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REVIEW



A priori dietary patterns and cardiovascular disease incidence in adult population-based studies: a review of recent evidence

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ABSTRACT

Cardiovascular disease (CVD) is the leading cause of death worldwide. Studies using the *a priori* dietary pattern approach have been criticized for the heterogeneity of their scoring methods. This review aimed to evaluate the evidence on the association between *a priori* dietary patterns and CVD incidence in recent adult population-based studies. Similar to the conclusions of previous systematic reviews and meta-analyses, our review found that the majority of recent studies suggested that Mediterranean diet (6 out of 10 studies), Dietary Approaches to Stop Hypertension diet (4 out of 6 studies), Dietary Guidelines-based (11 out of 13 studies) patterns, and other emerging dietary patterns, including carbohydrate quality, Dietary Inflammatory Index, Plant-based Diet Index and Healthy Nordic Food Index, were cardioprotective in the general population; however, there was substantial heterogeneity among the studies, possibly due to differences in scoring methods and analytical approaches used and inclusion of different confounders, as well as other methodological drawbacks, such as low numbers of cases and short follow-up periods. Future studies should simultaneously examine and compare multiple *a priori* dietary patterns in a specific population using a uniform statistical approach. A consensus on the scoring methods for each *a priori* dietary pattern is also necessary.

KEYWORDS

Dietary pattern; cardiovascular disease; healthy diet; Mediterranean diet; DASH diet; population-based studies

Introduction

Cardiovascular disease (CVD), a class of disease which includes coronary heart disease (CHD), stroke, heart failure (HF) and peripheral artery disease, is the leading cause of death globally (Benjamin et al. 2019), with 17.9 million deaths attributable to it in 2015 (Roth et al. 2017). It is expected to cause more than 23.6 million deaths and an economic burden of one trillion United States (US) dollar by 2030 (Bloom et al. 2011; Smith et al. 2012). To prevent and manage the global epidemic of CVD, the United Nations set a target of a 33% reduction in CVD morbidity and mortality by 2030 in the third Sustainable Development Goals Statement (Zoghbi et al. 2014). Expert panels from Europe and US have recommended diet modification as an effective strategy for the prevention of CVD (Eckel et al. 2014; Piepoli et al. 2016).

Nutritional epidemiological research has provided valuable evidence on the relationship between diet and CVD. In terms of food groups, previous literature have reported that high intakes of fruits and vegetables (Aune et al. 2017), fish (Chowdhury et al. 2012; Hou et al. 2012; Whelton et al. 2004), nuts (Aune et al. 2016a), and whole grains (Aune et al. 2016b) may reduce CVD risk, while a high intake of processed meat increases the risk of CHD and stroke (Chen

et al. 2013; Micha, Wallace, and Mozaffarian 2010). High consumption of sugar-sweetened beverages is also associated with increased risks of CHD, stroke, and myocardial infarction (Huang et al. 2014; Narain, Kwok, and Mamas 2016). Higher intakes of fiber (Threapleton et al. 2013) and potassium (D'Elia et al. 2011) were shown to be associated with reduced CVD risk, whereas high salt intake increased CVD risk (Strazzullo et al. 2009). The findings on other food and nutrients such as dairy products (Mullie, Pizot, and Autier 2016; Qin et al. 2015; Soedamah-Muthu et al. 2011), vitamins and antioxidants (Myung et al. 2013) have remained inconclusive.

As many epidemiological analyses have focused on individual food groups and nutrients without considering their interactions, the generalization of their findings is limited, because individuals consume meals, not isolated foods and nutrients. Therefore, to investigate the overall impact of diet, dietary pattern analysis has become a new focus in nutritional epidemiology (Hu 2002). While randomized controlled-feeding trials providing subjects with specific diets can examine their efficacy in certain groups, dietary pattern analyses in population-based studies provides insights on diet adherence and its relationship with health outcome(s) in the population.

Two methodological approaches have been proposed in dietary pattern analysis: *a posteriori* and *a priori* analyses (Panagiotakos 2008). The former approach involves the use of explorative data analysis such as cluster, factor, and principal component analyses. A recent meta-analysis of prospective studies using the *a posteriori* approach found that healthy dietary patterns reduced the risk of CVD, CHD, and stroke (Rodriguez-Monforte, Flores-Mateo, and Sanchez 2015). However, the dietary patterns developed using this approach varied among populations, as they were based on available empirical data without *a priori* hypotheses (Hu 2002). In contrast, the *a priori* approach uses pre-defined dietary pattern scores to test the hypothesis related to certain dietary patterns. Using this approach, a higher adherence to the Healthy Eating Index (HEI), Alternative Healthy Eating Index (AHEI), and Dietary Approaches to Stop Hypertension (DASH) diet was found to be associated with a reduced CVD incidence and mortality (Schwingshackl, Bogensberger, and Hoffmann 2018), while a higher Mediterranean diet score (MDS) was associated with reduced risks of CHD and ischemic stroke, but not hemorrhagic stroke (Rosato et al. 2019). Nevertheless, significant heterogeneity between studies was noted among these meta-analyses (Rosato et al. 2019; Schwingshackl, Bogensberger, and Hoffmann 2018).

Findings from studies employing the *a priori* approach have been challenged by researchers due to the inconsistency of the scoring methods used in these studies (D'Alessandro and De Pergola 2015). Together with the differences in the study populations and the statistical models used, as well as the inclusion of different covariates, these have led to different conclusions on the association between the same dietary pattern and CVD. Furthermore, there is a lack of review regarding the associations between other emerging dietary patterns including Dietary Inflammatory Index (DII) (Georgousopoulou et al. 2016; O'Neil et al. 2015) and Plant-based Diet Index (PDI) (Satija et al. 2017) and CVD risk. Hence, this review aimed to evaluate and summarize the recent evidence on the relationship between *a priori* dietary patterns and CVD incidence in adult population-based studies. This review focused on studies published between Oct 2013 to Jan 2020, as the relationship between specific dietary patterns and CVD has been summarized previously (Rosato et al. 2019; Schwingshackl, Bogensberger, and Hoffmann 2018).

Materials and methods

This review adopted the Patient problem, Intervention, Comparison, and Outcome (PICO) (Schardt et al. 2007) framework to guide the research question, eligibility criteria, and outcome measures (Supplementary Table 1). The literature search was conducted according to the principles in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al. 2009) (Supplementary Table 2), using a combination of synonyms for dietary pattern and CVD incidence: (diet* pattern* OR diet* intake* OR diet* habit* OR diet* score OR diet*

index OR diet* indices OR nutri* habit OR nutri* pattern OR eating habit* OR eating pattern* OR food pattern* OR food habit* OR food quality OR diet* quality OR nutri* quality) AND (cardiovascular disease* OR CVD OR ischemic heart disease OR angina OR heart attack OR myocardial infarction OR coronary heart disease OR coronary artery disease OR CHD OR oedema OR edema OR heart failure OR HF OR stroke OR cerebrovascular disease OR atherosclerosis OR peripheral vascular diseases OR peripheral arterial disease) AND (incidence OR occurrence OR risk) on MEDLINE and EMBASE from October 2013 to January 2020. The inclusion criteria were population-based studies, studies with adult subjects (aged 18 or above), English full-text, and those using an *a priori* analysis applying pre-defined dietary pattern scores. Reviews, editorials, non-research letters, case reports, case series, and ecological studies were excluded. An example of the search strategy is provided in Supplementary Table 3.

