Clínica e Investigación en Arteriosclerosis 35 (2023) 155–163

Sociedad Española de Arteriosclerosis

CLÍNICA E INVESTIGACIÓN EN ARTERIOSCLEROSIS

www.elsevier.es/arterio

CONSENSUS STATEMENT

Nutritional recommendations in the prevention and treatment of atherogenic dyslipidemia☆☆

Vicente Pascual[a,b,c], **José Luis Díaz**[b,d], **Jesús Millán Nuñez-Cortés**[b,e], **Pablo Pérez-Martínez**[a,c,f,g,*]

[a] *Centro de Salud Palleter, Universidad CEU-Cardenal Herrera, Castellón, Spain*
[b] *Grupo de Trabajo Dislipemia Aterogénica, Sociedad Española de Arteriosclerosis (SEA), Spain*
[c] *Grupo de Trabajo Nutrición y Estilo de Vida, Sociedad Española de Arteriosclerosis (SEA), Spain*
[d] *Unidad de Lípidos y Riesgo Cardiovascular, Medicina Interna, Hospital Universitario A Coruña, A Coruña, Spain*
[e] *Hospital General Universitario Gregorio Marañón, Universidad Complutense. Madrid, Spain*
[f] *Unidad de Lípidos y Arterioesclerosis, Universidad de Córdoba/Hospital Universitario Reina Sofía/Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Córdoba, Spain*
[g] *CIBER Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Madrid, Spain*

Available online 1 June 2023

KEYWORDS
Atherogenic dyslipidemia;
Mediterranean diet;
Nutrition;
Hypertriglyceridemia

Abstract The incorporation of a healthy diet, regular physical exercise and smoking cessation are the initial measures to reduce cardiovascular risk in patients with atherogenic dyslipidemia. In these patients, the nutritional quality of their diet should be improved, replacing foods with a greater atherogenic effect for others with a healthier effect. There is strong evidence that plant-based dietary patterns, low in saturated fatty acids, cholesterol and sodium, with a high content of fiber, potassium and unsaturated fatty acids, are beneficial and reduce the expression of cardiovascular risk factors. This document focuses on the role of nutrition in the prevention and treatment of atherogenic dyslipidemia, providing current evidence to serve as a tool for health professionals in its clinical management. To facilitate the reading of these recommendations, they are presented in a user-friendly table format, with a hierarchy of different levels of evidence.

DOI of original article: https://doi.org/10.1016/j.arteri.2022.09.002
☆☆ The enclosed Appendix lists the members of the Atherogenic Dyslipidemia Work Group.
* Corresponding author.
E-mail address: pabloperez@uco.es (P. Pérez-Martínez).

PALABRAS CLAVE
Dislipemia aterogénica;
Dieta mediterránea;
Nutrición;
Hipertrigliceridemia

Recomendaciones nutricionales en la prevención y tratamiento de la dislipemia aterogénica. Grupo de Trabajo Dislipemia Aterogénica, Sociedad Española de Arteriosclerosis

Resumen La incorporación de una dieta saludable, ejercicio físico regular junto a la supresión del hábito tabáquico son las primeras medidas para reducir el riesgo cardiovascular en los pacientes con dislipemia aterogénica. En estas personas, se debe mejorar la calidad nutricional de su alimentación, sustituyendo los alimentos con mayor efecto aterogénico, por otros de efecto más saludable. Hay una sólida evidencia de que los patrones alimentarios de base vegetal, bajos en ácidos grasos saturados, colesterol y sodio, con un alto contenido en fibra, potasio y ácidos grasos insaturados, son beneficiosos y reducen la expresión de los factores de riesgo cardiovascular. Este documento se centra en el papel que juega la nutrición en la prevención y tratamiento de la dislipemia aterogénica, aportando las evidencias actuales que sirvan de herramienta a los profesionales de la salud en su manejo clínico. Para facilitar su lectura dichas recomendaciones se expondrán en un formato de tablas amigable, jerarquizando por diferentes niveles de evidencia.

Introduction

Atherogenic dyslipidemia (AD) is a common process in western countries, and its association with obesity, metabolic syndrome and diabetes explains its high level of prevalence in our society. It is defined by increased plasma levels of total triglycerides (TG) and a fall in high density lipoprotein cholesterol (HDL-c). This is usually combined with an increase in TG-rich lipoproteins (TRL) and apolipoprotein B (apoB) transporters, together with a discrete increase in the concentration of low-density lipoprotein cholesterol (LDL-c), with a predominance of small dense LDL particles.[1] From a clinical point of view, the presence of AD, above all in the case of diabetes, increases the risk of myocardial ischemia, so that it therefore increases cardiovascular risk (CVR). This is a metabolically complex process, given that it involves the presence in plasma of different atherogenic molecules, even though no single one of them is an exclusive diagnostic marker. Nor are they easy to detect with the diagnostic methods that are available in clinical practice. On the other hand, AD is a critical element that clearly adds to the residual risk that persists even with a correct lipid-lowering treatment and appropriate control of LDL-c. Different groups of experts such as the Atherogenic Dyslipidemia Group of the Spanish Society of Arteriosclerosis have now reached agreements that make it possible, using markers that are accessible and often indirect, to achieve acceptable levels of evidence for the presence of this entity, making it possible to take effective decisions about how to treat it. However, in spite of all this, AD is currently a clinical entity that unfortunately fulfils the 3 ''u''s, as it is underdiagnosed, undertreated and undercontrolled.

