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## CLINICAL RESEARCH

# Dietary fibre intake and mortality from cardiovascular disease and all cancers: A meta-analysis of prospective cohort studies



*Consommation de fibres diététiques et mortalité cardiovasculaire et par cancer : méta-analyse des études de cohortes prospectives*

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### KEYWORDS

Fibre;  
Cardiovascular disease;  
Mortality;  
Prospective cohort studies;  
Meta-analysis

### Summary

**Background.** — Accumulating evidence supports health benefits of dietary fibre, such as improving lipid profiles, lowering blood pressure and improving insulin sensitivity, but evidence from comprehensive investigation of dietary fibre intake and mortality from cardiovascular disease (CVD) and all cancers is limited.

**Aims.** — To quantitatively assess the association between dietary fibre intake and mortality from CVD and all cancers.

**Methods.** — We performed a meta-analysis of prospective cohort studies. Eligible studies were identified by searching PubMed and Embase databases for all articles published up to September 2014 and via hand searching. Study-specific estimates adjusting for potential confounders were combined to calculate pooled relative risks (RRs) with 95% confidence intervals (CIs), using a random-effects model.

**Results.** — We found 15 studies that examined the association between dietary fibre and mortality from CVD, coronary heart disease (CHD) and all cancers. The pooled RRs of CVD, CHD and all-cancer mortality for the highest versus lowest category of dietary fibre were 0.77 (95% CI: 0.71–0.84), 0.76 (95% CI: 0.67–0.87) and 0.86 (95% CI: 0.79–0.93), respectively. In a

**Abbreviations:** BMI, Body mass index; CI, Confidence interval; CHD, Coronary heart disease; CVD, Cardiovascular disease; IHD, Ischaemic heart disease; RR, Relative risk.

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dose-response meta-analysis, the pooled RRs for an increment of 10 g/day in dietary fibre intake were 0.91 (95% CI: 0.88–0.94) for CVD, 0.89 (95% CI: 0.85–0.93) for CHD and 0.94 (95% CI: 0.91–0.97) for all cancers.

**Conclusions.** — Our findings suggest that high dietary fibre intake is associated with a reduced risk of mortality from CVD and all cancers. These results support the current recommendation that high dietary fibre intake should be part of a healthy diet.

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## MOTS CLÉS

Fibres ;  
Maladies  
cardiovasculaires ;  
Mortalité ;  
Étude de cohortes  
prospectives ;  
Méta-analyses

## Résumé

**Justification.** — Des données convergentes sont en faveur du bénéfice des fibres diététiques, qui contribuent à améliorer le profil lipidique, à réduire le niveau de pression artérielle et à améliorer la sensibilité à l'insuline, mais la preuve de cette hypothèse reste à démontrer en particulier en ce qui concerne le rôle de la prise de fibres diététiques sur le pronostic, mortalité cardiovasculaire, en particulier chez les patients souffrant d'un cancer.

**Objectif.** — Évaluer de façon quantitative l'association entre la consommation des fibres diététiques et la mortalité cardiovasculaire et par cancer en utilisant une méthodologie standard, méta-analyse des études de cohortes prospectives.

**Méthode.** — Des études éligibles ont été identifiées au travers d'une recherche PubMed et Embase pour tous les articles jusqu'en septembre 2014 complétée par une recherche manuelle. L'estimation a été obtenue après ajustement sur les variables de confusion, afin de calculer un risque relatif global, l'IC 95 % en utilisant un modèle aléatoire.

**Résultats.** — Parmi les 15 études qui ont examiné l'association entre prise de fibres diététiques et mortalité cardiovasculaire, coronaire et par cancer, la valeur du risque relatif de la mortalité en comparant la consommation la plus élevée de fibres diététiques par rapport à la consommation la plus faible était respectivement de 0,77 (IC 95 % : 0,71–0,84), 0,76 (IC 95 % : 0,67–0,87) et 0,86 (IC 95 % : 0,79–0,93). Dans une méta-analyse dose-réponse, le risque relatif global pour l'augmentation des consommations de fibres diététiques de 10 g/j donne le résultat suivant pour le risque relatif : 0,91 (IC 95 % : 0,88–0,94) pour la mortalité cardiovasculaire 0,89 (IC 95 % : 0,85–0,93) pour la mortalité coronaire et 0,94 (IC 95 % : 0,91–0,97) pour la mortalité par cancer.

**Conclusion.** — Cette méta-analyse suggère que la consommation élevée de fibres diététiques est associée à une réduction significative de la mortalité cardiovasculaire et par cancer. Ces résultats sont en faveur d'une recommandation accrue de fibres diététiques faisant partie intégrante d'un régime préservant le niveau de santé.

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## Background

Cardiovascular disease (CVD) and cancer are the leading causes of death worldwide [1,2]. In particular, a large portion of premature deaths (death before the age of 75 years) were from CVD [3] and cancer [2], so we need to develop effective preventive strategies to reduce mortality from CVD and cancer. Several modifiable factors (i.e. smoking, physical activity, body mass index [BMI] and healthy dietary pattern) have been found to be related to CVD [1] and cancer [2]. Dietary fibre is rich in fruits, vegetables and whole grains, and consists of portions of plant foods that are edible and non-digestible by humans [4]. Dietary fibre intake is widely recognized as a part of a healthy diet, and higher intake is inversely associated with disease risk factors such as dyslipidaemia, obesity, hypertension and diabetes [5].

Accumulating evidence from epidemiological studies has shown that high intake of dietary fibre is inversely associated with the incidence of CVD (9% reduction in risk of CVD for an increase in dietary fibre of 7 g per day) [6]. Previous research into dietary fibre intake and CVD focused on the incidence of CVD as an endpoint. Recently, a meta-analysis of prospective cohort studies showed a significant inverse association between dietary fibre intake and all-cause mortality [7]. There is a growing body of epidemiological studies on dietary fibre intake and mortality from CVD, coronary heart disease (CHD) or all cancers [8–22], but a comprehensive assessment of dietary fibre intake and mortality from CVD, CHD and all cancers has not been carried out. Therefore, we conducted a systematic review and meta-analysis of prospective cohort studies to assess the risk of mortality from CVD, CHD and all cancers in relation to dietary fibre intake in the general population.

## Methods

### Literature search and study selection

We used the electronic PubMed and Embase databases to search for eligible studies published in English up to September 2014. The following key terms were used in searching: ("fibre" or "fiber") combined with ("cardiovascular disease" or "CVD" or "coronary disease" or "CHD" or "ischaemic disease" or "IHD" or "cancer" and "mortality" or "death"). Additionally, we reviewed the reference lists of the selected articles and published reviews to identify more studies. We selected studies according to following criteria: prospective cohort design; the exposure of interest was dietary fibre intake; the outcome of interest was mortality from CVD, CHD, ischaemic heart disease (IHD) or all cancers; and RRs with 95% confidence intervals (CIs) were provided. Studies that reported relative risks (RRs) from incidence of CVD, CHD, IHD or cancer were not included. Studies conducted in patients with specific diseases were excluded.

### Data extraction

Data extraction was conducted by two investigators (Y.K. and Y.J.), independently, according to the Meta-analysis of observational studies in epidemiology (MOOSE) guidelines [23], and any discrepancies were resolved by referencing original articles and having a further discussion. The following information was extracted from each included study: first author's last name; year of publication; cohort name; geographical region; follow-up period; number of cases; number of subjects or person-time; adjustment factors; RR and 95% CI for the association between various levels of fibre intake and mortality from CVD, CHD, IHD or all cancers. We used the RR from multivariate models with the greatest degree of adjustment for potential confounders if the study reported several RRs on this subject.

