

# Diet and nutrition in cardiovascular disease prevention: a scientific statement of the **European Association of Preventive Cardiology** and the Association of Cardiovascular Nursing & Allied Professions of the European Society of **Cardiology**

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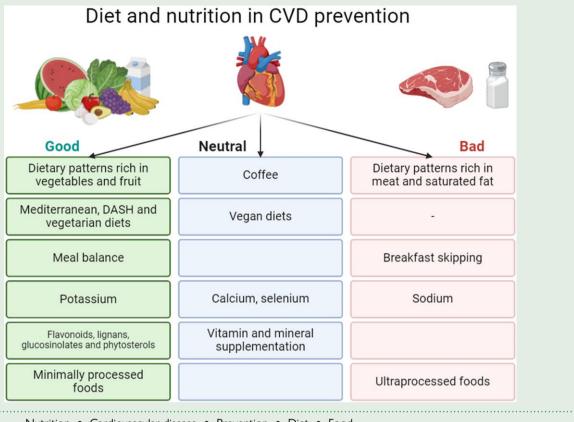
What we eat is a cornerstone of cardiovascular disease (CVD) prevention, but health professionals may not have a clear understanding of the current evidence-based research to underpin eating habits and recommendations. This study aims to appraise existing evidence-based research on the importance of diet on CVD risk biomarkers, specifically, the effects of dietary patterns, specific foods, and constituents including vitamins/minerals and plant-derived bioactive compounds on CVD risk. Plant-based dietary patterns rich in minimally processed foods, vegetables, and fruits reduce CVD risk, while patterns rich in ultra-processed foods, meat, salt, sugar, and saturated fat increase risk. The Mediterranean, Dietary Approaches to Stop Hypertension, and vegetarian diets reduce CVD risk, while vegan diets offer no additional benefit. Low-carbohydrate diets may be beneficial, but their long-term effect remains to be confirmed. Balanced distribution of caloric intake through different meals is associated with favourable effects. Fasting (e.g. alternate-day, intermittent, time-restricted, and periodic) can reduce CVD risk but is often challenging. Moderate coffee consumption is not associated with increased risk of CVD. The consumption of one unit of alcohol/day may contribute to a reduced cardiovascular risk without presenting an unfavourable risk profile. Generally, there is no evidence that vitamin and mineral supplementation reduces CVD risk. High potassium intake is beneficial in healthy individuals, calcium or selenium supplementation shows no added benefit, and high sodium intake is detrimental. Diet is a major component of CVD prevention, and health professionals should include dietary assessment and evidence-based recommendations in their clinical practice.

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#### **Graphical Abstract**



**Keywords** 

Nutrition • Cardiovascular disease • Prevention • Diet • Food

# Introduction: nutrition for cardiovascular disease

Diet is a key risk factor for the development of cardiovascular disease (CVD). Early studies focused on specific nutrients/dietary constituents and their effect on cardiovascular health. However, it soon became clear that total food intake and dietary patterns may be a more appropriate way to broadly examine diet and cardiovascular health associations. Dietary patterns encompass the totality of a diet, while allowing for various ways to achieve a healthy diet. As such, public health recommendations will be more readily translated into eating behaviours when defined by recommending foods and not nutrients. Expanding the work in our previous clinical consensus statement on the promotion of healthy nutrition in CVD prevention,<sup>1</sup> in this scientific statement from the European Association of Preventive Cardiology (EAPC) and the Association of Cardiovascular Nursing & Allied Professions (ACNAP) of the European Society of Cardiology (ESC), we summarize the scientific evidence regarding dietary patterns, specific foods, and their constituents in relation to cardiovascular risk. For each dietary pattern and food group, we interpret the available scientific evidence and highlight areas where further research is required to enhance our evidence base. The aim is to empower preventive cardiologists, physicians, nurses, and allied health professionals regarding the benefits of targeted evidence-based nutrition knowledge to patients.

#### Review of evidence

The authors of this statement were asked to review literature without any restrictions, across available databases including PubMed, Embase, and the Cochrane Library until December 2023. The search covered any aspect relating to nutrition and the focus of this statement as detailed through the subheadings below. The evidence was reviewed by the group in an iterative process, and gaps in knowledge were generated with the agreement of all co-authors.

# Dietary patterns and diets

Dietary intake is characterized by variety, and the effects of individual nutrients or foods are hard to identify as they are not consumed as single entities but combined with other nutrients and foods. Food components can interact to have synergistic effect, and a diet that is relatively high in carbohydrates will automatically be relatively low in fat and/or protein. Hence, dietary patterns have emerged to understand the combined impact of nutrients when considered together, rather than in isolation. The combined estimate of favourable dietary habits reflected by the total dietary pattern highlights the overall preventive potential of diet.

# Naïve dietary patterns

Naïve dietary patterns reflect the complex behaviour behind an individual's eating habits and food consumption. A dietary pattern is defined

Aspect	Mediterranean diet	DASH diet
General scope	Promotes overall heart health and longevity	Lowers blood pressure and improves heart health
Main foods	Vegetables, fruits, wholegrains, olive oil, legumes, nuts, fish, moderate dairy, and moderate alcohol intake (especially red wine)	Vegetables, fruits, low-fat dairy products, wholegrains, lean protein (especially poultry and fish), and nuts.
Fats	Increased fat content with special focus on the quality (mainly from olive oil and nuts)	Low in fat
Meat consumption	Limits red meat; encourages fish and poultry	Emphasizes lean meats (poultry, fish) and low red meat
Dairy	Moderate; mostly fermented dairy products	Focuses on low-fat or fat-free dairy products
Sodium intake	Not specifically restricted but naturally lower due to the recommendation for least processed foods; use of herbs and spices in food preparation.	Limits sodium intake to 1500–2300 mg per day
Wine/alcohol	Moderate wine consumption, typically red wine; focus on drinking pattern (alongside meals, socializing)	Alcohol is not emphasized but can be consumed in moderation

by the individual food choices and is characterized by the food that is most frequently consumed by a person. Naïve dietary patterns may include elimination of entire food groups such as carbohydrates or fats, overconsumption of certain foods, emotional eating, or regularly skipping meals.

