

Dutch dietary guidelines for people with atherosclerotic cardiovascular disease

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Health Council of the Netherlands



contents

Summary	3	04 Functional foods and supplements	33
01 Introduction	6	4.1 Recommendations	34
1.1 Reason for advisory report	7	4.2 Explanation	34
1.2 Atherosclerotic cardiovascular disease	8	05 Weight reduction and maintenance	39
1.3 Users of this advisory report	9	5.1 Recommendation	40
1.4 Scope	9	5.2 Explanation	40
1.5 Reading guide	10	06 Recommendations	43
02 Methodology	11	6.1 Dietary recommendations	44
2.1 Working group and consulted experts	12	6.2 Points to consider in implementing dietary recommendations	45
2.2 Dutch dietary guidelines 2015 as a starting point	12	6.3 Recommendations for future research	48
2.3 Selection of dietary factors	13	References	52
2.4 Selection of health outcomes	14		
2.5 Literature review and evaluation	15		
03 Dutch dietary guidelines	18		
3.1 Recommendation	19		
3.2 Explanation	19		



summary

In the *Dutch dietary guidelines 2015*, the Health Council of the Netherlands specifies the recommended intake of foods and beverages to prevent chronic diseases. These guidelines are meant for the general Dutch population. This group also includes the roughly 1.5 million people with chronic cardiovascular diseases, such as a previous heart attack (myocardial infarction), a stroke and peripheral arterial disease (intermittent claudication). In many cases these cardiovascular diseases are caused by atherosclerosis. However, for the *Dutch dietary guidelines 2015* it was not separately assessed whether the guidelines were fully tailored to people with atherosclerotic cardiovascular disease. It is possible that disease-specific adjustments or additions are needed for this group. At the request of the State Secretary for Health, Welfare and Sport, the Health Council of the Netherlands is now issuing specific advice on this matter. The Permanent

Committee on Nutrition prepared the advisory report.

Dietary guidelines an appropriate basis

The *Dutch dietary guidelines 2015* contain specific guidelines for the consumption of foods and beverages. The Committee evaluated whether the guidelines for dairy products, fish, fats and oils, coffee, meat, alcohol and table salt are also appropriate for people with atherosclerotic cardiovascular disease. The point of departure here is that the *Dutch dietary guidelines 2015* form an appropriate basis, unless proven otherwise.

The selection of the foods and beverages for evaluation was based on existing national and international dietary guidelines for people with cardiovascular disease and on the expert judgement of the Committee. For its evaluation, the Committee used the same health outcomes as for the *Dutch dietary guidelines 2015*:

morbidity and mortality caused by the top ten chronic diseases in the Netherlands, body weight, LDL cholesterol level and blood pressure. For the current advisory report, the Committee also evaluated all-cause mortality, cardiac arrhythmia, glucose metabolism and kidney function.

The Committee concludes that the *Dutch dietary guidelines 2015* are an appropriate basis for people with atherosclerotic cardiovascular disease. With regard to coffee, fats and oils and alcohol the Committee found sufficient research in this group for conclusions to be drawn and the results did not give cause for deviating from the existing guidelines. Hence the recommendations are to replace unfiltered coffee with filtered coffee, to replace butter, hard margarines and cooking fats with soft margarines, liquid cooking fats or vegetable oils, and not to drink alcohol or at least no more than 1 glass per day. With regard to fish the Committee concludes on the



basis of the available studies that eating 1 to 2 portions a week (instead of 1 portion a week, as recommended in the *Dutch dietary guidelines 2015*) can be beneficial for the health of people with atherosclerotic cardiovascular disease. There is currently too little research available on table salt, dairy products and meat for people with atherosclerotic cardiovascular disease. Hence there is no basis for adjusting these guidelines.

The other foods and beverages from the *Dutch dietary guidelines 2015* were not evaluated, because there is no reason to assume that different recommendations apply to people with atherosclerotic cardiovascular disease than to the general population. This means that also for people with atherosclerotic cardiovascular disease, it is recommended, among other things, that they eat at least 200 grammes of vegetables, 200 grammes of fruit and 90 grammes of whole-grain products every day as well as legumes every week, that they minimise the consumption of sugar-containing beverages

and that they eat more plant-based and less animal-based products.

The Committee is aware that the dietary recommendations not only affect health but also sustainability aspects of dietary patterns. The Committee outlines how sustainability aspects can be taken into account when applying these guidelines, but it did not evaluate sustainability aspects when drawing up the dietary recommendations.

Plant sterols and stanols can also help to reduce LDL cholesterol levels

A healthy dietary pattern in line with the *Dutch dietary guidelines 2015* can help to lower LDL cholesterol levels and reduce the risk of cardiovascular disease and other chronic diseases. The Committee evaluated whether foods fortified with plant sterols and/or stanols can also help people with atherosclerotic cardiovascular disease to reduce their level of LDL cholesterol.

It concludes that these products are effective in lowering LDL cholesterol levels, also in people who use statins. It is not yet sufficiently clear whether this also works for people who use other cholesterol-lowering medicines than statins. Furthermore, there are no studies that have investigated whether the use of foods fortified with plant sterols and/or stanols does in fact help to reduce the risk of cardiovascular disease.

No reason to recommend supplements

The Committee also examined whether dietary supplements may possibly help to reduce the risk of (worsening or subsequent) cardiovascular disease for people with atherosclerotic cardiovascular disease. The Committee cannot make any recommendation about supplements with monacolin K from red yeast rice because insufficient studies were available on this subject. The Committee also cannot make any recommendation about high dosages of fish fatty acids. Sufficient studies are available in this case, but they do not provide a clear picture.



In the opinion of the Committee, a lower dosage of fish fatty acids – comparable to 1 to 3 portions of fish a week – probably does not yield any health benefit.

If overweight or obese, aim for weight reduction

A large proportion of people with atherosclerotic cardiovascular disease are overweight or obese. Being overweight or obese is a risk factor for, among other things, elevated blood pressure and cholesterol levels, and development of type 2 diabetes, cancer and cardiovascular disease. The Committee advises people with atherosclerotic cardiovascular disease who are overweight or obese to aim for a weight reduction of at least 5% and to maintain this reduced weight in the long term. An energy-restricted diet based on the *Dutch dietary guidelines 2015* can be compiled for people who wish to lose weight and it is recommended they seek guidance from a dietician. However, reducing weight and above all maintaining the reduced weight is complex and usually requires

addressing multiple factors, including lifestyle-related factors, at the same time, both at the individual level and in the living environment.

Integrating dietary recommendations in a broader approach

The recommendations of the Committee can be used in public information on nutrition for people with atherosclerotic cardiovascular disease, provided for instance by the Netherlands Nutrition Centre, by healthcare professionals such as cardiologists and general practitioners and their assistant practitioners and for dietary treatment by dietitians. It is preferable that the Committee's dietary recommendations be integrated into a broader multidisciplinary approach that also focuses on other factors, such as not smoking and taking sufficient exercise.

Future research

The Committee indicates that more research is required in people with atherosclerotic cardiovascular disease in order for more specific

recommendations to be given. This relates, for instance, to research on the health effects of dietary factors for which the Committee found too little research (such as dairy products and table salt) and on dietary interventions combined with the use of cardiovascular medication. In addition, follow-up research is needed into how the Committee's recommendations can be combined with increasing sustainability of dietary patterns.



01 introduction



This advisory report addresses the question of whether the Health Council's *Dutch dietary guidelines 2015* can also be applied to people with cardiometabolic disorders and whether any disease-specific adjustments or additions are required for this group. The first part of the advisory report, which focuses on people with type 2 diabetes, was published in November 2021.¹ The present, second part of the advisory report focuses on people with cardiovascular disease caused by atherosclerosis (calcification of the arteries).

1.1 Reason for advisory report

For the general Dutch population (from 2 years of age), the *Dutch dietary guidelines 2015* specify the recommended intake of foods and beverages to prevent chronic diseases, including cardiovascular disease, type 2 diabetes and some forms of cancer.²

A significant part of the Dutch population already has chronic diseases, such as the cardiometabolic diseases type 2 diabetes and cardiovascular diseases. The Health Council's Committee on Nutrition, which drafted the *Dutch dietary guidelines 2015*, assumes that these guidelines are also suitable for people with cardiometabolic disorders, as these guidelines are largely based on studies in the general population and not only in healthy populations. People with cardiometabolic disorders are therefore also covered in the evaluations that form the basis of the *Dutch dietary guidelines 2015*. Several Dutch treatment guidelines for people with type

2 diabetes or cardiovascular disease therefore recommend following the *Dutch dietary guidelines 2015*.³⁻⁵

At the time, it was not separately assessed whether the *Dutch dietary guidelines 2015* are entirely appropriate for people with cardiometabolic disorders. More research is now available that has been specifically carried out in people who already have type 2 diabetes or cardiovascular disease.⁶⁻¹⁰ These studies allow improved insight into whether the *Dutch dietary guidelines 2015* apply to those groups and whether any disease-specific adjustments or additions are required. In 2019, the State Secretary for Health, Welfare and Sport requested the Health Council to issue an advisory report on this matter. The request for advice can be found on the Council's website. The first part of the advisory report, on people with type 2 diabetes, was published in 2021.¹ The present, second advisory report focuses specifically on people with cardiovascular disease caused by atherosclerosis.

This report was prepared by the Health Council's Permanent Committee on Nutrition, with experts from nutritional, behavioural, medical and paramedical disciplines, amongst others. A list of the Committee's members can be found at the end of this advisory report. Stakeholders have been given the opportunity to comment on drafts of the advisory report and the associated background documents. All comments received



and the Committee's responses to them have been published on the Council's website.

1.2 Atherosclerotic cardiovascular disease

In 2020, around 1.5 million people in the Netherlands were known to have a chronic cardiovascular disease. The percentage of males and females is almost even (slightly more males).¹¹ Cardiovascular disease is an umbrella term for various disorders of the heart and blood vessels. In this advisory report, the Committee focuses specifically on cardiovascular disease caused by calcification of the arteries, also known as atherosclerosis. This is the most common form of cardiovascular disease in the Netherlands.¹¹ An unhealthy diet is a risk factor for atherosclerotic cardiovascular disease.^{2,12}

Atherosclerosis causes narrowing of the arteries. When the narrowing of the arteries occurs around the heart (coronary arteries), this can lead to acute coronary syndrome and stable angina pectoris (chest pain on exertion). Acute coronary syndrome is an umbrella term for unstable angina pectoris (chest pain without direct cause such as physical exertion) and myocardial infarction (heart attack). Narrowing of an artery that carries blood to the brain can lead to an ischaemic stroke (stroke) and narrowing of the artery that carries blood to the leg can lead to peripheral vascular disease (also known as intermittent claudication). In 2018, 251200 people in the Netherlands had had an acute myocardial infarction.