Results

The PRISMA flowchart with reasons for exclusion at each stage is shown in Figure 1. A total of 2,303 records were identified through the database searches. After the removal of duplicates ($n = 624$), an initial screening of the titles and abstracts was conducted to exclude ineligible articles ($n = 1,679$). The full-texts of 47 articles were obtained to assess their eligibility for inclusion. Finally, 29 articles were included in this review. Their methodological quality was assessed using the National Institutes of Health quality assessment tools for observational cohort and cross-sectional studies (National Institutes of Health 2014b) and case-control studies (National Institutes of Health 2014a) (Supplementary Tables 4, 5, 6, 7 and 8). The articles were then classified into four groups: (1) Mediterranean diet, (2) DASH diet, (3) Dietary Guidelines-based dietary patterns such as AHEI, AHEI-2010 and the Dutch Dietary Guidelines, and (4) other emerging dietary patterns that could not be classified in the previous three groups. The information in each article regarding country, study design and follow-up period, participant characteristics, dietary assessment and pattern, outcome measurement, covariates, and main results presented as hazard ratios (HRs), odds ratios (ORs) or relative risk (RR) with confidence intervals (CIs) were extracted using a pre-defined extraction form to create tables for comparison. A “data microarray” (Wallach et al. 2020) illustrating the confounders adjusted for in the included studies is presented as Figure 2.

Mediterranean diet and CVD risk

Ten studies examined the relationship between the adherence to the Mediterranean diet and CVD risk (Table 1). Six of these studies showed a significant inverse association between adherence to the Mediterranean diet and CVD (Figure 3). These studies used the MDS ($n = 4$), the modified MDS by Trichopoulou and the EPIC-Elderly Prospective Study Group (2005) ($n = 2$), the amended

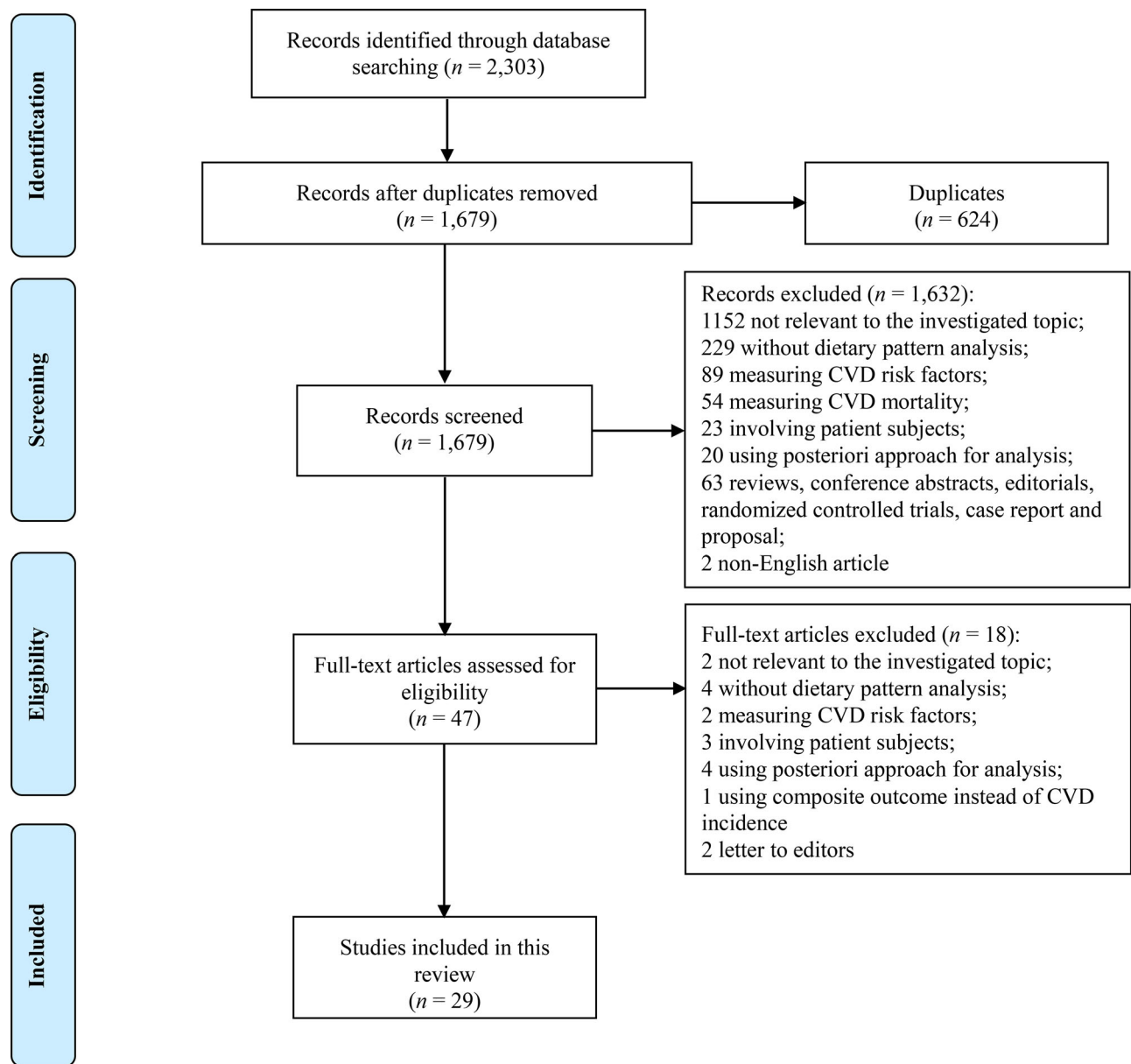


Figure 1. PRISMA flowchart of study selection.

versions of MDS according to population's characteristics ($n=3$), and literature-based adherence score to the Mediterranean diet (MED-LITE) ($n=1$) to examine adherence to the Mediterranean diet (**Supplementary Table 9**). Most of these studies adjusted for smoking ($n=10$), participants' age ($n=9$), physical activity ($n=9$), body mass index/obesity ($n=9$) and total energy intake ($n=8$) (**Figure 2**). Overall, in studies which reported that adherence to the Mediterranean diet was associated with a significant reduction in CVD risk, the risk reduction ranged from 21–45% when comparing the highest to the lowest scores; and 3–15% per unit or 20-percentile increase in the Mediterranean dietary pattern scores.

Four recent studies found no association between Mediterranean diet adherence and incidence of CHD (Turati et al. 2015), HF (Wirth et al. 2016), aortic valve stenosis (AVS) (Larsson, Wolk, and Back 2019), and total CVD

(Atkins et al. 2014). A possible reason may be due to the adjustment for cardiovascular risk factors and diabetes, which can serve as mediating factors to the association. Chan, Chan, and Woo (2013) reported a significant positive association with incident stroke which was only present in older Chinese males (HR: 0.55, 95%CI: 0.31–0.99) but not females (HR: 0.72, 95%CI: 0.28–1.87) for MDS score 6–9 compared with 0–3.

Five recent studies provided further supportive evidence between the protective effect of the Mediterranean diet on CVD incidence (Bonaccio et al. 2017; Hoevenaar-Blom et al. 2014; Sotos-Prieto et al. 2015; Tognon et al. 2014; Trébuchet et al. 2019). Hoevenaar-Blom et al. (2014) measured diet three times over 12 years in Dutch adults and found that a higher MDS was associated with a 35% reduction in risk of CVD incidence when comparing the highest and lowest MDS. In another study, Sotos-Prieto et al. (2015) showed