The aim of current recommendations for the management of AD is to normalize LDL-c and to control hypertriglyceridaemia, which necessitates reducing apoB levels and the number of LRP, together with non-HDL-c, while increasing HDL-c. This strategy includes recommendations for a healthy lifestyle, followed by the use of drugs including statins, fibrates, n-3 fatty acids, ezetimibe and PCSK9 inhibitors to a lesser degree. Appropriate changes in lifestyle significantly reduce CVR, so that a healthy eating pattern should be recommended, together with regular physical exercise and smoking cessation. This document centres on the role played by diet in the prevention and treatment of AD, offering the latest evidence to be used as tools by healthcare professionals in its clinical management. Different patterns of healthy diet will therefore be analysed based on existing evidence, as well as the main recommendations for each group of foods. To aid reading these recommendations will be shown in the form of accessible tables, ranked according to different levels of evidence.

The recommendations made are classified into 3 types:

1 Strong: based on clinical trials and meta-analyses which include quality criteria.
2 Moderate: based on prospective cohort studies and case studies with controls.
3 Weak: justified by expert agreement and opinion, or based on long clinical practice.

Healthy dietary patterns and edible fats

The different healthy diets have many components in common, some of which, such as fruit, vegetables, nuts, pulses and fish are recommendable, while others should be restricted. The latter include foods that are rich in saturated fat, those which contain added sugar, large amounts of salt or foods that have been processed. There is strong evidence that vegetable-based diets which are low in saturated fatty acids, cholesterol and sodium, and which have a high content of fibre, potassium and unsaturated fatty acids, are beneficial and reduce the expression of CVR factors.[2] Within the context of the relationship between nutrition and AD it

is also fundamental to prevent weight gain or reduce excess weight when patients are overweight or obese.

The Mediterranean diet, the DASH diet, a vegan-vegetarian diet and the Alternative Healthy Eating Index all stand out as beneficial. They are all vegetable-based and contain abundant complex carbohydrates (CH). The data from large cohort studies and, in the case of the Mediterranean diet, the randomized clinical study PREDIMED, indicate that adherence to these diets leads to a clear cardiovascular benefit. Of the edible fats, virgin olive oil is the one that is the most effective in preventing cardiovascular diseases. A few years ago, the PREDIMED study showed that the participants assigned to a Mediterranean diet supplemented with extra virgin olive oil or nuts had an average reduction of 30% in major cardiovascular events,[3] apart from other benefits which included a lower risk of type 2 diabetes mellitus (DM2). We recently published the results of the CORDIOPREV study, a randomized clinical trial of 1,002 patients with established coronary disease. They either received a Mediterranean diet rich in virgin olive oil or a low-fat diet that was rich in complex carbohydrates during 7 years. Those who followed a Mediterranean diet were found to have a 26% reduction in major cardiovascular events compared to those who followed the low-fat diet.[4] These results are relevant for clinical practice, and they support the use of the Mediterranean diet to prevent the recurrence of cardiovascular (CV) disease and reduce residual risk of the same even when appropriate lipid reducing treatment is given. The Mediterranean diet should therefore be considered in patients with AD, according to their preferences.

Food groups

The main recommendations regarding the different food groups for the prevention and treatment of AD are shown below (Table 1). The food groups that are recommended or not recommended for the prevention and treatment of AD are also shown, together with the level of available evidence (Table 2).

Table 1 The main recommendations for different food groups for the prevention and treatment of atherogenic dyslipidemia.

Edible fats

- Replacing dietary sources of saturated fats with foods that contain unsaturated fat improves the lipid profile, the components of the metabolic syndrome,[5] the control of glycaemia and insulin resistence.[6]
- Replacing dietary carbohydrates with unsaturated fat reduces triglyceridaemia, increases HDL-c and reduces blood pressure.[7]

Moderate evidence.

- Virgin olive oil is the most recommendable for use as a dressing and everyday cooking.[2–4] As well as its high level of monounsaturated fat (oleic acid), its high micronutrient content, of which the polyphenols stand out, may be the cause of its effects in improving the lipid and atherogenic profile.[8]

Strong evidence.

- At high temperatures, sunflower, maize and soya oils undergo oxidative phenomena and produce free radicals and other pro-inflammatory molecules, so that they are not recommendable for use in frying.[9] The consumption of fried foods is associated with a higher risk of ischemic cardiomyopathy.[10] This association did not arise in the follow-up of a Spanish cohort,[11] and nor was any increased risk of ictus found,[12] which was probably due to the nature of the cooking fat used in our country (olive oil in the majority of cases).

Weak evidence.

Meat

- Meat consumption (no more than 4 portions per week) is not prejudicial for CVR or DM2.[13] Lean meat is preferable, and the skin and visible fat should be removed before cooking.
- Replacing red meat with sources of vegetable protein improves the lipid profile[14] and may reduce the risk of ischemic cardiomyopathy.[15]

Weak evidence.