longevity

Limits refined sugars and processed foods

Lowers risk of heart disease, stroke, certain cancers, and diabetes; promotes

Sugar Health benefits

Although there are no specific definitions, there are several patterns that have been observed over the years in numerous studies. Some examples include the 'meat and fries' pattern, the 'fruits and vegetables' pattern, and the 'fatty and sugary'. Another study observed the 'Western' pattern, characterized by consumption of refined cereals, processed and red meats, high-fat milk and dairy products, and the 'prudent' pattern that consists of high amounts of fruit, vegetables, white meats, and reduced-fat milk derivatives. Regardless of the label, some of these patterns may represent dietary habits that may be oversimplified or not well informed, and, as such, they may often lack the nutritional requirements of a balanced diet. More importantly, as certain diets quickly become popular on a global level through social media, many people with various underlying medical conditions adopt inappropriate dietary habits that may harm their overall well-being.

An individual's food choices and dietary pattern are influenced by multiple factors, including cultural, religious, medical, psychological, and personal circumstances. Limited nutritional awareness and low socioeconomic status have been shown to have a major impact on eating habits by steering them towards an unhealthy direction. However, the opposite is observed in low- and middle-income countries where people of higher socioeconomic status tend to adopt a 'westernized' dietary pattern that may translate to more processed foods and saturated fats and less traditional locally sourced options. More recently, social media have been shown to have a significant impact on eating habits, although it is unclear yet whether this effect is beneficial.

A balanced diet translates to adequate nutritional intake, which is of paramount importance for a person's health. Fad diets, for example, which promise fast weight loss, may be accompanied with significant deficiencies in nutrients and micronutrients, which may be of great concern particularly for those with underlying chronic diseases. Achieving nutritional balance also has a protective impact on physical and mental status by preventing diseases. Overconsumption of red

and processed meats and saturated fats is linked with increased risk of diabetes and CVD. 9 It is therefore essential to adopt a dietary pattern that is well balanced and tailored to the individual's needs and lifestyle.

Limits sugar and sugary beverages

risk of heart disease

Effectively reduces high blood pressure, cholesterol, and

In addition, more and more impact of dietary choices on planetary health is recognized, leading to dietary recommendations that are beneficial for both human and planetary health. <sup>10</sup> In this paper, we will focus on human health.

#### Gaps in knowledge

- Large epidemiological studies are needed to evaluate the effect of naïve dietary patterns of different populations across the globe on CVD events.
- (2) Implementation of the results of such studies considering individual motivation and knowledge is also essential.
- (3) Nutritional education and awareness may limit imbalances in naïve dietary patterns observed in the population level. However, there is a lack of large population studies investigating the effect of behavioural interventions and change of naïve dietary patterns on peoples' overall health and the prevalence of diseases such as cardiometabolic diseases.

# Mediterranean Diet and Dietary Approaches to Stop Hypertension diets

A shift from animal-based to plant-based dietary patterns has been associated with many cardiometabolic health benefits. <sup>11</sup> The Mediterranean-type diet has been long investigated for its potential beneficial effects on a range of chronic disease outcomes, cumulating in the PREDIMED (Prevención con Dieta Mediterránea) trial. <sup>12</sup> The Mediterranean diet is characterized by high intake of fruits, vegetables, legumes, wholegrain products, fish, and unsaturated fatty acids (especially olive oil), moderate consumption of alcohol (mainly wine, preferably consumed with meals), and low consumption of red meat, dairy products, and saturated fatty acids. <sup>13</sup> Several observational and intervention studies have shown reduced mortality and morbidity from CVD following greater adherence to a Mediterranean dietary pattern <sup>14</sup> as well as beneficial effects on

cardiometabolic disorders including metabolic syndrome. <sup>15</sup> In a comprehensive meta-analysis of prospective cohort studies, a 2-point increase in adherence score to the Mediterranean diet was associated with a 10% reduced risk of CVD. <sup>16</sup> A recent meta-analysis of 37 randomized controlled clinical trials (RCTs) suggests that there is still uncertainty regarding the effects of a Mediterranean-style diet on clinical endpoints and CVD risk factors. <sup>17</sup> However, based on supportive observational evidence and the biological mechanisms to explain the beneficial effect of the Mediterranean diet, it remains a popular cardioprotective dietary pattern.

The Dietary Approaches to Stop Hypertension (DASH) diet, which emphasizes fruit, vegetables, fat-free/low-fat dairy, wholegrains, nuts, and legumes and limits saturated fat, cholesterol, red and processed meats, sweets, added sugars, salt, and sugar-sweetened beverages, is recommended by the ESC guidelines on CVD prevention in clinical practice and the European Association for the Study of Diabetes guidelines. 18,19 A recent meta-analysis and umbrella review of meta-analyses concluded that the DASH diet is associated with decreased CVD incidence and improves blood pressure with evidence of other cardiometabolic advantages in people with and without diabetes.<sup>20</sup> In particular, a pooled analysis revealed that DASH diet contributed to a 20% reduced CVD incidence and has blood pressure benefits, which may translate to ~20% reduction in CVD risk, along with meaningful benefits in other established CVD risk factors in those with and without diabetes.<sup>21</sup> The similarities and differences between the Mediterranean and the DASH diets are indicated in Table 1.

#### Gaps in knowledge

(1) Effective nutrition policies and public health strategies to make the adherence to such diets feasible, affordable, and sustainable for the majority of the population are still under investigation.