		Mediterranean		DASH	Dietary guidelines based			Emerging diets		
		♂ + ♀		♂ + ♀	♂ + ♀			♂ + ♀	♂	♀
		Bonaccio et al., 2017		Chan et al., 2013	Adriouch et al., 2017			AlEsa et al., 2018		
		Chan et al., 2013		Jones et al., 2018	Akbaraly et al., 2013			Georgousopoulou et al., 2016		
		Hoeveraar-Bloom et al., 2014		Larsson et al., 2016	Herbers et al., 2020			Hansen et al., 2017		
		Larsson et al., 2019		Larsson et al., 2019	Kulezic et al., 2019			Satija et al., 2017		
		Sotos-Prieto et al., 2015		Sotos-Prieto et al., 2015	Neelakantan et al., 2016			Turati et al., 2015		
		Tognon et al., 2014		Sotos-Prieto et al., 2015	Sotos-Prieto et al., 2015			O'Neill et al., 2015		
		Trébuchet et al., 2019		Struijk et al., 2014	Streppel et al., 2014			Yu et al., 2016		
		Turati et al., 2015			Trébuchet et al., 2019					
		Wirth et al., 2016			Voortman et al., 2017					
		Atkins et al., 2014			Atkins et al., 2014					
					Fung et al., 2016					
					Fung et al., 2018					
Biological	Age									
	Sex									
Dietary	Race/Ethnicity									
	Weight change									
Lifestyle behavior	Menopausal status									
	Total energy intake									
CVD risk factors	PUFA:SFA									
	SFA and/or trans-fat									
SES-related	Dietary quality									
	Margarine intake									
Drug	Egg intake									
	Potato intake									
Other	MDS									
	Glycaemic load									
Dietary	Diet prescription									
	Dietary assessment method									
CVD risk factors	# of dietary records									
	Smoking									
Lifestyle behavior	Smoking intensity									
	Physical Activity									
CVD risk factors	Alcohol consumption									
	BMI / obesity									
SES-related	WC									
	TG									
Drug	HDL or Total chol:HDL ratio									
	SBP/DBP									
Other	Atrial fibrillation									
	Diabetes									
CVD risk factors	CRP									
	Hypertension									
Lifestyle behavior	Hypercholesterolaemia									
	Family Hx									
CVD risk factors	von Willebrand factor									
	Education level									
SES-related	Household income									
	Social class									
Drug	Marital status									
	Occupation / employment status									
Other	Cohabiting status									
	HRT									
CVD risk factors	Oral contraceptive									
	Anti-hypertensive									
Lifestyle behavior	Lipid-lowering drugs									
	Multivitamin									
CVD risk factors	Vitamin E									
	Aspirin									
Other	Birth cohort									
	Date/Season of enrolment									

Figure 2. Data “microarray” showing confounders being adjusted for in the included studies. BMI, body mass index; chol, cholesterol; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HRT, hormone replacement therapy; Hx, history; MDS, Mediterranean Diet Score; PUFA, poly-unsaturated fatty acid; SBP, systolic blood pressure; SFA, saturated fat; TG, triglycerides; WC, waist circumference;

that an improvement in Mediterranean diet adherence through 4-year dietary changes in middle- and old-aged healthcare professionals in the US significantly reduced CVD incidence by 3% per 20-percentile increase in the MDS.

Tognon et al. (2014) disaggregated mixed dishes when examining Mediterranean dietary patterns in a study of Danish older population to improve accuracy. Their results showed that a per point increase in the score was associated with a 6% reduction in CVD risk. Furthermore, when wine was used instead of total alcohol in the scoring, the reduction was larger (HR: 0.92, 95%CI: 0.87–0.97), indicating that the beneficial effect of alcohol in the Mediterranean diet may be due to the wine, which has a high antioxidant activity (Fernández-Pachón et al. 2004). Bonaccio et al. (2017)

found that the beneficial effect of the Mediterranean diet was only limited to those with high education and high income, and who had higher fish consumption. In the most recent study, Trébuchet et al. (2019) examined the association between CVD risk and the MED-LITE score, which is based on absolute scoring for each food group at an individual level (Sofi et al. 2014). When the extreme quartiles were compared, the results showed that a higher MED-LITE score was associated with a 21% risk reduction in CVD.

DASH diet and CVD risk

The characteristics of studies examining the association between the DASH diet and CVD risk are summarized in

Table 1. Brief summary of the characteristics of studies examining the association between adherence to the Mediterranean diet and cardiovascular diseases risk.

First author, country, year	Study design, follow-up period and participant characteristics	Dietary assessment and pattern	Outcome measures
Atkins, UK (2014)	Prospective cohort study Mean follow-up 11.3 years 3,328 males aged 60-79 y	86-item validated self-administered FFQ 8 of 9 components of modified MDS by Trichopoulou <i>et al.</i> (2005) without scoring on alcohol	Incident CVD (MI + stroke + HF) 1. Through National Health Service Central Register for death 2. <i>Ad hoc</i> reports from general practitioners supplemented by a 2-yearly review of the clinical and hospital record
Bonaccio, Italy (2017)	Prospective cohort study Median follow-up 4.3 years 18,991 participants aged ≥ 35 y (55.4% female)	Validated Italian EPIC FFQ on 47 dishes MDS	Incidence CHD and stroke Linkage to hospital discharge file, regional Registro Nominativo delle Cause di Morte registry and death certificates
Chan, Hong Kong (2013)	Prospective cohort study Median follow-up 5.7 years 2,735 participants aged 65 y and over (51.1% female)	280-item validated FFQ through interview MDS	Incident stroke Retrieved from the Clinical Management System database of the Hong Kong Hospital Authority
Hoevenaer-Blom, The Netherlands (2014)	Prospective cohort study Mean follow-up 12 years 3,417 participants aged 20-65 y (51.0% female)	178-item validated FFQ Modified MDS by Trichopoulou <i>et al.</i> (2005) with amendment on alcohol scoring	Composite CVD (fatal CVD + nonfatal MI & stroke) 1. Morbidity through the National Medical Register using the Dutch Hospital Discharge data 2. Mortality through "Statistics Netherlands"
Larsson, Sweden (2019)	Prospective cohort study Mean follow-up 15.2 years 74,401 participants aged 45-83 y (46.3% female)	96-item validated FFQ Modified MDS by Larsson <i>et al.</i> (2017)	Incident AVS Retrieved from the Swedish National Patient Register and Swedish Cause of Death Register
Sotos-Prieto, US (2015)	Prospective cohort study 1,394,702 person-years of follow-up 29,343 males aged 40-75 y and 50,195 females aged 30-55 y	131-item validated self-administered FFQ Amended MDS by Sotos-Prieto <i>et al.</i> (2015)	Incident CVD (CHD + stroke) 1. Nonfatal event: reported by participants and examined through medical records 2. Death: identified from the state vital statistics records and the National Death Index or reported by families and the postal system
Tognon, Denmark (2014)	Prospective cohort study Mean follow-up 14 years 1,849 participants (51.3% female) born in 1922, 1932, 1942 and 1952	Weighed 7-day food record Modified MDS by Knoop <i>et al.</i> (2004)	Incident CVD Retrieved from the National Patient Registry of Hospital Discharges, the Cause of Death Register and the Central Person Register
Trébuchet, France (2019)	Prospective cohort study Mean follow-up 5.4 years 94,113 participants aged above 18 (78.6% female)	Three self-administrated nonconsecutive validated 24-hour dietary records MEDI-LITE	Incident CVD Through self-declared health events, medical records and medico-administrative databases of the National health insurance
Turati, Greece (2015)	Prospective cohort study Median follow-up 10.4 years 20,275 participants aged 20-86 y (59.3% female)	150-item validated semi quantitative FFQ through interview MDS	Incident CHD Through hospital discharge data, medical records or death certificate
Wirth, Germany (2016)	Prospective cohort study Mean follow-up 8.2 years 24,008 participants aged 35-65 y (61.6% female)	148-item validated self-administered FFQ MDS	Incident HF Through self-reported, death certificates, linkage to hospital information system and validation of participants who suffered from incident MI or reported the use of medications typical for HF treatment

AMI: acute myocardial infarction; AVS, aortic valve stenosis; CHD: coronary heart disease; CVD: cardiovascular disease; EPIC: European Prospective Investigation into Cancer and Nutrition; FFQ: food frequency questionnaire; HF: heart failure; MDS: Mediterranean diet score; MEDI-LITE: literature-based adherence score to the Mediterranean diet; MI: myocardial infarction.