In 2019, 421700 people in the Netherlands had angina pectoris and 345200 had had a stroke (of which a large percentage is expected to be ischaemic). In 2014, 85000 people aged 55 and over in the Netherlands had peripheral vascular disease, and this number is likely to be an underestimate.^{11,13}

People with atherosclerotic cardiovascular disease have a relatively high risk of a manifestation, or recurrent manifestation of this disease, such as a myocardial infarction or stroke. Atherosclerotic cardiovascular disease can reduce quality of life and life expectancy. Myocardial infarction can be followed by arrhythmia and heart failure. A stroke can be followed by motor, sensory and cognitive symptoms, which can manifest in problems affecting areas such as balance, speech and memory, as well as a reduction or loss of sensation in the extremities. The symptoms of peripheral vascular disease often include pain and unpleasant sensations when walking.¹⁴⁻¹⁷

There are a number of risk factors for the occurrence or acceleration of atherosclerosis, including smoking, high LDL cholesterol levels in the blood, high blood pressure and being overweight. The treatment of atherosclerotic cardiovascular disease focuses on influencing these risk factors, which can be done by promoting a healthy lifestyle and through medication. In serious cases, there is the option of surgery to eliminate



(percutaneous coronary intervention) or bypass (bypass surgery) the narrowing.¹⁴

1.3 Users of this advisory report

This advisory report is intended as a basis for the public information provided by the Netherlands Nutrition Centre and patient organisations for people with atherosclerotic cardiovascular disease. Dietitians can, in cooperation with other healthcare professionals such as cardiologists, general practitioners (GPs) and general practice nurses, provide tailored dietary advice to people with atherosclerotic cardiovascular disease.

These healthcare professionals can use this advisory report as a reference work. The advice can also be integrated into broader interventions aimed at promoting a healthy lifestyle for people with cardiovascular disease, such as cardiac rehabilitation programmes.

The Committee discusses this in greater detail in Chapter 6.

1.4 Scope

A healthy diet is part of a healthy lifestyle, but other lifestyle factors such as getting ample exercise and refraining from smoking are important for people's general health, including those with cardiovascular disease.

This advisory report is limited to dietary recommendations and does not address other lifestyle factors.

In this advisory report, the Committee uses the term 'dietary factors' as an umbrella term for foods, beverages, nutrients and dietary patterns.

As many people with atherosclerotic cardiovascular disease are overweight or obese and dietary intake is inextricably linked to energy balance, the Committee also addresses the importance of weight reduction in this advisory report. However, the Committee did not evaluate how people with atherosclerotic cardiovascular disease can best lose weight. It therefore does not make any recommendations on the type of weight-loss diet.

In this advisory report, the Committee focuses on people with clinically established coronary heart disease (this includes people with acute coronary syndrome, those with stable angina pectoris and people who have undergone a percutaneous coronary intervention or bypass surgery), peripheral vascular disease or ischaemic stroke. People who have heart failure alone and no (underlying) atherosclerotic cardiovascular disease fall outside this group.

In principle, the Committee did not include people who have a high risk of atherosclerotic cardiovascular disease but who have not been diagnosed with cardiovascular disease in its evaluation. Risk factors for atherosclerotic cardiovascular disease are common. For example, in 2020, one and a half million people in the Netherlands had a lipid metabolism disorder, including hyperlipidaemia (elevated cholesterol and/or



triglyceride levels), and 2.8 million people had hypertension (high blood pressure).¹⁸ The *Dutch dietary guidelines* apply to these high-risk groups since, as part of the general population, they have already been included in the studies that contribute towards these guidelines. In a few exceptional cases, the Committee has incorporated studies among high-risk groups (without established atherosclerotic cardiovascular disease). For further information see section 2.5.2.

The Committee did not evaluate the extent to which the recommendations in the advisory report also apply to people with cardiovascular disease who already receive dietary advice for other conditions, such as kidney disease.

1.5 Reading guide

In Chapter 2, the Committee discusses the methodology used for this advisory report. In Chapter 3, the Committee discusses findings on the evaluated foods and beverages from the *Dutch dietary guidelines 2015*, indicating whether these findings give rise to any changes to the recommendations for people with atherosclerotic cardiovascular disease. In Chapter 4, the Committee addresses the effects of several functional foods and food supplements. In Chapter 5, it briefly discusses the importance of weight reduction for people with cardiovascular disease who are overweight or obese. Finally, Chapter 6 lists the Committee's

recommendations along with additional points for consideration and research recommendations.

There are 12 English-language background documents to this advisory report on the methodology and on the various dietary factors evaluated.



02 methodology



A structured approach was followed in preparing this advisory report, as is described in detail in the background document *Methodology for the evaluation of evidence*.¹⁹ The approach is summarised below.

2.1 Working group and consulted experts

The Committee set up a working group that prepared the background documents and drew sub-conclusions for each dietary factor and health outcome. The working group also drew conclusions as to whether, based on all of the sub-conclusions, there are grounds to amend the *Dutch dietary guidelines 2015* for people with atherosclerotic cardiovascular disease. A list of members of the Cardiovascular Disease Working Group can be found at the end of this advisory report.

During the advisory process, the Working Group and the Committee consulted experts including a cardiologist and an internist-vascular medicine specialist for a cardiovascular perspective on the advice. A list of all experts consulted on an incidental basis can also be found at the end of this advisory report.

2.2 Dutch dietary guidelines 2015 as a starting point

The Committee used the *Dutch dietary guidelines 2015* as a starting point and considered whether there were any indications that adjustments or additions might be needed for people with atherosclerotic cardiovascular disease. This means that the Committee recommends that people with

atherosclerotic cardiovascular disease follow the *Dutch dietary guidelines 2015*, unless proven otherwise. Various treatment guidelines for people with existing, or a high risk of developing, atherosclerotic cardiovascular disease, such as the Cardiovascular risk management standard of the Dutch College of General Practitioners (in Dutch: *Nederlands Huisartsen Genootschap*)³, currently already recommend following the *Dutch dietary guidelines 2015*. The Committee also assumes that the *Dutch dietary guidelines 2015* are appropriate for people with atherosclerotic cardiovascular disease because they are based on research primarily carried out in the general population: thus not just in healthy people, but also in people with cardiovascular disease and a high risk of developing it. In addition, a number of the studies used for the *Dutch dietary guidelines 2015* were specifically carried out in people with cardiovascular disease, including that caused by atherosclerosis.

As people with atherosclerotic cardiovascular disease are at an increased risk of worsening of the disease and of recurrence of the same or another cardiovascular disease, disease-specific adjustments or additions to the *Dutch dietary guidelines 2015* may be needed for this group. In order to assess this, the Committee has exclusively focused in this advisory report on studies in people who already have atherosclerotic cardiovascular disease. For dietary factors on which insufficient research is available in people with atherosclerotic cardiovascular disease, the Committee recommends that people with atherosclerotic cardiovascular disease



should follow the respective recommendations from the *Dutch dietary guidelines 2015*, unless the dietary factors in question had not been evaluated for those guidelines. In that case, the Committee has carried out an evaluation based on studies in high-risk groups (without established atherosclerotic cardiovascular disease).

2.3 Selection of dietary factors

Based on national and international reports with dietary guidelines for cardiovascular disease^{3,14,20-22} and its expert opinion, the Committee has identified dietary factors for which there are indications that adjustments or additions may be needed to the existing recommendations in the *Dutch dietary guidelines 2015* and for which healthcare professionals consider there to be a need for advice. The Committee evaluated this, amongst others, by comparing the information supporting the *Dutch dietary guidelines 2015* with existing reports containing guidelines for people with cardiovascular disease. An overview of this comparison can be found in the background document *Methodology for the evaluation of evidence*.¹⁹ In selecting the dietary factors to be evaluated, the Committee considered the following questions:

1. Which dietary factors are (especially) relevant for people with atherosclerotic cardiovascular disease and the health outcomes evaluated in this regard?
2. For which dietary factors are deviations from the *Dutch dietary guidelines 2015* to be expected for people with atherosclerotic

cardiovascular disease?

3. Which dietary factors are the subject of (considerable) discussion among healthcare professionals?

Based on these considerations, the Committee saw reasons to conduct a specific evaluation for people with atherosclerotic cardiovascular disease in the case of seven of the existing dietary recommendations in the *Dutch dietary guidelines 2015*. This concerns the 2015 guidelines on dairy products, fish, fats and oils, coffee, meat, alcohol and table salt. For the other 2015 guidelines on foods and beverages, such as those on vegetables and fruit, legumes and wholegrain products, the Committee saw no indications that deviations would be required. The Committee also assumes that there is no need to change the overall 2015 guideline to eat a more plant-based and less animal-based diet (based primarily on studies of a Mediterranean diet). This assumption is based on the Committee's expertise and the previously mentioned evidence-based dietary guidelines published by other organisations.

The *Dutch dietary guidelines 2015* advise that the use of nutrient supplements (in other words multivitamins, vitamins and minerals) are not needed, except for people from a specific target group. The Committee judged that it is specifically relevant for people with atherosclerotic cardiovascular disease to evaluate products that are fortified with plant sterols and/or stanols, supplements containing red yeast rice and



supplements containing fish fatty acids. These products are addressed in the existing guidelines for cardiovascular disease mentioned above and the Committee believes that there is a need for advice in this area among both healthcare professionals and people with atherosclerotic cardiovascular disease.

Besides the existing dietary factors in the *Dutch dietary guidelines 2015*, the Committee only addresses additional dietary factors that are specifically relevant for people with atherosclerotic cardiovascular disease in this advisory report. Dietary factors that may be additional to the *Dutch dietary guidelines 2015* and that are relevant for the entire population, such as ultra-processed foods and plant-based meat, fish or dairy substitutes, are not included in this advisory report. Such additional dietary factors will be addressed in the update of the Dutch dietary guidelines for the general population, which will commence in 2023. During the update, it will also be considered whether there is a need for specific recommendations for people with atherosclerotic cardiovascular disease (and people with type 2 diabetes) in relation to these additional dietary factors.

2.4 Selection of health outcomes

In this advisory report, the Committee focuses on promoting the long-term health of people with atherosclerotic cardiovascular disease.

The Committee used the same health outcomes as used for the *Dutch*

dietary guidelines 2015 for its evaluation. To this end, it looked at the top ten chronic diseases in the Netherlands measured in terms of mortality, years of life lost and burden of disease. This includes coronary heart disease, stroke, type 2 diabetes and various types of cancer, amongst others. In addition, the Committee searched for studies with all-cause mortality and cardiac arrhythmia as health outcomes. Where possible, the Committee looked more specifically at endpoints that fall under coronary heart disease, such as undergoing a percutaneous coronary intervention, and suffering a myocardial infarction. This was not possible for the endpoint stroke based on the available literature.

As with the *Dutch dietary guidelines 2015*, the Committee also considered so-called surrogate endpoints, which can be seen as substitute health outcomes for chronic disease and reflect the causal pathway leading from a dietary factor to chronic disease.²³ High LDL cholesterol, for example, is a surrogate endpoint for coronary heart disease. An advantage of such surrogate endpoints is that they make it possible to observe the effects of nutrition relatively soon. For example, effects on LDL cholesterol can be visible in a few weeks, whereas it takes years to observe effects on coronary heart disease. Surrogate endpoints included in this advisory report are body weight, systolic blood pressure, LDL cholesterol (in accordance with the *Dutch dietary guidelines*), kidney function (estimated glomerular filtration rate, eGFR) and glucose metabolism (fasting blood glucose and HbA1c).