# Vegetarian and vegan diets

Vegetarian diets have increased in popularity and may be deemed a cost-effective and low-risk intervention for many chronic diseases, including CVDs, yet the hitherto evidence is inadequate and in some cases of poor quality. A meta-analysis of 13 cohort studies suggested that a vegetarian diet was associated with ~15% lower risk of CVD and 20% lower risk of ischaemic heart disease (IHD) compared with non-vegetarian diets (any kind).<sup>22</sup> The CARDIVEG RCT showed that a low-calorie, vegetarian diet was as effective as the Mediterranean diet in reducing surrogate markers related with increased CVD risk factors, although no information on major CVD endpoints was provided.<sup>23</sup> The role of vegan diets on cardiometabolic health has also been investigated. In the aforementioned meta-analysis, the pooled analysis of six cohort studies, focusing on vegan diets, overall, showed no statistically significant benefit on the risk of either CVD or stroke. However, a vegan diet was associated with an 18% lower risk of IHD when compared with other non-vegetarian diets.<sup>22</sup> The smaller effect of vegan diets on CVD might be due to the consumption of ultraprocessed meat substitutes, which can be rich in sodium and total even unhealthy—fats.<sup>24</sup> Still, for individuals adopting a vegan diet, the ethical commitment to avoiding animal products can be deeply ingrained and non-negotiable, making it challenging to alter their dietary choices, even when health concerns arise.<sup>25,26</sup>

Recent evidence from umbrella reviews supports the notion that vegetarian and vegan dietary patterns may play a role in reducing certain cardiometabolic risk factors, such as blood pressure, LDL cholesterol, and body mass index (BMI). These dietary patterns have also been associated with reduced levels of inflammatory markers, such as

C-reactive protein. However, their implementation should be carefully monitored to ensure adequate intake of critical nutrients, including vitamin  $B_{12}$ , iron, and omega-3 fatty acids. When tailored appropriately to individual needs and nutritional requirements, these diets could potentially complement CVD prevention strategies, although further research is warranted to solidify their long-term benefits and address existing uncertainties.  $^{27}$ 

#### Gaps in knowledge

- Well-designed RCTs are needed to carefully examine the role of vegetarian diets in CVD prevention.
- (2) Large studies with long-term follow-up are also needed to assess vegan diets in relation to overall cardiovascular health.

## Low-carbohydrate diets

Low-carbohydrate diets, which limit carbohydrates and increase the percentage of fat or protein, are a popular weight-loss strategy investigated for their cardiometabolic properties as well. <sup>28</sup> Carbohydrates can be categorized as refined (i.e. sugar and white bread) or non-refined (i.e. wholemeal bread and pulses). Refined carbohydrates typically have a higher glycaemic index, which refers to their ability to raise blood glucose levels. <sup>29</sup>

Increased intake of carbohydrates, especially refined or high glycaemic index carbohydrates, is associated with hypertension, coronary heart disease (CHD), obesity, Type 2 diabetes, metabolic syndrome, and increased risk of mortality. 30 A meta-analysis on this issue pooling data from 12 RCTs revealed the beneficial effect of low-carbohydrate diets on surrogate, conventional CVD risk factors, including excess weight, lipid profile, and blood pressure, yet their long-term effect remains unclear.<sup>31</sup> A more recent meta-analysis suggested that BMI is an important mediator, and LDL increased within the normal range, but not in obese.<sup>32</sup> In the Prospective Urban Rural Epidemiology (PURE) study, higher-carbohydrate intake was associated with higher all-cause mortality risk, yet the association with CVD mortality was not significant.<sup>30</sup> On the other side, a recent analysis of two large-scale cohort studies suggested that it is the quality of low-carbohydrate diets that determines their cardiometabolic effects; in particular, a lowcarbohydrate diet based on animal sources was associated with higher allcause mortality risk, whereas a vegetable-based low-carbohydrate diet was associated with lower all-cause and CVD mortality risk. 33 Lately, in a large-scale study of >130 000 participants, a diet with a high glycaemic index resulted in 21 and 51% higher risk of major CVD events, including death, in participants free of disease at baseline or with established CVD at baseline, respectively, after a median follow-up time of 9.5 years.34 Similar results were revealed in case of glycaemic load yet only in case of participants with established CVD at the recruitment phase.<sup>34</sup>

#### Gaps in knowledge

 The substitution potential of carbohydrates in terms of quality as well as with other macronutrients in relation to cardiometabolic health needs to be better defined.

# Very low-carbohydrate diets: ketogenic diets

Ketogenic diets refer to very low-carbohydrate diets with the biggest part of daily calorie intake (i.e. 70-80% to up to 90% in the treatment of epilepsy) coming from dietary fat, followed by protein 15-20% while carbohydrates do not exceed the 50 g.  $^{35}$  In the current ESC guidelines,

these dietary protocols are presented with potential benefits on appetite control, lowering triglycerides and limiting medication in patients with Type 2 diabetes.<sup>36</sup> The ketogenic diets have been mostly investigated in relation to glycaemic and weight control. The latest meta-analysis of eight RCTs with patients with Type 2 diabetes and obesity revealed better glycaemia control and decreased body weight for up to 6 months and better lipidaemic control for up to 12 months in relation to the typical, recommended diet.<sup>37</sup> However, the quality of evidence remains poor and the compliance of individuals to such strict dietary protocols guestionable.<sup>37</sup> Recent work from the UK Biobank study revealed that a self-reported diet low in carbohydrates and high in fat was associated with increased levels of LDL cholesterol and apolipoprotein B as well as an increased risk of incident atherosclerotic cardiovascular events,<sup>38</sup> and a recent meta-analysis concluded that ketogenic diet or a diet low in carbohydrates significantly reduced body weight, BMI, and body fat percentage.<sup>39</sup>

#### Gaps in knowledge

1. Larger intervention studies of longer duration are needed to determine if the potential benefits of very low-carbohydrate diets outweigh the risks in CVD prevention.