Table 2. The DASH diet was originally developed to reduce blood pressure (Appel *et al.* 1997). As hypertension is one of the strongest risk factors for CVD (Kjeldsen 2018), six recent studies investigated the relationship between the DASH diet and CVD incidence among various populations (Chan, Chan, and Woo 2013; Jones *et al.* 2018; Larsson, Wallin, and Wolk 2016; Larsson, Wolk, and Back 2019; Sotos-Prieto *et al.* 2015; Struijk *et al.* 2014) using two scoring methods (Supplementary Table 10). Four of these studies showed a significant inverse association between adherence to the DASH diet and CVD risk (Figure 3). One study used Mellen's method (Mellen *et al.* 2008) which relied on nutrient recommendations to develop scoring, and five studies used Fung's method (Fung *et al.* 2008) which separated food

intake into quintiles according to the population's consumption. All six studies adjusted for participants' age, total energy intake and smoking, and most studies also adjusted for physical activity ($n = 5$), alcohol intake ($n = 4$), participants' sex ($n = 4$), education level ($n = 4$), and history of diabetes and hypertension ($n = 4$) (Figure 2). Studies which found statistically significant results reported a 7–14% reduction in CVD risk when comparing the highest to the lowest quantile, and 6–8% per unit/SD/20-percentile increase in the DASH dietary pattern scores.

Using Mellen's method (Mellen *et al.* 2008), the DASH diet was not associated with incident stroke among Chinese older adults in a study with a low number of cases ($n = 156$) and a short follow-up period of 5.7 years (Chan, Chan, and

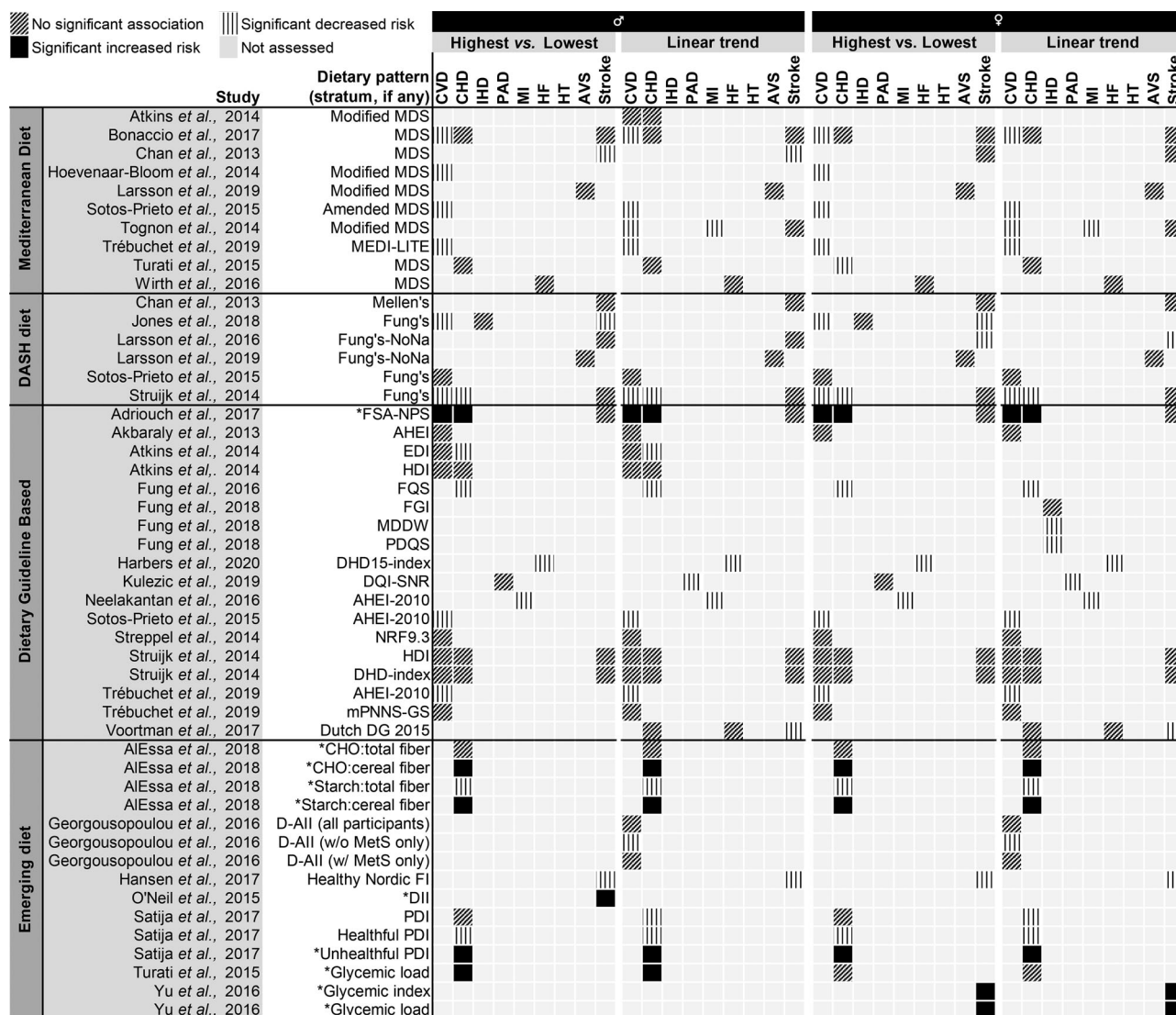


Figure 3. “Data microarray” summarizing the results of the included studies. Identical results were logged under each sex for studies which examined both sexes in the same analysis without stratification. *higher score indicates poorer diet. AHEI, alternative healthy eating index; AVS, aortic valve stenosis; CHD, coronary heart disease; CHO, carbohydrates; CVD, cardiovascular disease; D-AII, Dietary Anti-inflammatory Index; DG, Dietary Guidelines; DHD15-index, Dutch Healthy Diet 2015 Index; DHD-index, Dutch Healthy Diet Index; DII, Dietary Inflammatory Index; DQI-SNR, diet quality index assessing adherence to the Swedish nutrition recommendations; EDI, Elderly Diet Index; FGI, Food Group Index; FQS, Food Quality Score; FSA-NPS, the British Food Standards Agency Nutrient Profiling System; Fung’s-NoNa, Fung’s method without sodium; HDI, Healthy Diet Index; HF, heart failure; HT, hypertension; IHD, ischemic heart disease; MDDW, Minimum Dietary Diversity for Women; MDS, Mediterranean diet score; MEDI-LITE, literature-based adherence score to the Mediterranean diet; MetS, metabolic syndrome; MI, myocardial infarction; mPNNS-GS, mPNNS-GS: modified and “penalized” Programme National Nutrition Sante guideline score; NRF9.3, nutrient-rich food with limited nutrients; PAD, peripheral artery disease; PDI, Plant-based Diet Index; PDQS, new Prime Diet Quality Score.

Woo 2013). In contrast, a higher adherence to the DASH scoring by Fung’s method (Fung et al. 2008) was associated with a 14% reduction in CVD risk in Danish adults (Struijk et al. 2014), a 12% reduction in CVD risk in middle-aged and older UK adults (Jones et al. 2018), and a 14% reduction in the risk of stroke in middle-aged and older Swedish population when comparing the extreme quartiles (Larsson, Wallin, and Wolk 2016). Sotos-Prieto et al. (2015) also observed a 6% reduction in CVD incidence per 20-percentiles increase in the 4-year change in DASH-style diet score in a study of US middle- and old-aged healthcare professionals. When interpreting studies adopting Fung’s method, consideration should be given that the scores are relative to the population’s consumption, rather than the quantitative recommendation by the US authority (US Department of Health and Human Services 2006). Thus, these results

implied that adopting a DASH-style diet, rather than true adherence to the official DASH diet, could reduce CVD incidence in the European and American populations.

Dietary guidelines-based dietary patterns and risk of CVD

Various scoring methods have been developed to quantify adherence to Dietary Guidelines-based dietary patterns (Table 3 and Supplementary Table 11). These included the AHEI and AHEI-2010 from various versions of the Dietary Guidelines for Americans ($n = 4$), Dutch Healthy Diet-Index (DHD-index) from the Dutch Dietary Guidelines 2006 and 2015 ($n = 3$), Healthy Diet Indicator (HDI) from the World Health Organization (WHO) ($n = 2$), Diet Quality Index

Table 2. Brief summary of the characteristics of studies examining the association between adherence to the DASH diet and cardiovascular diseases risk.

