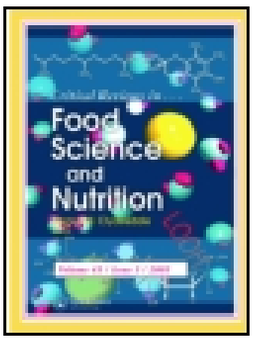

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REVIEW

Is eating a mixed diet better for health and survival?: A systematic review and meta-analysis of longitudinal observational studies

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ABSTRACT

The role of dietary diversity in chronic disease or survival is controversial. This meta-analysis quantified the health impact of dietary diversity. Random-effects models pooled risk ratios (RRs) and 95% confidence intervals (CIs) of 20 longitudinal studies. Total dietary diversity was associated with a 22% lower risk of all-cause mortality (RR 0.78 [95%CI: 0.64, 0.96]), and was inversely associated with incident cancer- or CVD-specific mortality only in subgroup analyses (RR range: 0.53 to 0.90, $p < 0.05$). Similarly, diversity across healthy foods was inversely associated with all-cause mortality (RR 0.84 [95%CI: 0.73, 0.96]). An inverse association between total diet diversity and incident CVD was significant in non-European populations consuming diets with diverse food groups (RR: 0.93 [95% CI: 0.86-0.99]). Effects on cancer risk are unstudied. Diversity within fruits and/or vegetables showed null associations for all outcomes, except potentially for squamous cell-type carcinomas. More robust research is warranted. Findings indicated greater dietary diversity may benefit overall survival.

KEYWORDS

Cancer; cardiovascular diseases; dietary diversity; food variety; meta-analysis; mortality

Introduction

In 2017, cardiovascular diseases (CVDs) and cancer were the leading causes of mortality, accounting for more than 2 million deaths among adults worldwide (Ritchie and Roser 2018). These chronic conditions can contribute to a lower quality of life and greater disability (Roser and Ritchie 2016). Also, in the United State alone, CVDs and cancer were responsible for US$318.8 million national total expenditure in 2013 (3). Therefore, prevention is critical to reducing this growing chronic disease burden (Roser and Ritchie 2016). Diet has been identified as one of the key modifiable risk factors in the etiology of cancer (Theodoratou et al. 2017), CVDs (Marhuenda et al. 2019), and related mortalities (Schwedhelm et al. 2016; Meier et al. 2019).

For decades, the dietary impact on CVDs (Cheng et al. 2019), cancer (Demeyer et al. 2016), and related mortalities have been investigated in terms of specific nutrients or foods (Giovannucci 2005; Becerra-Tomás et al. 2019). However, people do not eat single and isolated nutrients/foods but rather consume meals consisting of a diversity of foods with complex combinations of components that are likely to be synergistic or interactive (Hu 2002). Hence, nutritional epidemiologic studies are increasingly taking a whole-diet approach that takes such interactions of dietary components into account (Hu 2002). Dietary diversity/food variety is a holistic food-based dietary measure to assess whether a diet is mixed and diverse, and is a cornerstone of healthy eating in national guidelines. This dietary measure can be practical for population-based nutrition education and intervention as it can be easily understood and disseminated to the public (Lundkvist et al. 2010; Ruel 2003).

Dietary diversity has been traditionally defined as the total number of different food items in a diet, but it also refers to the variation of different food groups or different foods within a given group (Ruel 2003). Since the late 1970s, dietary diversity has been considered as an inseparable part of healthy eating as it helps to maintain an adequate balance of nutrients which the body needs to stay healthy (Randall, Nichaman, and Contant 1985). Thus, to promote a desirable eating pattern that supports overall health and prevents diet-related chronic conditions, several dietary guidelines have incorporated general recommendations on consuming a diversity of foods. These include: the new American (U.S. Department of Health and Human Services 2015), Chinese (Wang et al. 2016), and Australian (Australian Guide to Healthy Eating 2017) dietary guidelines as well as Canada's previous Food Guide (Bush et al. 2007) that was updated to be a plate of only three food groups and little mention of eating more diversity.

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Effective nutrition, healthcare and health policy should be informed by robust evidence that, to date, has been inconsistent regarding the association of dietary diversity with cancer, CVDs, and related mortalities (Bhupathiraju et al. 2013; Blekkenhorst et al. 2020; Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Conrad, Thomson, and Jahns 2018; Fung et al. 2018; Gicevic et al. 2018; Griep et al. 2012; Jeurnink et al. 2012; Kaluza et al. 2009; Kobayashi et al. 2020; Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b; Lee et al. 2011; Leenders et al. 2015; Letois et al. 2016; Masset et al. 2015; McNaughton, Bates, and Mishra 2012; Reedy et al. 2008; Smyth et al. 2016; Lv et al. 2020; Otsuka et al. 2020; Tao, Xie, and Huang 2020). Some studies have shown that greater total dietary diversity is inversely associated with incident cancer (Reedy et al. 2008), CVDs (Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b), and even mortality (Kobayashi et al. 2020; Lee et al. 2011; McNaughton, Bates, and Mishra 2012), but others report null associations (Fung et al. 2018; Letois et al. 2016; Smyth et al. 2016). Other studies highlighted the inverse associations of diversity within certain food groups with these adverse health outcomes (Blekkenhorst et al. 2020; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Jeurnink et al. 2012). By contrast, it is possible that greater diversity across, or within, food groups might increase energy intake, and thereby increase the risk of adiposity and consequent negative outcomes (Vadiveloo, Dixon, and Parekh 2013). To inform preventive action and improve health promotion through evidence-based dietary guidelines, this meta-analysis study aimed to comprehensively assess and quantify the health impact of dietary diversity.

Methods

Data sources and searches

Peer-reviewed literature was systematically searched using three bibliometric databases (PubMed/Medline, Web of Science, and Scopus) and hand-searched using references in retrieved full-texts and other reviews (Mozaffari et al. 2021). We followed PRISMA guidelines for systematic reviews (Moher et al. 2009) and used established evaluation tools for quality assessment of observational studies (Conklin et al. 2018). Free-text and thesaurus terms for 'food variety' or 'diet diversity' were applied using database-specific syntax (Appendix); the 'Recommended Food Score' was used in targeted searches of each database. The search strategy was deliberately broad and thus no outcome was pre-specified. Searches were performed separately by JL and AC (2008-2018) and then by HM (2018-2019). A rapid update was also performed by HM for studies published in January-June 2020. Results were imported to EndNote vX9 (Thomson Reuters, Philadelphia, PA, USA) for duplicate removal and eligibility screening. This study has been registered with PROSPERO (CRD42020167115).

Study selection

Studies with a longitudinal design (cohort, nested case-cohort, panel data, randomized clinical trials (RCTs)) examining morbidity and/or mortality outcomes of dietary diversity in developed settings (World Bank high-income and OECD countries) were considered eligible. Studies reporting effect sizes in English, French, and Persian languages, and published between 2008 and 2020, were included. For multiple publications using the same dataset, the longer study duration and/or larger sample size was selected for inclusion to avoid potential reporting of any skewed findings.

Exclusion criteria were as follows: 1) non-prospective studies (e.g. cross-sectional and case-control studies); 2) not reporting effect sizes (ORs or HRs or RRs, β, mean change); 3) exposure of interest lacking (i.e. diet education, nutrition counseling, food insecurity); 4) dietary diversity as an outcome measure; 5) studies from low-income countries; 6) qualitative studies; 7) studies on clinical populations; 8) no health outcome measured (e.g. diet cost, energy intake, nutrient profile); 9) weight management interventions; 10) position papers or editorials; 11) measurement validation studies; and 12) feeding practices/behavior studies.

HM, JL and AC independently screened titles and abstracts for potential eligibility and removed unrelated publications based on predefined criteria. Abstracts were examined further for full-text retrieval and retrieved papers were read in full with references followed up. When the eligibility of titles and abstracts was unclear, studies were reviewed in full. References of eligible full-texts revealed additional keywords for the targeted search on the Recommended Food Score.

Data extraction and quality assessment

HM and AC performed data extraction using a standardized evidence table with pre-defined headings: source, location and population, duration and time period, definition of dietary diversity, scoring system, exposure assessment tool, outcome(s) measured and incident cases, outcome assessment tool, comparison, the documented effect sizes (ORs or HRs or RRs, β, mean change), and covariates. Estimates were extracted from models that adjusted for the highest number of potential confounders, if available.