- The consumption of processed meat is associated with a higher risk of cardiovascular disease, DM2 and mortality due to any cause.[13,16]
- Higher consumption of processed meat is associated with a higher BMC and a larger waist perimeter, as well as deterioration of the lipid profile.[17] It is not advisable to consume cold meats or other processed meats.

Weak evidence.

Eggs

- Consuming up to one egg per day is not associated with increased risk of cardiovascular disease.[18]
- Consuming eggs leads to a slight increase in total cholesterolaemia. It favours the development of large LDL particles that are less atherogenic and is accompanied by an increase in HDL-c with improved functionality.[19] It does not increase atherogenic coefficients (LDL-c: HDL-c, CT: HDL-c) or triglyceridaemia.[20]
- There seems to be no reason to restrict egg consumption to improve the lipid profile or for cardiovascular prevention. Within the context of a healthy diet, it may be safe to consume up to one egg per day.[21]

Weak evidence.

Table 1 (*Continued*)

Fish

- Increased consumption of fish is associated with a fall in the risk of cardiovascular disease and myocardial infarct.[22] It is recommendable to consume fish or shellfish at least three times a week, two of which should take the form of blue fish.[23] Replacing meat with fish as the main dish in meals will offer a healthy source of protein, and it may also contribute to reducing CVR.[24]
- Fish, and especially blue fish (sardines, mackerel and salmon, etc.), is rich in ω-3 polyunsaturated fatty acids (EPA and DHA) which have a triglyceride-lowering action. At a pharmacological dose of 4 g/day ethyl eicosapentaenoic acid reduces triglyceridaemia (−21.5%; $P < .0001$) and other atherogenic inflammatory parameters without increasing LDL-c,[25] and it also significantly reduces cardiovascular events (HR: 0.75; CI 95%: 0.68−0.83).[26]-

Although fish (especially larger fish and predators) may contain mercury, within the context of a Mediterranean-type diet the benefit of consuming fish seems to exceed the potential risk of exposure to mercury.[27]

Moderate evidence.

Dairy products

- Whole milk dairy products are no worse in terms of cardiometabolic health than those which are low in fat or skimmed.[28]
- Consuming whole milk or skimmed milk dairy products does not increase CVR. The total intake of dairy products, as well as low fat or whole milk dairy products, has an inverse relationship with the risk of ictus.[29]

Moderate evidence.

- The consumption of yogurt is associated with a fall in the risk of DM2 and metabolic syndrome in the general population.[30]

Moderate evidence.

- Cheese consumption is not associated with increased CVR,[31,32] and it does not cause the lipid profile alterations which could be expected because of its content in saturated fat. There is a J-curve shaped association between cheese consumption and CVR, where the greatest benefit is found for a daily intake (40 g).[33]

Moderate evidence.

- It is advisable to consume at least 2 portions a day of whole - or skimmed milk dairy products (a portion is equivalent to 200 ml milk, 125 g yogurt or 40 g cheese), although it is not advisable to consume dairy products that contain added sugar. If the aim is to reduce dietary calories, dairy products should be selected that are either low fat or skimmed.[2]

Moderate evidence.

Fruit and vegetables

- Individuals who eat more fruit and vegetables have a lower CVR for ictus and ischemic cardiomyopathy.[34]
- Fruit and vegetables contain phytochemicals that have beneficial effects on vascular health, including antioxidant and anti-inflammatory properties.[35]
- Consuming more than 3 portions a day of fruit and vegetables gives rise to a reduction in triglyceridaemia and blood pressure.[36]
- The recommendation is to consume at least 5 portions a day of vegetables and fruit. Consumption should be varied, avoiding prepared foods with added sugar, while preferentially selecting fresh seasonal produce.[2]

Moderate evidence.

Nuts

- A moderate consumption of nuts (30 g/day) seems to be associated with reduced cardiovascular morbimortality.[3,37]
- In intervention studies the consumption of nuts reduces total cholesterolaemia and LDL-c, while it also improves endothelial functioning without affecting bodyweight.[38]
- There is an inverse relationship between nut consumption and the development of metabolic syndrome.[39]
- It is recommendable for the general population and subjects with hypercholesterolemia or hypertension, metabolic syndrome and/or obesity to eat nuts. It is advisable to consume a handful of raw nuts (about 30 g) often (every day or at least 3 times a week), avoiding salted nuts.[2]

Strong evidence.

Cereals

- Consuming whole grain cereals instead of refined products reduces total cholesterolaemia, LDL-c, HbA1c and C-reactive protein.[40] It is advisable to promote the consumption of whole grain cereals as opposed to refined ones due to their higher content in fibre, vitamin B and other antioxidants.[2]
- Higher consumption of dietary fibre is directly associated with a reduction in cardiovascular mortality and mortality due to any cause, as well as the incidence of heart disease, cerebrovascular accidents and DM2. This benefit arises with the consumption of whole grain cereals.[41,42]

Moderate evidence.

- Although consuming white or brown rice does not increase CVR,[43] white rice seems to be associated with a higher risk of metabolic syndrome.[44]

Weak evidence.