2.5 Literature review and evaluation

The Committee based its evaluation primarily on meta-analyses, pooled analyses and systematic reviews of studies carried out in people with atherosclerotic cardiovascular disease. Two types of studies were described and assessed: randomised controlled trials (RCTs) and prospective cohort studies. In RCTs, the participants are divided into random groups. One of these groups receives the treatment whose effect the researchers plan to measure, while the other group serves as a control. A prospective cohort study examines the relationship between diet and chronic disease, by monitoring a group of individuals for an extended period of time. Both study types have their own advantages and disadvantages and complement each other. When RCTs are available, the Committee speaks of effects; for findings based on cohort studies, the Committee uses the term associations. In addition to meta-analyses, pooled analyses and systematic reviews, the Committee searched for individual RCTs and cohort studies. For some dietary factors and health outcomes, the Committee carried out its own meta-analysis based on the results of the available studies. The Committee only opted to do this where it considered such an approach necessary for the purpose of drawing conclusions.

Cardiac rehabilitation programmes or other combined lifestyle interventions that include a diet component can be implemented in people with atherosclerotic cardiovascular disease. In studies of such interventions, it

is difficult to isolate the effect of diet from the other components.

The Committee therefore specifically evaluated studies that investigated only the dietary factors described above.

2.5.1 Strength of evidence for deviation from the *Dutch dietary guidelines 2015*

For each effect or association identified by the Committee between a dietary factor and a health outcome, the Committee has indicated whether the strength of evidence is strong or limited. Strength of evidence is determined on the basis of the size (number of studies and participants), quality (such as risk of bias of the results due to insufficient correction for confounding factors and whether the measured food intake reflects the usual intake after the atherosclerotic cardiovascular disease) and uniformity of the studies. It drew these conclusions separately for evidence from RCTs and cohort studies.

Subsequently, it weighted all evidence for each food group in its entirety. This means that the Committee considered the evidence from RCTs and cohorts together for each health outcome. The Committee considers an effect on an outcome convincing if strong evidence from cohort studies and RCTs supports each other or if there is strong evidence from RCTs. If strong evidence from cohort studies is supported by a separate RCT with disease as a health outcome (proof of principle), the Committee also



considers the effect convincing. If there is only strong evidence based on cohort studies, the Committee considers an association plausible.

The difference between a ‘convincing’ and ‘plausible’ effect or association is usually reflected in the precise content of the associated guideline.

If there is ‘convincing’ evidence, the associated guideline will usually contain a quantitative recommendation (eat or take a certain amount); while no quantitative recommendation will usually be given if the evidence is only ‘plausible’. Only convincing evidence can give rise to modifying an existing recommendation in the *Dutch dietary guidelines 2015* for people with atherosclerotic cardiovascular disease.

2.5.2 Evaluation of functional foods and supplements

The Committee evaluated the effects of fish fatty acid supplementation in people with atherosclerotic cardiovascular disease according to the methodology described above (in line with the *Dutch dietary guidelines 2015*).

Products fortified with plant sterols and/or stanols are functional foods. Their effectiveness has been assessed by the European Food Safety Authority (EFSA), which has issued a positive opinion on a health claim that doses of between 1.5 and 3 grammes per day lower LDL cholesterol.^{24,25} In the European Union, these products are considered foods (and not medicines) from a legal perspective. The Committee

therefore evaluated the effectiveness of these products as foods (using the standard methodology outlined earlier in this chapter), although it feels that these products actually fall within a grey area between regular food and medicines.

The Committee found too few studies on products fortified with plant sterols and/or stanols and supplements containing red yeast rice in people with cardiovascular disease, whether or not caused by atherosclerosis. As a result, it has carried out its evaluation on the basis of research into the effect of these products in people with an increased risk of (but not established) atherosclerotic cardiovascular disease. In many cases, this concerned people with high LDL cholesterol levels in the blood. High LDL cholesterol often occurs in people with atherosclerotic cardiovascular disease and products fortified with plant sterols and/or stanols and supplements containing red yeast rice are specifically aimed at reducing LDL cholesterol. Consequently, the Committee expects that any effects of these products observed in people with high LDL cholesterol also apply to people with atherosclerotic cardiovascular disease.

The Committee used EFSA scientific evaluation reports as a basis for its own evaluation of the efficacy of products fortified with plant sterols and/or stanols and supplements containing red yeast rice in people with high LDL cholesterol.²⁴⁻²⁶ In addition, the Committee used assessments and advisory reports published by EFSA and the European Commission on the



safety of products fortified with plant sterols and/or stanols and of monacolin K from red yeast rice.²⁷⁻³⁰

2.5.3 Influence of cardiovascular medication

Over the last two decades, there has been a significant increase in the use of cardiovascular medication, such as cholesterol-lowering drugs (known as statins) and blood pressure-lowering drugs, in the treatment of people with atherosclerotic and other cardiovascular disease. Use of such medication lowers the risk of recurrence of cardiovascular disease.

This can mean that certain dietary interventions are less effective than when no medication is used or that it is more difficult to demonstrate a potential effect of a dietary intervention on top of the effects of adequate medication. The Committee examined whether it saw indications in the available research that effects of the evaluated dietary factors are different in people who use cardiovascular medication than in people who do not.

2.5.4 Gender differences

There is growing evidence that the development of cardiovascular disease and symptoms of this disease, and if possible also its treatment, is different in men and women.¹⁴ Where possible, the Committee evaluated whether the associations between dietary factors and health outcomes differed between men and women.



03 Dutch dietary guidelines



The *Dutch dietary guidelines 2015* describe the recommended intake of 15 groups of foods and beverages for the prevention of chronic diseases in the general population. Studies are available that specifically address these dietary factors from the guidelines in relation to the health of people with atherosclerotic cardiovascular disease. Based on the studies found, the Committee concludes that the *Dutch dietary guidelines 2015* are also appropriate for this group. The Committee also observes that this group may benefit from a slightly higher fish intake.

3.1 Recommendation

The *Dutch dietary guidelines 2015* are a suitable basis for a healthy and varied diet for people with atherosclerotic cardiovascular disease.

A slightly higher fish intake (1 to 2 portions instead of 1 portion per week) can provide health benefits for this group.

3.2 Explanation

The Committee evaluated the 2015 dietary guidelines for dairy products, fish, fats and oils, coffee, meat, alcohol and table salt for people with atherosclerotic cardiovascular disease. In this chapter, the Committee describes its findings for each of the 2015 dietary guidelines it evaluated.

For the remaining 2015 guidelines, the Committee assumes, based on its expertise and evidence-based dietary guidelines published by other organisations^{3,14,20-22}, that no adjustments are needed for people with

atherosclerotic cardiovascular disease. The same applies to the overall 2015 guideline to follow a dietary pattern that involves eating more plant-based and less animal-based food. The Committee has therefore not evaluated these dietary guidelines, but does consider them relevant for people with atherosclerotic cardiovascular disease. This specifically refers to the following 2015 guidelines:

- Eat at least 200 grammes of vegetables and at least 200 grammes of fruit daily.
- Eat at least 90 grammes of brown bread, wholemeal bread or other wholegrain products daily.
- Eat legumes weekly.
- Eat at least 15 grammes of unsalted nuts daily.
- Drink three cups of tea daily.
- Replace refined cereal products with wholegrain products.
- Minimise consumption of sugar-containing beverages.
- Nutrient supplements are not needed, except for specific groups for which supplementation applies.



3.2.1 Findings on dairy products

Evaluated dietary factors

By dairy products, the Committee means milk and products made from milk, such as yoghurt and cheese. The Committee searched for studies on the intake of dairy products in general and for studies that distinguished between sub-groups of dairy: whole, semi-skimmed and skimmed milk products and specific (groupings of) dairy products such as milk, fermented products, yoghurt and cheese. In this advisory report, butter is not classified with dairy products but with spreads and cooking fats (see section 3.2.3 Fats and oils).

The Committee did not find sufficient studies that could be used for its evaluation of dairy products in general or for sub-groups of dairy.

The Committee did not find sufficient relevant research on health effects of dairy products in people with atherosclerotic cardiovascular disease. It therefore concludes that, for people with atherosclerotic cardiovascular disease, there is no basis for deviating from the recommendation in the *Dutch dietary guidelines 2015* to take several portions of dairy a day.

The recommendation on dairy products in the *Dutch dietary guidelines* does not distinguish between the fat content of dairy products, because at that time there was insufficient scientific basis for doing so based on research into whole, semi-skimmed and skimmed milk. The Committee investigated whether sufficient research is available into potential

differences in the health effects of whole versus skimmed or semi-skimmed milk in people with atherosclerotic cardiovascular disease, however that proved not to be the case. The Committee therefore sees no basis for deviating from the recommendation on dairy products in the *Dutch dietary guidelines 2015* for people with atherosclerotic cardiovascular disease.

More information on the Committee's evaluation of dairy products can be found in the background document *Dairy products*.³¹



3.2.2 Findings on fish

Evaluated dietary factors

For the recommendation about the amount of fish, the Committee focused on studies that investigated the consumption of different amounts of fish. Most studies evaluated fish intake of between 1 and 6 portions per week and compared this to no or occasional fish consumption. In its evaluation, the Committee compared three levels of fish consumption to no or occasional fish consumption: 1 portion per week, 2 portions per week and 3 to 6 portions per week, with 100 grammes counting as one portion. The studies reviewed looked at a combination of different types of fish, both oily and lean. Examples of oily fish are salmon, mackerel and herring. Examples of lean types of fish are pangasius, plaice, tilapia and whiting.

The Committee had planned to make a distinction between oily and lean fish in its recommendation, however there were not enough studies that evaluated associations or effects of oily and lean fish consumption separately. In addition, the Committee evaluated RCTs that looked at the effects of supplementation with low doses of fish fatty acids (≤ 1 gramme/day). These doses are comparable to the amounts of fish fatty acids in 1 to 3 portions of oily fish per week. Fish fatty acids are the omega-3 fatty acids mainly found in fish: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Some of the health effects of fish may be attributable to these nutrients. However, fish also contain other nutrients that could play a role.

The recommendation in the *Dutch dietary guidelines 2015* is to eat 1 portion of fish per week, preferably oily fish. This recommendation is

based on cohort studies that show an association between the consumption of fish at least once a week and lower mortality due to coronary heart disease. This finding was supported by RCTs that looked at fish fatty acid supplementation and a large-scale RCT examining oily fish consumption, which also reported beneficial effects on this health outcome.

The Committee's conclusions based on studies in people with atherosclerotic cardiovascular disease can be found in table 1 (fish consumption) and table 2 (supplementation of fish fatty acids of ≤ 1 gramme/day). More information on how the Committee reached these conclusions can be found in the background documents *Fish*³² and *EPA & DHA*.³³

The Committee did not find sufficient cohort studies to assess whether consumption of 1 portion of fish per week compared to no or occasional fish consumption is associated with a lower risk of mortality due to coronary heart disease or other sub-types of cardiovascular disease in people with atherosclerotic cardiovascular disease. It did, however, find that eating 1 portion of fish compared to no or occasional fish is unlikely to be associated with the risk of overall (i.e. all-cause) mortality.