### Quality assessment of individual studies

Two investigators (Y.K. and Y.J.) independently assessed the quality of studies included in meta-analysis by applying the Newcastle-Ottawa Scale [24] for the following aspects: selection of study groups (0–4 points); comparability of groups (0–3 points); and ascertainment of outcome (0–6 points). Disagreements between the investigators on more than one score were resolved by consensus. Studies with a total of more than 10 points (out of 13) were considered to be of high quality, and those with 7–9 points were considered to be of good quality.

### Statistical analysis

To compute a pooled RR and its 95% CI for the highest versus lowest category of dietary fibre intake from original studies, we combined the natural logarithm of the RRs from each study, using the DerSimonian and Laird random-effects models, which incorporate both within- and between-study variations [25]. For studies that had not used the lowest category as a reference, the RRs and 95% CIs were recalculated. If studies provided RRs for both total dietary fibre intake and

dietary fibre intake from each food source, we included a RR for total dietary fibre intake in the main analysis. The RRs of dietary fibre intake from each food source were used in the subgroup analyses by source of fibre. The study-specific RRs as well as a pooled RR are presented as forest plots, where the size of data markers (squares) corresponds to the inverse of variance of the natural logarithm of RR from each study, and a diamond indicates a pooled RR. We assessed statistical heterogeneity among the studies using the Cochran  $Q$  statistic [26] and inconsistency was quantified by the  $I^2$  statistic [27].

To examine dose-response relationships across various categories of dietary fibre intake, we used a generalized least-squares trend estimation analysis based on the method developed by Greenland and Longnecker [28–30]. After estimating study-specific slopes from the correlated natural logarithm of the RRs across dietary fibre categories in each study [12,15,18,19,22], we combined the generalized least-squares trend-estimated study-specific slopes with studies that reported slope estimates [8–10,13,14,17,20,21] to derive an overall average slope. If the studies did not report mean or median levels of dietary fibre intake, we considered the midpoint of the category as a dose. The lowest and highest open-ended categories were assumed to have an equal interval of intake as the adjacent category. As two studies did not report the number of deaths or person-time across dietary fibre categories [11,16], a total of 13 studies were included in the dose-response meta-analysis for CHD mortality [10,14,15,17,19–22], CVD mortality [8–10,12,13,15,18,21] and all-cancer mortality [13,18].

To evaluate whether the pooled RR in the main analysis was affected markedly by a single study, we carried out a sensitivity analysis, excluding one study at a time. We also performed subgroup analyses stratified by sex, geographical region (Europe/USA/others), adjustment for covariates (age, BMI, smoking, alcohol and physical activity), source of dietary fibre (cereals/vegetables/fruits/legumes) and water solubility (soluble/insoluble), and conducted meta-regression analyses to test for variations in pooled RRs among the subgroups. Finally, publication bias was evaluated through a funnel plot as well as the statistical tests of Begg and Mazumdar [31] and Egger et al. [32]. A two-tailed  $P$ -value  $< 0.05$  was considered statistically significant. All statistical analyses were performed by using Stata/SE software, version 12.0 (Stata Corporation, College Station, TX, USA).

## Results

### Study characteristics

We identified a total of 15 studies from 12 cohorts that reported RRs of dietary fibre intake and mortality from CVD, CHD, IHD or cancers [8–22] (Fig. 1). The main characteristics of the studies included in meta-analysis are presented in Table 1. Six studies provided RRs of mortality from CVD only [8,9,11–13,18], four studies provided RRs of mortality from CHD only [16,19,20,22], two studies provided RRs of IHD only [14,17] and three studies provided RRs of mortality from both CVD and CHD [10,15,21]. Among the

**Table 1** Characteristics of prospective cohort studies included in the meta-analysis of dietary fibre intake and mortality from cardiovascular disease, coronary heart disease or all cancers.

| Reference                          | Study location           | Follow-up period (years) | Age at baseline (years) | Study size                   |  |  | RR (95% CI)   | Adjustment factors   |
|------------------------------------|--------------------------|--------------------------|-------------------------|------------------------------|--|--|---|--|
|                                    |                          |                          |                         | Subjects (n)                 | Deaths (n)                               | Fibre category (g/day)   |   |  |
| Khaw and Barrett-Connor, 1987 [17] | USA <sup>a</sup>         | 12                       | 50–79                   | All: 859<br>M: 356<br>F: 503 | IHD: all: 65<br>IHD: M: 42<br>IHD: F: 23 | Per 6<br><br>< 16 vs > 16  | All: 0.79 (0.63, 0.98)<br>M: 0.85 (0.64, 1.11)<br>F: 0.67 (0.45, 1.00)<br>M: 0.33 (0.14, 0.77)<br>F: 0.37 (0.11, 1.24)  | Age, systolic BP, cholesterol, fasting plasma glucose, BMI, cigarette smoking, plus oestrogen use (F only)<br>Age  |
| Pietinen et al., 1996 [19]         | Finland <sup>b</sup>     | 6.1                      | 50–69                   | M: 21,930                    | CHD: M: 635                              | 16.1<br>20.7<br>24.3<br>28.3<br>34.8   | 1.00<br>0.91 (0.72–1.15)<br>(0.83 0.64–1.06)<br>(0.72 0.55–0.93)<br>(0.73 0.56–0.95)  | Age, smoking, BMI, BP, intake of energy, alcohol and saturated fatty acids, education, physical activity, intake of beta-carotene, vitamin C and vitamin E   |
| Wolk et al., 1999 [22]             | USA <sup>c</sup>         | 10                       | 37–64                   | F: 68,782                    | CHD: F: 162                              | 11.5<br>14.3<br>16.4<br>18.8<br>22.9   | 1.00<br>0.83 (0.52, 1.31)<br>0.74 (0.46, 1.18)<br>0.73 (0.46, 1.16)<br>0.41 (0.23, 0.70)  | Age  |
| Bazzano et al., 2003 [10]          | USA <sup>d</sup>         | 19                       | 25–74                   | 9248                         | CHD: 668<br><br>CVD: 1198                | < 7.7 <sup>n</sup><br>7.7–11.0 <sup>n</sup><br>11.1–15.9 <sup>n</sup><br>> 15.9 <sup>n</sup><br>Per 10 <sup>n</sup><br>< 7.7 <sup>n</sup><br>7.7–11.0 <sup>n</sup><br>11.1–15.9 <sup>n</sup><br>> 15.9 <sup>n</sup><br>Per 10 <sup>n</sup> | 1.00<br>0.87 (0.68, 1.12)<br>0.79 (0.63, 0.99)<br>0.85 (0.65, 1.10)<br>0.92 (0.84, 1.01)<br>1.00<br>0.95 (0.78, 1.15)<br>0.84 (0.72, 0.97)<br>0.93 (0.77, 1.12)<br>0.97 (0.93, 1.02)<br>0.87 (0.71, 1.07) | Age, alcohol intake, BMI, smoking, education level, DM, physical activity, sex, race, systolic BP, serum total cholesterol concentration, saturated fat intake, total calorie intake   |
| Streppel et al., 2008 [20]         | Netherlands <sup>e</sup> | 40                       | 49 ± 6                  | M: 1373                      | CHD: M: 348                              | Per 10   | 0.87 (0.71, 1.07)   | Age, total intake of energy, intake of saturated fat, trans unsaturated fatty acids and cis polyunsaturated fatty acids, intake of alcohol, wine and fish, prescribed diet, number of cigarettes smoked, duration of cigarette smoking, cigar or pipe smoking, BMI, socioeconomic status |