# **Eating patterns**

## Meal timing and frequency

Eating patterns are important determinants of nutrition, vary over time, geographic region, and culture/religion, such that some recognize our common heritage as hunter-gatherers as a major reason to maintain flexible and varying patterns (Supplementary material online).<sup>40</sup> Two main types of dimensions of eating patterns can be recognized: withinday meal timing and frequency, including breakfast skipping, and intermittent fasting.<sup>41</sup> The prototypical meal pattern includes three main meals every day (breakfast, lunch, and dinner), with additional intake of smaller quantities of food, typically two smaller, but still sizable portions.<sup>12</sup> Notably, meal definition is typically any food consumption episode (drink or solid meal) providing 200 kcal or more of energy.<sup>42</sup> However, substantial variability exists in such pattern, with differences in timing of each of the above meals, as well as the potential occasional skipping of one or more of them.

Furthermore, each meal may be composed differently, in terms of caloric intake as well as nutrient composition, occasionally leading to major imbalances. Social trends have been accompanied by major changes in eating patterns, with skipping breakfast (and occasionally also lunch) becoming more and more common.<sup>40</sup> Another dimension of eating pattern is represented by intermittent fasting, which can be limited to food, with *ad libitum* intake of fluids, or also include fluids.<sup>41</sup> Clearly, individual diet recommendations cannot disregard lifestyle and activity patterns, including sleeping.

Careful review of the pertinent evidence base shows that most studies to date are observational or short term and that some habits may appear risky just because of confounding. Variable-quality evidence suggests that breakfast skipping may be associated with a higher risk of overweight/obesity, <sup>43</sup> as well as derangements in glucose and insulin metabolism, <sup>44</sup> but possibly weight loss. Skipping breakfast is also associated, albeit in observational studies, with increased risk of cardiovascular morbidity and mortality. <sup>45,46</sup>

Higher meal frequency may improve cardiovascular risk profile and reduce body weight. 47 Accordingly, a more balanced intake of food

during the day, thus avoiding meal skipping, late dinners, or exceedingly abundant dinners, can be associated with a lower risk of overweight/obesity and improved cardiovascular risk profile. Notably, meal skipping is most often attributed to lack of time, rather than dieting or other similar personal choices, with men more frequently skipping breakfast and women lunch or dinner. A recent meta-analysis suggested that meal skipping can be associated with weight loss <sup>48</sup>; however, this would also depend on the total amount of calories consumed, with the possibility of even weight gain if the daily calorie intake exceeds the required amount.

Alternate-day, intermittent, time-restricted, and periodic fasting is associated with weight loss, and a lower overall cardiovascular risk, especially if liberal drinking is allowed. Even in apparently fit individuals, Ramadan-type intermittent fasting is safe and can improve weight balance and cardiovascular risk profile. So,51 Still, long-term compliance to such diets is difficult, and following an initial transient weight loss, a rebound gain in weight can be seen (Table 2).

Intriguingly, some patterns may be informed by genetic traits, for instance the preference for breakfast skipping or eating heavily at dinner. Finally, another piece of the puzzle is eating rate, with several studies suggesting that having longer (rather than quicker) meals may be associated with lower overall caloric intake.

#### Gaps in knowledge

- (1) Few mechanistic studies have elucidated how eating patterns impact on the pathophysiology of CVD. In addition, individualization of dietary pattern recommendations (e.g. according to sex, ethnicity, and lifestyle) still merits further research efforts.
- (2) Randomized studies on the effect of different types of fasting on CVD risk biomarkers are lacking.
- (3) The exploration of artificial intelligence and expert systems in directing dietary patterns remains a subject of active research.

# **Specific foods**

Several umbrella reviews have already presented information on the impact of specific foods on cardiovascular outcomes, so a further detailed review will not be presented in this paper. A recent review by Miller et al. <sup>56</sup> also highlighted these and included in *Table 3*. They identified 10 foods and 3 beverages that had probable or convincing evidence of being associated with cardiometabolic health outcomes including protective associations with increased intakes of fruits, vegetables, nuts/seeds, wholegrains, fish/seafood, chocolate, milk, tea, and harmful associations from higher intakes of red meat, processed meats, and sugar-sweetened beverages.

Of note, the 2021 scientific statement from the American Heart Association<sup>57</sup> provided an evidence-based guidance on dietary choices to improve cardiovascular health including:

- Maintaining a healthy body weight.
- Eating a variety of fruits and vegetables.
- Opting for wholegrains over refined carbohydrates.
- Choosing healthy sources of protein (predominantly from plant sources, fish and seafood, and low-fat or fat-free dairy products) and to choose lean and unprocessed forms of meat/poultry.
- Using liquid plant oils rather than tropical oils and partially hydrogenated fats.
- Choosing minimally processed foods instead of ultra-processed foods and minimizing the intake of beverages and foods with added sugars.

- indicates unclear or neutral result.

Table 2 Summary of main features and effects of meal timing/balance/frequency, breakfast skipping, and fasting

Intervention	Definition	Impact on CV risk	Compliance	Reference
Breakfast skipping	Avoidance of meals before noon	Increase	Low	45,46
Eating rate	Increasing time devoted to a meal	_	_	52
Intermittent fasting	Alternate or periodic episodes of fasting lasting at least one day	Increase	Low	53
Meal balance	Balanced distribution of caloric intake through different meals	Increase	_	54
Meal frequency	Higher number of meals per day	Increase	_	47
Meal skipping	Skipping meals during a day	Decrease	_	48
Meal timing	Delaying meals (particularly dinner) compared with standard routine	Decrease	_	54
Ramadan intermittent fasting	Periodic periods of fasting (including no drinking)	Increase	Low	50,51

• Choosing and prepare foods with little or no salt.

We have therefore not further reviewed existing evidence for these. However, an examination of coffee and alcohol consumption has been included, as both are ubiquitously consumed and exert a significant influence on the cardiovascular system.

#### **Coffee**

Coffee is one of the most popular consumed beverages worldwide. Because of its popularity, the investigation of the association between coffee consumption and chronic disease development is of crucial importance for public health.