First author, country, year	Study design, follow-up period and participant characteristics	Dietary assessment and pattern	Outcome measures
Chan, Hong Kong (2013)	Prospective cohort study Median follow-up 5.7 years 2,735 participants aged 65 and over (51.1% female)	280-item validated FFQ through interview Mellen's method	Incident stroke Retrieved from the Clinical Management System database of the Hong Kong Hospital Authority
Jones, UK (2018)	Prospective cohort study Mean follow-up 12.4 years 23,655 participants aged 39-79 y (54.4% female)	130-item validated FFQ; Fung's method, with energy adjustment using residual method	Incident CVD (IHD + stroke) Linkage to hospital admissions and death certificates
Larsson, Sweden (2016)	Prospective cohort study Mean follow-up 11.9 years 74,404 participants (aged 45-79 for male; aged 49-83 for female, 46.3% female)	96-item validated FFQ 7 of 8 components in Fung's method without scoring on sodium	Incident stroke Linkage with the Swedish National Patient Register and the Swedish Cause of Death Register
Larsson, Sweden (2019)	Prospective cohort study Mean follow-up 15.2 years 74,401 participants aged 45-83 years (46.3% female)	96-item validated FFQ Fung's method without scoring on sodium	Incident AVS Retrieved from the Swedish National Patient Register and Swedish Cause of Death Register
Sotos-Prieto, US (2015)	Prospective cohort study 1,394,702 person-years 29,343 males aged 40-75 y and 50,195 females aged 30-55 y	131-item validated self-administered FFQ Fung's method	Incident CVD (CHD + stroke) 1. Nonfatal event: reported by participants and examined through medical records, 2. Death: identified from the state vital statistics records and the National Death Index or reported by families and the postal system
Struijk, The Netherlands (2014)	Prospective cohort study Mean follow-up 12.2 years 33,671 participants aged 20-70 y (74.1% female)	178-item validated FFQ Fung's method	Incident CVD (CHD + stroke + PAD + HF), CHD and stroke 1. Morbidity obtained from the Dutch Center for Health Care Information with hospital discharge diagnosis 2. Vital statistics was obtained through linkage with the municipal registries 3. Cause of death collected from Statistics Netherlands

AVS, aortic valve stenosis; CHD: coronary heart disease; CVD: cardiovascular disease; DASH: Dietary Approaches to Stop Hypertension; FFQ: food frequency questionnaire; HF, heart failure; IHD, ischemic heart disease; PAD, peripheral artery disease.

Assessing Adherence to the Swedish Nutrition Recommendations (DQI-SNR; $n=1$), Elderly Diet Index (EDI; $n=1$), the British Food Standards Agency Nutrient Profiling System (FSA-NPS; $n=2$), amended Food Group Index (FGI; $n=1$), amended Food Quality Score (FQS; $n=1$), Minimum Dietary Diversity for Women (MDDW; $n=1$), modified and "penalized" Programme National Nutrition Sante Guideline Score (mPNNS-GS; $n=1$), Nutrient-rich Food index with nine beneficial and three limited nutrients (NRF9.3; $n=1$), and new Prime Diet Quality Score (PDQS; $n=1$). Although the Healthy Eating Index (HEI) is also a popular *a priori* dietary pattern that has been investigated in many previous studies, none of the recent studies included in this review utilized the HEI. Among the 13 studies included, 11 of them showed a beneficial effect of the Dietary Guidelines-based dietary pattern on CVD (Figure 3). All 13 studies adjusted for participants' age and smoking, and most studies also adjusted for total energy intake ($n=12$), physical activity ($n=12$) and BMI/obesity ($n=10$) (Figure 2).

Akbaraly et al. (2013) reported that a better adherence to the AHEI was associated with a significant reduction in the odds of fatal CVD (OR: 0.60, 95%CI: 0.39–0.92), but not nonfatal CVD in UK middle-aged adults when comparing extreme tertiles, which is consistent with another study in the UK on mortality (Akbaraly et al. 2011). In a nested

case-control study of middle-aged and older Singaporeans (Neelakantan et al. 2016), each 10 out of 100 points increase in AHEI-2010 significantly reduced the odds of CVD incidence, morbidity and mortality by 21%, 23% and 22% respectively. Similarly, in the middle-aged and older French population, each point increase in the AHEI-2010 was associated with a 9% reduction in CVD risk (Trébuechet et al. 2019). The discrepancy could be explained by the updates to the AHEI-2010 scoring system that discouraged sodium intake, which is a strong risk factor of CVD (Kjeldsen 2018), to reduce blood pressure (Chiuev et al. 2012; He, Li, and MacGregor 2013; Strazzullo et al. 2009).

In another study, Sotos-Prieto et al. (2015) examined the CVD risk association with 4-year dietary changes of middle-aged and older healthcare professionals in three US cohorts and concluded that the improvement in AHEI-2010 adherence was associated significantly with an 8% reduction in CVD incidence comparing the extreme quintiles.

Apart from AHEI and AHEI-2010, several studies also examined the association between the Dutch dietary guidelines and CVD. The study by Struijk et al. (2014) used the DHD-index for Dutch adults comparing extreme tertiles, and even without involving physical activity scores, concluded that a higher DHD-index adherence did not reduce incident CVD significantly. In another study, Voortman et al. (2017) used an updated version of the Dutch Dietary

Table 3. Brief summary of the characteristics of studies examining the association between Dietary Guidelines-based dietary patterns and cardiovascular diseases risk.

First author, country, year	Study design, follow-up period and participant characteristics	Dietary assessment and pattern	Outcome measures
Adriouch, France (2017)	Prospective cohort study Median follow-up 4.59 years 76,647 participants aged above 18 y (78.2% female)	Three nonconsecutive validated web-based 24-hour dietary records Dietary index based on the FSA-NPS	Incident CVD (CHD + stroke) 1. Self-declared health events through the yearly health status questionnaire, a specific checkup questionnaire every three months and any time on the study website 2. Then medical record was required to participants 3. Then medical data were reviewed for the validation of major health events
Akbaraly, UK (2013)	Prospective cohort study Mean follow-up 16 years 5,350 participants aged 35-55 y (29.4% women)	127-item validated semi quantitative FFQ AHEI	Nonfatal CVD (MI + angina + stroke) 1. CHD (MI & angina) based on clinically verified events 2. Stroke based on self-reported measure of physician diagnosis Fatal CVD (MI + angina + stroke) Identified through the national mortality register kept by the National Health Services Central Registry
Atkins, UK (2014)	Prospective cohort study Mean follow-up 11.3 years 3,328 males aged 60-79 y	86-item validated self-administered FFQ HDI and EDI without alcohol	Incident CVD (MI + stroke + HF), CHD 1. Through National Health Service Central Register for death 2. <i>Ad hoc</i> reports from general practitioners supplemented by a 2-yearly review of the clinical and hospital record
Fung, US (2016)	Prospective cohort study Up to 26 years follow-up Females (71,415 aged 35-55 y, 42,495 aged 40-75 y and 93,131 aged 25-42 y from 3 cohort studies)	About 135-item validated FFQ FQS	Incident CAD 1. First self-reported during the follow-up period 2. Reviewed in medical records for confirmation by study physicians 3. Fatal CVD identified from state vital records, the National Death Index, or reported by participants' next of kin or the postal system
Fung, US (2018)	Prospective cohort study Up to 28 years follow-up Females (75,045 aged 35-55 y, 43,966 aged 40-75 y and 93,131 aged 25-42 y from 3 cohort studies)	About 135-item validated FFQ; Amended FGI by Fung <i>et al.</i> (2018), MDDW and PDQS	Incident IHD 1. Self-reported event in biennial follow-up questionnaire 2. Verified by medical record 3. Death identified from state vital records or the National Death Index, or reported by participants' next of kin or the postal system
Harbers, The Netherlands (2020)	Prospective cohort study Median follow-up 15.2 years 37,468 participants aged 20-70 years (74.7% females)	178-item validated FFQ DHD15-index without scoring on coffee	Incident HF 1. Hospitalization obtained from the Hospital Discharge Register 2. Vitality information obtained from the municipal registry 3. Death information obtained from Statistics Netherlands
Kulezic, Sweden (2019)	Prospective cohort study Median follow-up 21.7 years 26,010 participants (mean age: 57.8 y, 62.3% female)	7-day food diary record combined with 168-item FFQ and 1-hour interview DQI-SNR	Incident PAD Identified through the Cause of Death Register and the Inpatient and Outpatient Registers
Neelakantan, Singapore (2016)	Nested case-control study [†] N/A 751 incidence cases aged 45-74 y and 1,443 matched control aged 45-74 y (both 35.0% female)	165-item validated semi-quantitative FFQ administered through face-to-face interview 10 of 11 components of AHEI-2010 without <i>trans</i> -fat	Incident AMI 1. Identified through electronic record linkages of the cohort database with a centralized, population-based Singapore MI Registry or a nationwide hospital discharge database (1990-2010) 2. Verified by a consulting cardiologist using the Multi-Ethnic Study of Atherosclerosis criteria for AMI
Soto-Prieto, US (2015)	Prospective cohort study 1,394,702 person-years follow-up 29,343 males aged 40-75 y and 50,195 females aged 30-55 y	131-item validated self-administered FFQ; AHEI-2010	Incident CVD (CHD + stroke) 1. Nonfatal event: reported by participants and examined through medical records 2. Death: identified from the state vital statistics records and the National Death Index or reported by families and the postal system
Streppel, The Netherlands (2014)	Prospective cohort study 56,389 person-years follow-up	Two-stage approach	Incident CVD (CHD + stroke)