Table 1 (Continue)

| Reference                 | Study location         | Follow-up period (years) | Age at baseline (years) | Study size             |                              |                                   | RR (95% CI)               | Adjustment factors  |
|---------------------------|------------------------|--------------------------|-------------------------|------------------------|------------------------------|-----------------------------------|---------------------------|---|
|                           |                        |                          |                         | Subjects (n)           | Deaths (n)                   | Fibre category (g/day)            |                           |   |
| Kaushik et al., 2009 [16] | Australia <sup>f</sup> | 13                       | ≥ 49                    | 2897                   | CHD: NR                      | Tertile 1: 3.0                    | 0.94 (0.73, 1.22)         | Age, sex, systolic BP, diastolic BP, use of antihypertensives, BMI, smoking status, educational qualifications, fair or poor self-rated health, history of MI and stroke, DM, energy intake   |
|                           |                        |                          |                         |                        |                              | Tertile 2: 6.5<br>Tertile 3: 11.0 | 1.22 (0.95, 1.58)<br>1.00 |   |
| Eshak et al., 2010 [15]   | Japan <sup>g</sup>     | 14.3                     | 40–79                   | M: 23,119<br>F: 35,611 | CVD: M: 1063<br>CVD: F: 1017 | Q1: M < 7.8                       | M: 1.00                   | Age, BMI, history of hypertension, history of DM, alcohol intake, smoking, education level, hours of exercise, hours of walking, perceived mental stress, sleep, intake of fish, saturated fatty acids, (n-3) fatty acids, sodium, folate and vitamin E |
|                           |                        |                          |                         |                        |                              | Q1: F < 8.5                       | F: 1.00                   |   |
|                           |                        |                          |                         |                        |                              | Q2: M: 7.8–9.4                    | M: 1.06 (0.92, 1.22)      |   |
|                           |                        |                          |                         |                        |                              | Q2: F: 8.5–9.9                    | F: 1.21 (0.94, 1.44)      |   |
|                           |                        |                          |                         |                        |                              | Q3: M: 9.5–10.8                   | M: 0.92 (0.80, 1.06)      |   |
|                           |                        |                          |                         |                        |                              | Q3: F: 10.0–11.1                  | F: 1.06 (0.82, 1.19)      |   |
|                           |                        |                          |                         |                        |                              | Q4: M: 10.9–12.6                  | M: 0.86 (0.55, 1.55)      |   |
|                           |                        |                          |                         |                        |                              | Q4: F: 11.2–12.7                  | F: 0.85 (0.69, 0.99)      |   |
|                           |                        |                          |                         |                        |                              | Q5: M > 12.6                      | M: 0.83 (0.63, 1.09)      |   |
|                           |                        |                          |                         |                        |                              | Q5: F > 12.7                      | F: 0.82 (0.57, 0.97)      |   |
|                           |                        |                          |                         |                        |                              |                                   |                           |   |
|                           |                        |                          | F: 1.00                 |                        |                              |                                   |                           |   |
|                           |                        |                          | M: 0.83 (0.62, 1.12)    |                        |                              |                                   |                           |   |
|                           |                        |                          | F: 1.03 (0.76, 1.48)    |                        |                              |                                   |                           |   |
|                           |                        |                          | M: 0.69 (0.51, 0.93)    |                        |                              |                                   |                           |   |
|                           |                        |                          | F: 0.86 (0.61, 1.13)    |                        |                              |                                   |                           |   |
|                           |                        |                          | M: 0.59 (0.43, 0.81)    |                        |                              |                                   |                           |   |
|                           |                        |                          | F: 0.81 (0.52, 0.99)    |                        |                              |                                   |                           |   |
|                           |                        |                          | M: 0.81 (0.61, 1.09)    |                        |                              |                                   |                           |   |
|                           |                        |                          | F: 0.80 (0.57, 0.97)    |                        |                              |                                   |                           |   |

| Reference                 | Study location         | Follow-up period (years) | Age at baseline (years) | Study size         |                            |  | RR (95% CI)  | Adjustment factors   |
|---------------------------|------------------------|--------------------------|-------------------------|--------------------|----------------------------|--|--|--|
|                           |                        |                          |                         | Subjects (n)       | Deaths (n)                 | Fibre category (g/day)   |  |  |
| Buyken et al., 2010 [12]  | Australia <sup>f</sup> | 13                       | ≥ 49                    | M: 1245<br>F: 1490 | CVD: M: 151<br>CVD: F: 109 | Tertile 1: M: 18.4<br>Tertile 1: F: 19.7<br>Tertile 2: M: 25.9<br>Tertile 2: F: 24.8<br>Tertile 3: M: 36.4<br>Tertile 3: F: 36.2 | M: 1.00<br>F: 1.00<br>M: 0.74 (0.49, 1.13)<br>F: 0.90 (0.55, 1.46)<br>M: 0.84 (0.53, 1.34)<br>F: 0.88 (0.53, 1.46) | Age, energy intake, total fibre residuals, dietary glycaemic index residuals, total fat intake, whether underweight, current smoking, use of corticosteroid drugs at baseline  |
| Baer et al., 2011 [9]     | USA <sup>e</sup>       | 18                       | 52.5                    | 50,112             | CVD: 1026                  | Per 4  | 0.82 (0.69, 0.97)  | Age, BMI, weight change since age 18 years, height, smoking status, smoking amount/duration, physical activity, alcohol intake, nut consumption, polyunsaturated fat intake, glycaemic load, dietary cholesterol, systolic BP, use of antihypertensives, personal history of DM, parental MI before age 60 years, time since menopause |
| Akbaraly et al., 2011 [8] | UK <sup>h</sup>        | 18                       | 49.5 (39–63)            | 6926               | CVD: 141                   | Per 4.5  | 0.91 (0.74, 1.12)  | Age, modified total AHEI score excluding the component considered in the analysis, sex, ethnicity, occupational grade, marital status, smoking status, total energy intake, physical activity, BMI categories, prevalent CVD, type 2 DM, hypertension, dyslipidaemia, metabolic syndrome, inflammatory markers                         |

Table 1 (Continue)

