)	All cause = 4893 CVD = 1026 Smoking related cancer = 931 Cancers not related to Smoking = 1430 All other causes = 1506	Semi-quantitative FFQ	Cereal fiber, (energy adjusted)	Per 4 g, energy adjusted	Good
3	Bazzano/2003	Prospective Cohort	United States	(NHANES 1) survey 1	19	25–74	9776/(38.3 % Men)	Civilian – No CVD (Healthy)	All cause = 2632 (Q4 = 740) CVD = 1198 (Q4 = 344) Stroke = 233 (Q4 = 67) CHD = 668 (Q4 = 192)	Standardized protocol used (24-h dietary recall)	Total fiber Soluble fiber	4 Quartile - Total fiber Q1 (<7.7) Q2 (7.7–11) Q3 (11.1–15.9) Q4 (>15.9) 4 Quartile - soluble fiber Q1 (<1.3) Q2 (1.3–2.3) Q3 (2.4–4) Q4 (>4)	Good
4	Belle/2011	Prospective Cohort	United States	Health, Eating, Activity, and Lifestyle (HEAL) study	6.7	>18 Mean = 55.3	688/(0 % Men)	Women with breast cancer stage 0–3A survivors	All cause = 106 Breast cancer = 83	FFQ	Total fiber	4 Quartiles/Q1 (<8.8) Q2 (8.8–12.8) Q3 (12.8–18.3) Q4 (>18.3)	Good
5	Buck/2011	Prospective Cohort	Germany	two German study regions (Hamburg and Rhein-Neckar-Karlsruhe (RNK))	6.4	50–74	2653/(0 % Men)	Postmenopausal women with diagnosed breast cancer	All cause = 321 Breast cancer = 235	FFQ	Total fiber	5 Quintiles/Q1 (13.3) Q2 (16.9), Q3 (19.9), Q4 (23.2), Q5 (28.9)	Good
6	Buil-Cosiales/2014	Prospective Cohort	Spain	Prevenio'n con Dieta Mediterra'nea (PREDIMED) trial,	5.9	55–75 m/60–75 f/	7216/(43 % Men)	No CVD + T2DM or 3 CVD risk factor	All cause = 425 Cancer = 169 No cancer no CVD death = 153 CVD = 103	Validated FFQ	Total fiber	5 Quintile (medians) Q1 = 17, Q2 = 21, Q3 = 24, Q4 = 28, Q5 = 35	Good
7	Burger/2012	Prospective Cohort	Denmark, Germany, Italy, Netherlands, Spain, Sweden	(EPIC)	9.2	35–70 Mean = 57.4	6192/(54.2 % Men)	DM individuals (Median time = 4.4 y)	All cause = 791 (m = 533/f = 258) CVD = 306 (m = 215) Cancer = 163 (m = 103) Other known causes = 118 (m = 74)	Validated dietary questionnaires	Total fiber	per SD increase of fiber (6.4)	Good
8	Buyken/2010	Prospective Cohort	Australia	The Blue Mountains Eye Study (BMES)	13	≥49	2735 (45.5%Men)	≥49 Postmenopausal women and men, No CVD – No Cancer, (Healthy)	All-cause = 838 (f = 380/m = 458) Inflammatory Death = 170 (f = 84/m = 86) CVD = 260 (f = 109/m = 151)	Validated FFQ	Total Fiber Vegetable Fiber, Fruit Fiber, Cereal Fiber	3 Tertile Total fiber Women/ T1:19.7, T2:24.8, T3:36.2 3Tertile Total fiber Men/ T1:18.4, T2:25.9,T3:36.4 3 Tertile Vegetable Women/ T1:6.5, T2:9.2, T3:13.5 3Tertile Vegetable Men/T1:6, T2:9.1, T3:13.7 3 Tertile fruit Women/T1:2.8,T2:6,T3:11.7 3 Tertile fruit Men/ T1:2.4,T2:5.3,T3:11.1 3 Tertile cereal women/ T1:62.9,T2:6.1,T3:10.9 3 Tertile cereal Men/T1:3,T2:6.5,T3:11.5	Good
9	Chan/2016	Prospective Cohort	United States	Survey III, (NHANES)	13.74	≥20 Mean = 44.53	15740/(46.60 % Men)	US residents – No Cancer (Healthy)	All cause = 3164 Cancer = 656 Colorectal anal cancer = 68	24-h dietary recall	Total fiber Insoluble fiber Soluble fiber	4 Quartiles Q1 (<9.3), Q2=(9.3–14.5) Q3=(14.5–22.1), Q4 (≥22.1) Insoluble fiber Q1<5.9, Q2 (5.9–9.6), Q3 (9.6–15.3) Q4 ≥15.3, Soluble fiber Q1<3.4, Q2 (3.4–5.2), Q3 (5.2–7.7), Q4 ≥7.7,	Good
10	Chuang/2012	prospective	Denmark, France, Germany, Greece, Italy, Netherland, Norway, Spain,	(EPIC)	12.7	25–70 Mean = 50.8	452717 (29 %Men) (m = 130564, f = 322153)	No-Cancer, No-CVD, No DM, (Healthy)	All cause = 23582 (m = 10366/f = 13216) Cancer: (m = 4039/f = 5575) Smoking-related cancers: (m = 2640/f = 2478) Non-smoking-related cancers:	Semi-quantitative FFQ	Total fiber	5 Quintile (medians) Q1= <16.4 Q2 = 16.4 to <20.1 Q3 = 20.1 to <23.6 Q4 = 23.6 to <28.5 Q5 = ≥ 28.5	Good

(continued on next page)

Table 1 (continued)