To avoid the likelihood of reporting skewed findings, we did not enter any duplicate population or risk estimate to the meta-analysis (Parohan et al., 2019). For instance, two studies on CVDs (Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b) and mortality (Lv et al. 2020; Tao, Xie, and Huang 2020) were found to have similar datasets. For CVD and mortality, the meta-analysis only included the study wherein dietary diversity was the primary exposure, different definitions of diversity were studied, the sample size was largest and follow-up was longest (Larsson, Åkesson, and Wolk 2014b; Lv et al. 2020). Duplicate study IDs on the forest plots are due to the same study having different populations (e.g. female-only, male-only). When a single study reported multiple dependent risk estimates for different exposures (e.g. diversity of healthy and less healthy

foods) or outcomes (e.g. chronic heart disease versus stroke for CVDs), we used averaging before meta-analysis as the preferred method for dealing with dependent risk estimates since other approaches need large numbers of studies or a specified correlation value for the dependent risk estimates (Scammacca, Roberts, and Stuebing 2014).

Two studies reported outcomes for renal-cause mortality (Smyth et al. 2016) or CVDs and cancer combined (Letois et al. 2016). Given that death due to CVDs, cancers, and renal diseases were in the definition of all-cause mortality in the included studies, we entered data from those cause-specific studies into the meta-analysis of all-cause mortality similar to other meta-analyses (Sadeghi et al. 2019; Parohan et al., 2019). One study reported associations between low dietary diversity with mortality such that the highest category of dietary diversity was considered as the reference category (Conrad, Thomson, and Jahns 2018). To be able to pool this study with risk estimates from other studies, we modified the reference group into the lowest category (Conrad, Thomson, and Jahns 2018). Since our study included risk estimates and 95% CIs of different categories, changing the reference category was possible as described by the Oxford Center for Evidence-Based Medicine (Taylor 2020).

Two reviewers (HM and ZH) separately assessed quality using a tool adapted from the Effective Public Health Practice Project (EPHPP) (Thomas 2003) and Newcastle-Ottawa Scale (NOS), (Peterson et al. 2011) which were both reported as 'best' tools for critical appraisal of observational studies by the UK's Health Technology Assessment Programme (Deeks et al. 2003). The 27 criteria were coded with three categories ('yes', 'no' and 'unknown/cannot tell'); quality was determined based on the percent of criteria coded 'yes': ≥80% (high quality); 20-80% ('medium quality'); <20% (low quality) (Appendix).

Data synthesis and analysis

Log-transformed RRs as well as corresponding standard errors (SEs) were obtained using risk ratios (ORs, RRs or HRs and related 95% CIs) extracted from three or more studies reporting associations between dietary diversity and risk of cancer, CVDs, or mortality (all-cause and cause-specific).

For CVD and mortality outcomes, high versus low intake of dietary diversity were pooled in meta-analyses. Since included studies varied in exposure definition, a random-effects model was used as the pooling method regardless of heterogeneity (I^2). Cochran's Q and I^2 statistics were used to assess study heterogeneity; $I^2 > 50\%$ and $P < 0.10$ were considered to indicate statistically significant heterogeneity (Higgins and Wells 2021). Subgroup analyses using fixed-effects models (Parohan et al., 2019) helped to understand the main findings and potential sources of variation. Sources included: definition of dietary diversity (individual foods vs. food groups); comparator groups (≥3 vs. <3 categories of diversity); assessment tools (food frequency questionnaire vs. other tools); population (European, non-European); sample size (≥10 000 vs. <10 000); confounding by energy intake (yes vs. no) and by body mass index (BMI) (yes vs. no); and, study quality (high vs. medium). Subgroup characteristics were considered if at least two independent effect sizes were available for analysis. Publication bias was assessed by constructing funnel plots and conducting Egger's test (Egger et al. 1997). Sensitivity analysis was done to determine whether pooled risk estimates were affected by one or more specific studies.

Cancer was the only outcome analyzed in relation to both categorical and continuous dietary diversity scores in the existing literature, thus separate analyses pooled the risk of cancer for both categorical (high versus low) and continuous scores of diet diversity. All the risk estimates for the association between fruits and/or vegetables diversity and different types of cancers came from similar populations of European Prospective Investigation into Cancer (EPIC) Study. Thus, rather than meta-analysis, we used the averaging approach to obtain aggregated risk estimates with an assumed correlation of 1.0 between estimates following Borenstein's method (Borenstein et al. 2011). This is considered as the most conservative method when other approaches of dealing with dependent risk estimates are not possible (Scammacca, Roberts, and Stuebing 2014). Averaging of dependent risk estimates was conducted in R version 3.6.3. All other data analyses were conducted using Stata, version 11.2 (Stata Corp, College Station, TX), with significance of pooled estimates set at $p < 0.05$.

Results

Study selection

The search identified 4 950 publications eligible for inclusion, following duplicate removal (1 763). Screening titles and abstracts removed 4 832 and 118 retrieved full-texts were assessed for eligibility. Twenty-three studies (Bhupathiraju et al. 2013; Blekkenhorst et al. 2020; Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Conrad, Thomson, and Jahns 2018; Fung et al. 2018; Gicevic et al. 2018; Griep et al. 2012; Jeurnink et al. 2012; Kaluza et al. 2009; Kobayashi et al. 2020; Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b; Lee et al. 2011; Leenders et al. 2015; Letois et al. 2016; Masset et al. 2015; McNaughton, Bates, and Mishra 2012; Reedy et al. 2008; Smyth et al. 2016; Lv et al. 2020; Otsuka et al. 2020; Tao, Xie, and Huang 2020) met criteria for data extraction and quality review, and 20 were pooled (Figure 1). Included studies mainly reported on the count of individual foods across the diet or different fruits and vegetables in relation to mortality as an outcome between the 1990s and 2000s. Most studies came from European countries or the US, but a few came from the Pacific region (Table 1).

Study characteristics

Study quality was generally good (Appendix). Thirteen studies were rated as of high (Blekkenhorst et al. 2020; Büchner

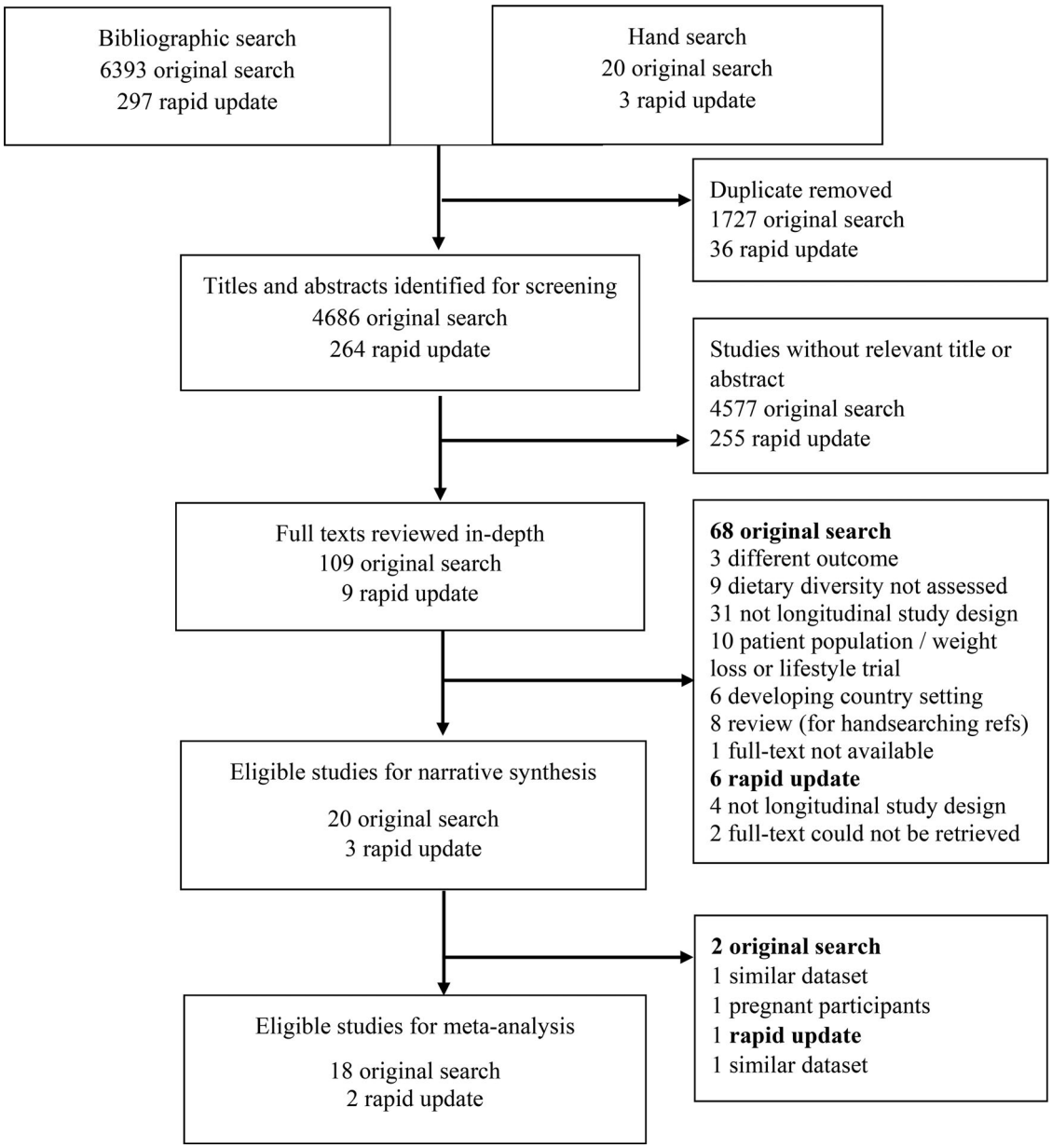

Figure 1. PRISMA diagram of search strategy and study selection.