| Reference                | Study location       | Follow-up period (years) | Age at baseline (years) | Study size               |                              | Fibre category (g/day) | RR (95% CI)          | Adjustment factors  |
|--------------------------|----------------------|--------------------------|-------------------------|--------------------------|------------------------------|------------------------|----------------------|---|
|                          |                      |                          |                         | Subjects (n)             | Deaths (n)                   |                        |                      |   |
| Park et al., 2011 [18]   | USA <sup>i</sup>     | 9                        | 50–71                   | M: 219,123<br>F: 168,999 | CVD: M: 5248<br>CVD: F: 2147 | Q1: M: 12.6            | M: 1.00              | Age, race/ethnicity, education, marital status, health status, BMI, physical activity, smoking status, time since quitting, smoking dose, intake of alcohol, red meat and total fruit/vegetables, total energy intake     |
|                          |                      |                          |                         |                          |                              | Q1: F: 10.8            | F: 1.00              |   |
|                          |                      |                          |                         |                          |                              | Q2: M: 16.4            | M: 0.89 (0.82, 0.96) |   |
|                          |                      |                          |                         |                          |                              | Q2: F: 14.3            | F: 0.85 (0.75, 0.96) |   |
|                          |                      |                          |                         |                          |                              | Q3: M: 19.4            | M: 0.82 (0.75, 0.90) |   |
|                          |                      |                          |                         |                          |                              | Q3: F: 17.0            | F: 0.78 (0.68, 0.90) |   |
|                          |                      |                          |                         |                          |                              | Q4: M: 22.9            | M: 0.80 (0.73, 0.89) |   |
|                          |                      |                          |                         |                          |                              | Q4: F: 20.1            | F: 0.72 (0.61, 0.84) |   |
|                          |                      |                          |                         |                          |                              | Q5: M: 29.4            | M: 0.76 (0.68, 0.85) |   |
|                          |                      |                          |                         |                          |                              | Q5: F: 25.8            | F: 0.66 (0.55, 0.79) |   |
|                          |                      |                          |                         |                          |                              | Cancer: M: 8244        | M: 1.00              |   |
|                          |                      |                          |                         |                          |                              | Cancer: F: 4927        | F: 1.00              |   |
|                          |                      |                          |                         |                          |                              | Q2: M: 16.4            | M: 0.98 (0.91, 1.04) |   |
|                          |                      |                          |                         |                          |                              | Q2: F: 14.3            | F: 0.93 (0.85, 1.01) |   |
|                          |                      |                          |                         |                          |                              | Q3: M: 19.4            | M: 0.94 (0.87, 1.01) |   |
| Q3: F: 17.0              | F: 0.88 (0.80, 0.97) |                          |                         |                          |                              |                        |                      |   |
| Q4: M: 22.9              | M: 0.87 (0.81, 0.94) |                          |                         |                          |                              |                        |                      |   |
| Q4: F: 20.1              | F: 0.88 (0.79, 0.98) |                          |                         |                          |                              |                        |                      |   |
| Q5: M: 29.4              | M: 0.83 (0.76, 0.92) |                          |                         |                          |                              |                        |                      |   |
| Q5: F: 25.8              | F: 0.96 (0.85, 1.08) |                          |                         |                          |                              |                        |                      |   |
| Crowe et al., 2012 [14]  | Europe <sup>j</sup>  | 11.5                     | 40–85                   | 306,331                  | IHD: 2381                    | < 17.5                 | 1.00                 | Age, alcohol intake, BMI, physical activity, marital status, highest education level, current employment, hypertension, hyperlipidaemia, angina pectoris, DM, polyunsaturated to saturated fat ratio, total energy intake |
|                          |                      |                          |                         |                          |                              | 17.5–22.4              | 0.80 (0.71, 0.89)    |   |
|                          |                      |                          |                         |                          |                              | 22.5–27.4              | 0.78 (0.69, 0.89)    |   |
|                          |                      |                          |                         |                          |                              | ≥ 27.5                 | 0.77 (0.66, 0.89)    |   |
|                          |                      |                          |                         |                          |                              | Per 10                 | 0.85 (0.73, 0.99)    |   |
| Chuang et al., 2012 [13] | Europe <sup>k</sup>  | 12.7                     | 25~70                   | M: 130,564               | CVD: M: 2489                 | < 16.4                 | M: 1.00              | Age, education, smoking, alcohol intake, BMI, physical activity, total energy intake, plus anytime use of menopausal hormone therapy (F only)   |
|                          |                      |                          |                         |                          |                              |                        |                      |   |

| Table 1 (Continue)  |                |                          |                         |                                    |              |  |   |
|---|----------------|--------------------------|-------------------------|------------------------------------|--------------|--|---|
| Reference   | Study location | Follow-up period (years) | Age at baseline (years) | Study size                         |              | RR (95% CI)  | Adjustment factors  |
|   |                |                          |                         | Subjects (n)                       | Deaths (n)   |  |   |
|   |                |                          |                         | F: 322,153                         | CVD: F: 2115 | F: 1.00  |   |
|   |                |                          |                         |                                    |              | 16.4 to <20.1  | M: 0.91 (0.79, 1.03)<br>F: 0.83 (0.72, 0.95)  |
|   |                |                          |                         |                                    |              | 20.1 to <23.6  | M: 0.82 (0.71, 0.94)<br>F: 0.80 (0.69, 0.93)  |
|   |                |                          |                         |                                    |              | 23.6 to <28.5  | M: 0.81 (0.70, 0.94)<br>F: 0.73 (0.61, 0.86)  |
|   |                |                          |                         |                                    |              | ≥ 28.5   | M: 0.83 (0.71, 0.98)<br>F: 0.67 (0.55, 0.82)  |
|   |                |                          |                         |                                    |              | Per 10   | M: 0.84 (0.74, 0.94)<br>F: 0.79 (0.67, 0.94)  |
|   |                |                          |                         | Cancer: M: 4039<br>Cancer: F: 5575 | < 16.4       | M: 1.00<br>F: 1.00   |   |
|   |                |                          |                         |                                    |              | 16.4 to <20.1  | M: 0.93 (0.84, 1.03)<br>F: 0.88 (0.81, 0.95)  |
|   |                |                          |                         |                                    |              | 20.1 to <23.6  | M: 0.84 (0.75, 0.93)<br>F: 0.92 (0.84, 1.00)  |
|   |                |                          |                         |                                    |              | 23.6 to <28.5  | M: 0.92 (0.82, 1.03)<br>F: 0.90 (0.81, 0.99)  |
|   |                |                          |                         |                                    |              | ≥ 28.5   | M: 0.82 (0.72, 0.93)<br>F: 0.82 (0.73, 0.92)  |
|   |                |                          |                         |                                    |              | Per 10   | M: 0.91 (0.84, 0.99)<br>F: 0.86 (0.78, 0.95)  |
| Threapleton UK <sup>1</sup><br>et al., 2013<br><a href="#">[21]</a> |                | 14.3                     | 51.8                    | F: 31,036                          | CHD: F: 113  | Q1: 21.0<br>Q2: 30.0<br>Q3: 36.8<br>Q4: 44.8<br>Q5: 63.0<br>Per 11 | 1.00<br>1.18 (0.68, 2.03)<br>0.82 (0.43, 1.58)<br>0.99 (0.52, 1.86)<br>0.72 (0.28, 1.83)<br>0.96 (0.73, 1.26) |
|   |                |                          |                         |                                    | CVD: F: 230  | Q1: 21.0<br>Q2: 30.0<br>Q3: 36.8<br>Q4: 44.8<br>Q5: 63.0<br>Per 11 | 1.00<br>0.84 (0.56, 1.25)<br>0.62 (0.39, 0.98)<br>0.72 (0.46, 1.13)<br>0.61 (0.32, 1.17)<br>0.91 (0.76, 1.08) |



**Table 1** (Continue)

| Reference                       | Study location     | Follow-up period (years) | Age at baseline (years) | Study size   |             |                        | RR (95% CI)       | Adjustment factors  |
|---------------------------------|--------------------|--------------------------|-------------------------|--------------|-------------|------------------------|-------------------|---|
|                                 |                    |                          |                         | Subjects (n) | Deaths (n)  | Fibre category (g/day) |                   |   |
| Buil-Cosiales et al., 2014 [11] | Spain <sup>m</sup> | 5.9 years                | M (55–75)<br>F (60–75)  | 7216         | CVD: 103    | Q1: 17                 | 1.00              | Age, sex, smoking status, DM, BMI, baseline systolic and diastolic arterial BP, intervention group use of statins, alcohol intake, educational level, physical activity, total energy intake, plus stratification by recruitment centre |
|                                 |                    |                          |                         |              |             | Q2: 21                 | 0.55 (0.31, 0.95) |   |
|                                 |                    |                          |                         |              |             | Q3: 24                 | 0.57 (0.32, 1.02) |   |
|                                 |                    |                          |                         |              |             | Q4: 28                 | 0.65 (0.35, 1.19) |   |
|                                 |                    |                          |                         |              |             | Q5: 35                 | 0.46 (0.23, 0.93) |   |
|                                 |                    |                          |                         |              | Cancer: 169 | Q1: 17                 | 1.00              |   |
|                                 |                    |                          |                         |              |             | Q2: 21                 | 0.67 (0.42, 1.06) |   |
|                                 |                    |                          |                         |              |             | Q3: 24                 | 0.78 (0.50, 1.23) |   |
|                                 |                    |                          |                         |              |             | Q4: 28                 | 0.59 (0.35, 0.98) |   |
|                                 |                    |                          |                         |              |             | Q5: 35                 | 0.69 (0.42, 1.14) |   |

AHEI: alternative healthy eating index; BMI: body mass index; BP: blood pressure; CI: confidence interval; CVD: cardiovascular disease; DM: diabetes mellitus; F: females; IHD: ischaemic heart disease; M: males; METs: metabolic equivalents; MI: myocardial infarction; NR: not reported; RR: relative risk.