Coffee is a complex chemical mixture, including caffeine, diterpenes, purinic alkaloids, theophylline, polyphenols, and various lipid-soluble substances, containing more than one thousand bioactive compounds that may influence human health. Those effects may differ according to the type of coffee consumed and way of preparation (i.e. boiled, filtered, and instant). Secondary contents to the type of coffee consumed and way of preparation (i.e. boiled, filtered, and instant).

Over the past three decades, the association between coffee consumption and CVD outcomes including stroke, heart failure, and cardiac mortality has been extensively studied. In 2014, a meta-analysis reported a non-linear, dose-response inverse relationship between coffee consumption and mortality, with the largest risk reductions observed for 4 cups/day for all-cause mortality and 3 cups/day for CVD mortality.<sup>60</sup> In a recent meta-analysis of US prospective cohorts, there was a significant inverse association between caffeinated coffee consumption, CVD mortality, and CVD morbidity, while no risk reduction was observed above 3-4 cups/d.<sup>61</sup> This comes in accordance with a large prospective study from the UK Biobank, where consumers of moderate amount of caffeine (200-300 mg/day) had the lowest risk for new-onset cardiometabolic multimorbidity compared with nonconsumers or consumers of <100 mg caffeine per day.<sup>62</sup> Additionally, a recent prospective study showed that heavy coffee consumption ( $\geq 2$ cups/day) was associated with an increased risk of CVD mortality among people with severe hypertension, attributed to increased catecholamine release, but not people without or with Grade 1 hypertension.<sup>63</sup> Furthermore, another prospective study reported U-shaped associations of unsweetened coffee consumption, sugar-sweetened coffee, or artificially sweetened coffee with mortality during a 7-year follow-up period.<sup>64</sup> Even decaffeinated coffee consumption has been associated with decreased risk of diabetes mellitus in an 11-year follow-up study, but no robust evidence exists regarding CVD outcomes.<sup>65</sup> Recently, one Mendelian randomization (MR) study failed to find an association

between coffee and CVD events,  $^{66}$  while another reported a reduction in obesity and Type 2 diabetes.  $^{67}$  Neither of the MR studies could assess whether there was a U-shaped association between coffee consumption and cardiovascular outcomes, and pleiotropy could not be tested in one of them.  $^{67}$ 

Notably, a recent analysis from the UK Biobank study reported consistent findings across different coffee subtypes, as decaffeinated, ground, and instant coffee—particularly at 2–3 cups/day—was associated with significant reductions in incident CVD and mortality. Still, consumption should be limited during pregnancy and avoided in children and adolescents. 68

#### Gaps in knowledge

- Mendelian randomization studies considering pleiotropic effects of coffee-related genotypes and collider bias are needed.
- (2) Analysis of existing data is needed considering the specific type of coffee, sugar and cream added to coffee, unhealthy behaviours, and consumption pattern because caffeine is included in tea, chocolate, and some soft and energy drinks besides coffee.
- (3) More studies are needed regarding the role of decaffeinated coffee on cardiovascular health.

## **Alcoholic beverages**

The impact of alcohol on CVD is complex and depends not only on the amount and pattern of alcohol intake but also on the type of CVD manifestation. The type of alcohol—whether from fermented drinks or distilled spirits—also plays a pivotal role in determining the cardiometabolic benefits. The increased anti-inflammatory and the bioactive compounds in fermented drinks have the potential to confer greater cardiovascular benefits.<sup>69</sup> On the one hand, there seems to be a direct and linear association between alcohol intake and the risk of haemorrhagic stroke or atrial fibrillation. On the other hand, historically a Jor U-shaped association between alcohol and cardiometabolic health has been postulated—principally in the context of Mediterranean diet<sup>13</sup> and mainly for CHD—with the lowest risk at low alcohol intake and higher risks at no intake or higher intake. A meta-analysis of 45 cohort studies suggested that moderate drinkers (up to 2 drinks/day) and drinkers, in general, presented lower CHD risk compared with abstainers. 70 In a recent study, a J-shaped dose-response relationship between alcohol consumption and CVD incidence was found only in men, while in men with three to four comorbidities, there were no protective effects of light to moderate and moderate consumption on