No	First Author/year	Study type	Country	Cohort name	F/U (Year)	Age range/mean age (at base line)	Sample size (n)	Population	Outcomes (Causes and Number of death)	Dietary assessment method	Fiber types	Dietary fiber categories (g/day)	Quality score
11	Crowe/2012	Prospective Cohort	Sweden, United Kingdom	(EPIC) study and its component (EPIC-Heart)	11.5	40–85 Mean = 53.8	306331 (37.6 %Men)	Men and Women No CVD, No stroke (Healthy)	(m = 1399/f = 3097) Circulatory diseases: (m = 2489/f = 2115) Respiratory diseases: (m = 323/f = 597) Digestive diseases: (m = 310/f = 311) Non-CVD non cancer inflammatory diseases: (m = 909/f = 1110) External causes: (m = 489/f = 418) IHD = 2381 (f = 785/m = 1596)	Country specific FFQ and a 24-h diet recall	Total fiber Cereal fiber Fruit fiber Vegetable fiber Other sources of fiber	4 Quartile Total fiber/Q1 (<17.5) Q2 (17.5–22.4) Q3 (22.5–27.4) Q4 (>27.5) 4 Quartile cereal/Q1 (<5) Q2 (5–7) Q3 (8–10) Q4 (>11) 4 Quartile fruit and vegetable/Q1 (<2) Q2 (2–3) Q3 (4–5) Q4 (>6) 4 Quartile other sources/Q1 (<3) Q2 (3–4) Q3 (5–6) Q4 (>7)	Good
12	Dominguez/2018	Prospective cohort	Italy	Mediterranean population of the SUN ("Seguimiento Universidad de Navarra") longitudinal study	10.1	Mean = 37.55	19703(39 % Men)	No (cancer, DM, CVD, HTN, Hypercholesterolemia) Healthy	All cause = 323	Validated FFQ	Vegetables fiber, Fruit fiber, Other sources fiber, Cereals fiber, Legumes fiber	Dietary fiber intake (g/1000 kcal of total energy) 0–100 (0–15) > 15 mean (sd) T1 = 7.9 (1.5) T2 = 12.2 (1.4) T3 = 18.9 (4.0) 3 Tertile	Good
13	Dray/2003	Prospective Cohort	France	case control study (1985–1987) in the Côte d'Or area (Burgundy, France)	5	30–79 Mean = 64.4	148/(65.54 %)	Individuals with colorectal cancer	Colorectal cancer = 70	Questionnaire	Total fiber		Good
14	Eshak/2010	Prospective Cohort	Japan	The Japan Collaborative Cohort Study for Evaluation of Cancer Risks	14.3	40–79	58730(39.36%Men)	No (cancer, stroke, or CHD) (Healthy)	CVD = 2080 (m = 1063/f = 1017) Stroke = 983 (m = 499/f = 484) CHD = 422 (m = 231/f = 191) Other CVD = 675 (m = 333/f = 342)	FFQ	Total fiber, insoluble fiber, soluble fiber, cereal fiber, fruit fiber, vegetable fiber,	5 Quintile Total fiber/(male/ Q1<7.8, Q2 (7.8–9.4), Q3 (9.5–10.8), Q4 (10.9–12.6), Q5>12.6) //Female/Q1 <8.5, Q2 (8.5–9.9), Q3 (10–11.1), Q4 (11.2–12.7), Q5>12.7) 3 Tertile/T1 = 27 T2 = 51 T3 = 87.8 50 Quintile/Q1 (<2.57) Q2 (2.57–3.4), Q3 (3.41–4.22), Q4 (4.23–5.30), Q5 (5.31–22.50) Q2 (12.7–15.6) Q3 (15.7–19.3) Q4 (>19.3) 5 Quintiles/Q1 (<12.5) Q2 (12.6–14.7), Q3 (14.8–16.9), Q4 (17–20), Q5 (>20) Quintile	Good
15	Ha/2021	Prospective Cohort	United States	1999–2010 NHANES	9.3	>30 Mean = 51.2	20602/(48.7 % Men)	Nationally representative, No cancer	All cause = 3529 CVD = 798 Cancer = 714	24-h dietary recall	Total fiber		Good
16	He/2010	Prospective Cohort	United States	NHS	26	30–55	7822(0 % men)	Women with T2DM, No-CVD, No-Cancer	All cause = 852 CVD = 295 (CHD = 195, Stroke = 100)	Validated questionnaire	Cereal fiber		Good
17	Hertog/1996	Prospective Cohort	United Kingdom	The Caerphilly Study	13.8	45–59	2112/(100 % men)	Men, Nationally representative	All cause cancer = 114 Digestive tract cancer = 45 respiratory tract cancer = 51 other site cancer = 18	FFQ	Total fiber		Good
18	Holmes/1998	Prospective Cohort	United States	NHS	13	Mean = 54	1982 (0 % Men)	Females with invasive breast carcinoma	Breast Cancer = 326	Validated FFQ	Total fiber		Good
19	Holmes/2009	Prospective Cohort	United States	NHS	6.9	30–55	3846(0 % Men)	Females with diagnosed stage I-III breast cancer	Breast cancer = 446	FFQ	Cereal fiber		Good
20	Huang/2015	Prospective Cohort	United States	prospective NIH-AARP Diet and Health Study (1995–2009).	14	50–71 Mean = 61.7	367442 (56.1 % Men)	No cancer, no CVD, no diabetes, no stroke, no ESRD.	All cause = 46067 CVD = 11283 Cancer = 19043 Diabetes = 371 Respiratory disease = 3796 Infectious = 922 Other causes = 5223	FFQ	Cereal fiber	5 Quintile/Q1 = 2.02, Q2 = 4.15, Q3 = 5.27, Q4 = 6.65, Q5 = 10.22	Good

21	Jacobs/2000	Prospective Cohort	United States	The Iowa Women's Health Study	11.3	55–69	11040 (0% Men)	Post menopausal women	All cause = 1341 Cancer = 527 CHD = 247 Other CVD = 180	FFQ	Total fiber	2 Groups (Whole grain fiber intake*/Refined grain fiber intake*) 71 % of total grain fiber 77 % of total grain fiber 10 % of mean intake Total fiber = 3.32	Good
22	Jansen/1999	Prospective Cohort	USA, Finland, Japan, Greece, Italy, Netherland, Serbia, Croatia	from 16 cohorts were enrolled in the Seven Countries Study,	25	40–59	12763/(100% Men)	Nationally representative	All cause = 5974 Cancer = 1580 Colorectal cancer = 162 (Colon cancer = 100 Rectum cancer = 62) All cause = 19400 (m = 11773/ f = 7627) Total CVD: (m = 2831/f = 2069) Heart disease: (m = 1506/ f = 1050) Cerebrovascular disease: (m = 1085/f = 828) Respiratory disease: (m = 1000/ f = 511) Injury: (m = 850/f = 426)	7 days recall	Total fiber	5 Quintile/Total fiber (male/ Q1–8.7 Q2 = 8.8–10.8/Q3 = 10.8 –12.9/Q4 = 12.9–15.7/ Q5→15.7) – (Female/Q1 = <10.6/ Q2 = 10.6–12.7/Q3 = 12.7 –14.7/Q4 = 14.7–17.4/ Q5→17.4) 5 Quintile/Soluble fiber (male/Q1 = <2.6 – Q2 = 2.6–3.1/Q3 = 3.1–3.7/ Q4 = 3.7–4.5/Q5→4.5) – (female/Q1 = <3.1/Q2 = 3.1 –3.7/Q3 = 3.7–4.2/Q4 = 4.2 –5/Q5 = >5) 5 Quintile/Insoluble fiber (female/Q1 = <7.2/Q2 = 7.2 –8.8/Q3 = 8.8–10.3/ Q4 = 10.3–12.3/Q5→12.3) – (male/Q1 = <6.0/Q2 = 6.6 –8.1/Q3 = 8.1–9.5/Q4 = 9.5 –11.4/Q5→11.4)	Poor
23	Katagiri/2020	Prospective Cohort	Japan	(Japan Public Health Center-based prospective study)/JPHC	16.8	45–74	92924/(46% Men)	No CVD, No stroke, No cancer, Healthy individuals	All cause = 1287 Stroke = 95 CHD = NR	FFQ	Total fiber Soluble fiber, insoluble fiber	Good	
24	Kaushik/2008	Prospective Cohort	Australia	(BMES)/until 2005	13	>49	2897/(43.96% Men)	Nationally representative	IHD = 65 (m = 42, f = 23)	validated FFQ	Cereal fiber	Good	
25	Khaw/1987	Prospective Cohort	United States	Caucasian community in Rancho Bernardo, California, a survey of heart disease risk factors	12	50–79	859/(41.44% Men)	No CVD - No Stroke (Healthy)	All cause = 2027 (Breakfast eater = 1719, Non-BF eater = 308) CVD = 469 (Breakfast eater = 383, Non-BF eater = 86) All cause = 2141	24-h Dietary recall	Total fiber	Good	
26	King/2021	Prospective Cohort	United States	(NHANES)/2015	12.3	>40	5761/(49.5% Men)	Nationally representative	All cause = 602 CVD = 149	validated FFQ	Total fiber	Good	
27	Krishnamurthy/2012	Prospective Cohort	United States	(NHANES III)/until 2000	8.4	>20 Mean = 45	14533/(48% Men)	Adults with eGFR<150 mL/min per 1.73 m ²	All cause = 5436 CVD = 985	24-h Dietary recall	Total fiber Insoluble fiber Soluble fiber	Good	
28	Kwon/2022	Prospective Cohort	Korea	Korean Genome and Epidemiology Study (KoGES)	10.1	40–69	3892/(38.41% Men)	Individuals with eGFR <60 mL/min/1.73 m ²	All cause = 602 CVD = 149	validated FFQ	Total fiber	Good	
29	Kwon/2022	Prospective Cohort	Korea	(KoGES)–Ansan–Ansung study (2001–2002), KoGES health examinee study (2004–2013), and the KoGES cardiovascular disease association study (2005–2011), NIH-AARP Diet and Health (AARP) Study	10.1	≥40 mean = 53.9	143050/(35.6% Men)	Nationally representative	All cause = 5436 CVD = 985	FFQ	Total fiber	Good	
30	Lan/2021	Prospective Cohort	United States	NIH-AARP Diet and Health (AARP) Study	8	50–70 Mean = 61.8	150671 (100% men)	No cancer	Prostate cancer = 760	Risk factor questionnaire FFQ	Total fiber	Good	
31	Li/2014	Prospective Cohort	United States	(NHS)/until 2008	F = 32 M = 22	30-55 Female 40-75 Male	4098/(44.89% Men)	No CVD, stroke, or cancer at base line + incident MI	All cause = 1133 (m = 451/ f = 682) CVD = (m = 222/f = 336) women	FFQ	Total fiber	Good	
32	Lin/2021	Prospective Cohort	China	multicentre prospective cohort study in China.	3.8	≥ 18 Mean = 54	1044/(57.7% Men)	Individuals who underwent maintenance hemodialysis for minimum of 90 days	All cause = 354 CVD = 210	24-h dietary recalls 3 day	Total fiber Insoluble fiber Soluble fiber	Good	