et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Griep et al., 2012; Jeurnink et al. 2012; Kaluza et al. 2009; Kobayashi et al. 2020; Lee et al., 2011; Leenders et al. 2015; Reedy et al. 2008; Smyth et al. 2016; Lv et al. 2020; Otsuka et al. 2020) and ten of medium quality (Bhupathiraju et al. 2013; Conrad, Thomson, and Jahns 2018; Fung et al. 2018; Gicevic et al. 2018; Larsson et al., 2014a; Larsson, Åkesson, and Wolk 2014b; Letois et al. 2016; Masset et al. 2015; McNaughton, Bates, and Mishra 2012; Tao et al., 2020). Limited comparability (e.g. uncontrolled confounders) and lack of completeness (e.g. likely effects outside the study timescale) were major concerns in most included studies. Medium quality studies also had sampling (e.g. strategy unclear or not justified) and representativeness (e.g. results not generalizable) limitations.

Study periods varied between 1984 to 1999 and the follow-up duration ranged from 5 to 28 years (Table 1). Study populations were also diverse: 11 studies included European populations (Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Griep et al. 2012; Jeurnink et al. 2012; Kaluza et al. 2009; Larsson et al., 2014a; Larsson, Åkesson, and Wolk 2014b; Leenders et al. 2015; Letois et al. 2016; Masset et al. 2015; McNaughton, Bates, and Mishra 2012), six used samples from the US (Bhupathiraju et al. 2013; Conrad, Thomson, and Jahns 2018; Fung et al. 2018; Gicevic et al. 2018 Reedy et al., 2008; Smyth et al. 2016), five used samples from Asia (China (Lee et al. 2011; Lv et al. 2020; Tao, Xie, and Huang 2020), and Japan (Kobayashi et al. 2020; Otsuka et al. 2020) and one came from Australia (Blekkenhorst et al. 2020). Studies' sample sizes varied between 954 to 492 382 participants. A total of 18 studies included both sexes, but only four reported results by sex (Bhupathiraju et al. 2013; Fung et al. 2018; Kobayashi et al. 2020; Reedy et al. 2008). Four studies included only females

Table 1. Characteristics of included studies.

Study (source)	Location & Population	Follow-up (time period)	Exposure	Exposure assessment	Health outcome (incident cases)	Outcome assessment	Comparison	Effect sizes for high vs. low intake	Covariates
Reedy et al. (2008) (Medline)	USA M: 293,615 (50-71 y) F: 198,767 (50-71 y)	5y (1995-96 to 2000)	Recommended Food Score (RFS)	124-item FFQ	Colorectal cancer (M: 2,151; F: 959) Proximal colon cancer Distal colon cancer Rectal colon cancer	Cancer registry; ICD 10	Q5 vs. Q1 M: (16-38 vs. 0-6) F: (17–38 vs. 0–6)	For M: **RR: 0.75 (0.65, 0.87)** **RR: 0.68 (0.53, 0.86)** **RR: 0.76 (0.59, 0.97)** RR: 0.86 (0.66, 1.11) For F: RR: 1.01 (0.80, 1.28) RR: 1.09 (0.77, 1.53) RR: 0.90 (0.56, 1.42) RR: 1.03 (0.64, 1.66)	Demographics Socio-economic status Health behaviors Anthropometry Other factors
Büchner, Bueno-de-Mesquita, Linseisen, et al. (2010) (Medline)	10 European countries 445,923 (25-70y)	8.7y (1991-2000 to 2002-5)	Fruits and vegetables diversity Fruit diversity Vegetable diversity Vegetable subgroup diversity	FFQ or food records	Lung cancer (1,607)	Regional or national registries, health insurance records, cancer and pathology hospital registries, and active follow-up; ICD10	Q4 vs. Q1 (23-40 vs. 0-10) (9-14 vs. 0-2) (16-26 vs. 0-6) (8 vs. 0-4)	HR: 0.96 (0.75,1.21) HR: 0.94 (0.76,1.17) HR: 0.94 (0.74,1.18) HR: 0.77 (0.64,0.94)	Demographics Health behaviors Anthropometry
Büchner et al. (2011) (Medline)	10 European countries 452,185 (25-70y)	8.7y (1991-2000 to 2002-5)	Fruits and vegetables diversity Vegetable subgroup diversity Vegetable diversity Fruit diversity	FFQ or food records	Bladder cancer (870)	Regional or national registries, health insurance records, cancer and pathology hospital registries, and active follow-up; ICD10	T3 vs. T1 (20–40 vs. 0-11) (8 vs. 0-5) (14–26 vs 0-7) (8–14 vs. 0-3)	HR: 1.30 (1.00,1.69) HR: 1.19 (0.94,1.51) HR: 1.16 (0.90,1.50) HR: 0.99 (0.77,1.28)	Demographics Health behaviors
Leenders et al. (2015) (Medline)	10 European countries 442,961 (25-70y)	13y (1992-2000 to 2004-8 or 2006-10)	Fruit and vegetable diversity Vegetable subgroup diversity Vegetable diversity Fruit diversity	FFQ or food records	Colon cancer (2,128) Rectal cancer (1,242)	Regional or national registries, health insurance records, cancer and pathology hospital registries, and active follow-up; ICD10	Q4 vs. Q1	HR: 0.96 (0.79,1.16) HR: 1.26 (0.97,1.63) HR: 1.08 (0.92,1.28) HR: 0.98 (0.78,1.22) HR: 1.07 (0.88,1.30) HR: 0.88 (0.68,1.14) HR: 0.87 (0.73,1.03) **HR:1.41 (1.11,1.78)**	Health behaviors Anthropometry
Jeurnink et al. (2012) (Medline)	10 European countries 452,269 (25-70y)	8.4y (1992-2000 to 2002-5)	Fruit and vegetable diversity Vegetable subgroup diversity Vegetable diversity Fruit diversity	FFQ or food records	Non-cardia adenocarcinoma (180) Esophageal, GEJ and cardia adenocarcinoma (185) Esophageal squamous cell carcinomas (98)	Regional or national registries, health insurance records, cancer and pathology hospital registries, and active follow-up; ICD10	T3 vs. T1 (20-40 vs. 0-11) (8 vs. 0-5) (14-26 vs. 0-7) (8-14 vs. 0-3)	**HR: 1.82 (1.02,3.25)** R: 0.76 (0.43,1.33) HR: 0.42 (0.17,1.04) HR: 1.10 (0.62,1.94) HR: 1.17 (0.70,2.94) HR: 0.59 (0.29,1.22) HR: 1.09 (0.61,1.94) HR: 0.81 (0.46,1.43) HR: 0.72 (0.32,1.62) HR: 1.33 (0.76,2.33) HR: 0.83 (0.46,1.49) HR: 0.48 (0.21,1.11)	Demographics Health behaviors

(*continued*)

Table 1. Continued.