Table 1 (*Continued*)

Pulses
- Pulse consumption does not seem to be associated with a higher risk of metabolic syndrome.[45]
- Pulse consumption is associated with a lower risk of cardiovascular disease and ischemic cardiomyopathy.[46] It is recommendable to consume a portion of pulses at least 4 times a week.[2]

Moderate evidence.

Tubers
- There is no relationship between a higher consumption of potatoes and cardiovascular risk[47] or mortality due to all causes.[48]
- Daily consumption of potatoes (especially if they are fried) may lead to an increased risk of DM2.[47,49]

Weak evidence.

Cacao and chocolate
- The high flavonoid content of cacao seems to have antioxidant, antihypertensive and antiaggregant effects, as well as improving endothelial functioning.[50]
- In intervention studies the consumption of black chocolate with ≥70% cacao improves vascular function and insulin resistance, while in observational studies a fall in the risk of myocardial infarct, cerebrovascular accidents, DM2 and cardiovascular mortality was observed.[51,52]
- Black chocolate with ≥70% cacao may be consumed in moderate amounts (up to 30 g/day), although it is not recommendable to habitually consume chocolate which contains a smaller percentage of cacao or its derivates, when they contain other fats or sugars.[2]

Weak evidence.

Coffee and tea
- Coffee infusions contain polyphenols including chlorogenic acid. This has been said to have antioxidant and anti-inflammatory properties, as well as regulating the hydrocarbonate metabolism.[53]
- Prospective studies have shown a direct association between higher coffee consumption and a reduction in the risk of DM2, without any differences between coffee with and without caffeine.[54]
- There is a non-lineal inverse association (a U-shaped curve) between coffee consumption and cardiovascular mortality, as well as mortality due to all causes.[55] A 15% fall in CVR arises with the consumption of from 3 to 5 cups per day of coffee, with similar benefits for cerebrovascular accidents and ischemic cardiomyopathy.[56]
- Meta-analyses of prospective cohort studies show that the habitual consumption of black or green tea is associated with a lower CVR and lower mortality due to all causes.[57,58]
- The habitual consumption of up to 5 cups per day of coffee (filtered or instant, complete or decaffeinated) or tea (green or black) is beneficial for cardiovascular health, although any added sugar should be restricted to the maximum.[2]

Moderate evidence.

Processed foods
- The consumption of ultraprocessed foods is associated with a higher incidence of being overweight or obese,[59] the risk of DM2,[60] all cardiovascular, coronary and cerebrovascular diseases, as well as mortality due to any cause.[61–63]
- A higher intake of ultraprocessed foods is associated with increased risk of metabolic syndrome, lower levels of HDL-c and greater weight circumference.[63]
- Ultraprocessed foods should be avoided in the diet, while promoting the consumption of fresh foods. The consumption of precooked, tinned and salted foods or sausages should be restricted, as they also usually contain more sodium and other additives.[2]

Moderate evidence.

Alcoholic drinks
- In comparison with abstinence or the excessive consumption of alcoholic drinks, consuming up to one fermented drink per day for women and 2 for men (where a unit equals the equivalent of 330 ml beer or one 150 ml glass of wine), is associated with a fall in CVR,[64] although the risk of cancer or mortality due to any cause gradually rises with the increased consumption of alcoholic drinks.[65]
- Alcohol consumption increases the hepatic synthesis of triglycerides and very low-density lipoproteins (VLDL), and is also involves increased calorie consumption, so that in patients with hypertriglyceridaemia no alcohol consumption is acceptable.[66]

Moderate evidence.

Drinks with added sugar or artificial sweeteners
- The frequent consumption of drinks which contain added sugar favours insulin resistance, visceral obesity, metabolic syndrome and the incidence of DM2, and it also increases CVR.[67]

Strong evidence.
- Drinks with added sugar should not be consumed, not only soft drinks but also artificial fruit juices and dairy-based drinks. Substituting sugared drinks with water or unsweetened infusions would be important in reducing calorie intake as well as CVR, obesity, metabolic syndrome and DM2.

Table 1 (*Continued*)

- The latest evidence indicates that increased consumption of artificially sweetened drinks increases cardiovascular mortality and mortality due to any cause, the risk of cerebrovascular accident and coronary disease,[68,69] so that even though there is no definitive evidence for this, consumption of these drinks should not be recommended.
Weak evidence.

Dietary sustainability

- The amount food contributes to global heating depends as much on how it is produced as well as its transportation, so that we should consume locally produced seasonal foods, avoiding food from farther away.[70] Furthermore, seasonal foods are richer in nutrients and keep their natural flavour.
Moderate evidence.
- To increase dietary sustainability, it is advisable for the population in general to reduce the consumption of meat and processed foods, while increasing the consumption of plant-based foods.[71,72]
Moderate evidence.

BMI, body mass index; CI 95%, 95% confidence interval; CV, cardiovascular; CVR, cardiovascular risk; DHA, docosahexaenoic acid; DM2, type 2 diabetes mellitus; EPA, eicosapentaenoic acid; HbA1c, glycated haemoglobin; HDL-c, high density lipoprotein cholesterol; HR, hazard ratio; HT, hypertension; LDL-c, low density lipoprotein cholesterol.