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Table 1 (continued)

No	First Author/year	Study type	Country	Cohort name	F/U (Year)	Age range/mean age (at base line)	Sample size (n) Men (%)	Population	Outcomes (Causes and Number of death)	Dietary assessment method	Fiber types	Dietary fiber categories (g/day)	Quality score
33	Liu/2021	Prospective Cohort	United States	(NIH)-(AARP) Diet and Health Study/untill 2011	15.5	Mean = 61.5	485717 (59.8 % Men)	No cancer, no CLD Healthy individuals	Chronic liver disease = 993	FFQ	Total fiber Fruit fiber Vegetable fiber Bean fiber Grain fiber	5 Quintile (Q1 = 9.1, Q2 = 13.7, Q3 = 17.5, Q4 = 22, Q5 = 32.5) <25 g/day and >25 g/day	Good
34	Lubini/2003	Prospective cohort	Israel	Israeli Central Population	18	41–70 Mean = 55.2	623 (48 % men)	No chronic disease (Healthy)	All cause = 151 Cancer = 34 CVD = 38 Cerebrovascular = 10 Other causes = 25 Unavailable causes = 44	FFQ	Total fiber		Good
35	Mann/1997	Prospective cohort	United Kingdom	Vegetarian Society, controls were their friends and relatives	13.3	16–79	10802 (38 % Men)	Vegetarian participants, no cancer	All cause = 392 IHD (CHD) = 64	FFQ	Total fiber	3 Tertile Men (Median)/ T1:17.9,T2:7.3 T3:39.6 3 Tertile Women (Median)/ T1:16.5,T2:4.7 T3:35	Good
36	McEligor/2009	Prospective cohort	United States	breast cancer cases diagnosed in Orange County, California, during 1994.	6.6	Mean = 64.78	516 (0 % Men)	Post menopausal Women with breast cancer	All cause = 96 Breast cancer = 41 Other cancers = 9 CVD = 13 Other causes = 22 Unknown = 11	NCI-Block FFQ	Total fiber	3 Tertile Women (Median)/ T1:NR, T2 = 8.74 T3:13.28	Good
37	Miyazawa/2019	Prospective cohort	Japan	Non-communicable Disease and its Trends in the Aged (NIPPON DATA) in Japan	24	30–79 (m = 50/ f = 50.2)	8925 (43.87 % Men)	Healthy - no CVD	CVD = 823 (m = 419/f = 404) CHD = (m = 83/f = 82) Cerebral hemorrhage (m = 46/ f = 38) Cerebral infarction (m = 126/ f = 85) All stroke type (m = 205/f = 180) IHD = 220	In person interview	Total fiber	4 Quartile(median)/men(Q1 = 5.8,Q2 = 6.9,Q3 = 8.3,Q4 = 9.6 Female(Q1 = 7.02 = 8.3,Q3 = 9.6,Q4 = 11.6	Good
38	Mozaffarian/2003	Prospective Cohort	United States	Cardiovascular Health Study	8.6	>65 Mean = 72	3588 (NR)	No CVD, No stroke (Healthy)	All cause = 2383 (f = 923/ m = 1460) Cancer = 975 CVD = 681 All cause = 317	FFQ	Cereal fiber, Fruit fiber	5 Quintile (Cereal fiber Q1<1.7 Q2 (1.7–3.3), Q3 (3.4–4.7) Q4 (4–6.3) Q5>6.3 5 Quintile/Fruit fiber Q1<2.8 Q2 (2.8–4.2), Q3 (4.3–5.7) Q4 (5.8–7.5) Q5>7.5 Median	Good
39	Nilsson/2012	Cohort	Sweden	Västerbotten Intervention Program (VIP) cohort	10	>30 Median = 49	77319 (48.68 % men)	Nationally representative	All cause = 2383 (f = 923/ m = 1460) Cancer = 975 CVD = 681 All cause = 317	semi-quantitative FFQ	Total fiber		Good
40	Palli/2000	Prospective Cohort	Italy	Population in several areas in Italy	10	NR	382 (63 % Men)	Individuals diagnosed with gastric cancer	Cancer = 681 All cause = 317	FFQ	Total fiber	Tertile	Good
41	Park/2011	Prospective cohort	United States	The NIH-AARP Diet and Health Study/untill 2005	9	50–71	388122 (56.45 % Men)	No cancer, no CVD, no diabetes, no stroke, no ESRD.	Total = 31456 (m = 20126/ f = 11330) CVD = 8365 (m = 5248/f = 2417) Cancer = 13171 (m = 8244/ f = 4927) Infectious = 498 (m = 275/f = 223) Respiratory = 2446 (m = 1415/ f = 1031) Accident = 1019 (m = 734/ f = 285) Other causes = 1565 (m = 992/ f = 573)	FFQ and 24-h recall	Total fiber Fruit fiber Vegetable fiber Bean fiber Grain fiber	5 Quintile (Median (male/ Q1 = 12.6, Q2 = 16.4, Q3 = 19.4, Q4 = 22.9, Q5 = 29.4) Female(Q1 = 10.8, Q2 = 14.3, Q3 = 17, Q4 = 20.1, Q5 = 25.8)	Good
42	Partula/2020	Prospective cohort	France	NutriNet-Santé prospective cohort (2009–2019).	5	> 18 Mean = 42.8	107377	Nationally representative	All cause = 635 Cancer or cardio- and cerebrovascular = 408	24-h recall	Total fiber, Fruit fiber, Vegetable fiber, Legumes fiber, Potato and Tubers fiber, Soluble fiber Insoluble fiber	5 Quintile/Total fiber mean Q1 = 11.3, Q2 = 15.5, Q3 = 18.6, Q4 = 22.1 Q5 = 30.1	Good