<sup>a</sup> Southern California population-based cohort.

<sup>b</sup> Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study.

<sup>c</sup> Nurses' Health Study.

<sup>d</sup> National Health And Nutrition Examination Survey (NHANES) I epidemiological follow-up study.

<sup>e</sup> Zutphen Study.

<sup>f</sup> Blue Mountains Eye Study.

<sup>g</sup> Japan Collaborative Cohort Study.

<sup>h</sup> Whitehall II cohort.

<sup>i</sup> National Institutes of Health-American Association of Retired Persons (NIH-AARP) Diet & Health Study.

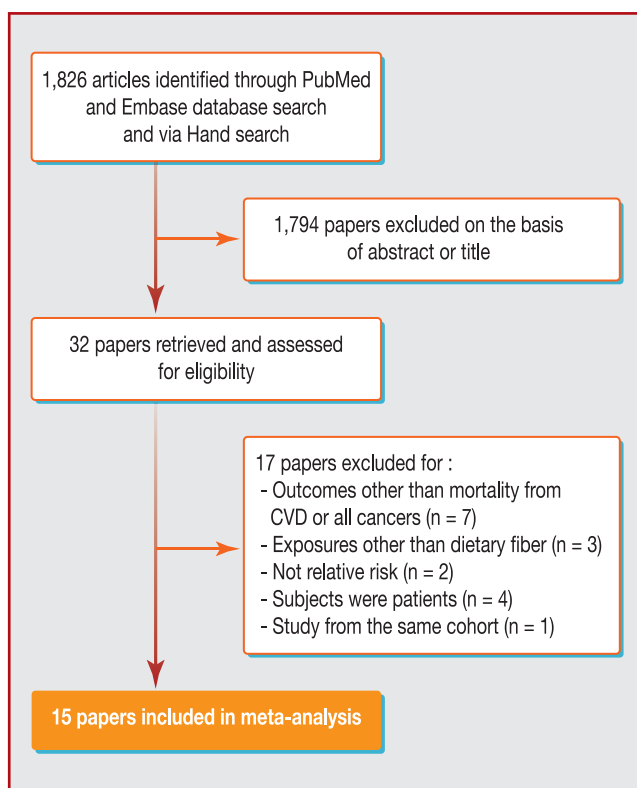
<sup>j</sup> European Prospective Investigation into Cancer and Nutrition (EPIC)-Heart.

<sup>k</sup> EPIC.

<sup>l</sup> UK Women's Cohort Study.

<sup>m</sup> Prevencion con Dieta Mediterranea (PREDIMED) Study.

<sup>n</sup> g/1735 kcal.



**Figure 1.** Process used to select prospective cohort studies for a meta-analysis of the association between dietary fibre intake and mortality from cardiovascular disease (CVD) and all cancers.

15 studies, only three studies reported RRs of mortality from all cancers [11,13,18]. By geographical region, seven studies were conducted in Europe [8,11,13,14,19–21], five in the USA [9,10,17,18,22], two in Australia [12,16] and one in Japan [15]. The follow-up periods ranged from 5.9 to 40 years; the mean follow-up time was 14.5 years. The age of the subjects ranged from 20 to 85 years. Most of the studies assessed dietary fibre intake using food frequency questionnaires [8,9,11–16,18,19,22], while two studies used 24-hour dietary recall [10,17] and one study used a cross-check dietary history method [20]. One study from the UK assessed dietary fibre intake using both food frequency questionnaires and a 7-day food diary [21]. All of the 15 studies adjusted for age and 13 studies adjusted for BMI [8–11,13–21] or smoking [8–13,15–21]. Ten studies adjusted for alcohol intake [9–11,13–15,18–21] or physical activity [8–11,13–15,18,19,21]. With regard to quality assessment, the mean quality assessment score was 10 (range 8–13). Six studies had more than 10 points, indicating high quality [10,12,15–17,20]; the other nine studies had 8 or 9 points, indicating good quality [8,9,11,13,14,18,19,21,22].

## Highest versus lowest dietary fibre intake

### Dietary fibre intake and mortality from cardiovascular disease

Seven studies were included in the analysis for the highest versus lowest categories of dietary fibre intake

[10–13,15,18,21]. The pooled RR of CVD mortality was 0.77 (95% CI: 0.71–0.84), with no significant heterogeneity among the studies ( $P=0.33$ ,  $I^2=12.5\%$ ) (Fig. 2A). When we conducted a sensitivity analysis that excluded one study at a time, the pooled RRs ranged from 0.75 (95% CI: 0.69, 0.80) to 0.79 (95% CI: 0.73, 0.86) (data not shown). The results of subgroup analyses by study characteristic are summarized in Table 2. There were no significant differences by sex, geographical region or water solubility ( $P: 0.1$  for all comparisons). When the analysis was limited to five studies that adjusted for age, BMI, smoking, alcohol and physical activity, the inverse association was slightly attenuated (RR=0.81, 95% CI: 0.72–0.92). By source of dietary fibre, cereal fibre intake was strongly associated with reduced mortality from CVD (RR=0.77, 95% CI: 0.71–0.82), and dietary fibre intake from legumes also showed an inverse association (RR=0.89, 95% CI: 0.82–0.98). On the other hand, vegetable fibre (RR=0.95, 95% CI: 0.89–1.02) and fruit fibre (RR=0.96, 95% CI: 0.83–1.11) showed no significant inverse associations. The differences by source of dietary fibre were all statistically significant ( $P \leq 0.01$  for all comparisons).

### Dietary fibre intake and mortality from coronary or ischaemic heart disease

Eight studies that provided data on dietary fibre intake and CHD mortality [10,15,16,19,21,22] or IHD mortality [14,17] were included in the analysis for the highest versus lowest categories of dietary fibre intake. The pooled RR of CHD or IHD mortality was 0.76 (95% CI: 0.67–0.87), with no significant heterogeneity ( $P=0.10$ ,  $I^2=40.1\%$ ) (Fig. 2B). A sensitivity analysis showed that the pooled RRs ranged from 0.74 (95% CI: 0.64–0.85) to 0.79 (95% CI: 0.71–0.88) (data not shown). There were no significant differences by sex, geographical region, adjustment for covariates, source of dietary fibre or water solubility ( $P>0.2$  for all comparisons) (Table 2).

### Dietary fibre intake and mortality from all cancers

Three studies reported data on dietary fibre intake and all-cancer mortality [11,13,18]. The pooled RR was 0.86 (95% CI: 0.79–0.93), with no significant heterogeneity ( $P=0.14$ ,  $I^2=46\%$ ) (Fig. 2C). A sensitivity analysis showed that the pooled RRs ranged from 0.82 (95% CI: 0.77–0.88) to 0.87 (95% CI: 0.75–0.99). There were no significant differences by sex or geographical region ( $P>0.4$  for all comparisons) (data not shown).