Study (source)	Location & Population	Follow-up (time period)	Exposure	Exposure assessment	Health outcome (incident cases)	Outcome assessment	Comparison	Effect sizes for high vs. low intake	Covariates
Griep et al. (2012) (Hand search)	Netherlands 20,069 (20-65y)	10y (1993-1997 to 2006)	Fruits and vegetables diversity Fruits diversity Vegetables diversity	178-item FFQ	CHD (245) Stroke (233)	Municipal population register, Statistics Netherlands, hospital discharge register; ICD9,10	T3 vs. T1 (≥13 vs. ≤8) (≥7 vs. ≤3) (≥8 vs. ≤4)	HR: 0.99(0.63,1.57) HR: 0.90(0.58,1.41) HR:0.80(0.50,1.29) HR: 0.99(0.62,1.58) HR: 1.26(0.89,1.79) HR: 0.76(0.52,1.10)	Demographics Socio-economic status Health behaviors Anthropometry Health status Other factors
Fung et al. (2018) (Medline)	USA NHS F:75,045 (43-63 y) HPFS M: 43,966 (40-75 y) NHS2 F:93,131 (27-44y)	28y NHS: (1984 to 2012) HPFS:(1986 to 2010 NHS2: (1991 to 2011)	Minimal Diet Diversity Score (MDDS) Food Group Index (FGI)	135-item FFQ	Ischemic heart disease (NHS: 2,908 HPFS:3,722 NHS2:531)	Non-fatal: self-report verified by physicians (medical record); WHO criteria / Fatal: state vital records or the National Death Index, and family report verified by hospital record	For MDDS: Q5 vs. Q1 (>6 vs. 0-3) (>6 vs. 0-3) (>6 vs. 0-3) For FGI: Q5 vs. Q1 (8 vs. 0-5) (8 vs. 0-5) Q4 vs. Q1 (≥7 vs. 0-5)	For MDDS: RR: 0.84 (0.70, 1.01) RR: 0.92 (0.78, 1.08) RR: 0.79 (0.52, 1.20) For FGI: RR: 0.94 (0.74, 1.19) RR: 1.04 (0.86, 1.27) RR: 0.83 (0.56, 1.24)	Demographics Health behaviors Anthropometry Health status Other factors
Bhupathiraju et al. (2013) (WOS)	USA F: 71,141 (43-57 y) M: 42,135 (44-62 y)	NHS: 24 y (1984 to 2008) HPFS:22y (1986 to 2008	Fruits and vegetables diversity (cumulative average)	135-item FFQ	CHD (NHS/F:2,582 HPFS/M:3,607)	Nonfatal CHD: (medical records reviewed by physicians who were blinded; WHO criteria) a + probable cases Fatal CHD: (hospital record or autopsy report or death certificate) + presumed cases	Q5 vs. Q1 F: (16.4 vs. 5.3) M: (16.1 vs. 4.7)	For total sample: RR: 1.05 (0.97, 1.13) For F: RR: 1.12 (0.99, 1.27) For M: RR: 1.01 (0.91, 1.11)	Demographics Health behaviors Anthropometry Health status Other factors
Larsson, Åkesson, and Wolk (2014a) (Medline)	Sweden F: 31,696 (49-83 y)	10.4 y (1997 to 2008)	Recommended Food Score (RFS)	96-item FFQ	Total stroke (1,554) Cerebral stroke (1,155) Hemorrhage stroke (246)	National registries; ICD10	2 categories (top 50% vs. bottom 50%)	**RR: 0.85(0.76,0.95)** **RR: 0.87(0.76,0.99)** RR: 0.77(0.58,1.01)	Demographics Socio-economic status Health behaviors Anthropometry Health status Other factors
Larsson, Åkesson, and Wolk (2014b) Medline)	Sweden F: 33,911 (49-83 y)	10.4 y (1997 to 2008)	Recommended Food Score (RFS) Non-Recommended Food Score (NRFS)	96-item FFQ	Total stroke (1,687) Cerebral stroke (1,260) Hemorrhage stroke (256)	National registries; ICD10	Q5 vs. Q1 (23-25 vs. 1-16) (17-21 vs. 1-10)	For RFS: **RR: 0.80 (0.67,0.95)** RR: 0.86 (0.70,1.05) RR: 0.66 (0.42,1.04) For NRFS: **RR: 1.22 (1.02,1.46)** **RR: 1.27 (1.03,1.56)** **RR: 1.25 (0.80,2.94)**	Demographics Socio-economic status Health behaviors Anthropometry Health status Other factors

Gicevic et al. (2018) (Medline)	USA Pregnant women: 19,917 (27- 44 y)	10 y (1991 to 2001)	Minimal Diet Diversity score (MDDS) Food Group Index (FGI)	131-item FFQ	Hypertensive disorders of pregnancy (HDPs) (1,421)	Self-report verified by medical record	Q5 vs. Q1	For MDDS: RR: 0.92 (0.75, 1.12) For FGI: RR:0.97 (0.79, 1.17)	Demographics Socio-economic status Health behaviors Anthropometry Health status
Letois et al. (2016) (Medline)	France 8,937 (65-85 y)	10 y (1999-2000 to 2008-9)	Dietary Diversity Score (DDS) Fat diversity	Brief FFQ	CVD and Cancer mortality (931)	Civil registry; ICD10	Median split (4–5 vs. 0–3) (>3 vs. ≤3)	For DDS: HR: 0.94 (0.85,1.04) For Fat diversity: HR:0.90 (0.80,1.01)	Demographics Socio-economic status Health behaviors Anthropometry Health status Other factors
Lee et al. (2011) (Medline)	Taiwan 1,743 (65-90y)	10y (1999-2000 to 2008)	Dietary Diversity Score (DDS)	18-item FFQ & 24-h recall	All-cause mortality (624) Cancer mortality (164) Diabetes mortality (48) CVD mortality (156) Cerebrovascular Disease mortality (63) Pneumonia mortality (38)	National Death Registry; ICD9	4 categories (6 vs ≤3)	**HR: 0.50 (0.31,0.81)** HR: 0.46 (0.20,1.07) HR: 0.31 (0.07,1.49) HR: 0.31 (0.07,1.36) HR: 0.52 (0.11,2.51) HR: 0.52 (0.10,2.54)	Demographics Socio-economic status Health behaviors Anthropometry Health status
Conrad, Thomson, and Jahns (2018) (Medline)	USA 29,133 (20-85 y)	6.5 y (1999 to 2011)	Vegetable subgroups diversity	24-h dietary recalls	All-cause mortality (2,861) Cardiometabolic mortality (829) CVD mortality (726) CHD mortality (556)	National registries	3 categories (0.48 vs. 0)	**HR: 0.78 (0.62, 1.00)** HR: 0.70 (0.43, 1.11) **HR: 0.67(0.47,1.00)** **HR: 0.62(0.41,1.00)**	Demographics Socio-economic status Health behaviors Anthropometry Other factors
Kobayashi et al. (2020) (Hand search)	Japan M: 37,240 (48-64 y) F: 42,664 (48-64 y)	17y (1995 to 2012)	Dietary diversity Fish diversity Meat diversity Vegetables diversity Fruits diversity Soy diversity	138-item FFQ	All-cause mortality (M: 7,596) (F:4,334) Cancer mortality (M:3,104) (F:1,656) CVD mortality (M:1,791) (F:1,151) Other mortality (M:2,701) (F:1,527)	Death certificates	Q5 vs. Q1 For DDS: M:(35.9 vs. 13.4) F: (39.8 vs 15.5) For fish: M:(3.5 vs. 0.7) F:(3.6 vs. 0.8) For meat: M:(2.3 vs. 0.3) F:(2.3 vs. 0.3) For vegetables: M:(8.4 vs. 1.7) F:(9.4 vs. 2.3) For fruits: M:(5.7 vs. 0.6) F:(7.1 vs. 1.0) For soy: M:(3.5 vs. 1.1) F:(3.6 vs. 1.1)	For DDS/M: HR: 0.96 (0.87–1.06) HR: 0.95 (0.82–1.11) HR: 0.95 (0.77–1.16) HR: 0.97 (0.83–1.15) For DDS/F: **HR: 0.82 (0.71,0.94)** HR: 1.00 (0.80,1.25) **HR: 0.65 (0.49,0.85)** **HR: 0.78 (0.62,0.98)** For fish/M: **HR: 1.12 (1.02,1.22)** HR: 1.04 (0.91,1.20) **HR: 1.20 (1.00,1.44)** **HR: 1.15 (1.00,1.34)** For fish/F: HR: 0.99 (0.87–1.11) HR: 0.99 (0.81–1.21) HR: 1.06 (0.84–1.33) HR: 0.94 (0.77–1.16)	Demographics Socio-economic status Health behaviors Anthropometry Other factors

(*continued*)

Table 1. Continued.