43	Pietinen/1996	Prospective cohort	Finland	The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study	6.1	50–69	21930 (100%men)	smoking men – no CVD, no DM	CHD = 635	Validated questionnaire	Total fiber/Soluble fiber, Insoluble fiber, Insoluble NCP, Cellulose, Lignin, Cereal fiber, Vegetable fiber, Fruit fiber	5 Quintile dietary fiber Median/Q1 (16.1) Q2 (20.7),Q3 (24.3),Q4 (28.3),Q5 (34.8) 5 Quintile Soluble fiber/Q1 (3.7) Q2 (5.7),Q3 (5.4),Q4 (6.2),Q5 (7.4) 5 Quintile Insoluble fiber/Q1 (12.2) Q2 (15.9),Q3 (18.9),Q4 (22.3),Q5 (27.7) 5 Quintile Insoluble NCP/Q1 (6.8) Q2 (8.9),Q3 (10.7),Q4 (12.6),Q5 (15.9) 5 Quintile lignin/Q1 (2.1) Q2 (3),Q3 (3.7),Q4 (4.5),Q5 (5.8) 5 Quintile Cellulose/Q1 (3.1) Q2 (3.9),Q3 (4.6),Q4 (5.2),Q5 (6.3) 5 Quintile cereal/Q1 (8.8) Q2 (12.4),Q3 (16),Q4 (19.9),Q5 (26.3) 5 Quintile vegetable fiber/Q1 (2.9) Q2 (3.9),Q3 (4.7),Q4 (5.6),Q5 (7.1) 5 Quintile fruit fiber/Q1 (0.7) Q2 (1.5),Q3 (2.4),Q4 (3.4),Q5 (5.3)	Good
44	Pocobelli/2010	Prospective cohort	United States	13-county area of western Washington State	5	50–76	77673 (48 % Men)	Nationally representative	All cause = 3577	FFQ	Total fiber	High-use category low-use category	Good
45	Qi/2022	Prospective cohort	United States	NHANES (2003–2014) cohort	11	≥18	31,164 (48.18 % Men)	Nationally representative	All cause = 2915 Cancer = 631 CVD = 836	2 days 24 h dietary recall	Total fiber	none	Good
46	Rebello/2014	Prospective cohort	Singapore and China	The Singapore Chinese Health Study cohort	15	45–74	53469 (43.9 % Men)	no (cancer, heart attack or angina, stroke, or diabetes.) Healthy	IHD = 1660 (m = 1022/f = 638)	semi-quantitative FFQ	Total fiber	5 Quintiles/men/Q1 = 783, Q2 = 1040, Q3 = 1213, Q4 = 1418, Q5 = 1777 5 Quintiles/Female/ Q1 = 850, Q2 = 1046, Q3 = 1215, Q4 = 1418, Q5 = 1781	Good
47	Ricci/2020	Prospective cohort	United States	NHANES surveys (1999–2014)	5.7	>18	2371 (4686 % Men)	Cancer survivors	All cause = 532 Cancer = 180	24-h dietary recall	Total fiber	Tertile	Good
48	Ricci/2020	Prospective cohort	United States	NHANES surveys (1999–2014)	5.6	Median = 69	2473 (557 % men)	Nationally representative	All cause = 761 CVD = 199	24 h dietary recall interview	Total fiber	T1 = (<11-93 g),T2&T3 (18-9 -52-39)	Good
49	Rimm/1996	Prospective cohort	United States	The Health Professionals Follow-up Study (HPPS)	6	40–75	43757 (100%Men)	Healthy make health professional. No CVD No DM	CHD = 229	Dietary Questionnaire	Energy adjusted total fiber	Q1 (12.4) Q2 (16.6) Q3 (19.6) Q4 (23.0) Q5 (28.9)	Good
50	Schoemaker/2012	Prospective cohort	Europe	The EURODIAB Prospective Study (PCS)	7.4	15–60 Mean = 32.07	2108 (51 % Men)	Individuals with type 1 diabetes mellitus free of CVD at baseline	All cause = 46	3 days dietary record	Total fiber/Soluble fiber Insoluble fiber	T2 = 18.6 T3 = 25.2	Good
51	Skiba/2019	Prospective cohort	United States	Women's Health Initiative (WHI) study.	15.4	Mean = 63.2	160195 (0 % Men)	Post menopausal women without history of colorectal cancer	All cause = 35746 Colorectal cancer = 841	Questionnaire	Probiotic supplement fiber type (soluble, insoluble)	Probiotic supplement yes or no	Good
52	Song/2017	Prospective cohort	United States	(NHS) and (HPPS)	8	30–75 Mean = 68.6	1575 (38.9 % Men)	Health care professionals with stage I-III colorectal cancer	All cause = 773 Colorectal cancer = 174	FFQ	Total fiber Cereal fiber Vegetables fiber Fruits fiber	4 Quartiles/median Q1 (14.4) Q2 (18.2) Q3 (22.2) Q4 (28.9)	Good

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Table 1 (continued)