Table 2 Food groups that are recommended and not recommended for the prevention and treatment of atherogenic dyslipidemia.

Recommended Food group	Level of evidence
Virgin olive oil as a dressing and for cooking	Strong
Nuts (±30 g) raw and unsalted ≥3 times/week	
Replace saturated fat and carbohydrates with unsaturated fat	Moderate
Consume ≥2 portions/day dairy products	
Consume fish or shellfish ≥3 times/week, 2 of which are blue fish	
Consume a portion of pulses ≥4 times/week	
Consume ≥5 portions/day of fruit and/or vegetables	
Consume whole grain cereals and dietary fibre	
Consume ≥5 cups of coffee or tea/day without added sugar	
Replace red meat with vegetable-based protein	Weak
Consumption of drinks with added sugar	Strong
Consumption of processed foods	Moderate
Consumption of alcohol by patients with hypertriglyceridaemia	
Consumption of processed meat	Weak
Using sunflower, maize or soya oil for frying	

Conclusions

A healthy diet, regular physical exercise and smoking cessation are the first measures to reduce cardiovascular risk in patients with AD. The nutritional quality of their diet should be improved, replacing the foods with the greatest atherogenic effect with others that are healthier. There is solid evidence that vegetable-based diets that are low in saturated fatty acids, cholesterol and sodium, and with a high fibre, potassium and unsaturated fatty acids, are beneficial and reduce the expression of cardiovascular risk factors. Patients are therefore recommended to consume pulses, whole-grain cereals, nuts, greens and fruit (foods with a higher content of complex carbohydrates and dietary fibre); salt intake should be reduced; and products with added sugar or which are refined or processed should be avoided. The Mediterranean diet rich in virgin olive oil is a good example of such a diet. Additionally, given the link between nutrition and this disease, it is fundamental to try to prevent weight gain or reduce excess weight, personalizing treatment to favour patient empowerment.

Conflict of interests

The authors have no conflict of interests to declare.

Appendix A. Members of the Atherogenic Dyslipidemia Work Group

Mariano Blasco, Ángel Díaz, José Luis Díaz, Alipio Mangas, Jesús Millán Cortés, Vicente Pascual, Juan C. Pedro-Botet, Pablo Pérez Martínez and Xavier Pintó.

References

1. Ascaso JF, Millán J, Hernández-Mijares A, Blasco M, Brea A, Díaz A, et al. Dislipidemia aterogénica 2019. Documento de consenso