Study (source)	Location & Population	Follow-up (time period)	Exposure	Exposure assessment	Health outcome (incident cases)	Outcome assessment	Comparison	Effect sizes for high vs. low intake	Covariates
								For meat/M: **HR: 1.15 (1.06,1.25)** HR: 1.00 (0.88,1.14) **HR: 1.23 (1.04,1.46)** **HR: 1.29 (1.12,1.48)** For meat/F: HR: 1.00 (0.90–1.12) HR: 0.91 (0.76–1.09) HR: 0.95 (0.76–1.18) HR: 1.15 (0.96–1.38) For vegetables/M: HR: 1.04 (0.95,1.14) HR: 0.93 (0.80,1.08) HR: 1.08 (0.89,1.31) HR: 1.15 (0.98,1.34) For vegetables/F: HR: 0.95 (0.84–1.07) HR: 1.01 (0.83–1.23) HR: 1.01 (0.80–1.28) HR: 0.85 (0.69–1.04) For fruits/M: **HR: 0.87 (0.79,0.95)** HR: 0.96 (0.83,1.10) HR: 0.89 (0.73,1.07) **HR: 0.76 (0.66,0.89)** For fruits/F: HR: 0.94 (0.83–1.06) HR: 1.06 (0.87–1.29) HR: 0.81 (0.64–1.03) HR: 0.91 (0.74–1.12) For soy/M: HR: 0.97 (0.89–1.06) HR: 1.01 (0.88–1.15) HR: 0.98 (0.82–1.17) HR: 0.93 (0.80–1.07) For soy/F: **HR: 0.89 (0.79,1.00)** HR: 0.90 (0.75,1.08) **HR: 0.77 (0.61,0.96)** HR:1.00 (0.83,1.20)	
Kaluza et al. (2009) (Medline)	Sweden M: 40,837 (45-79 y)	7.7y (1997 to 2003-05)	Recommended Food Score (RFS) Non-Recommended Food Score (NRFS)	FFQ	All-cause mortality (4,501) CVD mortality (1,394) Cancer mortality (759)	National registries; ICD9	3 categories: high vs. low (≥28 vs. ≤20) 3 categories: high vs. low (≥5 vs. ≤2)	For RFS: HR: **0.81 (0.71,0.91)** HR: **0.71 (0.54,0.93)** HR: 1.09 (0.84,1.41) For NRFS: **HR: 1.21 (1.09,1.34)** **HR: 1.27 (1.05,1.54)** HR: 1.17 (0.94,1.46)	Demographics Socio-economic status Health behaviors Anthropometry Health status Other factors
McNaughton, Bates, and Mishra (2012) (Medline)	UK 972 ≥65y	14y (1994-1995 to 2008)	Recommended Food Score (RFS)	4-day record	All-cause mortality (654)	Local registries	Q4 vs. Q1	**HR: 0.67 (0.52, 0.86)**	Demographics Socio-economic status Health behaviors Anthropometry

Smyth et al. (2016) (Medline)	USA 544,635 (51-70 y)	14.3y (1995-1996 to 2011)	Recommended Food Score (RFS)	124-item FFQ	Death due to a renal cause (4,848)	Social Security Administration Death Master File and National Death Index.; ICD9 & 10	Q5 vs. Q1 (>3 vs. 0)	HR: 0.95 (0.85,1.07)	Demographics Socio-economic status Health behaviors Anthropometry Health status
Lv et al. (2020) (Medline)	China 28,790 (80-99 y)	16y (1998 to 2014)	Dietary Diversity Score (DDS)	FFQ	All-cause mortality (23,503)	Interviews with close family members or the village doctor	1-unit increment 6 categories (≥6 vs. <2)	**HR: 0.910 (0.904, 0.916)** **HR: 0.56 (0.53, 0.58)**	Demographics Socio-economic status Health behaviors Health status Other factors
Tao, Xie, and Huang (2020) (WOS)	China 15,033 (65-99 y)	6y (2008 to 2014)	Dietary Diversity Score (DDS)	FFQ	All-cause mortality (8,445)	Interviews with close family members or the village doctor	5 categories (8-9 vs. 0-1)	**HR: 0.70 (0.60, 0.80)**	Demographics Socio-economic status Health behaviors Anthropometry Health status Other factors
Otsuka et al. (2020) (Medline)	Aichi Prefecture, Japan 799 (60-79 y)	16y (1997-2000 to 2017)	Quantitative Index for Dietary Diversity (QUANTID)	3-day record	All-cause mortality (289) Cancer mortality (92) Cardiovascular mortality (38) Cerebrovascular mortality (31)	National Vital statistics records; ICD10	T3 vs. T1	**HR:0.69 (0.51–0.94)** **HR:0.57 (0.33–0.98)** HR:0.86 (0.37–1.98) HR:0.48 (0.16–1.27)	Demographics Socio-economic status Health behaviors Anthropometry Health status
Blekkenhorst et al. (2020) (Hand search)	Perth, Western Australia F: 924-1,226 (70-85 y)	13y (1998 to 2011)	Vegetable subgroups diversity (cumulative average)	75-item FFQ	Atherosclerotic vascular disease mortality (238) Carotid plaque severity Mean CCA-IMT Maximum CCA-IMT	Linked mortality data; ICD9 and ICD10 Ultrasounds	3 categories (≥5 vs. ≤3) 3 categories (≥5 vs. ≤3) 1-unit increment	HR: 0.68 (0.42, 1.09) OR: 0.61 (0.30, 1.24) **Beta ± SE: −0.012 ± 0.005** **Beta ± SE:** − 0.014 ± 0.006	Demographics Socio-economic status Health behaviors Anthropometry Other factors
Masset et al. (2015) (Medline)	London (civil servants) 5,263 to 7,235 (35-55 y)	Up to 16.8 y (1991-1993 to 2009-10)	Food Variety Score (FVS) Diversity between (less)healthy foods based on Ofcom nutrient profile model Diversity between (less)healthy foods based on SIAN, LIM nutrient profile	127-item FFQ	CHD (220) All-cause mortality (372) Cancer mortality (185) CVD mortality (137)	For CHD: Questionnaire items on chest pain, doctor diagnoses and hospitalisations For mortality: National registries; ICD9, ICD10	Q4 vs. Q1 (50–99 vs. 0–34)	For FVS: HR: 0.70(0.44,1.09) HR: 0.77(0.55,1.08) HR: 0.68(0.43,1.07) HR: 0.66(0.36,1.20)	Demographics Socio-economic status Health behaviors Anthropometry Health status

Abbreviation: F: Female; M: Male; NHS: Nurse Health Study (NHS); Health Professionals Follow-Up Study (HPFS); FFQ: Food Frequency Questionnaire; CHD: Coronary Heart Disease; ICD: International Statistical Classification of Diseases and Related Health Problems;T: Tertile; Q: Quartile or Quintile; OR: Odds Ratio; RR: Relative Risk; HR: Hazard Ratio. Adjustment for covariates included: Demographics (age, sex, race, region); Socio-economic status (education, income, income-to-poverty ratio, occupation, marital status, enough money, social class, parity, living pattern); Health behaviors (physical activity, sedentary time, smoking status, duration of smoking, number of cigarettes, alcohol); Anthropometry (weight, height, BMI, waist-to-hip ratio); Health status (Self-rated health, specific conditions, number of specific conditions, chewing ability, dependence); Diet components (energy, quality, quantity); Other factors (drugs, supplements, hormone therapy, oral contraceptive, menopausal status).

(Blekkenhorst et al. 2020; Gicevic et al. 2018; Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b), and one had males only (Kaluza et al. 2009). Although the majority of included studies were population-based, some assessed special populations such as healthcare workers (Bhupathiraju et al. 2013; Fung et al. 2018; Gicevic et al. 2018) or civil servants (Masset et al. 2015).

The majority of studies assessed dietary diversity using a semi-quantitative Food Frequency Questionnaire (FFQ) (Bhupathiraju et al. 2013; Blekkenhorst et al. 2020; Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Fung et al., 2018; Gicevic et al. 2018; Griep et al. 2012; Jeurnink et al. 2012; Kaluza et al. 2009; Kobayashi et al. 2020; Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b; Lee et al. 2011; Leenders et al. 2015; Letois et al. 2016; Masset et al. 2015; Reedy et al., 2008; Smyth et al. 2016; Lv et al. 2020; Tao et al., 2020); other methods included food records (Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Jeurnink et al. 2012; Leenders et al. 2015; McNaughton, Bates, and Mishra 2012; Otsuka et al. 2020) or 24-hour recall (Conrad, Thomson, and Jahns 2018; Lee et al. 2011). All dietary assessments were performed at baseline, except for three studies with repeated dietary assessments that used a cumulative average of dietary diversity (Bhupathiraju et al. 2013; Blekkenhorst et al. 2020; Fung et al. 2018). The reference period ranged from 1 to 7 days (Bhupathiraju et al. 2013; Blekkenhorst et al. 2020; Fung et al. 2018; Gicevic et al. 2018; Kobayashi et al. 2020; Lee et al. 2011; Leenders et al. 2015; Letois et al. 2016; Masset et al. 2015; Reedy et al., 2008), but 14 days (Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Griep et al. 2012; Jeurnink et al. 2012; Leenders et al. 2015) was also used and periods of up to 30 days have been reported (Kaluza et al. 2009; Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b).