No	First Author/year	Study type	Country	Cohort name	F/U (Year)	Age range/mean age (at base line)	Sample size (n) Men (%)	Population	Outcomes (causes and Number of death)	Dietary assessment method	Fiber types	Dietary fiber categories (g/day)	Quality score
53	Strepel/2008	Prospective cohort	Netherlands	Zuiphen Study	40	>30 Mean = 49	1373 (100% Men)	Nationally representative	All cause = 1130 CHD = 348	In person interview	Total fiber Cereal fiber Potatoes fiber Legumes fiber Vegetables fiber Fruits fiber NSP fiber, AOC fiber, Soluble fiber, Insoluble fiber, nuts, seeds fiber, Legume fiber, Vegetable fiber, Fruit fiber, breakfast cereals fiber, Total cereal fiber	Per 10 gr/d increment	Good
54	Threapleton/2013	Prospective cohort	United Kingdom	United Kingdom Women's Cohort Study (UKWCS)	14.3	Mean = 51.8	31036 (0% Men)	no CVD no stroke no heart attacks	All CVD = 258 (Stroke = 130 - CHD = 128)	FFQ		Quintiles	Good
55	Ward/2016	Prospective cohort	Sweden, Denmark, Norway, Netherlands, UK, France, Germany, Spain, Italy, Greece	(EPIC) cohort	4.1	25–70	3789 (42.3% men)	Unhealthy patients with colorectal cancer	All cause = 1262 Colorectal cancer = 1008	FFQ	Total fiber	4 Quartiles (Q1 (14.5), Q2 (19.5), Q3 (24.1), Q4 (31.2))	Good
56	Wolk/1999	Prospective cohort	United States	(NHS) until 1994	10	37–64	68782 (0% Men)	Women no CVD, no hypercholesterolemia, no diabetes (Healthy)	CHD = 162	FFQ	Total fiber	5 Quintiles (Q1 (11.5), Q2 (14.3), Q3 (16.4), Q4 (18.8), Q5 (22.9))	Good
57	Xu/2014	Prospective cohort	Sweden	Uppsala Longitudinal Study of Adult Men (ULSAM)	10	69.5–71.9 Mean = 70.9	1110 (100% Men) GFR-60 = 604 GFR-60 = 506	Nationally representative	All cause = 300 (GFR-60 = 132 GFR-60 = 168) CVD = 138 (GFR-60 = 49 GFR-60 = 168) Cancer = 111 (GFR-60 = 56 GFR-60 = 55) infectious = 19 other causes = 33 All cause = 434 CVD = 178	7 day record of Validated precoded menu book	Total fiber	4 Quartiles (Q1 (4.8, 14.5), Q2 (0.14.5, 16.8), Q3 (0.16.8, 19.2), Q4 (0.19.2, 34.7))	Good
58	Xu/2019	Prospective cohort	China	a prospective cohort at the PD centre of Peking University First Hospital, Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial	3.75	Mean = 57.7	881 (46.3% Men)	Patients on peritoneal dialysis (PD)	All cause = 434 CVD = 178 Infection = 107 All-cause = 17536 CVD = 4842 Cancer = 5760	3–4 recall	Total fiber	Tertile of fibre intake (Low (<6.4 g/d) Middle (6–4) High (>9.1 g/d)) Total: Q1 (<11.12) Q2 (≥11.12 to <14.71) Q3 (≥14.71 to <18.41) Q4 (≥18.41 to <23.75) Q5 (≥23.75) Alive vs Dead (Total fibre (g/day) 3.98 (2.44) vs 3.21 (1.94) p < 0.001*)	Good
59	Xu/2022	Prospective Cohort	United States	Longitudinal Study on Neuroprotective Model for Healthy Longevity (LRGS TUA) cohort	17.1	Mean = 62.1	86642 (54.20% Men)	No cancer, no heart disease, no stroke, no diabetes (Healthy)	All cause = 336 CVD = 783 Cancer = 884	Dietary History Questionnaire (DHQ)	Total fiber, Insoluble fiber, Soluble fiber	4 Quartiles (Q1 (4.3), Q2 (6.5), Q3 (8.7), Q4 (12.6))	Good
60	You/2022	Prospective Cohort	Malaysia	Longitudinal Study on Neuroprotective Model for Healthy Longevity (LRGS TUA) cohort	5	>60	2322 (47.97% Men)	Nationally representative	All cause = 336	3-Day record Dietary history questionnaire	Total fiber	4 Quartiles (Q1 (<6.21) Q2 (6.21–8.81) Q3 (8.81–13.50) Q4 (>13.50))	Good
61	Zeng/2022	Prospective cohort	United States	NHANES survey/2001–2014	7.1	20–85 Mean = 46	35692	No cancer, No CVD, Healthy individuals	All cause = 3854 CVD = 783 Cancer = 884	24-h dietary recall	Total fiber	4 Quartiles (Q1 (<10.2), Q2 (10.2–14.45), Q3 (14.45–19.85), Q4 (>19.85))	Good
62	Zhang/2022	Retrospective Cohort	United States	Survey (NHANES) 2003–2014	5.8	>65 (mean = 74.1)	4906 (48.4% Men)	Adults with hypertension	All cause = 1369 CVD = 270	24-h dietary recall	Total fiber	4 Quartiles (Q1 (<6.21) Q2 (6.21–8.81) Q3 (8.81–13.50) Q4 (>13.50))	Good
63	Zhang/2022	Prospective Cohort	China	China Nutrition and Health Database (CHNS) until 2015	11	>18	8307 (39.2% Men)	No CVD - No Cancer/ Nationally representative	All cause = 468	3-day recall	Total fiber, Whole Grain fiber, Legumes fiber, Vegetable fiber, Fruit fiber	4 Quartiles (Q1 (<6.21) Q2 (6.21–8.81) Q3 (8.81–13.50) Q4 (>13.50))	Good
64	Zhao/2022	prospective cohort	Canada	The Newfoundland Familial Colorectal Cancer Study (NEFCCS) until 2010	6.4	20–75 Mean = 60.9	504 (60.71% Men)	CRC patients	All cause = 159 (f = 53/m = 106) CRC-specific = 83 (f = 29/m = 54)	FFQ	Total fiber	4 Quartiles (Q1 = 14.17, Q2 = 19.74, Q3 = 24.15, Q4 = 30.35)	Good

Table 2
The pooled associations between dietary fiber usage and mortality.

Variable	N Observations ^a	HR 95 % CI	Heterogeneity		
			I Squared%	Model	P-Value
All-Cause Mortality					
Overall	33	0.77 (0.73,0.82)*	67.89	Random	<0.001
By Sex					
Male	5	0.81 (0.75,0.87)*	49.61	Random	<0.001
Female	9	0.76 (0.67,0.85)*	58.11	Random	<0.001
Both Sexes	23	0.77 (0.71,0.83)*	67.92	Random	<0.001
By Population					
General	19	0.82 (0.77,0.86)*	71.13	Random	<0.001
Non-General ^b	14	0.67 (0.61,0.72)*	32.54	Fixed	0.11
By Diet Assessment					
FFQ	20	0.78 (0.72,0.84)*	59.50	Random	<0.001
24 h Recall	10	0.79 (0.67,0.90)*	78.67	Random	<0.001
By Fibre					
Cereal, Bran, Germ, Whole grain	10	0.84 (0.79,0.89)*	77.02	Random	<0.001
Soluble	8	0.84 (0.76,0.91)*	75.53	Random	<0.001
Insoluble, Cellulose, Lignin	7	0.77 (0.72,0.82)*	54.88	Random	0.04
Vegetable	8	0.87 (0.80,0.95)*	80.67	Random	<0.001
Fruit	8	0.94 (0.86,1.02)	81.83	Random	<0.001
Legume, Bean	7	0.92 (0.89,0.95)*	43.75	Fixed	0.10

N: number, HR: Hazard Ratio, CI: Confidence interval, FFQ: Food Frequency Questionnaire, 24 h: 24 h, CVD: Cardio-Vascular Diseases, NSP: Non-Starch Polysaccharides, CHD: Congestive Heart Disease.

*: Statistically significant (P-value < 0.05).

^a Refers to the number of reports, Not the number of studies, as some studies may have reported more than one HR or RR for different populations.

^b Participants who could not be categorized as the general population (e.g. cancer survivors, Smokers, individuals with type II diabetes mellitus, etc.).

Table 3
The pooled associations between dietary fiber usage and CVD-related mortality.