## Dose-response meta-analysis

### Dietary fibre intake and mortality from cardiovascular disease

Eight studies were included in the dose-response meta-analysis of dietary fibre intake and CVD mortality [8–10,12,13,15,18,21]. The pooled RR for a 10 g/day increment in dietary fibre intake was 0.91 (95% CI: 0.88–0.94), with no significant heterogeneity ( $P=0.15$ ,  $I^2=30.8\%$ ) (Fig. 3A). A sensitivity analysis that was carried out by omitting one study at a time showed the pooled RRs ranging from 0.90 (95% CI: 0.87–0.93) to 0.91 (95% CI: 0.89–0.94) (data

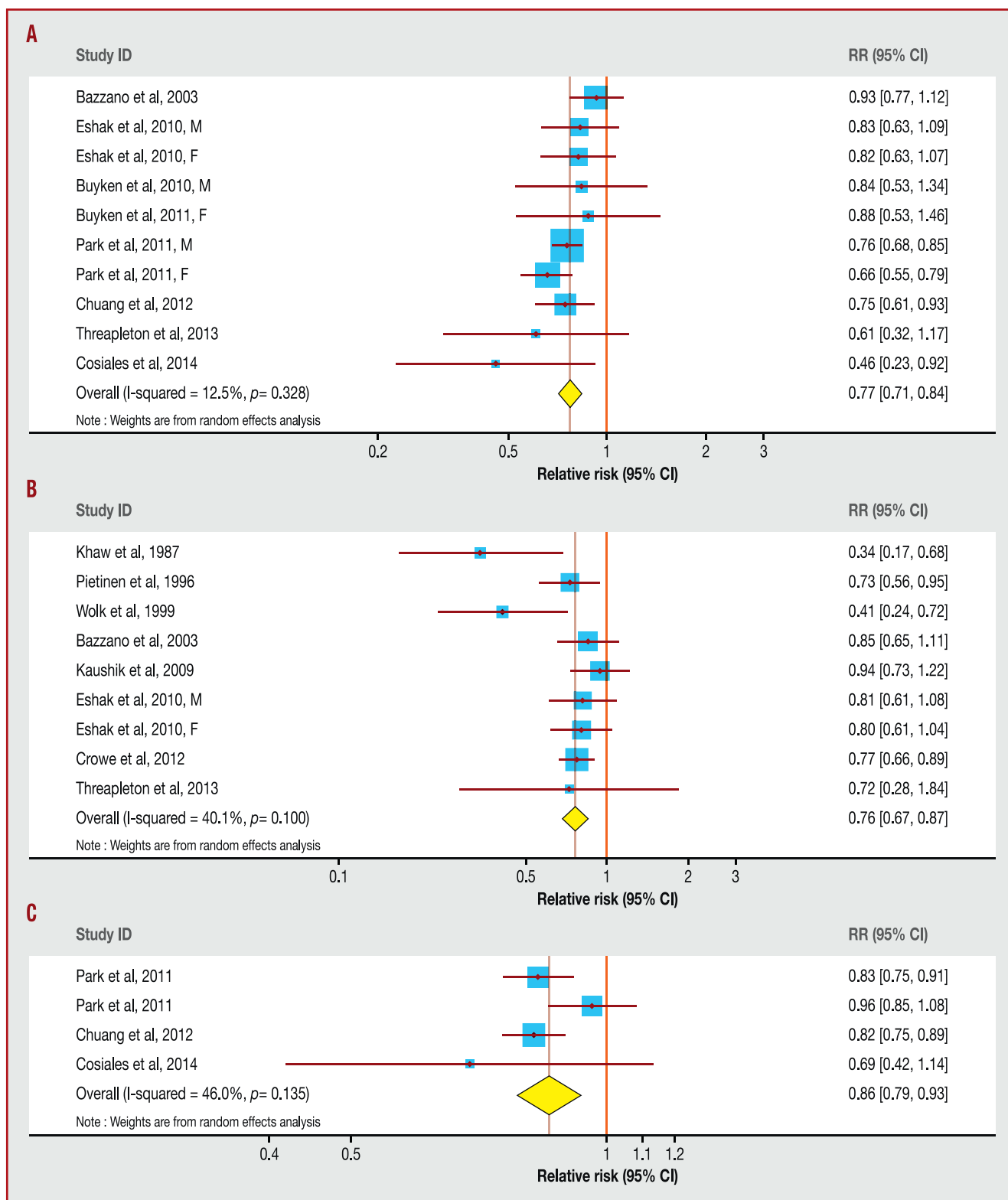
**Table 2** Pooled relative risks of mortality from cardiovascular disease and coronary heart disease according to dietary fibre intake in a meta-analysis of prospective cohort studies.

| Variable  | CVD mortality  |      |            |                         | CHD mortality  |      |            |                         |
|---|----------------|------|------------|-------------------------|----------------|------|------------|-------------------------|
|   | No. of studies | RR   | 95% CI     | <i>P</i> for difference | No. of studies | RR   | 95% CI     | <i>P</i> for difference |
| <i>High versus low fibre intake</i>                             |                |      |            |                         |                |      |            |                         |
| All studies   | 7              | 0.77 | 0.71, 0.84 |                         | 8              | 0.76 | 0.67, 0.87 |                         |
| Sex   |                |      |            |                         |                |      |            |                         |
| Male  | 4              | 0.79 | 0.72, 0.86 | 0.14                    | 3              | 0.70 | 0.52, 0.95 | 0.71                    |
| Female  | 5              | 0.70 | 0.62, 0.78 |                         | 4              | 0.60 | 0.39, 0.92 |                         |
| Region  |                |      |            |                         |                |      |            |                         |
| Europe  | 3              | 0.71 | 0.59, 0.86 |                         | 3              | 0.76 | 0.67, 0.86 |                         |
| USA   | 2              | 0.77 | 0.65, 0.91 | 0.46 <sup>a</sup>       | 3              | 0.52 | 0.28, 0.98 | 0.40 <sup>a</sup>       |
| Others  | 2              | 0.83 | 0.70, 0.98 | 0.27 <sup>a</sup>       | 2              | 0.85 | 0.73, 1.00 | 0.53 <sup>a</sup>       |
| Adjustment for age, BMI, smoking, alcohol and physical activity |                |      |            |                         |                |      |            |                         |
| Yes   | 5              | 0.81 | 0.72, 0.92 | 0.245                   | 4              | 0.79 | 0.69, 0.91 | 0.65                    |
| No  | 2              | 0.74 | 0.67, 0.81 |                         | 4              | 0.65 | 0.46, 0.91 |                         |
| Source of fibre   |                |      |            |                         |                |      |            |                         |
| Cereals   | 3              | 0.77 | 0.71, 0.82 |                         | 5              | 0.83 | 0.76, 0.92 |                         |
| Vegetables  | 3              | 0.95 | 0.89, 1.02 | 0.001 <sup>b</sup>      | 4              | 0.90 | 0.79, 1.02 | 0.46 <sup>b</sup>       |
| Fruits  | 3              | 0.96 | 0.83, 1.11 | < 0.001 <sup>b</sup>    | 4              | 0.68 | 0.49, 0.95 | 0.34 <sup>b</sup>       |
| Legumes   | 2              | 0.89 | 0.82, 0.98 | 0.01 <sup>b</sup>       | 1              | 1.33 | 0.65, 2.72 | 0.29 <sup>b</sup>       |
| Water solubility  |                |      |            |                         |                |      |            |                         |
| Soluble   | 2              | 0.85 | 0.75, 0.96 | 0.4                     | 4              | 0.73 | 0.62, 0.85 | 0.54                    |
| Insoluble   | 2              | 0.77 | 0.66, 0.90 |                         | 3              | 0.66 | 0.52, 0.83 |                         |
| <i>10 g/day increment in fibre intake</i>                       |                |      |            |                         |                |      |            |                         |
| All studies   | 8              | 0.91 | 0.88, 0.94 |                         | 8              | 0.89 | 0.85, 0.93 |                         |
| Sex   |                |      |            |                         |                |      |            |                         |
| Male  | 4              | 0.91 | 0.88, 0.94 | 0.82                    | 4              | 0.89 | 0.84, 0.95 | 0.96                    |
| Female  | 5              | 0.90 | 0.84, 0.97 |                         | 4              | 0.85 | 0.74, 0.98 |                         |
| Region  |                |      |            |                         |                |      |            |                         |
| Europe  | 3              | 0.89 | 0.78, 1.01 |                         | 4              | 0.92 | 0.87, 0.97 |                         |
| USA   | 3              | 0.89 | 0.86, 0.93 | 0.83 <sup>a</sup>       | 3              | 0.87 | 0.79, 0.96 | 0.40 <sup>a</sup>       |
| Others  | 2              | 0.95 | 0.89, 1.01 | 0.37 <sup>a</sup>       | 1              | 0.80 | 0.70, 0.92 | 0.14 <sup>a</sup>       |
| Adjustment for age, BMI, smoking, alcohol and physical activity |                |      |            |                         |                |      |            |                         |
| Yes   | 5              | 0.91 | 0.85, 0.96 | 0.86                    | 5              | 0.91 | 0.86, 0.96 | 0.12                    |
| No  | 3              | 0.90 | 0.87, 0.93 |                         | 3              | 0.83 | 0.75, 0.91 |                         |
| <i>5 g/day increment in fibre intake</i>                        |                |      |            |                         |                |      |            |                         |
| Source of fibre   |                |      |            |                         |                |      |            |                         |
| Cereals   | 4              | 0.94 | 0.90, 0.98 |                         | 5              | 0.95 | 0.89, 1.01 |                         |
| Vegetables  | 3              | 0.92 | 0.89, 0.95 | 0.57 <sup>b</sup>       | 5              | 0.92 | 0.86, 0.98 | 0.43 <sup>b</sup>       |
| Fruits  | 3              | 0.96 | 0.90, 1.01 | 0.5 <sup>b</sup>        | 5              | 0.89 | 0.73, 1.10 | 0.92 <sup>b</sup>       |
| Legumes   | 1              | 0.87 | 0.68, 1.13 | 0.63 <sup>b</sup>       | 2              | 0.90 | 0.78, 1.03 | 0.56 <sup>b</sup>       |
| Water solubility  |                |      |            |                         |                |      |            |                         |
| Soluble   | 3              | 0.87 | 0.74, 1.02 | 0.8                     | 4              | 0.83 | 0.71, 0.98 | 0.93                    |
| Insoluble   | 2              | 0.92 | 0.85, 1.00 |                         | 3              | 0.83 | 0.71, 0.98 |                         |