(continued)

Table 3. Continued.

First author, country, year	Study design, follow-up period and participant characteristics	Dietary assessment and pattern	Outcome measures
	3,629 participants aged 55 or above (43.7% female)	1. 170-item validated self-administered FFQ 2. Dietitian identified the quantity and frequency of food consumed	1. CHD: events coded by two independent research physicians 2. Stroke: events coded by two independent research physicians and an experienced neurologist
Struijk, The Netherlands (2014)	Prospective cohort study Mean follow-up 12.2 years 33,671 participants aged 20-70 y (74.1% female)	NRF9.3 including NuR9 and LIM3 178-item validated FFQ; HDI and 9 of 10 components of DHD-index without acidic drinks and foods	Incident CVD (CHD + stroke + PAD + HF) 1. Morbidity obtained from the Dutch Center for Health Care Information with hospital discharge diagnosis 2. Vital statistics was obtained through linkage with the municipal registries 3. Cause of death collected from Statistics Netherlands
Trébuchet, France (2019)	Prospective cohort study Mean follow-up 5.4 years 94,113 participants aged above 18 y (78.6% female)	Three self-administrated nonconsecutive validated 24-hour dietary records AHEI-2010 without scoring on <i>trans</i> -fat, mPNNS-GS without scoring on physical activity	Incident CVD Through self-declared health events, medical records and medico-administrative databases of the National health insurance
Voortman, The Netherlands (2017)	Prospective cohort study Mean follow-up CHD: 10.2 years, Stroke: 11.8 years; HF: 11.7 years 9,701 participants aged 45 y or above (58.1% female)	<i>First two cohorts:</i> Two-stage approach 1. 170-item validated self-administered FFQ 2. Dietitian identified the quantity and frequency of food consumed <i>Third cohort:</i> 389-item validated self-administered semi quantitative FFQ The Dutch Dietary Guidelines 2015	Incident CHD, stroke and HF 1. Monitored through linkage to medical record 2. Independently reviewed by two physicians

AHEI: Alternative Healthy Eating Index; AML: acute myocardial infarction; CAD: coronary artery disease; CHD: coronary heart disease; CVD: cardiovascular disease; DHD-index: Dutch Healthy-Diet Index; DHD15-index: the Dutch Healthy Diet 2015 Index; DQI-SNR: diet quality index assessing adherence to the Swedish nutrition recommendations; EDI: Elderly Eating Index; FGI: Food Group Index; FFQ: food frequency questionnaire; FQS: Food Quality Score; FSA-NPS: the British Food Standards Agency Nutrient Profiling System; HDI: Healthy Diet Indicator; HF: heart failure; IHD: ischemic heart disease; LIM: limited nutrient; MDDW: Minimum Dietary Diversity for Women; MI: myocardial infarction; mPNNS-GS: modified and "penalized" Programme National Nutrition Sante guideline score; NA: not applicable; NuR: nutrient rich; NRF: nutrient-rich food; PAD: peripheral artery disease; PDQS: new Prime Diet Quality Score.

†Follow-up period is not applicable as it is a case-control study in which participants were observed retrospectively.

Guidelines score and found a significant reduction in stroke risk, but not CHD and HF risk, for every guideline item adhered to in a group of Dutch middle-aged and older adults. Although both studies had long follow-up periods (>10 years) allowing CVD events to occur, the insignificant results could be due to the scoring methods of the two Dutch guidelines (Health Council of the Netherlands 2015; van Lee et al. 2012), where participants were only awarded the score for guideline items which they completely adhered to. The generally low vegetable, fruit, and fiber intake in the study population (Struijk et al. 2014) and poor adherence to legumes, nuts, and red and processed meat recommendations (Voortman et al. 2017) in these studies may have caused a lower total score and variation in the scores, decreasing the chance to detect an association. In contrast, when the updated Dutch Dietary Guidelines score was constructed on a continuous scale (Biesbroek et al. 2018; Looman et al. 2017), Harbers et al. (2020) found a significant inverse association between the Dutch Healthy Diet 2015 Index score and 15-year incidence of HF in the same cohort as Struijk et al. (2014).

Two other studies examined the association between the dietary guidelines from their respective countries and CVD risks. In a Swedish cohort study, higher adherence to the

DQI-SNR was inversely associated with incident peripheral artery disease in middle-aged individuals (Kulezic et al. 2019). Another study examined the relationship between the mPNNS-GS, which complies with the French dietary guidelines, and CVD among middle-aged and older French adults (Trébuchet et al. 2019). However, the inverse association was only significant when transient ischemic attack (TIA) cases were included. This may be attributed to increased statistical power.

Two studies examined HDI in Dutch adult and British older populations respectively (Atkins et al. 2014; Struijk et al. 2014), and both failed to find a significant association between HDI and CVD incidence, which could be due to lower variations in the scores. Furthermore, since the majority of HDI components are macro- and micronutrients (Supplementary Table 11) with high measurement error, due to the requirement for the transformation from food to nutrient intake, their accuracy depends on the completeness of food composition database and compliance to standard food portion size in the FFQ used (Willett 2013).

In clinical practice, scoring methods involving both food and nutrients are difficult to apply as they require the use of software/database to compute the nutrient intake for assessment. Simpler scoring tools based solely on food group

intake provide a quick way to assess an individual's dietary habits. Fung et al. (2016) assessed the association between FQS and incident coronary artery disease in three US cohorts of middle-aged and older healthcare professionals and identified an inverse association (RR: 0.61, 95%CI: 0.54–0.69) when comparing extreme deciles. However, as the scoring classified food intake into quintiles, it was heavily dependent on the consumption pattern of the sample population, implying that the same association may not exist in other populations with a different dietary intake pattern.

For scoring methods based on absolute cutoffs, Fung et al. (2018) examined the associations of FGI, MDDW, and PDQS with ischemic heart disease (IHD) risk using the same three cohorts. Although the three scores were positively correlated (Fung et al. 2018), only MDDW and PDQS had significant inverse associations with IHD incidence for each SD increase. It is possible that the higher number of items in the MDDW and PDQS increased their sensitivity to measure diet quality compared with the FGI. Furthermore, FGI assessed the frequency of consumption per week, which may be too simplistic and less sensitive to the general dietary patterns in developed countries where overconsumption is a major issue. Similar to FGI, which assessed consumption frequency, higher scores in the EDI were significantly associated with fewer CHD events when comparing extreme quartiles in British older males (Atkins et al. 2014); it was specifically developed to capture the recommendations in the Modified MyPyramid for Older Adults based on populations from developed countries (Kourlaba et al. 2009).