Variable	N Observations ^a	HR 95 % CI	Heterogeneity		
			I Squared%	Model	P-Value
CVD related mortality					
Overall	47	0.74 (0.71,0.77)*	20.31	Fixed	0.12
By Sex					
Male	19	0.76 (0.71,0.80)*	26.19	Fixed	0.14
Female	17	0.72 (0.67,0.77)*	6.67	Fixed	0.15
Both Sexes	13	0.74 (0.68,0.79)*	22.99	Fixed	0.21
By Population					
General	41	0.74 (0.71,0.78)*	24.82	Random	0.08
Non-General ^b	6	0.69 (0.58,0.79)*	<0.001	Fixed	0.62
By Diet Assessment					
FFQ	23	0.77 (0.73,0.81)*	8.42	Fixed	0.35
24 h Recall	9	0.75 (0.67,0.84)*	48.55	Random	0.05
Other Questionnaires ^c	13	0.74 (0.71,0.77)*	<0.001	Fixed	0.48
By Fibre					
Cereal, Bran, Germ, Whole grain	20	0.85 (0.80,0.89)*	34.05	Random	0.07
Soluble	16	0.80 (0.75,0.86)*	<0.001	Fixed	0.90
Insoluble, Cellulose, Lignin	15	0.74 (0.68,0.79)*	<0.001	Fixed	0.50
Vegetable	17	0.89 (0.85,0.93)*	<0.001	Fixed	0.91
Fruit	18	0.79 (0.70,0.88)*	77.63	Random	<0.001
Legume, Bean	11	0.87 (0.82,0.91)*	<0.001	Fixed	0.79
NSP	3	0.72 (0.39,1.04)	<0.001	Fixed	0.85
NSP Density	3	0.94 (0.65,1.23)	<0.001	Fixed	0.97
Nuts and Seeds	3	0.57 (0.38,0.77)*	<0.001	Fixed	0.47
By Type of CVD					
CHD	7	0.83 (0.73,0.92)*	<0.001	Fixed	0.87
Stroke	11	0.78 (0.69,0.87)*	22.23	Fixed	0.23

N: number, HR: Hazard Ratio, CI: Confidence interval, FFQ: Food Frequency Questionnaire, 24 h: 24 h, CVD: Cardio-Vascular Diseases, NSP: Non-Starch Polysaccharides, CHD: Congestive Heart Disease.

*: Statistically significant (P-value <0.05).

^a Refers to the number of reports, Not the number of studies, as some studies may have reported more than one HR or RR for different populations.

^b Participants who could not be categorized as the general population (e.g. cancer survivors, Smokers, individuals with type II diabetes mellitus, etc.).

^c Diet History Questionnaire (DHQ), Interview, Pre-coded Menu Book and other dietary questionnaires.

Table 4
The pooled associations between dietary fiber usage and malignancy-related mortality.

Variable	N Observations ^a	HR 95 % CI	Heterogeneity		
			I Squared%	Model	P-Value
Malignancy related mortality					
Overall	18	0.78 (0.68,0.87)*	77.81	Random	<0.001
By Sex					
Male	6	0.80 (0.68,0.92)*	52.07	Random	0.06
Female	5	0.97 (0.89,1.06)	23.65	Fixed	0.26
Both Sexes	9	0.70 (0.54,0.87)*	76.90	Random	<0.001
By Population					
General	10	0.85 (0.76,0.94)*	73.67	Random	<0.001
Non-General ^b	8	0.64 (0.44,0.85)*	62.39	Random	0.01
By Diet Assessment					
FFQ	11	0.79 (0.65,0.93)*	63.12	Random	<0.001
24 h Recall	3	0.65 (0.29,1.01)	88.90	Random	<0.001
By Fibre					
Cereal, Bran, Germ, Whole grain	7	0.85 (0.82,0.88)*	26.37	Fixed	0.23
Soluble	3	0.98 (0.67,1.29)	71.37	Random	0.03
Insoluble, Cellulose, Lignin	3	0.80 (0.73,0.88)*	48.39	Fixed	0.14
Vegetable	5	0.93 (0.85,1.01)	60.66	Random	0.04
Fruit	5	0.97 (0.92,1.02)	<0.001	Fixed	0.45
Legume, Bean	4	1.00 (0.96,1.05)	<0.001	Fixed	0.77
By Type of Malignancy					
Colorectal	4	0.82 (0.67,0.96)*	56.54	Random	0.06

N: number, HR: Hazard Ratio, CI: Confidence interval, FFQ: Food Frequency Questionnaire, 24 h: 24 h, CVD: Cardio-Vascular Diseases, NSP: Non-Starch Polysaccharides, CHD: Congestive Heart Disease.

*: Statistically significant (P-value < 0.05).

^a Refers to the number of reports, Not the number of studies, as some studies may have reported more than one HR or RR for different populations.

^b Participants who could not be categorized as the general population (e.g. cancer survivors, Smokers, individuals with type II diabetes mellitus, etc.).

HR:0.78; 95%CI (0.69,0.87) compared to CHD: HR: 0.83; 95 % CI (0.73,0.92)) (Table 3).

3.5.3. Meta-Regression

Meta-regression was performed for all-cause, CVD, and malignancy-related mortalities with sex, mean age of the participants, studied population, participants' follow duration, and dietary assessment as covariates; and only the type of studied population (general and non-general) was found to be a possible cause of heterogeneity among studies evaluating the association of all-cause mortality with dietary fiber usage. (Coefficient: -0.19, standard error (SE): 0.08 P-value: 0.01) and malignancy-related mortality with dietary fiber usage (Coefficient: -0.66, SE: 0.25 P-value: 0.007) (Supplementary Tables 2–4).

3.5.4. Publication bias and trim-fill analysis

Based on Egger's test, no publication bias was seen across studies assessing all-cause and CVD and malignancy-related mortalities. Upon trim fill analysis, no studies were imputed within CVD and malignancy-related mortality records. Three studies were imputed in all-cause mortality records in which the HR changed from HR:0.77 95%CI (0.73,82) to HR:80 95%CI (0.75,84) indicating that the findings of the analyses were not substantially affected by publication bias. Funnel plots for graphical diagnostics of small-study effects regarding all-cause, CVD-related, and Cancer-related mortalities were presented in Supplementary Fig. 2 (A, B, and C).

3.5.5. Leave one out meta-analysis

Leave-one-out analysis was performed to evaluate each study's effect on the overall pooled effect size; upon omitting each study, the overall significance of the findings did not change substantially. These sensitivity analyses are illustrated in Supplementary Fig. 3 (A, B, and C) for all-cause, CVD-related, and malignancy-related mortalities, respectively.

4. Discussion

4.1. Discussion

The current systematic review and meta-analysis of 64 prospective studies, provides a comprehensive overview of the reported association between dietary fiber intake and mortality risk. Our findings showed that the consumption of dietary fiber had a significant inverse association with the rate of total mortality and mortality due to specific causes, including CVD and cancer. Consistent with our results, multiple meta-analyses and large prospective cohort studies have found significant inverse associations between dietary fiber intake and mortality rate, and CVD- and cancer-related mortality [15,21–23,27–30].

In the current study, it has been showed that those with higher fiber intake had a 23 % lower total mortality rate. Kim et al. (2014) conducted a meta-analysis comparing individuals with high versus low dietary fiber intake and found a 23 % lower risk of total mortality in those with higher fiber intake [15]. Similarly, Liu et al. (2015) performed a meta-analysis and found that those who consumed the highest amount of fiber had a 23 % lower mortality rate for CVD, 17 % lower for cancer, and 23 % lower for all-cause mortality, as well as a strong dose-response relationship between dietary fiber intake and mortality from CVD [21]. However, it is worth noting that some earlier studies reported no significant association between fiber consumption and all-cause or CVD-related mortality, which is not consistent with the results of our study [31–37].

In total, consumption of dietary fiber has been linked to numerous health benefits and is believed to reduce the risk of premature mortality and incidence of NCDs [14,38–40]. In particular, dietary fiber protects against chronic diseases, such as CVD, type 2 diabetes, and certain cancers, which are the leading causes of death worldwide [41–53].