There were many different and complex descriptions of dietary diversity, and no common operational definition or nomenclature (Table 2), with the term 'diversity' used interchangeably with 'variety' even in the same study. Diversity, however named, was defined as either between- or within-group diversity: (a) counts of all individual foods eaten (n = 8) (Kaluza et al. 2009; Kobayashi et al. 2020; Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b; Masset et al., 2015; McNaughton, Bates, and Mishra 2012; Reedy et al. 2008; Smyth et al. 2016); (b) counts of food groups consumed (n = 6) (Fung et al. 2018; Gicevic et al. 2018; Lee et al. 2011; Letois et al. 2016; Lv et al. 2020; Tao, Xie, and Huang 2020); (c) counts of different food items within a given food group (e.g. fruits and vegetables) (n = 7) (Bhupathiraju et al. 2013; Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Griep et al. 2012; Jeurnink et al. 2012; Kobayashi et al. 2020; Leenders et al. 2015); (d) count of food subgroups within a given groups (n = 1) (Blekkenhorst et al. 2020); (e) relative contribution of food groups within a diet (n = 1) (Otsuka et al. 2020); and (f) relative contribution of the different food subgroups within a food group (n = 1) (Conrad, Thomson, and Jahns 2018). Among eight studies on dietary diversity across individual food items, three provided stratified analysis based on healthfulness of foods (Kaluza et al. 2009; Larsson, Åkesson, and Wolk 2014b; Masset et al. 2015), and four were only focused on diversity within healthy foods (Larsson, Åkesson, and Wolk 2014a; McNaughton, Bates, and Mishra 2012; Reedy et al. 2008; Smyth et al. 2016). Healthfulness of foods was mostly determined *a priori* (Kaluza et al. 2009; Larsson, Åkesson, and Wolk 2014a; Larsson, Åkesson, and Wolk 2014b; McNaughton, Bates, and Mishra 2012; Reedy et al. 2008; Smyth et al. 2016) versus *a posteriori* (Masset et al. 2015).

This review found relative risks of dietary diversity for three health outcomes. Five cohort studies (Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Jeurnink et al. 2012; Leenders et al. 2015; Reedy et al. 2008) of dietary diversity were conducted on different types of cancer (e.g. lung, bladder, colorectal cancers), including 2 285 720 participants and 9 420 cases of all cancers. Eight studies (Bhupathiraju et al. 2013; Blekkenhorst et al. 2020; Fung et al. 2018; Gicevic et al. 2018; Griep et al. 2012; Larsson et al., 2014a; Larsson, Åkesson, and Wolk 2014b; Masset et al. 2015) examined dietary diversity in relation to the risk of CVDs (437242 participants and 17 871 cases). All-cause mortality was reported in nine studies (Conrad, Thomson, and Jahns 2018; Kaluza et al. 2009; Kobayashi et al. 2020; Lee et al. 2011; Masset et al. 2015; McNaughton, Bates, and Mishra 2012; Lv et al. 2020; Otsuka et al. 2020; Tao, Xie, and Huang 2020) and cause-specific mortality due to all types of cancer and/or CVDs was examined in eight studies (Blekkenhorst et al. 2020; Conrad, Thomson, and Jahns 2018; Kaluza et al. 2009; Kobayashi et al. 2020; Lee et al. 2011; Letois et al. 2016; Masset et al. 2015; Smyth et al. 2016; Otsuka et al. 2020).

Meta-analysis findings

Table 3 summarizes pooled risk estimates for each outcome. Corresponding forest plots and subgroup analyses are provided in the Appendix. Sensitivity analysis showed the relationships between dietary diversity and each outcome did not depend on a single study (Appendix). Moreover, there was no evidence of publication bias, except for cancer mortality (Appendix).

Meta-analysis indicated that total dietary diversity was significantly associated with a 22% lower risk of all-cause mortality (RR: 0.78 [95% CI: 0.64, 0.96], I^2=97%). This association was consistently significant when diversity was defined by ≥3 categories and populations were non-European (RR range: 0.66 to 0.94, $p < 0.05$). Exposure assessment was the prime source of study heterogeneity. By contrast, total dietary diversity was not associated with cancer-specific mortality, and was inversely but non-significantly associated with CVD-specific mortality (RR: 0.83 [95% CI: 0.70, 1.00], I^2=46.1%). However, results for cause-specific mortality showed significant associations in subgroup analyses. Total dietary diversity was significantly associated with the risk of CVD-specific mortality (RR range: 0.81 to 0.90, $p < 0.05$)

when studies used >3 categories of exposure, measured diet using FFQ, were conducted on non-Europeans, had ≥10 000 participants, and adjusted for energy intake. These subgroup characteristics were major sources of study heterogeneity. Additionally, total dietary diversity was significantly associated with the risk of cancer-specific mortality when studies used non-FFQ assessment tool, had <10 000 participants, and excluded energy adjustment (RR range: 0.53 to 0.60, $p < 0.05$). Sources of heterogeneity were the exposure comparison and energy adjustment.

Total dietary diversity across healthy foods was only analyzed in relation to all-cause mortality. Pooled estimates of total diversity among only healthy foods showed a 16% lower risk of all-cause mortality (RR: 0.84 [95% CI: 0.73, 0.96], I^2=60.5%). Meta-analysis on other cause-specific mortalities and subgroup analysis were not conducted due to a limited number of studies.

There was a small inverse but non-significant association between total dietary diversity and CVD risk (RR: 0.93 [95% CI: 0.86, 1.00], I^2=31.7%) in pooled estimates, and this relationship was strengthened in subgroups analyses of non-European populations and the diversity exposure measured by food groups not foods (RR: 0.93 [95% CI: 0.86-0.99], I^2=34.6%). The impact of total dietary diversity on cancer could not be meta-analyzed as only one study was included.

Meta-analysis/averaging of diversity within specific food groups indicated that fruit and/or vegetable diversity was not associated with mortality (all-cause and CVD-specific), CVDs and all types of cancer. Null results were found for both continuous and binary analysis of within-group diversity with any health outcome analyzed. However, from a narrative point of view, two individual studies consistently showed that greater diversity within fruits and/or vegetables was associated with reduced risk of squamous cell-type carcinomas among smokers (RR range: 0.84-0.88, $p < 0.05$) (Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Jeurnink et al. 2012).

Discussion

This meta-analysis adds novel insights on the epidemiologic relationship between dietary diversity and prominent health outcomes. A key finding of this comprehensive quantitative evaluation was a protective effect of total diet diversity for overall mortality, with a 22% lower risk of death in adults consuming diets with four or more food groups. The association of dietary diversity with CVD morbidity and mortality was marginal and only observed significantly when studies had robust design characteristics and conducted in non-European populations. Diversity of healthy foods was also associated with a 16% lower risk of all-cause mortality. There was surprisingly no association observed between diversity of fruits and/or vegetables and health outcomes, with one exception (fruits and/or vegetables diversity and risk of squamous cell-type carcinomas). This review also highlighted major knowledge gaps and study weaknesses of existing literature on this topic.

This study provides Grade B evidence to demonstrate dietary diversity increases longevity and may lower CVDs and related mortality, but may have no impact on other health outcomes. Scope exists to examine how total dietary diversity impacts cancer risk or how diversity of other subgroups influences health. It is unclear whether greater diversity is linked to greater longevity by reducing CVD-specific mortality alone or in combination with other cause-specific mortalities that could not be studied in this review due to limited available evidence.

Dietary diversity scores may fail to completely distinguish between healthy and less healthy foods and may lead to awarding inappropriately high scores to some individuals that consume "more of all foods" including processed foods and refined grains, which may be a reason for null findings (Kobayashi et al. 2020; Lee et al. 2011; Masset et al. 2015). In support of this hypothesis, when we pooled estimates from stratified results for healthfulness of foods, diversity within total healthy foods was associated with reduced risk of all-cause mortality. Notably, the significant associations were observed in studies that defined healthy foods on *a priori* (RFS) (Kaluza et al. 2009; McNaughton, Bates, and Mishra 2012) rather than *a posteriori* basis (nutrient profile models such as Ofcom and SAIN, LIM) (Masset et al. 2015). Our finding is consistent with a recent meta-analysis of diet quality indices (e.g., Healthy Eating Index) reporting protective effects on mortality (Schwingshackl, Bogensberger, and Hoffmann 2018).