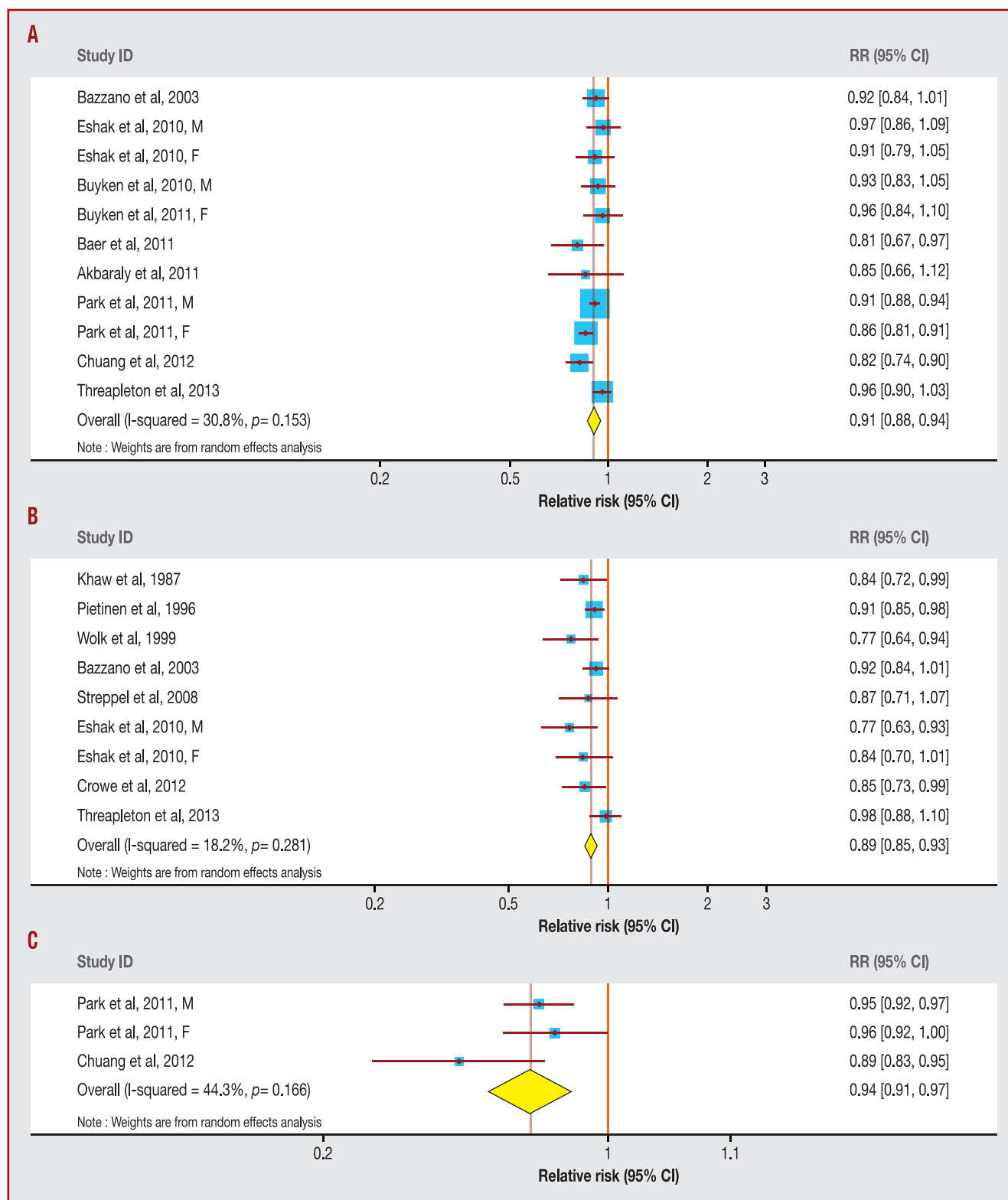
BMI: body mass index; CHD: coronary heart disease; CI: confidence interval; CVD: cardiovascular disease; RR: relative risk.

<sup>a</sup> *P*-value for the difference in RRs (when all geographical regions – Europe, USA and others – were included in the meta-regression model, simultaneously).

<sup>b</sup> *P*-value for the difference in RRs (when all sources of dietary fibre – cereals, vegetables, fruits and legumes – were included in the meta-regression model, simultaneously).



**Figure 2.** Forest plot of prospective cohort studies of (A) cardiovascular disease mortality, (B) coronary heart disease mortality and (C) all-cancer mortality for the highest versus lowest category of dietary fibre intake, using a random-effects model. CI: confidence interval; F: females; M: males; RR: relative risk.



**Figure 3.** Forest plot of prospective cohort studies of (A) cardiovascular disease mortality, (B) coronary heart disease mortality and (C) all-cancer mortality for an increment of 10 g/day in dietary fibre intake, using a random-effects model. CI: confidence interval; F: females; M: males; RR: relative risk.

not shown). The differences by sex, geographical region, adjustment for covariates, source of dietary fibre or water solubility were not statistically significant ( $P > 0.3$  for all comparisons).

### Dietary fibre intake and mortality from coronary or ischaemic heart disease

Eight studies reported RRs of dietary fibre intake and mortality from CHD or IHD [10,14,15,17,19–22]. The pooled RR for a 10 g/day increment in dietary fibre intake was 0.89 (95% CI: 0.85–0.93), and there was no significant heterogeneity among the studies ( $P = 0.28$ ,  $I^2 = 18.2\%$ ) (Fig. 3B). A sensitivity analysis showed that the pooled RRs ranged from 0.88 (95% CI: 0.83–0.93) to 0.90 (95% CI: 0.86–0.94) (data not shown). The pooled RRs did not differ by sex, geographical region, adjustment for covariates, source of dietary fibre or water solubility ( $P > 0.1$  for all comparisons) (Table 2).