The findings of the present study provide convincing evidence that a higher intake of total dietary fiber is associated with a 26 %

decreased risk of mortality from CVD. This is supported by multiple cohort studies and meta-analyses that have demonstrated the protective effects of dietary fiber in reducing the risk of CVD and CHD [31,33,36,37,46,54–60]. A meta-analysis of 18 studies found that people who consumed high amounts of dietary fiber had a 17 % reduced risk of mortality from CHD compared to those who had low dietary fiber intake. Additionally, a significant dose-response relationship between fiber intake and CHD risk has been observed [61]. Moreover, a meta-analysis of 15 prospective studies by Kim et al. (2016) observed an inverse association between CVD mortality and dietary fiber intake [8]. Notably, the World Health Organization (WHO) considers stroke to be a CVD. Stroke was the second leading cause of death and was responsible for approximately 11 % of all deaths globally in 2019 [62]. Therefore, we investigated the protective effect of fiber on stroke and found that higher fiber intake was associated with a 22 % lower incidence of stroke-related mortality. Another meta-analysis on stroke found that for each 7 g/day increase in dietary fiber intake, there was a corresponding 7 % reduction in the risk of hemorrhagic and ischemic stroke [51].

The relationship between dietary fiber intake and cancer-related mortality has been extensively studied. Previous studies have consistently shown that a high intake of dietary fiber is associated with a reduced risk of different cancers, particularly breast, colorectal, and stomach cancers [48–50,63–67]. Several meta-analyses have shown that a 10-g/day increase in dietary fiber intake is associated with a 5–44 % decrease in cancer risk [48–50]. The current study revealed that a higher intake of fiber is significantly associated with a 22 % reduced risk of mortality from cancer; this association was also significant for mortality from colorectal cancer. Consistent with these findings, a meta-analysis demonstrated that a daily increase of 10 g in fiber intake was associated with a 33 % decrease in mortality risk from colorectal cancer [65].

One of the defining features of dietary fiber is its resistance to digestion and absorption by endogenous enzymes in the human small intestine. Dietary fibers undergo partial or complete fermentation in the large intestine, which is crucial for the health of gut microbiota [28,68]. Some soluble fibers, such as pectin, gum, and β -glucan, can be fermented in the large intestine [69] with considerate synthesis of short-chain fatty acids (SCFAs) [70].

The current study revealed that the consumption of both soluble and insoluble fiber is associated with a reduced risk of total mortality and mortality from CVD and cancer. These associations were more evident in CVD-related mortality. According to previous studies, dietary fiber may have different health benefits depending on its solubility or source [8,9,61]. Soluble fiber, such as psyllium and β -glucan, can form a viscous gel in the intestinal tract. Normally, nutrients are delivered to the small intestine in the form of a thin liquid called chyme. However, when gel-forming fibers are added, the viscosity of the chyme increases significantly in a dose-dependent manner, leading to a thickening effect. This increase in viscosity slows nutrients' degradation as well as glucose and other nutrients absorption [71]. This mechanism effectively regulates blood glucose levels, thereby averting the risk of both hyperglycemia and hypoglycemia. This can reduce the risk of type 2 diabetes and other metabolic disorders [72]. As a result, soluble fiber may have health benefits and reduce mortality rates.

Soluble fiber lowers serum cholesterol concentration through two ways. First, it can bind to cholesterol particles in the small intestine, thereby reducing cholesterol absorption. Furthermore, soluble fiber alters the excretion of bile acids with fecal matter, causing the liver to absorb more cholesterol to generate more bile. This can lower blood cholesterol levels, and reduce the risk of heart disease and stroke [73,74].

Several potential biological mechanisms can explain the beneficial effects of dietary fiber consumption. One such mechanism is

that it supports digestive health. Research has demonstrated that dietary fiber can enhance stool volume and the rough texture of fiber aids in the stimulation of peristalsis. This prevents constipation and reduces the risk of hemorrhoids, diverticulitis, and other gastrointestinal disorders. In addition, this effect results in a reduction in exposure to carcinogens within the intestinal lumen as well as a decrease in the production of secondary bile acids by accelerating transit time. For instance, insoluble fiber binds and absorbs carcinogens, mutagens, and toxins, thereby avoiding their negative effects on the body by inhibiting their absorption and directing them toward elimination [45,75,76]. This quality of insoluble fiber prevents the negative impact of harmful substances on the body and protects against the development of cancer. Notably, in the current study, insoluble fiber intake tended to be more effective than soluble fiber intake in reducing the risk of total mortality and mortality due to CVD and cancer.

Moreover, fiber is filling and can help promote feelings of satiety after a meal and stimulate the cholecystokinin satiety hormone, which may promote weight loss and improve overall health [19,77–79].

Prebiotic dietary fiber refers to a type of dietary fiber that modifies the composition and function of the gut microbiota through its fermentation by microorganisms in the intestine, thereby providing a favorable physiological effect on the host [80]. SCFAs produced by the gut microbiota are one of the principal metabolites of dietary fiber [81] which reduces the intestinal pH and prevents the growth of pathogenic microorganisms [82]. One of the key properties of SCFAs is that they maintain the integrity of the intestinal barrier by reducing the inflammatory response in the intestinal epithelium [83]. Moreover, SCFAs have anti-inflammatory and immunomodulatory effects [84,85] and offer preventive effects against CVD, obesity, diabetes, and cancers, reducing their mortality rates [86–91].

Fiber-rich foods, such as fruits, vegetables, whole grains, and legumes, are also rich sources of biologically active components, including phytochemicals, antioxidants, and vitamins, which are capable of inhibiting cancer growth [92,93]. Therefore, as an indirect mechanism, increasing fiber intake through the consumption of these foods may also lead to an increase in the intake of these beneficial compounds. Overall, high-fiber diets are more effective than fiber supplementation in improving disease outcomes [94]. It should be noted that nutrients other than fiber may also contribute to the benefits of high-fiber diets. In contrast, King et al. (2007) showed that psyllium fiber supplementation can be as effective as a high-fiber diet in reducing CRP levels [95].

In the current study, dietary fiber intake from whole grains, cereals, and vegetables showed a reduction in the risk of all-cause mortality, whereas fiber from fruits did not show such an association. In line with our findings, multiple studies examining the association between fiber intake from different sources and the risk of diseases found that cereal fiber was strongly associated with lower risks of colorectal cancer, gastric cancer, type 2 diabetes, and stroke, whereas vegetable and fruit fiber was weakly associated with disease risk [50–53]. Moreover, in a meta-analysis, cereal and to a lesser extent, vegetable fiber were significantly associated with a decreased risk of total mortality; however, fruit fiber was not [15]. Similarly, Kim et al. (2016) conducted a meta-analysis and found that intake of cereal fiber was strongly associated with reduced mortality from CVD; however, vegetable and fruit fiber did not show any significant inverse association with mortality from CVD [8]. Moreover, a meta-analysis of 18 prospective studies revealed an inverse association between all-cause mortality and cereal fiber intake, and the same analysis showed an inverse relationship between cereal fiber intake and mortality from CVD and cancer [23]. The results were comparable to our own, which in that cereal fiber

demonstrated a higher inverse connection with total mortality than other food sources, particularly with regard to cancer-related mortality.