Stroke CVD	Dietary factor	Outcome	Strength	Consistency	Temporality	Coherence	Specificity	Analogy	Plausibility	Biological gradient	Experiment
CVD	Foods and beverages										
State   C-D    C-D	Fruits	CVD		‡	<b>+</b> +	<b>+</b> +	+	‡		+	+
Stroke		СНБ		‡	<b>+</b> +	‡	+	‡		+	+
Sectionary Groupe		Stroke		<b>+</b>	++	++	+	‡		+	+
Henomyage stroke + + + + + + + + + + + + + + + + + + +		Ischaemic stroke	+	<b>+</b>	++	++	+	‡		+	+
Stroke   CVD		Haemorrhagic stroke	+	++	++	++	+	‡		+	+
CHD	Vegetables	CVD		‡	++	‡	+	‡		+	+
Stockeds CVD		CHD		‡	++	++	+	‡		+	+
Steeds CVD		Stroke		‡	++	‡	+	‡		+	+
Stateds CVD ++ + + + + + + + + + + + + + + + + +		Ischaemic stroke		+	<b>+</b>	<b>+</b>	+	‡		+	+
CHO	Nuts/seeds	CVD	‡	<b>+</b>	++	‡	+	‡		+	++
CVD		CHD	‡	‡	<b>+</b>	<b>+</b>	+	‡		+	‡
CHD	Wholegrains	CVD	+	‡	++	‡	+	‡		+	++
Schaemic stroke		CHD	+	<b>+</b>	++	++	+	‡		+	<b>+</b>
CHD		Ischaemic stroke	+	‡	++	<b>+</b> +	+	‡		+	‡
Stroke   CHD	Red meats, unprocessed	CVD	‡	+	++	++	‡			+	+
Stroke CVD		СНБ	+	‡	++	‡	‡	1		+	+
CHD         ++		Stroke	‡	+	++	++	‡	1		+	+
Stroke	Processed meats	CVD	‡	+	<b>+</b> +	<b>+</b> +	+	‡		+	+
Stander Stroke		СНБ	‡	ı	<b>+</b> +	‡	+	‡		+	‡
Sedfood CHD CHD in patients with diabetes		Stroke	‡	‡	<b>+</b> +	<b>+</b> +	+	‡		+	‡
Seafood CHD in patients with diabetes - + + + + + + + + + + + + + + + + + +		Ischaemic stroke	‡	1	++	++	+	‡		+	‡
Choractered beverages CVD in patients with diabetes - + + + + + + + + + + + + + + + + + +	Fish/seafood	СНБ	1	1	++	++	+	‡		+	++
Mile         -         +		CHD in patients with diabetes		+	++	‡	+	‡		+	+
Stroke CVD		Σ		+	<b>+</b> +	<b>+</b> +	+	‡		+	‡
Colate         CVD         -         ++ <th< td=""><td></td><td>Stroke</td><td></td><td>+</td><td>++</td><td>‡</td><td>+</td><td>‡</td><td></td><td>+</td><td><b>+</b></td></th<>		Stroke		+	++	‡	+	‡		+	<b>+</b>
CHD       -       +       ++	Chocolate	CVD		‡	++	++	‡	+		+	‡
Mile		СНБ		+	++	‡	‡	+		+	<b>+</b>
Stroke         -         ++		Σ		‡	<b>+</b> +	<b>+</b> +	‡	+		+	‡
Haemorrhagic stroke - ++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++ +		Stroke		‡	++	‡	‡	+		+	<b>+</b>
Stroke       -       ++		Haemorrhagic stroke		‡	++	++	‡	+		+	‡
CHD + ++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++	Λiik	Stroke		‡	<b>+</b> +	‡	‡			+	
CHD + ++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++	Sugar-sweetened beverages	CVD		+	<b>+</b> +	<b>‡</b>	+	+		+	+
Schaemic stroke		CHD	+	‡	<b>+</b>	<b>‡</b>	+	+		+	+
Stroke . + + + + + + + + + + + + + + + + + +		Ischaemic stroke	+	+	<b>+</b> +	‡	+	+		+	+
Co	Теа	Stroke	1	+	++	++	+	+		+	++
											Pomitao

Dietary factor	Outcome	Strength	Consistency	Strength Consistency Temporality Coherence Specificity Analogy Plausibility	Coherence	Specificity	Analogy	Plausibility	Biological gradient	Experiment
Nutrients										
Dietary fibre	CVD	+	‡	++	++	+	‡	‡	++	‡
	CHD	‡	‡	++	++	+	‡	‡	++	‡
	Stroke	‡	‡	++	++	+	‡	‡	++	+
	Diabetes	+	‡	++	++	+	‡	‡	++	‡
Fruit fibre	Stroke	1	‡	<b>+</b>	<b>+</b>	+	‡	‡	++	+
Vegetable fibre	Stroke	1	‡	<b>+</b>	<b>+</b>	+	‡	‡	++	+
Glycaemic index	CHD	+	‡	++	++	+	+	+	++	+
Glycaemic load	CHD	‡	‡	++	++	+	+	+	++	+
PUFA replacing carbohy drate	СНО	ı	+	++	++	‡	‡	‡	++	ı
PUFA replacing SFA	CHD	1	+	<b>+</b>	<b>+</b>	‡	+	‡	++	‡
Trans-fatty acid	CHD	‡	‡	<b>+</b>	<b>+</b>	‡	+	‡	<b>+</b> +	‡
Sodium	Stroke	ı	+	<b>‡</b>	<b>‡</b>	+	‡	‡	<b>+</b>	‡
Potassium	Stroke	+	‡	++	++	‡	‡	‡	++	‡

++ indicates consistent evidence from well-designed studies with few limitations, + indicates evidence from several well-designed studies with some important limitations, and - indicates emerging evidence from a few studies or with conflicting results (adapted from Miller et al. <sup>56</sup> under a CC-BY License).

 Table 4
 Effect of vitamin or mineral intake or

 supplementation on cardiovascular disease events

	Effect	Reference
Lipid-soluble vitamins		70
Vitamin A	Deleterious	78
Vitamin D	No effect	78
Vitamin E	No effect	78
Vitamin K	No effect	78,91
Water-soluble vitamins		
Vitamin B <sub>1</sub> (thiamine)	No effect on heart failure	92
Vitamin B <sub>2</sub> (riboflavin)	No effect on blood pressure	93
Vitamin B <sub>5</sub>	_	
(pantothenic acid)		
Vitamin B <sub>6</sub> (pyridoxine)	Possibly beneficial	81
Vitamin B <sub>7</sub> (biotin)	_	
Vitamin B <sub>9</sub> (folic acid)	Beneficial	82
Vitamin B <sub>12</sub> (cobalamin)	Possibly beneficial (stroke)	78,94,95
	No effect (CVD mortality)	
Vitamin C	No effect	83
Multivitamins	No effect	78
Minerals		
Sodium	Deleterious	96
Potassium	Possibly beneficial (stroke)	85
Magnesium	Insufficient information	88
Calcium	No effect	78
Selenium	No effect	78
Iron	Deleterious (haem)	89
Iron	Beneficial if intravenous for	90
	heart failure with reduced	
	ejection fraction or heart	
	failure with mildly reduced	
	ejection fraction	