del Grupo de Dislipidemia Aterogénica de la Sociedad Española de Arteriosclerosis. Clin Investig Arterioscler. 2020;32(3):120–5.
2. Pérez-Jiménez F, Pascual V, Meco JF, Pérez-Martínez, Delgado Lista J, Domenech M, et al. Documento de recomendaciones de la SEA 2018. El estilo de vida en la prevención cardiovascular. Clin Invest Arterioscler. 2018;30:280–310.
3. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med. 2018;378(25):e34.
4. Delgado-Lista J, Alcala-Diaz JF, Torres-Peña JD, Quintana-Navarro GM, Fuentes F, Garcia-Rios A, CORDIOPREV Investigators, et al. Long-term secondary prevention of cardiovascular disease with a Mediterranean diet and a low-fat diet (CORDIOPREV): a randomised controlled trial. Lancet. 2022;399(10338):1876–85.
5. Julibert A, Bibiloni MDM, Tur JA. Dietary fat intake and metabolic syndrome in adults: a systematic review. Nutr Metab Cardiovasc Dis. 2019;29(9):887–905.
6. Imamura F, Micha R, Wu JH, de Oliveira Otto MC, Otite FO, Abioye AI, et al. Effects of saturated fat, polyunsaturated fat, monounsaturated fat, and carbohydrate on glucose-insulin homeostasis: a systematic review and meta-analysis of randomised controlled feeding trials. PLoS Med. 2016;13(7):e1002087.
7. Clifton P. Metabolic syndrome-role of dietary fat type and quantity. Nutrients. 2019;11(7):1438.
8. George ES, Marshall S, Mayr HL, Trakman GL, Tatucu-Babet OA, Lassemillante AM, et al. The effect of high-polyphenol extra virgin olive oil on cardiovascular risk factors: a systematic review and meta-analysis. Crit Rev Food Sci Nutr. 2019;59(17):2772–95.
9. Dobarganes C, Márquez-Ruiz G. Possible adverse effects of frying with vegetable oils. Br J Nutr. 2015;113 Suppl 2:S49–57.
10. Honerlaw JP, Ho YL, Nguyen XT, Cho K, Vassy JL, Gagnon DR, VA Million Veteran Program, et al. Fried food consumption and risk of coronary artery disease: the million veteran program. Clin Nutr. 2020;39(4):1203–8.
11. Guallar-Castillon P, Rodriguez-Artalejo F, Lopez-Garcia E, León-Muñoz LM, Amiano P, Ardanaz E, et al. Consumption of fried foods and risk of coronary heart disease: Spanish cohort of the European Prospective Investigation into Cancer and Nutrition study. BMJ. 2012;344:e363.
12. Rey-García J, Guallar-Castillón P, Donat-Vargas C, Moreno-Iribas C, Barricarte A, Rodriguez-Barranco M, et al. Fried-food consumption does not increase the risk of stroke in the Spanish cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC) study. J Nutr. 2020;150(12):3241–8.
13. Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. Circulation. 2010;121:2271–83.
14. Guasch-Ferré M, Satija A, Blondin SA, Janiszewski M, Emlen E, O'Connor LE, et al. Meta-analysis of randomized controlled trials of red meat consumption in comparison with various comparison diets on cardiovascular risk factors. Circulation. 2019;139(15):1828–45.
15. Al-Shaar L, Satija A, Wang DD, Rimm EB, Smith-Warner SA, Stampfer MJ, et al. Red meat intake and risk of coronary heart disease among US men: prospective cohort study. BMJ. 2020;371:m4141, http://dx.doi.org/10.1136/bmj.m4141.
16. Zhong VW, Van Horn L, Greenland P, Carnethon MR, Ning H, Wilkins JT, et al. Associations of processed meat, unprocessed red meat, poultry, or fish intake with incident cardiovascular disease and all-cause mortality. JAMA Intern Med. 2020;180(4):503–12.
17. Hobbs-Grimmer DA, Givens DI, Lovegrove JA. Associations between red meat, processed red meat and total red and processed red meat consumption, nutritional adequacy and markers of health and cardio-metabolic diseases in British adults: a cross-sectional analysis using data from UK National Diet and Nutrition Survey. Eur J Nutr. 2021, http://dx.doi.org/10.1007/s00394-021-02486-3.
18. Drouin-Chartier JP, Chen S, Li Y, Schwab AL, Stampfer MJ, Sacks FM, et al. Egg consumption and risk of cardiovascular disease: three large prospective US cohort studies, systematic review, and updated meta-analysis. BMJ. 2020;368:m513, http://dx.doi.org/10.1136/bmj.m513.
19. Blesso CN, Fernandez ML. Dietary cholesterol, serum lipids, and heart disease: are eggs working for or against you? Nutrients. 2018;10(4), http://dx.doi.org/10.3390/nu10040426, pii: E426.
20. Rouhani MH, Rashidi-Pourfard N, Salehi-Abargouei A, Karimi M, Haghighatdoost F. Effects of egg consumption on blood lipids: a systematic review and meta-analysis of randomized clinical trials. J Am Coll Nutr. 2018;37(2):99–110.
21. Khalighi Sikaroudi M, Soltani S, Kolahdouz-Mohammadi R, Clayton ZS, Fernandez ML, Varse F, et al. The responses of different dosages of egg consumption on blood lipid profile: an updated systematic review and meta-analysis of randomized clinical trials. J Food Biochem. 2020;44(8):e13263, http://dx.doi.org/10.1111/jfbc.13263.
22. Krittanawong C, Isath A, Hahn J, Wang Z, Narasimhan B, Kaplin SL, et al. Fish consumption and cardiovascular health: a systematic review. Am J Med. 2021;S0002-9343(21), 00009-7.
23. Rimm EB, Appel LJ, Chiuve SE, Djoussé L, Engler MB, Kris-Etherton PM, American Heart Association Nutrition Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Epidemiology and Prevention; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; and Council on Clinical Cardiology, et al. Seafood Long-chain n-3 polyunsaturated fatty acids and cardiovascular disease: a science advisory from the American Heart Association. Circulation. 2018;138:e35–47.
24. Key TJ, Appleby PN, Bradbury KE, Sweeting M, Wood A, Johansson I, et al. Consumption of meat, fish, dairy products, and eggs and risk of ischemic heart disease. Circulation. 2019;139:2835–45.
25. Miller M, Ballantyne CM, Bays HE, Granowitz C, Doyle RT Jr, Juliano RA, et al. Effects of icosapent ethyl (Eicosapentaenoic Acid Ethyl Ester) on atherogenic lipid/lipoprotein, apolipoprotein, and inflammatory parameters in patients with elevated high-sensitivity C-reactive protein (from the ANCHOR study). Am J Cardiol. 2019;124(5):696–701.
26. Bhatt DL, Steg PG, Miller M, Brinton EA, Jacobson TA, Ketchum SB, et al., REDUCE-IT Investigators. Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. N Engl J Med. 2019;380:11–22.
27. Downer MK, Martínez-González MA, Gea A, Stampfer M, Warnberg J, Ruiz-Canela M. Mercury exposure and risk of cardiovascular disease: a nested case-control study in the PREDIMED (PREvention with MEDiterranean Diet) study. BMC Cardiovasc Disord. 2017;17:9.
28. Hirahatake KM, Astrup A, Hill JO, Slavin JL, Allison DB, Maki KC. Potential cardiometabolic health benefits of full-fat dairy: the evidence base. Adv Nutr. 2020;11(3):533–47.
29. Alexander DD, Bylsma LC, Vargas AJ, Cohen SS, Doucette A, Mohamed M, et al. Dairy consumption and CVD: a systematic review and meta-analysis. Br J Nutr. 2016;115:737–50.
30. Companys JR, Pla-Pagà L, Calderón-Pérez L, Llauradó E, Solà R, Pedret A, et al. Fermented dairy products, probiotic supplementation, and cardiometabolic diseases: a systematic review and meta-analysis. Adv Nutr. 2020;11(4):834–63.
31. Drouin-Chartier JP, Brassard D, Tessier-Grenier M, Anne Côté J, Labonté ME, Desroches S, et al. Systematic review of the association between dairy product consumption and risk of cardiovascular-related clinical outcomes. Adv Nutr. 2016;7:1026–40.