Based on cohort studies, the Committee considers there to be a plausible association between the consumption of 2 to 6 portions of fish per week, compared to no or occasional fish consumption, and lower overall



mortality (strong evidence) and lower morbidity and/or mortality due to cardiovascular disease (partly limited and partly strong evidence) and heart attacks (limited evidence). Within this range of 2 to 6 portions of fish per week, the Committee has found no evidence of further risk reduction in the case of a higher fish intake. Moreover, a large-scale, high-quality RCT in people with a history of heart attack found that participants who were advised to consume 2 to 4 portions of oily fish per week had a lower risk of overall mortality and mortality due to coronary heart disease than those who were not given this advice.³⁴

Based on the above findings, the Committee concludes that there is convincing evidence that the consumption of 2 to 6 portions of fish per week lowers the risk of mortality and cardiovascular disease in people with atherosclerotic cardiovascular disease. The Committee also concludes that it cannot exclude an association between consumption of 1 portion of fish per week and lower mortality and/or morbidity due to cardiovascular disease in this group (as was found for the general population in the case of the *Dutch dietary guidelines 2015*), as it did not find enough research in this area.

Based on the amounts of fish investigated in studies and their findings, consumption up to and including 6 portions of fish per week could be considered. The Committee sees no reason to recommend more than 2 portions of fish, however, because consumption of more than 2 portions of

fish per week did not reduce the risk any further. Moreover, it is not advisable both from a sustainability perspective and due to potentially harmful substances in fish, such as heavy metals and dioxins, to increase fish consumption further than necessary to achieve the positive health effects.

The Committee therefore recommends that people with atherosclerotic cardiovascular disease consume 1 to 2 portions of fish per week.

Type of fish

The recommendation in the *Dutch dietary guidelines 2015* is to preferably eat oily fish, based on the finding that supplementation with EPA and DHA reduces mortality due to coronary heart disease. Oily fish contains significantly more fish fatty acids than lean fish.

The Committee could not make any statement about the preferred type of fish for people with atherosclerotic cardiovascular disease. Little research has been carried out in this group into the effects of fish fatty acid supplementation at amounts similar to the amount in 1 or 2 portions of oily fish (1 to 2 portions of oily fish per week corresponds to an average of 350 to 700 milligrammes [mg] of EPA and DHA per day). The RCTs that did investigate a relatively low dose of fish fatty acid supplementation (1 gramme per day or less) give the impression that there is likely no effect on mortality and cardiovascular disease. However, this cannot rule



out that eating oily or lean fish is beneficial. In addition to fish fatty acids, fish also contains other nutrients. The Committee also cannot exclude the possibility that fish consumption replaces the consumption of other products in a diet, and as such contributes to limiting the intake of foods such as red and processed meat.

The Committee found very few studies that distinguish between lean and oily fish. In the available cohort study on overall fish consumption, one third to a half of fish consumed was oily fish. Since a large proportion of fish consumption in the studies evaluated is lean fish, it cannot be ruled out that the positive associations are also attributable to lean fish.

Fish can also contain harmful substances, such as heavy metals, dioxins and PFAS (poly- and perfluoralkyl substances). Concentrations of these substances can vary significantly between fish, because they are determined by factors such as the type of fish and where they are caught. Oily fish generally contain more dioxins than lean fish, as dioxins are stored in fatty tissue. PFAS are found in both lean and oily fish species. In general, the Committee recommends eating a variety of fish species. It also recommends avoiding or severely limiting consumption of fish species that contain high concentrations of harmful substances. Examples include predatory fish such as shark, swordfish and eel. Some fish species can be eaten on a regular basis (for example weekly) without exceeding EFSA's thresholds for exposure to hazardous

substances, such as dioxins and PFAS. Examples include salmon, trout, herring and plaice.

A previous advisory report published by the Health Council contains a list of fish species that, in terms of PFAS, dioxin and methylmercury exposure, can be eaten frequently (1 or 2 times per week), less frequently (occasionally, not weekly) or that should be avoided, based on a risk assessment of fish species for pregnant women.^{35,36} This assessment included risks to offspring in relation to methylmercury, which will not be relevant for all people with atherosclerotic cardiovascular disease.

The Committee assumes that this list is at least also applicable to people with atherosclerotic cardiovascular disease, although it cannot rule out a need for minor adjustments for this group. A fish chain risk assessment recently published (September 2022) by the Netherlands Food and Consumer Product Safety Authority examines other chemical substances, in addition to PFAS, dioxins and methylmercury, that can be present in fish, such as arsenic.³⁷ However, the extent to which this is a concern in the Dutch context is not yet clear.



Table 1 Overview of conclusions on the associations between consumption of fish and health outcomes in people with atherosclerotic cardiovascular disease

Health outcome ^a	Type of study	Results
All-cause mortality	Cohort studies	<ul style="list-style-type: none"> Higher intake versus lower intake: 15% lower risk; strong evidence^b 1 portion of fish per week versus little or none: association unlikely 2 portions of fish per week versus little or none: 20% lower risk; strong evidence 3 to 6 portions of fish per week versus little or none: 20% lower risk; strong evidence
All-cause mortality	Proof-of-principle RCT	2 to 4 portions of oily fish per week versus no recommendation: lower risk ^c
Morbidity or mortality due to cardiovascular disease	Cohort studies	<ul style="list-style-type: none"> Higher intake versus lower intake: lower risk; strong evidence^b 1 portion of fish per week versus little or none: too little research 2 portions of fish per week versus little or none: lower risk; limited evidence 3 to 6 portions of fish per week versus little or none: lower risk; strong evidence
Mortality due to cardiovascular disease	Cohort studies	<ul style="list-style-type: none"> Higher intake versus lower intake: lower risk; limited evidence^b 1 portion of fish per week versus little or none: too little research 2 portions of fish per week versus little or none: lower risk; limited evidence 3 to 6 portions of fish per week versus little or none: lower risk; limited evidence
Morbidity or mortality due to coronary heart disease	Cohort studies	Too little research
Morbidity or mortality due to coronary heart disease	RCT	2 to 4 portions of oily fish per week versus no recommendation: too little research
Mortality due to coronary heart disease	Cohort studies	Too little research

^a The table lists the health outcomes for which (relevant) studies were found. For the outcomes not shown in the table, no (relevant) studies were found.

^b This concerns the average result of several studies that used different definitions of the highest category of fish consumption

and the lowest category of fish consumption.

^c The Committee found one high-quality RCT for this health outcome. This RCT confirms the findings from cohort studies with strong evidence and is therefore used as a proof-of-principle RCT in order to derive the guideline on fish. As it is a proof-of-principle RCT, the result of this sole RCT is presented in the table.

Table 2 Overview of conclusions on the effects of supplementation with 0.4 to 1 gramme of fish fatty acids per day on health outcomes based on RCTs in people with atherosclerotic cardiovascular disease

Health outcome ^a	Results
All-cause mortality	Likely no effect
Morbidity or mortality due to cardiovascular disease	Likely no effect
Mortality due to cardiovascular disease	Likely no effect
Morbidity due to cardiovascular disease	Too little research
Morbidity or mortality due to coronary heart disease	Too little research
Mortality due to coronary heart disease	Lower risk; limited evidence
Morbidity or mortality due to heart attack	Too little research
Mortality due to heart attack	Too little research
Morbidity due to heart attack	Too little research
Revascularisation ^b	Too little research
Angina pectoris	Too little research
Sudden cardiac death	Lower risk; limited evidence
Morbidity or mortality due to stroke	Too little research
Heart failure	Too little research
Arrhythmia	Too little research
Depression	Too little research
Cancer	Too little research
LDL cholesterol	Too little research
Systolic blood pressure	Too little research

^a The table lists the health outcomes for which (relevant) studies were found. For the outcomes not shown in the table, no (relevant) studies were found.

^b This usually involves a coronary cause.



3.2.3 Findings on fats and oils

Evaluated dietary factors

Fats and oils intake includes products such as olive oil, sunflower oil and coconut oil. There are many studies of the effect of fish oil (oil consisting of the fish fatty acids EPA and DHA), in which olive oil and sunflower oil are used as a control intervention. The very low dose of olive oil and sunflower oil often used in these types of studies means that they are less relevant from the perspective of spreads and cooking fats. As a result, the Committee has not included the studies on fish oil here, but instead in its evaluation of the recommendation on fish and fish fatty acid supplementation. To support the research on fats and oils, the Committee evaluated studies that examined the health effects of replacing saturated fat with other types of fats, carbohydrates or proteins.

The Committee did not find sufficient studies that could be used for its evaluation of fats and oils. It did, however, find sufficient studies to draw conclusions regarding the health effects of substituting saturated fat with polyunsaturated fat. The Committee did not find sufficient studies to draw conclusions regarding the substitution of saturated fat with fats other than polyunsaturated fat, proteins and carbohydrates.

Hard and soft spreads and cooking fats

The recommendation in the *Dutch dietary guidelines 2015* is to replace butter, hard margarines and cooking fats with soft margarines, liquid cooking fats and vegetable oils. The reason for this is that foods rich in cis-unsaturated fatty acids, such as soft margarines or vegetable oils,

lower the risk of coronary heart disease compared to foods rich in saturated fatty acids, such as butter and hard margarines. Because the fatty acid composition differs for each spread and cooking fat, the Committee aimed to evaluate the health effects in people with atherosclerotic vascular disease for each type of fat or oil. However, the Committee did not find sufficient research into different types of fats and oils and therefore concludes that there is no basis to deviate from the recommendation in the *Dutch dietary guidelines 2015* to replace hard spreads and cooking fats with soft spreads and cooking fats for people with atherosclerotic cardiovascular disease. More information on the evaluation of fats and oils can be found in the background document *Fats & oils*.³⁸

Saturated and polyunsaturated fat

The Committee did find sufficient studies on the effects of substituting saturated fat with polyunsaturated fat. The Committee's conclusions can be found in table 3. More information on how the Committee reached these conclusions can be found in the background document *Saturated fat substitution*.³⁹ Based on RCTs, the Committee found convincing evidence that substituting 6% of energy from saturated fat with polyunsaturated fat leads to a 15% lower risk of morbidity and mortality due to coronary heart disease and a 20% lower risk of morbidity and mortality due to myocardial infarction. The Committee's findings on the substitution of saturated fat with polyunsaturated fat are in line with the findings in the *Dutch dietary*



guidelines 2015. This is logical, since the literature review carried out for the *Dutch dietary guidelines 2015* largely identified the same RCTs (in people with cardiovascular disease) as the literature review carried out for this advisory report for people with atherosclerotic cardiovascular disease. On the basis of these findings, the Committee sees no reason to adjust the recommendation on fats and oils from the *Dutch dietary guidelines 2015* for people with atherosclerotic cardiovascular disease.

All RCTs that examined the substitution of saturated fat with poly-unsaturated fat were carried out in men. The effects in women with atherosclerotic cardiovascular disease are therefore unknown. Based on the RCTs in the general population on the effects of saturated fat on LDL cholesterol,⁴⁰ which included both men and women, the Committee sees no reason to expect different effects in men and women. As a result, the Committee considers the recommendation on fats and oils to apply to both men and women, as is also the case in the *Dutch dietary guidelines 2015*.