### Dietary fibre intake and mortality from all cancers

Two studies provided RRs of dietary fibre intake and all-cancer mortality [13,18]. The pooled RR for a 10 g/day increment in dietary fibre intake was 0.94 (95% CI: 0.91–0.97), with no significant heterogeneity ( $P = 0.17$ ,  $I^2 = 44.3\%$ ) (Fig. 3C). A sensitivity analysis showed that the pooled RRs ranged from 0.93 (95% CI: 0.87–0.98) to 0.95 (95% CI: 0.93–0.97). The differences by sex or geographical region were not statistically significant ( $P > 0.3$  for all comparisons) (data not shown).

### Publication bias

There was no indication of publication bias for the meta-analysis of the highest category of dietary fibre intake versus the lowest (Begg and Mazumdar:  $P > 0.1$ ; Egger et al.:  $P > 0.1$  for mortality from CVD, CHD and all cancers). For the dose-response meta-analysis of CVD and all-cancer mortality, there was no evidence of publication bias (Begg and Mazumdar:  $P > 0.6$ ; Egger et al.:  $P > 0.4$ ). For the dose-response meta-analysis of CHD mortality, however, there was some evidence of publication bias based on the test of Egger et al. ( $P = 0.03$ ), but not the test of Begg and Mazumdar ( $P = 0.12$ ).

## Discussion

In the current systematic review and meta-analysis, the association between dietary fibre intake and mortality from CVD, CHD and all cancers was explored through 15 prospective cohort studies with 1,409,014 subjects. We found that dietary fibre intake is inversely associated with mortality from CVD, CHD and all cancers. Overall, participants who had a high intake of dietary fibre (mean  $\sim 29.6$  g/day for CVD mortality,  $\sim 23.2$  g/day for CHD mortality and  $\sim 30.4$  g/day for all-cancer mortality) had a reduction in CVD mortality by 23%, CHD mortality by 24% and all-cancer mortality by 14%, respectively, compared with those who had a low intake of dietary fibre (mean  $\sim 14.0$  g/day for CVD mortality,  $\sim 12.5$  g/day for CHD mortality and  $\sim 15$  g/day for all-cancer mortality). The dose-response meta-analyses also indicated that a 10 g/day increment in dietary fibre intake

was inversely associated with a reduction in mortality from CVD by 9%, from CHD by 11% and from all cancers by 6%. There was no significant heterogeneity among the studies. Similar inverse associations were found by sex, geographical region, water solubility and adjustment factors (age, BMI, smoking, alcohol and physical activity). By source of dietary fibre, cereal fibre consistently showed a significant inverse association with CVD mortality both in the highest versus lowest analysis and in a dose-response analysis. By water solubility of dietary fibre, similar inverse associations were found, but the number of studies included in the analysis was limited.

Accumulating evidence from epidemiological studies suggests that higher dietary fibre intake is associated with a reduced risk of CVD [6] and CHD [6,33,34]. These studies reported that cereal fibre had a stronger inverse association with risks of CVD [6] and CHD [34] than the other sources of fibre, and these findings are consistent with our results. The one meta-analysis that mainly examined the incidence of CHD and dietary fibre intake also reported some results for CHD death as an outcome (i.e. a 27% lower risk of CHD death in people who had a high dietary fibre intake versus those who had a low intake) [34]. Our present meta-analysis of dietary fibre intake and CVD and CHD mortality included studies that the previous meta-analysis did not include [8,9,11–14,16–18,21].

Several studies have also shown an inverse association between high dietary fibre intake and risk of gastric [35], breast [36] and pancreatic cancer [37]. Furthermore, one study reported that a 10 g/day increment in dietary fibre intake was inversely associated with a reduction in colorectal cancer mortality by 33% [38].

An inverse association between dietary fibre intake and diseases such as CVD or cancer may be explained by several mechanisms. Dietary fibre has some beneficial effects on cardiovascular health by lowering serum cholesterol concentrations via an increase in the excretion of bile acids in faeces [39] and inhibiting fatty acid synthesis in the liver through the production of short-chain fatty acids resulting from fermentation [40]. Dietary fibre may also help to control body weight because of its slower digestion and greater satiety [41]. One meta-analysis reported that dietary fibre intake reduces systolic and diastolic blood pressure [42] by decreasing body weight [43], which could be a risk factor for hypertension and obesity. In addition, high consumption of dietary fibre has been associated with a reduced risk of type 2 diabetes by increasing insulin sensitivity [44]. As hypercholesterolaemia, hypertension, obesity and type 2 diabetes are all major risk factors for CVD [3], and dietary fibre is inversely associated with inflammatory markers [45] that are important for the progression of CVD and cancer, high dietary fibre intake may decrease deaths from CVD or cancer by slowing down the progression of these diseases.

### Study strengths and limitations

The present meta-analysis has several strengths. To the best of our knowledge, this is the first comprehensive meta-analysis of dietary fibre intake and CVD, CHD and all-cancer mortality that included a large number of subjects ( $n = 1,409,014$ ) from the general population who had no

specific diseases. We included only prospective cohort studies in the current analysis, so the possibility of recall or selection bias that can affect the results could be minimal. Many studies included in the meta-analysis had a relatively long duration of follow-up (mean of ~14.5 years) from various geographical regions. The results of quality assessment suggested that all of the studies included in the meta-analysis were of high or good quality. Furthermore, we found a significant dose-response relationship between dietary fibre and CVD, CHD or all-cancer mortality, and there was no significant evidence of heterogeneity among the studies included in the meta-analysis.

The current study also has several limitations that should be acknowledged. First, a meta-analysis cannot solve the problem of confounding factors that might exist in the original studies. People who consume high dietary fibre tend to have other healthy behaviours, such as higher levels of physical activity, avoidance of tobacco use and low alcohol intake [13,15,18,46]. The majority of studies included in this meta-analysis adjusted for potential confounding factors, such as BMI, smoking, alcohol and physical activity, and the inverse association between dietary fibre and CVD or CHD remained significant even in the analysis stratified by the adjustment for covariates. Nonetheless, there is still a possibility that unknown and/or residual confounding may have influenced the results in each study, and thus the pooled estimates in the meta-analysis. Second, some non-differential misclassification of self-reported dietary fibre intake is inevitable, as most of the studies included in our meta-analysis assessed dietary fibre intake using a food frequency questionnaire at a single timepoint only. The possible misclassification, however, would probably have biased the results toward the null, rather than strengthening the association between dietary fibre intake and CVD or all-cancer mortality. Third, results of subgroup analyses in the current meta-analysis were based on a limited number of studies, although the relatively large sample size of this study allowed us to conduct subgroup analyses. Lastly, publication bias, such as small-study effect, can be of concern in meta-analyses. In our meta-analysis, there was weak evidence of publication bias based on the test of Egger et al. in the dose-response analysis of CHD mortality.

## Conclusions

In conclusion, our meta-analysis of 15 prospective cohort studies indicates that high fibre intake, especially fibre from cereals, is significantly associated with lower mortality from CVD, CHD and all cancers. Although it is difficult to determine causality of this association because of the observational nature (i.e. consumption of fibre is self-selected, not randomized), large prospective data, adjustment for important confounders, consistency with results from previous publications and a trend towards a dose-response relationship with dietary fibre intake may suggest real protection from dietary fibre against death from CVD, CHD and all cancers. Our results support the current recommendation that high dietary fibre intake should be part of a healthy diet. More prospective cohort studies, which fully adjust for potential confounders and conduct subgroup analyses by source of dietary fibre, should be performed to verify the

association between dietary fibre intake and CVD, CHD and all-cancer mortality.

## Acknowledgements

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## Disclosure of interest

The authors declare that they have no competing interest.

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