32. Alexander DD, Bylsma LC, Vargas AJ, Cohen SS, Doucette A, Mohamed M, et al. Dairy consumption and CVD: a systematic review and meta-analysis. Br J Nutr. 2016;115(4):737–50.
33. Chen GC, Wang Y, Tong X, Szeto IMY, Smit G, Li ZN, et al. Cheese consumption and risk of cardiovascular disease: a meta-analysis of prospective studies. Eur J Nutr. 2017;56:2565–75.
34. Zurbau A, Au-Yeung F, Blanco Mejia S, Khan TA, Vuksan V, Jovanovski E, et al. Relation of different fruit and vegetable sources with incident cardiovascular outcomes: a systematic review and meta-analysis of prospective cohort studies. J Am Heart Assoc. 2020;9(19):e017728, http://dx.doi.org/10.1161/JAHA.120.017728.
35. Poulsen NB, Lambert MNT, Jeppesen PB. The effect of plant derived bioactive compounds on inflammation: a systematic review and meta-analysis. Mol Nutr Food Res. 2020;64(18):e2000473.
36. Toh DWK, Koh ES, Kim JE. Incorporating healthy dietary changes in addition to an increase in fruit and vegetable intake further improves the status of cardiovascular disease risk factors: a systematic review, meta-regression, and meta-analysis of randomized controlled trials. Nutr Rev. 2020;78(7):532–45.
37. Becerra-Tomás N, Paz-Graniel I, Kendall C, Kahleova H, Rahelić D, Sievenpiper JL, et al. Nut consumption and incidence of cardiovascular diseases and cardiovascular disease mortality: a meta-analysis of prospective cohort studies. Nutr Rev. 2019;77:691–709.
38. Kim Y, Keogh J, Clifton PM. Nuts and cardio-metabolic disease: a review of meta-analyses. Nutrients. 2018;10(12):1935, http://dx.doi.org/10.3390/nu10121935. PMID: 30563231; PMCID: PMC6316378.
39. Zhang Y, Zhang DZ. Relationship between nut consumption and metabolic syndrome: a meta-analysis of observational studies. J Am Coll Nutr. 2019;38(6):499–505.
40. Marshall S, Petocz P, Duve E, Abbott K, Cassettari T, Blumfield M, et al. The effect of replacing refined grains with whole grains on cardiovascular risk factors: a systematic review and meta-analysis of randomized controlled trials with GRADE clinical recommendation. J Acad Nutr Diet. 2020;120(11):1859–83, e31.
41. Zhang B, Zhao Q, Guo W, Bao W, Wang X. Association of whole grain intake with all-cause, cardiovascular, and cancer mortality: a systematic review and dose-response meta-analysis from prospective cohort studies. Eur J Clin Nutr. 2018;72:57–65.
42. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. Lancet. 2019;393(10170):434–45.
43. Muraki I, Wu H, Imamura F, Laden F, Rimm EB, Hu FB, et al. Rice consumption and risk of cardiovascular disease: results from a pooled analysis of 3 U.S. cohorts. Am J Clin Nutr. 2015;101:164–72.
44. Krittanawong C, Tunhasiriwet A, Zhang H, Prokop LJ, Chirapongsathorn S, Sun T, et al. Is white rice consumption a risk for metabolic and cardiovascular outcomes? A systematic review and meta-analysis. Heart Asia. 2017;9(2):e010909.
45. Jiang YT, Zhang JY, Liu YS, Chang Q, Zhao YH, Wu QJ. Relationship between legume consumption and metabolic syndrome: a systematic review and meta-analysis of observational studies. Nutr Metab Cardiovasc Dis. 2020;30(3):384–92.
46. Marventano S, Izquierdo Pulido M, Sánchez-González C, Godos J, Speciani A, Galvano F, et al. Legume consumption and CVD risk: a systematic review and meta-analysis. Public Health Nutr. 2017;20:245–54.
47. Borch D, Juul-Hindsgaul N, Veller M, Astrup A, Jaskolowski J, Raben A. Potatoes and risk of obesity, type 2 diabetes, and cardiovascular disease in apparently healthy adults: a systematic review of clinical intervention and observational studies. Am J Clin Nutr. 2016;104:489–98.
48. Hashemian M, Murphy G, Etemadi A, Liao LM, Dawsey SM, Malekzadeh R, et al. Potato consumption and the risk of overall and cause specific mortality in the NIH-AARP study. PLoS One. 2019;14(5):e0216348.
49. Schwingshackl L, Schwedhelm C, Hoffmann G, Boeing H. Potatoes and risk of chronic disease: a systematic review and dose-response meta-analysis. Eur J Nutr. 2019;58(6):2243–51.
50. Khan N, Khymenets O, Urpí-Sardà M, Tulipani S, Garcia-Aloy M, Monagas M, et al. Cocoa polyphenols and inflammatory markers of cardiovascular disease. Nutrients. 2014;6(2):844–80.
51. Veronese N, Demurtas J, Celotto S, Caruso MG, Maggi S, Bolzetta F, et al. Is chocolate consumption associated with health outcomes? An umbrella review of systematic reviews and meta-analyses. Clin Nutr. 2019;38:1101–8.
52. Ren Y, Liu Y, Sun XZ, Wang BY, Zhao Y, Liu DC, et al. Chocolate consumption and risk of cardiovascular diseases: a meta-analysis of prospective studies. Heart. 2019;105:49–55.
53. Tajik N, Tajik M, Mack I, Enck P. The potential effects of chlorogenic acid, the main phenolic components in coffee, on health: a comprehensive review of the literature. Eur J Nutr. 2017;56:2215–44.
54. Carlström M, Larsson SC. Coffee consumption and reduced risk of developing type 2 diabetes: a systematic review with meta-analysis. Nutr Rev. 2018;76:395–417.
55. Kim Y, Je Y, Giovannucci E. Coffee consumption and all-cause and cause-specific mortality: a meta-analysis by potential modifiers. Eur J Epidemiol. 2019;34:731–52.
56. Ding M, Bhupathiraju SN, Satija A, van Dam RB, Hu FB. Long-term coffee consumption and risk of cardiovascular disease. A systematic review and a dose–response meta-analysis of prospective cohort studies. Circulation. 2014;129:643–59.
57. Zhang C, Qin YY, Wei X, Yu FF, Zhou YH, He J. Tea consumption and risk of cardiovascular outcomes and total mortality: a systematic review and meta-analysis of prospective observational studies. Eur J Epidemiol. 2015;30:103–13.
58. Chung M, Zhao N, Wang D, Shams-White M, Karlsen M, Cassidy A, et al. Dose-response relation between tea consumption and risk of cardiovascular disease and all-cause mortality: a systematic review and meta-analysis of population-based studies. Adv Nutr. 2020:nmaa010, http://dx.doi.org/10.1093/advances/nmaa010.
59. Mendonça RD, Pimenta AM, Gea A, de la Fuente-Arrillaga C, Martinez-Gonzalez MA, Souza Lopes AC, et al. Ultraprocessed food consumption and risk of overweight and obesity: the University of Navarra Follow-Up (SUN) cohort study. Am J Clin Nutr. 2016;104:1433–40.
60. Srour B, Fezeu LK, Kesse-Guyot E, Allès B, Méjean C, Andrianasolo RM, et al. Ultraprocessed food consumption and risk of type 2 diabetes among participants of the nutrinet-santé prospective cohort. JAMA Intern Med. 2020;180:283–91.
61. Srour B, Fezeu LK, Kesse-Guyot E, Allès B, Méjean C, Andrianasolo RM, et al. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Santé). BMJ. 2019;365:l1451.
62. Schnabel L, Kesse-Guyot E, Allès B, Touvier M, Srour B, Hercberg S, et al. Association between ultraprocessed food consumption and risk of mortality among middle-aged adults in France. JAMA Intern Med. 2019;179:490–8.
63. Pagliai G, Dinu M, Madarena MP, Bonaccio M, Iacoviello L, Sofi F. Consumption of ultra-processed foods and health status: a systematic review and meta-analysis. Br J Nutr. 2021;125(3):308–18.
64. Xi B, Veeranki SP, Zhao M, Ma C, Yan Y, Mi J. Relationship of alcohol consumption to all-cause, cardiovascular, and cancer-related mortality in U.S. adults. J Am Coll Cardiol. 2017;70:913–22.
65. GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic anal-