Table 3 Overview of conclusions on the associations between substituting saturated fat with other types of fat, carbohydrates or proteins and health outcomes in people with atherosclerotic cardiovascular disease

Substitution	Health outcome ^a	Type of study	Results
SFA-PUFA	All-cause mortality	RCTs	Likely no effect
SFA-PUFA	Mortality due to cardiovascular disease	RCTs	Likely no effect
SFA-PUFA	Morbidity and mortality due to cardiovascular disease	RCTs	15% lower risk on substituting 6% of energy from saturated fat; strong evidence
SFA-PUFA	Mortality due to coronary heart disease	RCTs	Too little research
SFA-PUFA	Morbidity and mortality due to coronary heart disease	RCTs	15% lower risk on substituting 6% of energy from saturated fat; strong evidence
SFA-PUFA	Morbidity and mortality due to myocardial infarction	RCTs	20% lower risk on substituting 6% of energy from saturated fat; strong evidence
SFA-PUFA	Mortality due to myocardial infarction	RCTs	Too little research
SFA-PUFA	Morbidity and mortality due to stroke	RCTs	Too little research
SFA-MUFA	All-cause mortality; morbidity and/or mortality due to cardiovascular disease; morbidity and/or mortality due to coronary heart disease; morbidity and/or mortality due to myocardial infarction	RCTs	Too little research
SFA-UFA	Mortality due to cardiovascular disease; mortality due to coronary heart disease	Cohort studies	Too little research
SFA-PUFA	Mortality due to cardiovascular disease; mortality due to coronary heart disease	Cohort studies	Too little research
SFA-MUFA	Mortality due to cardiovascular disease; mortality due to coronary heart disease	Cohort studies	Too little research
SFA-LA	Type 2 diabetes	Cohort studies	Too little research



Substitution	Health outcome ^a	Type of study	Results
SFA-NS	All-cause mortality; morbidity and/or mortality due to coronary heart disease	Cohort studies	Too little research

Abbreviations: LA: linoleic acid; MUFA: monounsaturated fatty acid; NS: macronutrient(s) not specified; PUFA: polyunsaturated fatty acid; SFA: saturated fatty acid; UFA: unsaturated fatty acid.

^a The table lists the health outcomes for which (relevant) studies were found. For the outcomes not shown in the table, no (relevant) studies were found.

3.2.4 Findings on coffee

Evaluated dietary factors

The Committee focused on studies on coffee intake. Where possible, the Committee distinguished between filtered and unfiltered coffee and between caffeinated and decaffeinated coffee. Cohort studies on caffeine from coffee were also included, as these also reflect coffee consumption. Cohort studies on caffeine in general were not included, as caffeine is also found in other foods (such as tea and soft drinks) and the results of these studies therefore provide insufficient information about the health effects of coffee.

The *Dutch dietary guidelines 2015* recommend replacing unfiltered coffee with filtered coffee, because unfiltered coffee can increase LDL cholesterol while filtered coffee is unlikely to have such a negative effect.

The Committee found no studies on filtered versus unfiltered coffee in relation to LDL cholesterol (or other health outcomes) in people with atherosclerotic cardiovascular disease.

The Committee also specifically looked for studies on the association between coffee consumption and health outcomes, since protective associations with strong evidence were found between coffee consumption and the risks of coronary heart disease and stroke in the literature evaluated for the *Dutch dietary guidelines 2015*. Table 4 describes the Committee's conclusions on this subject for people with atherosclerotic cardiovascular disease. More information on how the Committee reached these conclusions can be found in the background document *Coffee*.⁴¹

Based on cohort studies, the Committee found that an association between drinking 1 to 2 cups of coffee per day compared to less than 1 cup per day and the risk of all-cause mortality and the risk of mortality or morbidity due to cardiovascular disease is unlikely. There was no conclusive evidence regarding the association between drinking 2 to 4 cups of coffee per day compared to less than 1 cup per day and the risk of these health outcomes, due to the substantial degree of heterogeneity in findings between studies. The Committee identified both protective and neutral associations with a higher coffee consumption, but no harmful associations. Most of the studies evaluated looked at filtered coffee. Not enough research is available on associations between coffee consumption and other health outcomes, such as stroke or type 2 diabetes, in people with atherosclerotic cardiovascular disease.



Since the Committee only found neutral or protective associations in cohort studies that largely examined filtered coffee, and no harmful associations, it sees no reason to adjust the recommendation on coffee from the *Dutch dietary guidelines 2015* for people with atherosclerotic cardiovascular disease.

Table 4 Overview of conclusions on the associations between coffee intake and health outcomes based on cohort studies in people with atherosclerotic cardiovascular disease

Health outcome ^a	Results
All-cause mortality	<ul style="list-style-type: none"> • 1 to 2 cups of coffee per day versus <1 cup per day: likely no association • 2 to 4 cups of coffee per day versus <1 cup per day: inconclusive evidence (both neutral and protective associations)
Morbidity or mortality due to cardiovascular disease	Too little research
Mortality due to cardiovascular disease	<ul style="list-style-type: none"> • 1 to 2 cups of coffee per day versus <1 cup per day: likely no association • 2 to 4 cups of coffee per day versus <1 cup per day: inconclusive evidence (both neutral and protective associations)
Mortality due to coronary heart disease	Too little research
Morbidity or mortality due to heart attack	Too little research
Sudden cardiac death	Too little research
Morbidity or mortality due to stroke	Too little research
Heart failure	Too little research
Arrhythmia	Too little research
Type 2 diabetes	Too little research

^a The table lists the health outcomes for which (relevant) studies were found. For the outcomes not shown in the table, no (relevant) studies were found.

3.2.5 Findings on meat

Evaluated dietary factors

The Committee focused on studies on meat intake. The recommendation in the *Dutch dietary guidelines 2015* focuses specifically on red meat and processed meat. The Committee defines red meat as meat from mammals, such as cows, pigs, goats, sheep and horses. White meat comes from poultry, such as chickens, turkeys, ducks and geese, and from domestic rabbits. The Committee defines processed meat as meat that has been processed to improve the flavour or extend the shelf life. The meat may be smoked or cured, or preserving agents such as nitrate, nitrite, herbs or breadcrumbs may have been added. Processed meat also includes all sliced meats. Most processed meat is red meat.

The Committee did not find sufficient studies that could be used for its evaluation of meat in general or for categories of meat.

In the *Dutch dietary guidelines 2015*, the recommendation is to limit consumption of red meat and particularly processed meat, because there is a plausible association between the consumption of red and processed meat and a higher risk of stroke, diabetes, colorectal cancer and lung cancer. The Committee's aim was to identify any potential differences in health effects between red and white meat and between processed and unprocessed meat in people with atherosclerotic cardiovascular disease. However, it did not find any studies on this. The Committee also did not find sufficient relevant research on the health effects of meat in general



(regardless of type of meat or processing method) in people with atherosclerotic cardiovascular disease. It therefore concludes that there is no basis for deviating from the recommendation in the *Dutch dietary guidelines 2015* for people with atherosclerotic cardiovascular disease. More information on the evaluation of meat can be found in the background document *Meat*.⁴²

3.2.6 Findings on alcohol

Evaluated dietary factors

The Committee focused on studies that examined alcohol (also referred to as ethanol) intake. The Committee evaluated various levels of alcohol intake compared to no or very little alcohol intake (<2 grammes/day): 2 to 15 grammes/day, 16 to 35 grammes/day (and within this subgroup analyses of 16 to 25 and 26 to 35 grammes/day) and >35 grammes/day. The Committee identified no difference in associations with the health outcomes examined for intakes of 2 to 15 and of 16 to 35 grammes/day (nor in the subgroup analyses within the latter intake category). The Committee has therefore drawn conclusions on the intake of 2 to 35 grammes/day. It has also drawn conclusions on alcohol consumption exceeding 35 grammes/day. A standard alcoholic beverage contains around 10 grammes of alcohol.

Most studies compare people who drink various degrees of alcohol to people who drink no alcohol at all. The non-drinker group can consist of people who have never drunk alcohol and people who have stopped. People can decide to stop drinking alcohol due to poor health and an unfavourable prognosis. Including this

Evaluated dietary factors (continued)

group in the reference group could lead to the false conclusion that consuming alcohol is more beneficial than not consuming alcohol. For this reason, the Committee looked at whether the results of studies that only used life-long non-drinkers as a reference group (compared to various levels of alcohol intake) differ from the result based on all studies (including studies that also included former drinkers). There were not enough studies for an independent evaluation based on studies that only used life-long non-drinkers as a reference group.

There were not enough studies according to type of alcoholic drink (for example beer, wine or spirits). The Committee is therefore unable to state whether the association between alcohol and health outcomes differs for different types of alcohol.

The *Dutch dietary guidelines 2015* recommend drinking no alcohol or no more than 1 glass (around 10 grammes of alcohol) per day. One of the conclusions on which this recommendation is based is that moderate alcohol consumption in the general population is associated with both a lower risk of cardiovascular disease and a higher risk of stroke and various types of cancer. Table 5 describes the Committee's conclusions based on research in people with atherosclerotic cardiovascular disease. More information on this and on how the Committee reached these conclusions for people with atherosclerotic cardiovascular disease can be found in the background document *Alcohol*.⁴³



Based on cohort studies, the Committee found it plausible that people with atherosclerotic cardiovascular disease who drink an average of around 2 to 35 grammes of alcohol per day have a 20% lower risk of all-cause mortality compared to people who drink no or very little alcohol. Based on these studies, the Committee also considers it plausible that this group has a 20 to 35% lower risk of morbidity and mortality due to cardiovascular disease. In the studies among the general population, on which the *Dutch dietary guidelines 2015* are based, a 15% lower risk of overall mortality was found for consumption of 6 grammes of alcohol per day and a 15% lower risk of coronary heart disease from 2.5 grammes per day. A possible explanation for this difference is that people with atherosclerotic cardiovascular disease have a higher background risk of cardiovascular morbidity and mortality than the general population. This means that, in this group, a larger percentage of morbidity and mortality is determined by cardiovascular disease than in the general population. Due to their relatively advanced age, people with atherosclerotic cardiovascular disease may display less alcohol-related risk-taking behaviour. This may contribute towards lower alcohol-related mortality than in younger people, for example because they are less likely to be involved in a road accident. These differences may mean that potential protective associations with cardiovascular disease and overall mortality emerge more strongly in this population than in the general population.

Within the range of 2 to 35 grammes of alcohol per day, the protective associations for mortality and cardiovascular disease were evident from 2 grammes of alcohol consumption per day. These associations remained the same for higher intakes. Increasing alcohol consumption within this range appears to have neither a beneficial nor harmful effect on the risk of mortality and cardiovascular disease. For other health outcomes, however, increasing alcohol consumption within this range can have a harmful effect. The Committee has been unable to evaluate this specifically for people with atherosclerotic cardiovascular disease. Nevertheless, it has been able to do so (based on the *Dutch dietary guidelines 2015*) for the general population (including people with cardiovascular disease). One of the findings the Committee made, based on the research underlying the *Dutch dietary guidelines 2015*, was a harmful association between alcohol in general and/or alcoholic beverages, such as beer and spirits, and stroke, colorectal cancer and breast cancer at intakes within this range.^{44,45}

The Committee did not find sufficient RCTs that examined alcohol consumption in people with atherosclerotic cardiovascular disease to draw conclusions on health effects of alcohol based on RCTs. This means that there is no convincing evidence (only plausible, from cohort studies, as described above) on alcohol consumption in relation to health outcomes in people with atherosclerotic cardiovascular disease.