CVD incidence, while in both sexes, the protective effects of light to moderate and moderate consumption on CVD incidence were evident among ages 41–65.<sup>71</sup> Another meta-analysis showed a linear positive association between baseline alcohol intake and changes in levels of blood pressure over time, with no suggestion of an exposure-effect threshold.<sup>72</sup> Of course, any intake of alcohol should be measured against all its potential harmful effects, including it being listed as a Group 1 carcinogen according to the World Cancer Research Fund statement.<sup>73</sup> It is important to note that a recent meta-analysis showed that the threshold for the lowest risk of all-cause mortality was  $\sim 100 \text{ g/}$ week, which corresponds to 1 serving/day. However, one should consider the effects of alcohol on different types of cardiac outcomes, stroke, and cancer. 74 In the same meta-analysis, alcohol consumption was roughly linearly associated with a higher risk of cardiac outcomes other than myocardial infarction, whereas increased alcohol consumption was log-linearly associated with a lower risk of myocardial infarction.<sup>74</sup> A RCT among adults with Type 2 diabetes (CASCADE) concluded that initiating moderate wine intake, especially red wine, among well-controlled diabetics as part of a healthy diet was apparently safe and modestly decreased cardiometabolic risk.<sup>75</sup> On balance therefore, consuming one unit of alcohol per day may contribute to a reduced cardiovascular risk without presenting an unfavourable risk profile. A recent systematic review illustrated that moderate wine consumption defined as one to four drinks per week was associated with a risk reduction in cardiovascular mortality when compared with beer or spirits; however, higher risk for CVD mortality was typically seen with heavier daily or weekly alcohol consumption across all types of beverages. <sup>76</sup> Still, most results originate from observational studies, and potential biases such as survivor bias or the inclusion of former drinkers in the abstinent group cannot be ruled out.

Moderate alcohol intake especially in the form of red wine is an important part of the Mediterranean diet. <sup>13</sup> In this case, the drinking pattern plays a pivotal role; alcohol intake alongside with food as well as social drinking as part of a balanced lifestyle, often in a relaxed, communal setting, further promotes well-being and mitigates stress. <sup>77</sup>

#### Gaps in knowledge

(1) Studies assessing whether it is alcohol, alcohol consumption behaviour, or non-alcohol components of alcoholic drinks should be promoted.

## Vitamins and minerals

## Lipid-soluble vitamins

Lipid-soluble vitamins include vitamins A D, E, and K. Dietary vitamin A is inversely associated with CVD mortality in population-based studies, but supplementation studies showed an increased risk of cardiovascular mortality. The associations between dietary intake of vitamin D and CVD are complicated to establish as this vitamin is predominantly produced from sun exposure. In one trial, vitamin D supplementation was not associated with reduced major adverse CVD events. Dietary vitamin E is inversely associated with the risk of stroke, but vitamin E supplementation did not affect CVD. Dietary vitamin K intake is negatively associated with CHD but not with total CVD or stroke, but no association between vitamin K levels and CVD was found.

#### Gaps in knowledge

(1) It is unclear if the effects of vitamin D on CVD depend on the vitamin D status of the population (normal, insufficiency, or deficiency). The evidence relating vitamin K to CVD is scarce prompting the need for further research.

#### Water-soluble vitamins

Water-soluble vitamins include the B vitamins and vitamin C (ascorbic acid). Niacin in high doses has been used as a lipid-lowering drug and will not be reviewed here. Dietary intake of vitamin  $B_6$  and vitamin  $B_9$  is associated with a reduced risk of stroke, while no association was found for vitamin  $B_{12}$  intake. Interventional studies supplementing B vitamins found a protective effect against stroke, with differing effects according to the combination used. Supplementation with vitamin  $B_9$  would reduce the risk of stroke by 10% and of overall CVD by 4%, the beneficial effect being partly related to the decrease in homocysteine levels. Dietary vitamin C is inversely associated with CVD, but interventional studies supplementing vitamin C failed to show any effect regarding CVD events. Teals Finally, the use of multivitamin supplements showed no beneficial effect on CVD.

#### Gaps in knowledge

(1) The effects of vitamin B supplementation on total CVD independently of their effect on homocysteine reduction remain to be assessed. The optimal combination of B vitamins to prevent CVD has not been defined.

### **Minerals**

Sodium and potassium are the most extensively studied minerals regarding CVD risk. Excessive sodium intake increases CVD risk, the increase being as high as 6% per each 1 g increase. Intervention studies replacing salt by low-sodium substitutes led to a slight decrease in CVD events and mortality. <sup>84</sup> Potassium intake is negatively associated with the risk of stroke, <sup>85</sup> but no association with CVD or CHD was found. <sup>86</sup> Potassium consumption decreases BP and could counter-regulate the increase in BP levels due to excessive sodium consumption. <sup>87</sup>

No association has been found between calcium supplementation and CVD<sup>78</sup> or between magnesium intake and CVD mortality. Selenium serum levels are negatively associated with CVD risk, while interventional studies with selenium supplementation failed to influence CVD mortality or events. Increased haem iron intake is positively associated with CVD mortality, while no associations were found between non-haem or total iron and CVD. The deleterious effect of haem iron intake might partly be due to the associated increased consumption of red or processed meat, a source of saturated fatty acids and sodium. Conversely, intravenous iron supplementation has been shown to be effective in alleviating heart failure symptoms among patients with heart failure with reduced ejection fraction or heart failure with mildly reduced ejection fraction. The effect of vitamins, mineral intake, and supplementation on CVD events is summarized in *Table 4*.

#### Gaps in knowledge

(1) Randomized controlled clinical trials assessing the effect of magnesium and soluble vitamin supplementation on CVD are lacking.

# Plant-derived bioactive compounds

Plant-based foods contain an array of bioactive constituents with growing evidence to support their cardioprotective effects. Among these, polyphenols—encompassing flavonoids, lignans, and phenolic acids—stand out due to their diverse bioactive properties and contributions to cardiovascular health. To date, the primary focus has been on dietary flavonoids, phytosterols, lignans, and glucosinolates.