Two studies examined food-based indices (Adriouch et al. 2017; Streppel et al. 2014). Streppel et al. (2014) used the NRF9.3 (Supplementary Table 11) to assess food consumed in Dutch middle-aged and older population, where no association between NRF9.3 and CVD incidence was observed. This could be because the food group contributing the second most to the index of the participants was dairy products, whose association with CVD is inconclusive (Mullie, Pizot, and Autier 2016; Qin et al. 2015; Soedamah-Muthu et al. 2011). Contrarily, Adriouch et al. (2017) examined the association between the FSA-NPS and CVD risk in a French adult population. With a higher score indicating a less healthy diet (e.g., fewer fruits and vegetable and more sodium and saturated fat), it was associated with an 8% increase in CVD incidence for every point increase.

Other emerging diets and CVD risks

Table 4 and Supplementary Table 12 summarize the characteristics of and scoring methods used in studies examining the association between emerging diets and CVD risks respectively.

The quality of carbohydrates in terms of glycaemic index (GI) and glycaemic load (GL) and its ratio to fiber was examined in three studies (AlEsa et al. 2018; Turati et al. 2015; Yu et al. 2016). These represented the cumulative effect of various nutrients such as starch, protein, fat and fiber on postprandial blood glucose response (Augustin

et al. 2002). Yu et al. (2016) examined the associations of GI and GL on various types of stroke in middle-aged and older Chinese females. Their results indicated that both GI and GL were associated with an 18% and 25% increased risks of ischemic stroke respectively comparing extremes deciles, but not hemorrhagic stroke, which could be due to the small number of hemorrhagic stroke cases ($n=241$), leading to insufficient power to detect the association. The relationship between GL and CHD incidence was assessed in a Greek adult population (Turati et al. 2015), where GL in the highest tertile was associated with a 41% increase in CHD incidence. AlEsa et al. (2018) tested the ratios between carbohydrates and various types of fiber in three US middle-aged and older healthcare professional cohorts and reported that participants in the highest quintile of the carbohydrate: cereal fiber and starch: cereal fiber ratios had a 20% and 17% increase in risk of CHD incidence respectively. This could be due to the nutrients and phytochemicals in cereal fiber in whole grains (Aune et al. 2016b).

Two studies (Georgousopoulou et al. 2016; O'Neil et al. 2015) examined the association between anti-inflammatory diets as assessed using DII or Dietary Anti-Inflammatory Index (D-AII) and CVD risk. The DII scores foods that exert effects on inflammatory markers based on the cumulative effect of various nutrients (Shivappa et al. 2014), with positive scores for food enhancing inflammation and vice versa; and D-AII could be seen as a reciprocal of DII. Both studies had relatively short follow-up periods (<10 years). O'Neil et al. (2015) concluded that a high DII was associated with a 100% increased CVD incidence (HR: 2.00, 95%CI: 1.01–3.96) in Australian adults when comparing extreme tertiles. In a Greek study with a longer follow-up period (mean = 8.4 years), Georgousopoulou et al. (2016) reported a 3% statistically significant decrease in risk of CVD per unit increase in D-AII among participants without metabolic syndrome only. The anti-inflammatory effect of foods may be attenuated among patients with metabolic syndrome (Czernichow et al. 2009; Hercberg et al. 2004; Steinhubl 2008), as pathological changes of CVD may have already started (Bonora 2006).

The study by Satija et al. (2016) showed that a high adherence to the PDI significantly reduced the CHD incidence (HR: 0.93, 95%CI: 0.9–0.97 per 10 out of 90 point increase), and higher adherence to the healthful PDI further reduced the risk significantly (HR: 0.88, 95%CI: 0.85–0.91) among middle-aged and older-aged healthcare professional in three US cohorts. A higher score in the unhealthful PDI, on the other hand, significantly increased the risk of CVD (HR: 1.10, 95%CI: 1.06–1.14).

Apart from the Mediterranean diet, another tradition diet called Nordic diet, which encourages high intake of fish, apples and pears, cabbages, root vegetables, rye bread and oatmeal (Olsen et al. 2011), was suggested to be beneficial to CVD (Aune et al. 2017; Chowdhury et al. 2012; Hou et al. 2012; Threapleton et al. 2013; Whelton et al. 2004). The study by Hansen et al. (2017) identified that a higher Healthy Nordic Food Index (4–6 vs. 0–1) was associated with a 17% reduced risk in stroke incidence.

Table 4. Summary of the characteristics of studies examining the association between adherence to emerging dietary patterns and cardiovascular diseases risk.

First author, country, year	Study design, follow-up period and participant characteristics	Dietary assessment and pattern	Outcome measures
AlEsa, US (2018)	Prospective cohort study 2,827,024 person-years, up to 28 years follow-up 42,865 males aged 40-75 y and 75,020 females aged 30-55 y from 2 cohort studies	Validated FFQ with adjustment on total energy intake using residual method and removal of extraneous variation Ratios of carbohydrate:total fiber, carbohydrate:cereal fiber, starch:total fiber and starch:cereal fiber	Incident CHD 1. Fatal CHD identified by next of kin or the National Death Index and confirmed by medical records 2. Non-fatal MI confirmed by medical records
Georgousopoulou, Greece (2016)	Prospective cohort study Mean follow-up 8.4 years 2,020 participants aged 18-89 y (50% female)	Validated semi quantitative FFQ D-AII, which was the reverse of DII	Incident CVD (CHD + stroke + fatal CVD) Detailed evaluation of medical records performed by investigator
Hansen, Denmark (2017)	Prospective cohort study Mean follow-up 13.5 years 55,338 participants aged 50-64 y (52.4% female)	192-item validated semi quantitative FFQ; Healthy Nordic Food Index	Incident stroke Linkage to the Danish National Patient Register
O'Neil, Australia (2015)	Prospective cohort study 5 years follow-up 1,540 male participants aged ≥ 18 y	80-item validated FFQ through interview DII	Incident CVD (cardiac death + nonfatal MI & stroke) with hospital presentation Extracted from catchment area hospital medical records
Satija, US (2017)	Prospective cohort study 4,833,042 person-years follow-up Females: 121,701 aged 30-55 y, 116,686 aged 25-42 y from 2 cohorts; 51,529 males aged 40-75 y	Validated FFQ; PDI, healthful PDI and unhealthful PDI	Incident CHD 1. Fatal CHD identified by next of kin or the National Death Index and confirmed by medical records 2. Non-fatal MI confirmed by medical records
Turati, Greece (2015)	Prospective cohort study Median follow-up 10.4 years 20,275 participants aged 20-86 y (59.3% female)	About 150-item validated semi quantitative FFQ through interview Glycaemic load	Incident CHD Through hospital discharge data, medical records or death certificate
Yu, China (2016)	Prospective cohort study Mean follow-up 10 years 64,328 females aged 40-70 y	77-item validated FFQ with adjustment on total energy intake using residual method Glycaemic index and glycaemic load	Incident ischemic stroke and hemorrhagic stroke Confirmed by reviewing medical records

CHD: coronary heart disease; CVD: cardiovascular disease; D-AII, dietary anti-inflammatory index; DII, dietary inflammatory index; FFQ: food frequency questionnaire; MI: myocardial infarction; NA: not applicable; PDI, plant-based diet index.

Discussion

In this review, the majority of the studies published between Oct 2013 to Jan 2020 showed the beneficial effects of the Mediterranean diet, DASH diet, Dietary Guidelines-based dietary pattern, and other emerging diets including low GI and GL, anti-inflammatory diet, plant-based diet especially healthful plant-based diet, and Nordic diet, on CVD risk.