On the basis of the above findings and considerations, the Committee has concluded that there are no reason to deviate from the recommendation in the *Dutch dietary guidelines 2015* to drink no alcohol or no more than 1 glass per day for people with atherosclerotic cardiovascular disease.

The Committee wishes to note that the recommendation relates solely to risks in terms of chronic diseases. The risk of alcohol dependence and related social and psychological issues can also affect recommendations on alcohol consumption. However, such risks fall outside the scope of the current advisory report.

Table 5 Overview of conclusions on the associations between alcohol consumption and health outcomes in people with atherosclerotic cardiovascular disease

Health outcome ^a	Type of study	Level of alcohol consumption ^b	Results
All-cause mortality	Cohort studies	2 to 35 grammes/day	20% lower risk; strong evidence
All-cause mortality	Cohort studies	>35 grammes/day	Likely no association
Mortality due to cardiovascular disease	Cohort studies	2 to 35 grammes/day	25 to 35% lower risk; strong evidence
Mortality due to cardiovascular disease	Cohort studies	>35 grammes/day	Too little research
Morbidity or mortality due to cardiovascular disease	Cohort studies	2 to 35 grammes/day	20% lower risk; strong evidence
Morbidity or mortality due to cardiovascular disease	Cohort studies	>35 grammes/day	Too little research
Systolic blood pressure	RCTs	Unknown	Too little research

^a The table lists the health outcomes for which (relevant) studies were found. For the outcomes not shown in the table, no (relevant) studies were found.

^b Compared to no or sporadic alcohol consumption; 2 to 35 grammes of alcohol roughly corresponds to one quarter of a standard alcoholic drink to three and a half standard alcoholic drinks.

3.2.7 Findings on table salt

Evaluated dietary factors

The Committee searched for studies on the intake of salt (sodium chloride) or sodium and on sodium chloride supplements, as it considers these to be similar to adding table salt. In the case of cohort studies, the Committee gave preference to studies where salt or sodium intake was measured in urine collected (preferably repeatedly) over 24 hours, as this method is more reliable than a questionnaire.⁴⁶

The Committee did not find sufficient studies that could be used for its evaluation of table salt.

The Committee did not find sufficient relevant research on health effects of table salt or sodium in people with atherosclerotic cardiovascular disease. It therefore concludes that, for people with atherosclerotic cardiovascular disease, there is no basis for deviating from the recommendation in the *Dutch dietary guidelines 2015* to limit table salt intake to a maximum of 6 grammes per day. More information on the evaluation of table salt can be found in the background document *Sodium*.⁴⁶

The Committee found one large RCT that investigated the effect of substituting sodium chloride with potassium chloride on the risk of stroke in people with a history of stroke in China.⁴⁷ This RCT is sufficiently large in scale to draw a conclusion based on this study. However, the



Committee has not included this study because the study participants had a much lower average potassium intake than people in the Netherlands. A low potassium intake is associated with a higher risk of cardiovascular disease.⁴⁸ The Committee cannot rule out the possibility that the effects of the intervention with potassium chloride are at least partly attributable to the increased potassium intake rather than the reduced salt intake.

3.2.8 Overall findings

The Committee wishes to note that the majority of the studies evaluated were carried out in people with coronary heart disease or people with cardiovascular disease in general, most of whom often have coronary heart disease. As a result, the findings mainly apply to people with coronary heart disease. As far as the Committee was able to ascertain, it saw no evidence that associations between dietary factors and health outcomes are different for people with stroke or peripheral vascular disease than for people with coronary heart disease.

The percentage of participants who used cardiovascular medication, such as LDL and blood pressure-lowering drugs, differed from study to study. The Committee saw no evidence in the available data that the associations or effects are different or not visible in populations who use statins and other medicines relatively often. However, the Committee is unable to draw any firm conclusions from this as there was often little information and, in some cases, only indirect information available on any

differences in effects and associations for people who do or do not use cardiovascular medication.

Finally, the Committee wishes to note that, in most of the studies evaluated, males were overrepresented in terms of numbers. Partly because of this, the volume of research examining the associations between dietary factors and health outcomes separately for men and women is limited. However, the Committee sees no evidence in the available data that these associations are different in males and females. Based on its findings, the Committee assumes that the dietary guidelines described apply to both men and women.



04 functional foods and supplements



A healthy diet in line with the *Dutch dietary guidelines* can help to lower LDL cholesterol and reduce the risk of atherosclerotic cardiovascular disease and other chronic diseases. For people with atherosclerotic cardiovascular disease and high LDL cholesterol, products fortified with plant sterols and/or stanols can also be considered. These products appear to be effective in lowering LDL cholesterol levels, including in people who use statins. The Committee cannot make any recommendations on supplements containing monacolin K from red yeast rice, also designed to lower LDL cholesterol because insufficient studies are available on this subject. The Committee does not consider a low dose of fish fatty acids to yield any health benefits. The Committee cannot make any recommendations on fish fatty acid supplements at higher doses, as studies have produced inconsistent findings on their effects on cardiovascular health.

4.1 Recommendations

- Treating physicians and dieticians can consider the use of products fortified with plant sterols and/or stanols to lower LDL cholesterol in people with atherosclerotic cardiovascular disease, including those who use statins.
- Too little research is available on the use of supplements containing less than 3 mg of monacolin K from red yeast rice to make a recommendation.
- There are no reasons to recommend supplements containing a low

dose of fish fatty acids (1 gramme per day or less). The Committee cannot make any recommendations on the use of supplements containing high doses of fish fatty acids (more than 1 gramme per day), as studies have produced inconsistent findings.

4.2 Explanation

The Committee has evaluated the scientific evidence on functional foods or supplements that may help to further lower the risk of cardiovascular disease. This concerns products fortified with plant sterols and/or stanols, supplements containing monacolin K from red yeast rice and supplements containing fish fatty acids. The first two products are specifically aimed at lowering LDL cholesterol.



4.2.1 Products fortified with plant sterols and stanols

Evaluated dietary factors

The Committee searched for studies on foods fortified with plant sterols and/or stanols. These nutrients naturally occur, at much lower doses, in plant products such as vegetables, fruit and grains. In most studies, the plant sterols and/or stanols were added to margarines/fatty spreads or dairy products, and doses of between 1.5 and 3 grammes of plant sterols and/or stanols per day were examined. The Committee evaluated products containing plant sterols alone, plant stanols alone and a combination of both.

The Committee did not evaluate studies on blood levels of plant sterols in relation to the occurrence of cardiovascular disease, because these studies do not say enough about the effects of consumption of products fortified with plant sterols.

Effectiveness

The Committee found strong evidence that consuming foods fortified with 1.5 to 3 grammes of plant sterols and/or stanols per day lowers LDL cholesterol by 7 to 11%. Such beneficial effects were also found in people who use statins and in people with a diet that is low in saturated fat.

The effect on LDL cholesterol increased as the dose of plant sterols and/or stanols increased within this range of 1.5 to 3 grammes. There were no differences in effects between plant sterols and plant stanols. In many cases, the people who took part in the research had high LDL cholesterol at the start of the study. The Committee found no studies on the effects of

consuming products fortified with plant sterols and/or stanols in relation to the occurrence of cardiovascular disease or other chronic diseases. For a detailed description of these findings see the background document *Foods fortified with plant sterols and stanols*.⁴⁹

Safety

For safety reasons, the European Commission has established a number of conditions of use that must be stated on products fortified with plant sterols and/or stanols. The mandatory statements include that these products may not be nutritionally appropriate for pregnant and breast-feeding women and young children, that the product is to be used as part of a balanced and varied diet that includes the regular consumption of fruit and vegetables to help maintain carotenoid levels, and that people who use cholesterol-lowering medication should only use these products under medical supervision.^{27,28,50} Of note, children fall outside the target group of this advisory report and most pregnant and breastfeeding women are not likely to have yet been diagnosed with atherosclerotic cardiovascular disease.

Findings in the context of treatment

In current practice, people with atherosclerotic cardiovascular disease are advised to follow a healthy diet as a first step in accordance with the treatment guidelines (alongside other lifestyle improvements such as stopping smoking) and receive drug treatment aimed at improving risk



factors such as high LDL cholesterol. A statin will regularly be prescribed to lower LDL cholesterol. Where statin use is not an option or where further lowering of LDL cholesterol is desirable, a possible second step is the use of other or additional LDL-lowering drugs such as ezetimibe and PCSK9 inhibitors.¹⁴

In people who use statins and in whom further reduction of LDL-cholesterol is desirable, products fortified with plant sterols and/or stanols can help to further lower LDL cholesterol. This is in line with expectations, because these drugs lower LDL cholesterol via other mechanisms in the body than the fortified products.⁵¹ The effect of statins (around 30% reduction in LDL cholesterol¹⁴) is greater than can be achieved with products fortified with plant sterols and/or stanols (7–11% reduction in LDL cholesterol). Products fortified with plant sterols and/or stanols therefore cannot fully replace the effect of statins, but can be used alongside statins or for people who are unwilling or unable to use statins.

The Committee also searched for studies that examined the effects of products fortified with plant sterols and/or stanols in people who use ezetimibe. Both inhibit LDL absorption in the body, making the effects of this combination more difficult to predict.⁵¹ However, the Committee found too few studies to be able to conclude whether these products have added value when used in combination with ezetimibe. Too little is also known

about the use of these products in combination with other cholesterol-lowering drugs, such as PCSK9 inhibitors.

The Committee emphasises that it does not consider products fortified with plant sterols and/or stanols to be an alternative, but merely an addition, to a regular, healthy diet. The reason for this is that products fortified with plant sterols and/or stanols have a very targeted effect: on LDL cholesterol alone and not on other health outcomes (such as blood pressure and body weight). Conversely, a healthy diet (in line with the *Dutch dietary guidelines 2015*) has positive effects on a wide range of health outcomes. It thus benefits health in a broad sense (pleiotropic effects).



4.2.2 Supplements containing monacolin K from red yeast rice

Evaluated dietary factors

Red yeast rice is traditionally consumed in East Asia. Red yeast rice is produced by fermentation of rice with specific fungus species. One of the products of this process is the substance monacolin K. This substance is similar to lovastatin, a cholesterol-lowering product that has not been registered as a drug in the Netherlands.

EFSA concluded in 2011 that there was scientific evidence that a dose of 10 mg of monacolin K from red yeast rice per day maintains normal blood levels of LDL cholesterol in people in the general population.²⁶ In 2018, however, EFSA identified safety risks.²⁹ This resulted in the reduction of the permitted dose of monacolins from red yeast rice to less than 3 mg per day in 2022.⁵² The Committee subsequently decided not to evaluate supplements containing 10 mg of monacolin K from red yeast rice, but instead those containing daily doses of less than 3 mg. The safety of these supplements is currently under debate, and the European Commission will decide in the coming years whether the use of monacolins from red yeast rice in foods will be prohibited or restricted to certain conditions.