Notably, in this study, dietary fiber intake from nuts and seeds resulted in a 43 % reduction in the risk of mortality from CVD. Nuts protect against CVD primarily by improving the lipid and apolipoprotein profiles. Increasing evidence also suggests that nut consumption may protect against CVD by reducing oxidative stress and inflammation and improving endothelial function. Besides fiber, unsaturated fatty acids, L-arginine, beneficial minerals, phenolic compounds, and phytosterols appear to be of utmost importance for the health benefits of nuts [96].

Another noteworthy point in this study was that only the consumption of insoluble fiber and fiber from cereal sources showed a 20 % and 15 % reduction in mortality due to malignancy, respectively. However, this relationship was not observed in fiber from other sources. Insoluble fibers have been shown to improve digestive health and reduce carcinogen exposure [14,97,98].

The current study presents various findings regarding the association between dietary fiber intake and health outcomes based on sex. The results indicated that the risk reduction for total and CVD mortality was greater in the women subgroup than that in the men subgroup, although the risk reduction for cancer mortality was greater in the men subgroup. In this context, a study found that a higher intake of dietary fiber, only in women and not in men, had a lower risk of CVD-related death [58]. A European study revealed a significant inverse relationship between dietary fiber consumption and all-cancer mortality in both men and women [99]. However, another study found a significant inverse association of cancer-related deaths in men but not in women, which is consistent with our findings [28]. Similarly, a meta-analysis of 21 studies found a greater protective effect in men than in women [100], which is in line with our findings on the association between dietary fiber intake and cancer-related mortality. In contrast, two meta-analyses of dietary fiber effects on mortality found no significant differences by sex [8,15]. Differences in the effect of dietary fiber on mortality between men and women may be attributed to several factors, such as differences in dietary preferences and hormonal profiles. Women have higher estrogen levels, particularly young women. Estrogen can assist in softening stools and facilitating their passage [101], and it increases the quantity of beneficial bacteria in the gut, which aids in the breakdown and absorption of dietary fiber [102], leading to improved gut health and general digestive performance.

Dietary fiber has different effects on the gut microbiota depending on the gender. When men and women consume the same amount of fiber, there are more *Proteus* and *Lactobacillus* in men than in women. Both are critical for the digestion of dietary fiber, and numerous forms of cancer may be prevented by them [103,104]. Overall, the reasons for the differences in the effects of dietary fiber on mortality between men and women are complex and multifactorial, and additional research is necessary to better understand these differences.

Our findings suggest that consuming dietary fiber can 33 % reduce the risk of death in the subgroup of subjects with certain diseases such as diabetes, kidney failure, and various types of cancer. Several studies have suggested that dietary fiber intake may be particularly beneficial for individuals with certain health conditions [32,39,72,88]. This demonstrates the importance of following a healthy, high-fiber diet for those with NCDs to improve disease management and prolong their lifetime.

Finally, dietary fiber provides many health benefits through its complex mechanisms of action. It is recommended that adults

consume at least 25–30 g of fiber per day from a variety of sources, including fruits, vegetables, whole grains, and legumes [97]. Therefore, greater adherence to a plant-based diet is related with a lower risk and incidence of NCDs, such as Type 2 diabetes, colon cancer, and CVD [47,105–110].

4.2. Strengths and limitations

We believe that the findings of this study summarize the majority of existing data on the relationship between dietary fiber intake and mortality. Compared to all previous meta-analysis studies, this study has a more comprehensive view, has examined a larger sample size, and has also considered different types of fiber. Also, the possible causes of heterogeneity were investigated, and performed subgroup analysis. Another advantage is that the quality of the included articles was assessed. Moreover, the use of FFQ to assess dietary fiber intake is a common method in epidemiological studies, and frequent validation of these questionnaires increases the reliability of the results. However, the use of the FFQ in the included studies may have resulted in an underestimation of dietary fiber intake. Additionally, like any observational study, bias and confounding variables are potential limitations [111,112]. Cohort studies can be biased due to informative censoring and measurement errors. Confounding is difficult to resolve because it might be difficult to account for all prevalent causes of exposure and their relationship with disease outcomes. Furthermore, observational studies only showed associations and correlations and did not establish causality; in this study, only observational cohort studies were included. Therefore, controlled trials are necessary to determine the causality of fiber in reducing mortality and to eliminate confounders, measurement errors, and selection biases. Additionally, the effects of dietary fiber consumption on mortality outcomes may vary by different variables, such as target population, study design, and quality of the included studies, as well as confounding variables. Moreover, while in this study, like many previous studies, HR and RR have been considered the same approximately. However, it is important to note that HR and RR are fundamentally distinct from each other. HR is a ratio of conditional probabilities while RR is a ratio of probabilities. For instance, even in the hypothetical scenario involving constant hazards and a constant HR, the corresponding RR would fluctuate over time. Consequently, an HR does not quantify the increase or decrease in the risk of mortality in a direct manner. Therefore, the interpretation of the results should be done with caution. In summary, the present meta-analysis contributes to the literature on dietary fiber and mortality; however, the limitations inherent in observational studies should be considered.

5. Conclusion

The results of the present meta-analysis confirmed the association between dietary fiber intake and total mortality risk reduction. This association was more significant for CVD-related mortality. In particular, insoluble fiber consumption was found to be more effective than soluble fiber intake in lowering the risk of mortality, especially cancer-related mortality. Fiber consumption confers greater benefits to subpopulations of women and individuals with compromised health. These findings support the current recommendation of the Academy of Nutrition and Dietetics to increase the consumption of fiber-rich foods as part of a healthy diet [113]. Overall, the findings of this study have significant implications for individuals, clinicians, and policymakers concerned with reducing mortality rates and improving population health.

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Authors contribution

HSE and MQ Came with the idea of this systematic review and designed the study. BL did the search strategy and FR and MG participated in the Screening of articles. FP, ME, and FR extracted the data. FR, FP, and ME drafted the main manuscript, and MQ and HSE revised the main manuscript. All of the authors read and approved the final version of the manuscript.

Conflict of interest

The authors declare they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnu.2023.11.005>.

Appendix

Quality assessment:

The quality of the included studies was appraised using the Newcastle–Ottawa Quality Assessment scale (NOS) for cohort studies. Two authors assessed the articles independently. Any disagreement between the two researchers was resolved by discussion until reaching a consensus. The NOS evaluates the methodological quality of the studies in eight items for cohort studies within three categories: (1) Selection of participants (maximum 4 scores), (2) Comparability of subjects (maximum 2 scores), (3) Assessment of outcome (maximum 3 scores). And eight items were as follows: (1) representativeness of the exposed cohort, (2) selection of the non-exposed cohort, (3) ascertainment of exposure, (4) demonstration that the outcome of interest was not present at the start of the study, (5) comparability of cohorts on the basis of the design or analysis controlled for confounders, (6) assessment of outcome, (7) follow-up was long enough for outcomes to occur, (8) adequacy of follow-up of cohorts.

Good quality: If a study gets 3 or 4 points in the selection part AND 1 or 2 points in the comparability part AND 2 or 3 points in the outcome part.

Fair quality: If a study gets 2 scores in the selection part AND 1 or 2 scores in the comparability part AND 2 or 3 points in the outcome part.

Poor quality: if a study scored 0 or 1 in the selection part OR 0 stars in the comparability part OR 0 or 1 star in the outcome part.

(**Reference:** Wells GA, Wells G, Shea B, Shea B, O'Connell D, Peterson J, et al., editors. The Newcastle–Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses 2014.)

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