Subgroup analyses revealed that the relationship between dietary diversity and health is sensitive to exposure assessment. The association of dietary diversity with all-cause and CVD-specific mortality was observed only in studies with more than three categories for dietary diversity. A large number of categories is necessary for statistical efficiency given that exposures with few categories, or median-dichotomised, can introduce random error and reduce statistical power (Naggara et al. 2011). However, exposures with many categories will show significant health effects only when studies have large sample sizes, or the association is strong (Naggara et al. 2011). It is therefore likely that the association between total dietary diversity and risk of all-cause mortality is indeed strong since subgroup analysis showed equally significant reduced risk in both large and smaller sized studies.

Subgroup analyses also showed the significant associations of total dietary diversity with CVD morbidity and mortality, and all-cause mortality, were observed in non-European populations. Notably, null findings for the association of fruits and/or vegetables diversity with all-cancers might be due to all included studies coming from Europe. This geographical disparity may be attributable to different food preferences and dietary patterns across the world. More specifically, Europeans have higher intakes of animal-based foods compared to Asian and North American populations (Ritchie and Roser 2017). Therefore, as not all the included studies adjusted for quality of diet or quantity of intakes, the adverse effect of excessive intake of animal protein on certain cancers (Corpet 2011), CVDs (Mariotti

Table 2. Definitions and measures used to assess dietary diversity and its impact on health outcomes.

			Food groups counted by studies							
Definition	Measures used	Scoring system	**Grains**[1]	**Dairy**[2]	**Protein – animal**[3]	**Protein – plant**[4]	**Fruits**[5]	**Vegetables**[6]	**Other**[7]	Source
Between-group diversity										
Number of different individual foods	Total count of unique food items reported across all foods or only (less) healthy foods (e.g. FVS, RFS, NRFS, Ofcom or SIAN, LIM nutrient profile model)	Total diet diversity (max score between 127 and 133 items); Total healthy food diversity (max score between 23 and 45 items);[8] Total less healthy food diversity (max score between 16 and 53 items)[8]	5	4	5	4	5	5	1	Kaluza et al. (2009); Kobayashi et al. (2020); Larsson, Åkesson, and Wolk (2014a); Larsson, Åkesson, and Wolk (2014b); Masset et al. (2015); McNaughton, Bates, and Mishra (2012); Reedy et al. (2008); Smyth et al. (2016)[j]
Number of different food groups	Total count of unique food groups across the whole diet. (e.g. DDS, MDDS, FGI)	Total diet diversity (max score between 5 and 10 food groups)	4	5	6	5	6	6	5	Fung et al. (2018); Gicevic et al. (2018); Lee et al. (2011); Letois et al. (2016); Lv et al. (2020); Tao, Xie, and Huang (2020)
Relative contribution of different food groups	Proportion of food groups to total energy consumption and the number of food groups in the diet (e.g. QUANTID)	Total diet diversity (13 food groups, score range: 0–1)	1	1	1	1	1	1		Otsuka et al. (2020)
Within-group diversity										
Number of different individual foods within a given food group	Total count of unique food items per food group.	Fruit & vegetable diversity (max score between 22 and 49 items); Fruit diversity (max score between 9 and 16 items); Vegetable diversity (max score between 13 and 33 items); Meat diversity (score: 0 – 16 items); Fish diversity (score: 0 – 19 items); Soy diversity (Not available)			1	1	7	7		Bhupathiraju et al. (2013); Büchner et al. (2011); Büchner, Bueno-de-Mesquita, Linseisen, et al. (2010); Griep et al. (2012); Jeurnink et al. (2012); Kobayashi et al. (2020); Leenders et al. (2015)
Number of different subtypes of food within a given food group	Total count of unique food subtypes per food group.	Vegetable subgroup diversity (between 6 and 8 subtypes)						5		Blekkenhorst et al. (2020); Büchner et al. (2011); Büchner, Bueno-de-Mesquita, Linseisen, et al. (2010); Jeurnink et al. (2012); Leenders et al. (2015)

Relative contribution of different subgroups within a food group	Proportion of each subtype to total energy consumption and recommended quantity of each subtypes	Vegetable subgroup diversity (5 subtypes, score: 0 – 0.64)	1	Conrad, Thomson, and Jahns (2018)

Abbreviation: FVS: Food Variety Score; RFS: Recommended Food Score; NRFS: Non-Recommended Food Score; Ofcom: UK Ofcom nutrient profiling model; SIAN, LIM: SAIN, LIM, score for the nutritional adequacy of individual foods, score for disqualifying nutrients; DDS: Dietary Diversity Score; MDDS: Minimum Dietary Diversity Score; FGI: Food Group Index; QUANTID: Quantitative Index for Dietary Diversity.

1Grain products included only whole grains for 3 studies (Kaluza et al. 2009, Larsson et al. 2014a, 2014b) or included starchy vegetables in 3 studies (Fung et al. 2018, Gicevic et al. 2018, Otsuka et al. 2020).

2Dairy items sometimes included only low-fat milk (Kaluza et al. 2009, Reedy et al. 2008).

3Animal protein includes red and processed meat, poultry, fish and/or egg (Fung et al. 2018, Gicevic et al. 2018, Griep et al. 2012, Kobayashi et al. 2020, Larsson et al. 2014a, 2014b, Letois et al. 2016, Smyth et al. 2016, Lv et al. 2020, Otsuka et al. 2020).

4Plant protein includes legumes, nuts, seeds, soy (Fung et al. 2018, Gicevic et al. 2018, Griep et al. 2012, Kobayashi et al. 2020, Larsson et al. 2014a, 2014b, Letois et al. 2016, Reedy et al. 2008, Lv et al. 2020, Otsuka et al. 2020, Tao et al. 2020).

5Fruits includes different types of fresh, dried, and canned fruits (Bhupathiraju etal. 2013, Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010, Büchner et al. 2011, Griep et al. 2012, Jeurnink et al. 2012, Leenders et al. 2015).

6Vegetables includes leafy, fruiting, vitamin-A rich, Stalk, allium and root vegetables; some studies include starchy vegetables such as potato (Blekkenhorst et al. 2020, Conrad et al. 2018, Reedy et al. 2008).

7Other includes items that are mostly fats and oils (Fung et al. 2018, Gicevic et al. 2018, Kaluza et al. 2009, Lee et al. 2011), but occasional only tea (Lv et al. 2020, Tao et al. 2020) or sweets (Kaluza et al. 2009).

8Range of score for healthy food diversity or unhealthy food diversity determined *a priori* (Kaluza et al. 2009, Larsson et al. 2014a, 2014b, McNaughton et al. 2012, Reedy et al. 2008, Smyth et al. 2016) or *a posteriori* (Masset et al. 2015).

2019), and related mortalities (Chen et al. 2020), may bias the beneficial effects of diversity toward the null.

It was surprising to find null associations for diversity within fruits and/or vegetables in analyses given these food groups are markers of diet quality. More detailed examination of included studies revealed that greater diversity within fruits and/or vegetables, however measured, was consistently associated with reduced risk of squamous cell-type carcinomas (but not other cancer subtypes) only among smokers (Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Jeurnink et al. 2012). This corroborates other research reporting an association between fruit and vegetable consumption and incident squamous cell-type carcinomas and not other carcinoma subtypes (Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Lucenteforte et al. 2008). This study observed the association in smokers only which may be due to residual confounders related to smoking (Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Jeurnink et al. 2012), or due to an insufficient number of cases (Jeurnink et al. 2012). Notably, risk estimates for specific cancers were not included in meta-analyses since all of them came from the EPIC cohort population. Nevertheless, averaging the estimates to obtain the pooled hazard for all-cancers was reliable since each study included 10 distinct populations across Europe and all studies were adjusted for quantity of fruits and/or vegetables consumption (Büchner et al. 2011; Büchner, Bueno-de-Mesquita, Linseisen, et al. 2010; Jeurnink et al. 2012; Leenders et al. 2015).

Dietary diversity may affect health and longevity through several biological pathways. Experimental evidence shows diversity in a diet can increase variety of intestinal microbiota and their adaptability to dietary perturbations (Heiman and Greenway 2016), thereby improving immune function and health outcomes (Sekirov et al. 2010). Dietary diversity can ensure a balance of micronutrients that interact with each other to maintain health and longevity (Randall, Nichaman, and Contant 1985). For instance, greater dietary diversity was shown to be associated with higher serum magnesium, which in turn was linked to reduced mortality (Huang et al. 2015). Moreover, the particular benefits of diversity within healthy foods, and not just vegetables, may be due to the inclusion of wider health-promoting aspects of a diet. Specifically, grains (McRae 2017) and legume fiber (Rebello, Greenway, and Finley 2014), as well as animal-based vitamins and/or minerals have greater bioavailability compared to their plant sources (Mahan and Raymond 2016). Moreover, the beneficial effect of vegetable diversity shown in individual studies, which was only observed for subtypes of vegetable (Blekkenhorst et al. 2020; Conrad, Thomson, and Jahns 2018) but not vegetable items (Griep et al. 2012), may reflect measurement precision since diversity of vegetable items can lead to a high score even if many of the items are consumed from only a single vegetable subtype. Thus, within-diversity of vegetable subtypes is more likely to include various nutrients and secondary plant metabolites (such as phytochemicals) that are unique to certain subtypes (Randall, Nichaman, and Contant 1985; Conklin et al. 2016).