The Committee found only 3 intervention studies that looked at the effects of a daily intake of less than 3 mg of monacolin K from red yeast rice. The studies had a number of methodological limitations, such as a high subject drop-out rate during the study and the absence of a placebo in the control group. As a result, the Committee sees no basis for issuing a recommendation on the use of supplements containing less than 3 mg of monacolin

K from red yeast rice. For a detailed description of these findings see the background document *Supplements with monacolin K from red yeast rice*.⁵³

4.2.3 Supplements containing fish fatty acids

Evaluated dietary factors

The Committee evaluated RCTs involving fish fatty acid supplementation at doses of 1 gramme per day or less and more than 1 gramme per day. The latter dose of fish fatty acids cannot be achieved through a typical Dutch diet. The Committee also looked separately at the scientific evidence for doses of 1 to 3 grammes and more than 3 grammes per day and saw no indications to draw different conclusions about these doses.

Supplements with a low dose of fish fatty acids

Table 2 in chapter 3 describes the Committee's conclusions on low doses of fish fatty acids (1 gramme per day or less; EPA and DHA doses similar to consumption of 1 to 3 portions of fish per week). Based on the research into supplements with a low dose of fish fatty acids, the Committee sees no reasons to recommend such supplements for people with atherosclerotic cardiovascular disease. The Committee cannot indicate whether any health effects of low doses of fish fatty acids are different in people who eat little to no fish than in people who do eat fish. The RCTs found provided too little information in this area.³³



Supplements with a high dose of fish fatty acids

Table 6 describes the Committee's conclusions on doses of fish fatty acids of 1 gramme per day or higher. The results of RCTs on high doses of fish fatty acids are inconsistent when it comes to the effects on overall mortality and cardiovascular health, such as cardiovascular disease and coronary heart disease. Although the Committee saw beneficial effects of supplementation with high doses of fish fatty acids for two (similar and partly overlapping) outcomes that fall under coronary heart disease, for many other cardiovascular health outcomes the results were inconsistent or there was likely no effect. Overall, the Committee also sees a high level of heterogeneity between studies, for which it can give no clear explanation based on the available data. The Committee does not rule out the possibility that fish fatty acid supplementation at a specific ratio (EPA:DHA), at a specific dose and in a specific form (highly purified or not) can have a positive effect on the health of people with atherosclerotic cardiovascular disease. Based on the available research, however, it cannot identify this specific ratio, dose and form. The Committee also cannot rule out the possibility that the heterogeneity is explained by other factors, such as characteristics of the study population (for example medication use) or the study design. Based on these observations, the Committee concludes that it cannot make any recommendation on the use of supplements with a high dose of fish fatty acids in people with atherosclerotic cardiovascular disease. For a detailed description of these findings see the background document *EPA & DHA*.³³

Table 6 Overview of conclusions on the effects of supplementation with more than 1 gramme of fish fatty acids per day on health outcomes based on RCTs in people with atherosclerotic cardiovascular disease

Health outcome ^a	Results
All-cause mortality	Likely no effect
Morbidity or mortality due to cardiovascular disease	EPA and DHA combined: likely no effect EPA alone: lower risk; limited evidence
Mortality due to cardiovascular disease	Likely no effect
Morbidity due to cardiovascular disease	Too little research
Morbidity or mortality due to coronary heart disease	Lower risk; strong evidence
Mortality due to coronary heart disease	Likely no effect
Morbidity due to coronary heart disease	Too little research
Morbidity or mortality due to heart attack	Likely no effect
Mortality due to heart attack	Too little research
Morbidity due to heart attack	Likely no effect
Angina pectoris	Inconclusive evidence (neutral and beneficial effects)
Revascularisation ^b	27% lower risk; strong evidence
Sudden cardiac death	Too little research
Morbidity or mortality due to stroke	Inconclusive evidence (neutral, beneficial and tendency towards harmful effects) ^c
Morbidity due to stroke	Too little research
Worsening of peripheral vascular disease ^d	Too little research
Heart failure	Too little research
Arrhythmia	Too little research
LDL cholesterol	Inconclusive evidence (neutral and harmful effects)
Systolic blood pressure	Likely no effect
Body weight	Too little research

^a The table lists the health outcomes for which (relevant) studies were found. For the outcomes not shown in the table, no (relevant) studies were found.

^b This involves a coronary cause.

^c EPA and DHA supplementation was found to have mainly neutral effects on the risk of stroke, with one (large) study that showed a beneficial effect and two studies that pointed towards a harmful effect (however these effects were not statistically significant).

^d Worsening of peripheral vascular disease includes the occurrence of symptoms caused by intermittent claudication, revascularisation of the legs or amputation.



05

weight reduction and maintenance



The Committee recommends that people with atherosclerotic cardiovascular disease who are overweight or obese should aim for weight reduction and maintain their reduced weight in the long term. For people who aim to lose weight, an energy-restricted diet can be compiled based on the *Dutch dietary guidelines 2015* and guidance from a dietician is recommended. However, weight loss and, in particular, the long-term maintenance of weight loss is complex and usually requires addressing multiple lifestyle-related factors at the same time at both individual level and in the living environment.

5.1 Recommendation

In the case of overweight and/or obesity, aim for at least 5% weight reduction and maintain this reduced weight in the long term.

5.2 Explanation

A large number of people with atherosclerotic cardiovascular disease are overweight or obese.⁵⁴ Being overweight and obese are risk factors for high blood pressure, hyperlipidaemia (high cholesterol and/or triglycerides), insulin resistance, albuminuria (the presence of protein in the urine) and the development of type 2 diabetes, cancer and cardiovascular disease.^{3,14,55} Because dietary intake is inextricably linked to energy balance, the Committee issues additional recommendations on weight reduction for people with atherosclerotic cardiovascular disease

who are overweight or obese, supplementing the recommendations given in the *Dutch dietary guidelines 2015*.

Definition of overweight and obesity

By overweight, the Committee means a Body Mass Index (BMI) between 25 and 30 kg/m² for adults up to the age of 70 and a BMI between 28 and 30 kg/m² for people over 70. Older adults have the lowest risk of mortality with a higher BMI than younger adults, which is why the lower limit for overweight in older adults is higher. The Committee defines obesity as a BMI of 30 kg/m² or higher for all adults. There are age-dependent cut-off points for children.⁵⁵⁻⁵⁸

The Committee also wishes to note that the health risks of being overweight or obese are not determined by BMI alone. The health risks of being overweight or obese for instance increase when people also have accumulations of abdominal fat.⁵⁹

A meta-analysis of cohort studies in a total of over 10000 people with coronary heart disease, of whom the majority were overweight or obese, shows that intentional weight loss of at least 5% compared to a stable (too high) body weight is associated with a lower risk of cardiovascular disease.⁶⁰ For the general population and people with type 2 diabetes (who have a high risk of cardiovascular disease), it is also stated that 5 to 10% weight reduction can result in substantial health benefits in people who are overweight or obese.^{14,61-63} In addition, a number of treatment guidelines for people with atherosclerotic cardiovascular disease



recommend aiming for 5 to 10% weight reduction in those who are overweight or obese.⁶⁴⁻⁶⁶

There are also studies that show that people with atherosclerotic cardiovascular disease who are overweight or mildly obese have a better prognosis than people with atherosclerotic cardiovascular disease and a healthy weight.⁶⁷⁻⁶⁹ This is also referred to as the ‘obesity paradox’.

The Committee has identified several methodological limitations in these studies. For example, most are cohort studies in people in the acute phase of atherosclerotic cardiovascular disease, where there is some uncertainty as to whether the measured BMI is representative for the longer term. The results of these studies may also be distorted by aspects such as insufficient correction for confounding factors such as smoking, disease severity, comorbidities and recent unintentional weight loss.

More recently, studies have been published on people in the stable phase of atherosclerotic cardiovascular disease.⁷⁰⁻⁷³ The Committee expects that the limitation in relation to representativeness of the BMI will play a lesser role in these studies. The Committee also notes that these studies generally make a greater allowance for the confounding factors smoking and comorbidities. These studies show that people who are overweight have the same or a lower risk of mortality than people of a normal weight. The Committee notes, however, that disease severity is often not taken into account as a confounding factor and that, in some studies, the reference group also includes people with a fairly low BMI (these people

may be less healthy/more vulnerable or have recent unintentional weight loss). Moreover, the number of studies in people in the stable phase is still limited. These aspects make the existence of the paradox uncertain.

On the basis of all the above, the Committee advises people with atherosclerotic cardiovascular disease who are overweight or obese to strive for a weight reduction of at least 5% and to maintain this reduced weight in the long term. Once the intended weight loss has been achieved and maintained for a prolonged period, further weight loss can be attempted where necessary.

Restricting energy intake plays a key role in weight loss. The *Dutch dietary guidelines 2015* are not designed with the primary goal of weight reduction. Nevertheless, an energy-restricted diet can be compiled based on the *Dutch dietary guidelines 2015*. Guidance from a dietician is recommended to ensure that this diet is complete and in keeping with the client’s preferences and other individual aspects (such as medication use).

Energy-restricted eating based on the *Dutch dietary guidelines 2015* should be seen in a wider context of weight-reduction interventions, as weight reduction can be achieved in several ways. In particular, the long-term maintenance of weight loss is complex and usually requires addressing multiple lifestyle-related factors at the same time (multifactorial



approach) at both individual level and in the living environment.^{55,62,74,75}

This is because, in some cases, the living environment can encourage overconsumption and insufficient exercise, thus promoting obesity (obesogenic environment).

5.2.1 Weight reduction in relatively vulnerable groups

Exceptions may apply to the above advice on weight reduction in the case of relatively vulnerable people with atherosclerotic cardiovascular disease, such as people with multimorbidity or older adults. These groups can be issued with tailored advice based on specific treatment guidelines.

For instance, a cautious approach to weight reduction is recommended in older adults because its effects can include, alongside a reduction in fat mass, undesired loss of bone and muscle mass. It is therefore important to ensure that the method of weight loss minimises loss of bone and muscle mass. In older adults, weight reduction is therefore only indicated in cases of both obesity and weight-related health problems. Furthermore, weight reduction should only be considered where it is expected to result in substantial health benefits that outweigh any risks of weight loss. It is also important that any dietary intervention is combined with exercise, preferably under the guidance of a professional.⁷⁶



06 recommendations



6.1 Dietary recommendations

The Committee makes the following recommendations for professionals who want to provide public information on nutrition and dietary treatment to people with atherosclerotic cardiovascular disease:

1. The *Dutch dietary guidelines 2015* are a suitable basis for a healthy and varied dietary pattern for people with atherosclerotic cardiovascular disease.
A slightly higher fish intake (1 to 2 portions instead of 1 portion per week) can provide health benefits for this group.
See the box below for an overview of all dietary guidelines for people with atherosclerotic cardiovascular disease.
2. Treating physicians and dieticians can consider the use of products fortified with plant sterols and/or stanols to lower LDL cholesterol in people with atherosclerotic cardiovascular disease, including those who use statins.
3. Too little research is available on the use of supplements containing less than 3 mg of monacolin K from red yeast rice to make a recommendation.
4. There are no reasons to recommend supplements containing a low dose of fish fatty acids (1 gramme per day or less). The Committee cannot make any recommendations on the use of supplements containing high doses of fish fatty acids (more than 1 gramme per day), as studies have produced inconsistent findings.
5. In the case of overweight and/or obesity, aim for at least 5% weight

reduction and maintain this reduced weight in the long term.