The results of the Mediterranean diet, DASH diet and Dietary Guidelines-based dietary patterns are consistent with previous meta-analyses (Rodriguez-Monforte, Flores-Mateo, and Sanchez 2015; Rosato et al. 2019; Schwingshackl, Bogensberger, and Hoffmann 2018) and feeding trials (Estruch et al. 2018). For the other emerging diets, the link between GI and CVD may be explained by the possible presence of chronic postprandial hyperglycemia, which can lead to excessive oxidative stress and hyperinsulinemia which then exert effects on blood pressure, lipids, coagulation factors, inflammatory mediators, and endothelial functions (Ludwig 2002). High antioxidant consumption with an adherence to an anti-inflammatory diet may mitigate the low grade systemic inflammation caused by atherosclerosis. Similarly, plant-based diets were found to reduce the level of inflammatory markers such as C-reactive protein and interleukin-6, in a recent meta-analysis of intervention studies

(Eichelmann et al. 2016). The results for the Nordic diet were consistent with other studies that demonstrated its effectiveness in reducing blood pressure and improving lipid profiles (Adamsson et al. 2011).

A recent review by Aljuraiban et al. (2020) showed the utility of various *a priori* dietary pattern scores in assessing the relationship between diet quality and cardiovascular risk factors, incidence and mortality. They also noted that there is a lack of consensus in the definition and utility of an *a priori* dietary pattern score between studies, which may lead to the misclassification and low comparability between score categories. For example, four different scoring systems were used to study the association between the Mediterranean dietary pattern and CVD. The original MDS (Trichopoulou et al. 2003) grouped fruits and nuts together, while the modified MDS by Trichopoulou and the EPIC-Elderly Prospective Study Group (2005) grouped legumes with nuts, and used different scoring criteria for alcohol. Three other studies (Larsson, Wolk, and Back 2019; Sotos-Prieto et al. 2015; Tognon et al. 2014) calculated their own MDS according to the population characteristics and limitations in dietary assessment. Furthermore, the disaggregation of mixed dishes, which helped provide a more precise estimation of consumption pattern (Fitt et al. 2010), was only performed in the study by Tognon et al. (2014). Similar limitations

were observed in studies examining the DASH diet-CVD association (Fung et al. 2008; Mellen et al. 2008). We propose that future studies on the DASH diet should adopt scoring systems with absolute cutoffs such as the Mellen's method (Mellen et al. 2008) so that the adherence and effect of the true DASH diet instead of a DASH-style diet can be examined and compared between populations.

In addition, Aljuraiban et al. (2020) also raised concerns regarding how diet components were scored. Similarly, we observed that some *a priori* dietary pattern scores (Struijk et al. 2014; Voortman et al. 2017) were constructed based on an *all-or-nothing* approach for each component item, which resulted in a narrow distribution of the participants' score, making it difficult to detect an association between the score and CVD risks. We therefore propose that methods with continuous scoring should be used in future studies.

Apart from the above points, our review further adds to the work of Aljuraiban et al. (2020) by identifying and discussing several important limitations of the current literature. First, although well-known confounders of CVD risks, such as age, sex, physical activity, and smoking, were commonly adjusted for in the multivariate analyses, they were unlikely to be the only confounders of the diet-CVD risks association. The inclusion of other potential confounders in the analysis was highly variable between the studies. This may have had an impact on the degree of residual confounding (Wallach et al. 2020). As previously discussed by Wallach et al. (2020), since confounders can either contribute favorably or adversely to the association with the study outcome, the inconsistent consideration of confounders in the different studies may have hampered the between-study comparisons. Indeed, in some cases, the confounders may have been incorrectly adjusted for, which may have biased the effect estimates.

Using studies on Mediterranean diet as an example, the adjustment for cardiovascular risk factors and diabetes as confounders in some studies (Atkins et al. 2014; Larsson, Wolk, and Back 2019; Turati et al. 2015; Wirth et al. 2016) may have nullified the association between the Mediterranean diet and risks of CVD outcomes, as these may have been intermediary variables (Zeraatkar et al. 2019) of the causal pathway in the association between the Mediterranean diet and CVD risks (Franquesa et al. 2019). While practical concerns (e.g. unavailability or poor quality of data) may have limited the ability of some researchers to include well-known/theoretical confounders in their multivariate analyses, and other researchers may have decided to drop a confounder in their final multivariate model because it did not change the effect estimates, a simulation study by Lee (2014) suggested that theoretical/known confounders should always be adjusted for regardless of the empirical evidence shown in the study. Future studies on diet-CVD relationship should therefore consider adopting a standard panel of known confounders based on current knowledge (e.g. age, sex, total energy intake, smoking status, physical activity level, saturated fat intake, *trans* fat intake, socioeconomic status, etc.) in the first multivariate model, which

would mandate the routine collection of these variable in all future studies. Any additional confounders being adjusted for, should be included in further multivariate models as exploratory analyses. Such an approach would ensure there is always a consistent model that could be used for between-study comparisons.

Second, the differences in the characteristics of the study population may also have confounded the association between dietary patterns and CVD risks, which would also reduce the between-study comparability. We therefore propose that future studies should simultaneously examine and compare multiple *a priori* dietary patterns in a specific population with a uniform statistical approach e.g. Alvarez-Alvarez et al. (2020) and Wong, Grech, and Louie (2020), which will minimize or eliminate some of the aforementioned limitations to allow better conclusions to be drawn regarding which dietary pattern(s) confers the best protective effect on chronic disease risks.

Furthermore, this review was limited by solely including articles published within the recent years, because the relationship between specific dietary patterns and CVD has been previously explored (Rosato et al. 2019; Schwingshackl, Bogensberger, and Hoffmann 2018). Instead of pooling the results in a meta-analysis, this review compared the results among studies and evaluated their methodological approaches to provide insights and suggestions for future research. Last, most included studies were conducted in developed regions (Adriouch et al. 2017; Akbaraly et al. 2013; AlEsa et al. 2018; Atkins et al. 2014; Bonaccio et al. 2017; Chan, Chan, and Woo 2013; Fung et al. 2018; Fung et al. 2016; Georgousopoulou et al. 2016; Hansen et al. 2017; Hoevenaar-Blom et al. 2014; Jones et al. 2018; Larsson, Wallin, and Wolk 2016; Neelakantan et al. 2016; O'Neil et al. 2015; Satija et al. 2017; Sotos-Prieto et al. 2015; Streppel et al. 2014; Struijk et al. 2014; Tognon et al. 2014; Turati et al. 2015; Voortman et al. 2017; Wirth et al. 2016), implying that the results may not be applicable to developing regions where the food consumption patterns would be different.

Last, other common methodological drawbacks, such as a low number of cases, which may have lowered the statistical power to detect an association, e.g. Wirth et al. (2016) and Chan, Chan, and Woo (2013), and short follow-up periods, were observed. As atherosclerosis, which is the main contributor to cardiovascular disease, is a gradual and lifelong process of arterial wall lesions with the accumulation of cholesterol-rich lipids and inflammatory response (Insull 2009), a long follow-up period is required to allow the effect of dietary pattern to show. Future studies should carefully consider the use of an appropriate sample size and proper follow-up period.

The strengths of this review included the use of the PICO framework (Schardt et al. 2007) and principles in PRISMA guideline for literature search (Moher et al. 2009). We have also assessed the quality of the included studies using the National Institutes of Health Quality assessment checklists. Furthermore, we have presented data on common confounders being adjusted for in the included studies as

well as the summary findings as “data microarrays” which visualized this information to allow *at-a-glance* comparisons.

To conclude, findings from this review agree with those of previous reviews, that most *a priori* dietary patterns are cardioprotective. However, we have found several drawbacks in the current literature on the topic, in particular the low between-studies comparability. Future studies should utilize standardized *a priori* dietary pattern scoring methods, and only make modifications to the original scoring method when formulating new dietary patterns. They should also simultaneously examine and compare multiple *a priori* dietary patterns in a specific population using a uniform statistical approach.

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