ysis for the Global Burden of Disease Study 2016. Lancet. 2018;392(10152):1015–35.
66. Pascual V, Perez Martinez P, Fernández JM, Solá R, Pallarés V, Romero Secín A, et al. Documento de consenso SEA/SEMERGEN 2019. Recomendaciones dietéticas en la prevención cardiovascular. Semergen. 2019;45:333–48.
67. Malik VS, Hu FB. Sugar-sweetened beverages and cardiometabolic health: an update of the evidence. Nutrients. 2019;11(8):1840.
68. Mullee A, Romaguera D, Pearson-Stuttard J, Viallon V, Stepien M, Freisling H, et al. Association between soft drink consumption and mortality in 10 European countries. JAMA Intern Med. 2019:e192478, http://dx.doi.org/10.1001/jamainternmed.2019.2478.
69. Mossavar-Rahmani Y, Kamensky V, Manson JE, Silver B, Rapp SR, Haring B, et al. Artificially sweetened beverages and stroke, coronary heart disease, and all-cause mortality in the women's health initiative. Stroke. 2019;50:555–62.
70. Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, et al. Food in the anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet. 2019;393(10170):447–92, 71.
71. Godfray HCJ, Aveyard P, Garnett T, Hall JW, Key TJ, Lorimer J, et al. Meat consumption, health, and the environment. Science. 2018;361(6399), eaam5324.
72. Clark MA, Springmann M, Hill J, Tilman D. Multiple health and environmental impacts of foods. Proc Natl Acad Sci USA. 2019;116(46):23357–62.