Table 3. Pooled risk estimates.

Exposure	Effect sizes (n)	I^2 (%)	$P_{\text{within heterogeneity}}$	ES (95%CI)	*P* value
High versus low dietary diversity scores					
All-cause mortality (meta-analysis) †					
Total food diversity	10	97.0	0.0001	**0.78 (0.64-0.96)**	**0.01**
Healthy food diversity	4	60.5	0.05	**0.84 (0.73-0.96)**	**0.01**
Vegetables diversity	3	62.8	0.06	0.95 (0.84-1.08)	0.45
CVD mortality (meta-analysis) †					
Total food diversity	6	46.1	0.09	**0.83 (0.70-1.00)**	**0.04**
Vegetable diversity	4	57.8	0.06	0.90 (0.71-1.12)	0.34
Cancer mortality (meta-analysis) †					
Total food diversity	6	63.9	0.01	0.90 (0.75-1.09)	0.28
Cardiovascular diseases (meta-analysis) †					
Total food diversity	5	31.7	0.21	**0.93 (0.86-1.00)**	**0.06**
All cancers (dependent hazard ratios averaged)*					
Fruits and vegetables diversity	7	–	–	0.98 (0.66-1.46)	0.92
Vegetables diversity	7	–	–	0.94 (0.64-1.38)	0.75
Fruits diversity	7	–	–	0.93 (0.64-1.36)	0.70
Vegetables subgroups diversity	7	–	–	0.96 (0.66-1.38)	0.81
Continuous dietary diversity scores (per 2 products or 1 group increment)					
All cancers (dependent hazard ratios averaged)*					
Fruits and vegetables diversity (per 2 products increment)	7	–	–	0.99 (0.94-1.04)	0.67
Vegetables diversity (per 2 products increment)	7	–	–	0.99 (0.92-1.06)	0.70
Fruits diversity (per 2 products increment)	7	–	–	0.99 (0.90-1.09)	0.81
Vegetables subgroups diversity (per 1 group increment)	5	–	–	0.98 (0.89-1.08)	0.69

†DerSimonian et al. (1986): meta-analysis based on random-effects model.
*Borenstein et al. (2009): averaging of dependent effect sizes.
Note: Given that death due to CVDs, cancers, and renal diseases were in the definition of all-cause mortality in the included studies, we entered data from those cause-specific studies into the meta-analysis of all-cause mortality similar to other meta-analyses (Sadeghi et al. 2019, Parohan et al. 2019).

This review has some weaknesses. Included studies were restricted to developed countries and the last ten years which may have introduced selection bias. However, earlier studies of dietary diversity and studies from developing countries focus on nutritional adequacy rather than health outcomes; and, dietary diversity in lower-income settings is used to address food penury rather than prevent chronic disease. The study also excluded grey literature and languages outside the authors' linguistic competencies. Although all types of longitudinal designs were eligible for inclusion in this review, our searches found only observational studies that are a weaker design than RCTs for causal inference. This meta-analysis was limited in using more accurate multivariable methods to account for dependency of multiple diversity definitions (e.g. RFS and NRFS) where high and low categories of diversity scores may represent different groups of individuals. Nevertheless, we obtained an overall estimate of total dietary diversity by averaging as this approach was statistically more conservative than selecting only RFS for analysis (Scammacca, Roberts, and Stuebing 2014); it was also more consistent with the literature in counting both healthy and less healthy foods in the concept of dietary diversity.

As the type, number, and units of dietary diversity scores varied across studies, this limitation of the published literature underscores this review's key finding of the need for standardization of dietary diversity studies which some researchers have initiated (Ruel 2003; Vadiveloo et al. 2014). Future research in this area should address whether dietary diversity should only include healthy foods or whether it should add different weighting to foods based on their health effects. Lack of key measurement characteristics also limited additional subgroup analysis. Although most studies measured dietary diversity at the baseline timepoint, the approach does not account for length of exposure and potential cumulative effects which only three studies examined (Bhupathiraju et al. 2013; Blekkenhorst et al. 2020; Fung et al. 2018). While many risk estimates conditioned on known confounders (e.g. energy intake, and BMI), covariates differed across studies and some included no statistical adjustments; over a third of studies failed to report whether analyses excluded participants with biologically implausible energy intakes. Notably, quality covariables were largely unmeasured and quantity was inconsistently included in studies, despite both dietary components likely to influence relations between dietary diversity and health. Although eight out of nine studies on diversity within food groups adjusted for quantity, results were mixed and not directly comparable. Nonetheless, four studies showed significant findings after accounting for quantity of intake (Blekkenhorst et al. 2020; Jeurnink et al. 2012; Kobayashi et al. 2020; Leenders et al. 2015), suggesting an independent health effect of dietary diversity. Only one study of total dietary diversity adjusted for diet quality (Letois et al. 2016) and results indicated an independent effect of diversity. Notwithstanding these study weaknesses, 13 studies were rated as of high quality since they met other quality criteria.

This meta-analysis is strengthened by the systematic and comprehensive approach to synthesizing all longitudinal evidence from the scientific peer-reviewed literature, with three reviewers searching interdisciplinary literature from three major health sciences databases. The search used broad

terms so as to capture the widest possible evidence for health impact on this topic. Two reviewers followed an established checklist to critically appraise the quality of the evidence which was found to be generally high, with health outcomes objectively measured using registries and hospital records, or self-reported outcomes verified by medical records. Another strength of this study is the large sample sizes of included studies that ensured statistical power of reported estimates for meta-analysis, and the prospective design that allowed for causal inferences. Despite a lack of standardization for dietary diversity, our operational definition more accurately reflected the current conceptualization of a diverse diet and thus included a diversity measure (RFS) that was omitted in previous reviews, particularly those assessing obesity outcomes (Vadiveloo, Dixon, and Parekh 2013; Salehi-Abargouei et al. 2016).

This review has implication for dietary guidelines promoting dietary diversity. Specifically, our findings corroborate the 2015-2020 American Dietary Guideline's recommendation on consuming a diversity of vegetables, however, we found limited evidence to support recommended meat diversity (U.S. Department of Health and Human Services 2015), suggesting that there is a paucity of sound scientific evidence for some US dietary recommendations (Nissen 2016). Specific thresholds for diversity are given in the 2016 Chinese Food Pagoda, that recommends citizens consume more than twelve kinds of food per day, and at least twenty-five kinds of food per week (Wang et al. 2016). However, the evidence is insufficient to determine a minimum amount of different foods in a diet as studies varied widely in their definition for dietary diversity. Moreover, the evidence indicates that guidelines need to consider diversity of food groups and subgroups, but the Chinese guideline does not communicate how many of the twelve foods should be consumed from which food groups. It is generally unclear whether, for example, eating two food items from each of six different food groups is enough to ensure that a diet is adequately diverse, or more foods should be consumed from only certain food groups. Finally, in Canada, the new Food Guide (Canada 2019) now only recommends eating a diversity of healthy foods and reduced the number of food groups to only three which, compared to six in previous versions (Canada 2019), is not supported by evidence and may increase the risk of morbidity, particularly type 2 diabetes (Conklin et al. 2016).

Conclusion

This meta-analysis provides Grade B evidence to support the protective role of dietary diversity for survival and specific health outcomes, notably CVDs. The effects of total diversity on cancer risk are unknown and greater diversity within fruits and/or vegetables did not impact health outcomes, except potentially for squamous cell-type carcinomas. Nutrition policy and clinical practice should encourage diversity in a diet, specifically a more diverse selection of healthy foods. Knowledge gaps are highlighted and, despite current research being good quality, future studies should adjust for quantity and quality. Further investigations of a standardized diversity measure are warranted.

Disclosure statement

No potential conflict of interest was reported by the authors.

Authors' contribution

HM and AC designed the study and oversaw its implementation. HM, JL, and AC contributed to screening and study selection. HM and ZH performed quality appraisal. HM and AC extracted data from included studies. HM conducted statistical analysis and wrote the original draft. AC reviewed the first draft. All authors approved the final version for submission.

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