#### **Flavonoids**

Dietary flavonoids represent a diverse range of polyphenolic compounds that are present in many commonly consumed fruits, vegetables, grains, herbs, and beverages. Flavonoids are emphasized in this section due to their significant representation in current cardiovascular research and their well-established association with improvements in key cardiovascular biomarkers and outcomes. While other polyphenol subclasses, such as phenolic acids and lignans, are also relevant, the focus here reflects the concentration of available evidence on flavonoids. Their structural complexity has led to their subclassification as flavonols, flavones, flavanones, flavan-3-ols (including their oligomeric and polymeric forms, proanthocyanidins), isoflavones, and

anthocyanins. This structural diversity contributes to differences in biological efficacy with subtle differences affecting both bioavailability and bioactivity. To date, the flavan-3-ol, flavonol, and anthocyanin classes have received most attention in relation to cardiovascular health with the totality of available evidence from large populationbased studies and RCTs suggesting that foods rich in these flavonoids reduce biomarkers of CVD risk including blood pressure, lipids, flowmediated dilatation, and lower risk of fatal and non-fatal IHD and cerebrovascular disease. 99 After ingestion, flavonoids undergo extensive metabolism with absorption occurring in both the small and large intestines with a substantial fraction of intake reaching the colon, where the flavonoids are exposed to the gut microbiome. The resident microbiome operates as a metabolic reactor, catabolizing unabsorbed flavonoids into smaller molecules such as phenolic and aromatic acids that are thought to be more bioactive. 97 The impact of metabolism and the gut microbiome in explaining the wide interindividual variability in cardiovascular response to a flavonoid-rich diet is an active area of research.

## Lignans

Lignans, another subclass of polyphenols, share some mechanisms of action with flavonoids, such as antioxidant and anti-inflammatory effects. 100 However, their unique metabolism by gut microbiota into mammalian lignans, such as enterodiol and enterolactone, provides distinct pathways potentially influencing cardiovascular health. 101 Dietary lignans are present in a range of wholegrain foods, but the richest source is flaxseed/linseed. After ingestion, these plant lignans are metabolized by the gut microbiome to form mammalian lignans, enterodiol, and enterolactone. Data from population-based studies have been mixed with one study showing that higher serum enterolactone levels were associated with reduced CHD- and CVD-related mortality while two others showed no association. <sup>102</sup> In a recent cohort study, a higher enterolactone level was associated with a reduction in coronary artery disease risk in women but not in men. 103 A recent meta-analysis of RCTs suggests that flaxseed intake improves total, LDL cholesterol and triglyceride concentrations, although the importance of lignans vs. its n-3 fatty acid constituents was not evaluated. 104

#### **Glucosinolates**

Glucosinolates are sulfur-containing compounds present in cruciferous vegetables and are hydrolysed following ingestion to biologically active compounds called isothiocyanates. Sulforaphane is an isothiocyanate with cardioprotective effects as it is a potent NrF2 inducer and modulates various pro-inflammatory (e.g. nuclear factor kappa B) and metabolic (e.g. peroxisome proliferator-activated receptor gamma) signalling pathways. There have been limited RCTs to date, but emerging data suggest sulforaphane may reduce CVD risk biomarkers including lowering LDL cholesterol and improving insulin resistance. However, the only large prospective study conducted to date, in over 200 000 US adults from the Nurses' Health Study and the Health Professionals Follow-Up Study, suggested that a higher habitual intake of glucosinolates (predominantly from cabbage and Brussel sprouts) was associated with a slightly higher risk of heart disease. 107

#### **Phytosterols**

Plant sterols and plant stanols (commonly known as phytosterols) are plant-derived compounds that are structurally related to cholesterol. They are present in vegetable, nut and olive oils, nuts and

seeds, wholegrains, and legumes. Although present in the diet in amounts similar to cholesterol, they are poorly absorbed, and blood concentrations tend to be low. Phytosterol activity is dependent on various factors including processing, formulation, and solubility in the food matrix. After absorption, they are actively excreted back into the intestinal lumen. They interfere with the intestinal absorption of dietary cholesterol by displacing cholesterol from micelles and facilitate excretion of biliary cholesterol via faeces. To date, numerous short-term trials have shown that daily intake of phytosterols from phytosterol-enriched foods can significantly lower LDL cholesterol. An average phytosterol intake of 2 g/day lowers serum LDL cholesterol by 8–10%. However, the effect of long-term intake of enriched phytosterol products is currently unknown.

## Gaps in knowledge

- (1) Identify the key role the gut microbiome plays in modulating and mediating the effects of plant bioactives on cardiovascular health.
- Long-term trials in secondary prevention and conduct head-tohead comparisons of extracts with flavonoid-rich foods.
- Identify the importance of inter-individual variability in metabolism on the cardioprotective effects of plant bioactives.
- (4) Investigate the specific contributions of other polyphenol subclasses, such as phenolic acids, to cardiovascular health and their interactions with flavonoids and lignans.

### Conclusion

This scientific statement from the EAPC and ACNAP of the ESC outlines dietary patterns and nutrition aiming to enhance cardiovascular health and reduce cardiovascular risk. Overall, healthcare professionals should recommend plant-based dietary patterns, as unrefined as possible, rich in vegetables and fruit; Mediterranean, DASH, or vegetarian (non-vegan) diets; high dietary potassium intake; and plant-based components such as flavonoids, lignans, glucosinolates, or phytosterols. On the other side, healthcare professionals should discourage dietary patterns rich in ultra-processed foods, meat and saturated fat, skipping breakfast or snacking between meals, and increased sodium consumption. Healthcare professionals should also abstain from prescribing vitamin or mineral supplements or recommend vegan diets, as they appear to exert no significant effect on CVD risk. Moderate coffee consumption appears to be unrelated to CVD risk. Consumption of one unit of alcohol might reduce cardiovascular risk, but healthcare professionals should focus on reducing alcohol consumption and should not motivate their patients to start drinking as a preventive measure towards CVD prevention. Finally, healthcare professionals should be made conscious that behavioural changes are not easily achievable by many patients, where willingness of change is determined by socioeconomic factors 109 or the type of food. 110

# Supplementary material

Supplementary material is available at European Journal of Preventive Cardiology.

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AstraZeneca, Balmed, Cardionovum, Cepton, Crannmedical, Endocore Lab, Eukon, Guidotti, Innovheart, Meditrial, Menarini, Microport, Opsens Medical, Synthesa, Terumo, and Translumina, outside the present work.

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