Dutch dietary guidelines for people with atherosclerotic cardiovascular disease

Eat a healthy, varied diet that is more plant-based and less animal-based in accordance with the following *Dutch dietary guidelines*:

- Eat at least 200 grammes of vegetables and at least 200 grammes of fruit daily.
- Eat at least 90 grammes of brown bread, wholemeal bread or other wholegrain products daily.
- Eat legumes weekly.
- Eat at least 15 grammes of unsalted nuts daily.
- Take a few portions of dairy products per day, including milk or yoghurt.
- Eat one to two portions of fish weekly.^a
- Drink three cups of tea daily.^b
- Replace refined cereal products with wholegrain products.
- Replace butter, hard margarines and cooking fats with soft margarines, liquid cooking fats and vegetable oils.
- Replace unfiltered coffee with filtered coffee.
- Limit consumption of red meat and, particularly processed meat.
- Minimise consumption of sugar-containing beverages.
- Don't drink alcohol or no more than 1 glass daily.
- Limit salt intake to 6 grammes daily.
- Nutrient supplements^c are not needed, except for specific groups for which supplementation applies.^d

^a In the *Dutch dietary guidelines 2015*, the recommendation for the general population is to eat 1 portion of fish per week.

^b This guideline relates to black and green tea.

^c The guideline on nutrient supplements relates to vitamins, multivitamins and minerals.

^d For example, vitamin D supplements are recommended for various groups of people, such as 0 to 4-year-olds, women aged 50 and over and everyone aged 70 and over.



6.2 Points to consider in implementing dietary recommendations

It is important to consider the following points of interest when implementing the recommendations.

6.2.1 Part of a multifactorial approach

The treatment of cardiovascular disease is multifactorial and promoting a healthy lifestyle is a major component of this multifactorial treatment.

For example, those affected by cardiovascular disease may be placed on a cardiac rehabilitation programme.³ The Committee's dietary recommendations should therefore be part of a multifactorial approach alongside other factors such as avoiding smoking and getting enough exercise. Furthermore, the strive for weight loss in overweight and obese people should be applied in a broad context of interventions aimed at weight reduction and weight maintenance, with the Committee's recommendations serving as a basis for dietary interventions.

6.2.2 Dietary guidelines versus clinical treatment guidelines

Treatment guidelines for people with atherosclerotic cardiovascular disease recommend a healthy diet as a standard part of non-pharmacological treatment.¹⁴ The Committee's dietary recommendations can be integrated into these treatment guidelines. The Committee notes in this regard that the strength of evidence is usually weighted differently for dietary guidelines than for medicine guidelines. By way of illustration:

whereas the Committee derives a dietary guideline when there is sufficient evidence from RCTs for effects on surrogate endpoints and/or on hard clinical outcomes, medicine use is only included in treatment guidelines if there is sufficient evidence for effects on hard clinical outcomes. This is due to the different properties of food and medicines. Food is consumed naturally and a healthy diet benefits various health outcomes (pleiotropic effects). Conversely, medicines contain substances at higher doses than humans would naturally ingest and are used because of targeted therapeutic effects or targeted influence of specific physiological processes. Moreover, the feasibility and interpretation of RCTs into long-term effects of foods and diets are more complex than for medicines. Reasons for this include the fact that the blinding of RCTs into food is virtually impossible and that participants may find it difficult to adhere to a dietary intervention for a prolonged period. In addition, foods and diets supply energy and the control group must obtain this energy from another food or diet. The effects identified in the research may be partly or entirely dependent on the foods or diets consumed by the control group.⁷⁷

With regard to the drug component of the treatment guidelines, the Committee notes that, in its view, products fortified with plant sterols and/or stanols, supplements containing monacolin K and supplements containing high doses of fish fatty acids fall into the twilight zone between regular food and medicines due to their targeting of specific health outcomes and/or very high doses. Supplements containing high doses of



fish fatty acids are also manufactured by the pharmaceutical industry as medicinal products. For example, Omacor and icosapent ethyl (IPE) have both been assessed as medicinal products by the EMA (European Medicines Agency). This raises the question of whether advice on the use of such products should be included in a dietary guideline or in a drug guideline. On the other hand, these types of products can be classified as food and assessed as such in the European Union (by EFSA) if the nutrients naturally occur in food. This is the case for products fortified with plant sterols and/or stanols, supplements containing red yeast rice and at least in part for supplements containing fish fatty acids (the status of purer forms of EPA may be a little more questionable, however this concerned the vast minority of studies evaluated by the Committee). The Committee has therefore included the use of these products in its advisory report, but can also imagine that this (particularly in the case of fish fatty acid supplements, as these are also produced as medicinal products) will be discussed as part of the drug therapy in treatment guidelines.

6.2.3 The importance of a healthy, complete diet

In order to compile a healthy, complete diet, dietary recommendations from this advisory report should be combined with dietary reference values for nutrients and energy when these are translated to specific dietary advice for people with atherosclerotic cardiovascular disease. The Netherlands Nutrition Centre is responsible for translating the Health Council's dietary guidelines and dietary reference values into advice on a

complete and healthy diet for the general population, for example in the form of the 'Wheel of Five'. The 'Wheel of Five' can also serve as a basis for a healthy and complete diet for people with atherosclerotic cardiovascular disease. A slightly higher fish intake can also provide health benefits for this group.

Dieticians, in cooperation with other healthcare professionals, can provide tailored dietary advice, for example on food quantities. In giving this advice, they can make use of the dietary guidelines and dietary reference values, and individual aspects such as dietary habits, other diseases or allergies, medication use (in consultation with the treating physician), working and living conditions and target body weight can be taken into account.

Dietary reference values are usually (but not exclusively) based on data obtained from healthy people. These reference values are generally also used for people with chronic diseases, unless professional associations have issued deviating recommendations. However, it cannot be ruled out that these people, for some nutrients, have different requirements than healthy people.

People with atherosclerotic cardiovascular disease often have multiple chronic conditions, such as diabetes and kidney disease.⁷⁸⁻⁸⁰ These people need tailored dietary advice from a dietician.



6.2.4 Functional foods

The Committee emphasises that a healthy diet can benefit health in a broad sense, by impacting on various health outcomes at the same time. Conversely, products fortified with plant sterols and/or stanols have very targeted effects on LDL cholesterol. The Committee therefore does not see products fortified with plant sterols and/or stanols as a substitute for, but instead as a possible addition to, a healthy diet. The Committee emphasises that aiming for a healthy diet and prescribing a statin is part of the standard treatment strategy for people with atherosclerotic cardiovascular disease. Where these measures fail to sufficiently lower LDL cholesterol, products fortified with plant sterols and/or stanols may be considered as a second step.

6.2.5 Weight reduction and maintenance

The Committee recommends weight reduction for people with atherosclerotic cardiovascular disease who are overweight or obese. The *Dutch dietary guidelines 2015* can be used to compile an energy-restricted diet. In older adults, weight reduction is only indicated where both obesity and weight-related health problems are present and where weight loss is expected to result in substantial health benefits.⁷⁶

When people aim to maintain their body weight or limit weight gain, it can be useful to pay attention to low-calorie product choices within the food groups on which the Committee advises. For example, semi-skimmed and

skimmed dairy products contain less saturated fat and calories than full-fat dairy products.

6.2.6 Cardiovascular medication use

The use of statins and blood pressure lowering drugs is a standard component of treatment for cardiovascular disease.¹⁴ Use of these drugs has increased in recent decades.

Products fortified with plant sterols and/or stanols have a specific LDL cholesterol lowering effect by inhibiting cholesterol absorption. They can be used alongside statins, which inhibit cholesterol production.

The Committee cannot indicate whether these products can also be used alongside ezetimibe or other LDL cholesterol lowering medicines because insufficient studies are available in this area.

With regard to the other dietary factors in the *Dutch dietary guidelines 2015* on which the Committee advises, it saw no evidence in the available data that the effects and associations would not be present in populations that use statins and other medicines. However, the Committee is unable to draw any firm conclusions from this as there was often little information and, in some cases, only indirect information available on any differences in effects and associations for people who do or do not use cardiovascular medication.



6.2.7 Sustainability

The Committee's dietary advice aims to promote long-term health. Another important focus area for the Committee is sustainability.^{81,82} Generally speaking, a less animal-based and more plant-based diet, as recommended in the *Dutch dietary guidelines 2015*, means a smaller environmental footprint. Consumers can take sustainability into account when making food choices for instance by more regularly substituting meat with legumes or unsalted nuts, by not eating more than necessary, and by looking for sustainability labels. In the case of fish, for example, consumers can opt for fish species that are not subject to overfishing and that have been caught or farmed as sustainably as possible. This can be done using the Good Fish Foundation and World Wide Fund for Nature VISwijzer and by opting for fish bearing an MSC or ASC label in the supermarket. These assessments pay no or very limited attention to CO₂ emissions, and also not to other sustainability aspects such as animal welfare. The Committee therefore calls for improvements to these labels.

6.3 Recommendations for future research

Based on its evaluation, the Committee makes a number of suggestions for future research that may help to further specify and justify dietary recommendations for people with atherosclerotic cardiovascular disease.

6.3.1 Dietary factors

For several of the 2015 dietary guidelines, the Committee found insufficient research in people with atherosclerotic cardiovascular disease to come to a conclusion, such as the guidelines for table salt and dairy products. In such cases, the Committee is of the opinion that the existing *Dutch dietary guidelines 2015* are a good basis for people with atherosclerotic cardiovascular disease. However, further research confirming (or disproving) this opinion is desirable.

For a number of dietary factors, such as fish and alcohol, the Committee found sufficient research but did not have enough information to specify conclusions according to subtypes, such as the type of alcoholic beverage (for example wine and beer) and the type of fish (oily versus lean fish). With regard to fish and fish fatty acids, further research is needed into low fish consumption (around 1 portion per week) compared to no fish consumption and into the effects of fish fatty acid supplementation in people who do not eat fish.

6.3.2 Sustainability

The Committee's recommendations are based on effects on health. How these recommendations can go hand in hand with improving diet sustainability is a subject for further research. The Committee recommends focusing on research into sustainable alternatives to foods



such as meat, fish and dairy and into the health effects of their consumption.

6.3.3 Safety

A slightly higher fish intake can be associated with higher exposure to potential contaminants in fish. In this context, the Committee calls for more extensive monitoring of contaminants in fish regularly consumed in the Netherlands. This can help consumers to opt for less contaminated fish species. The Committee notes in this regard that the entire diet influences exposure to contaminants that may or may not also occur in fish.

6.3.4 Health outcomes

Health in a broader sense

For most of the dietary factors the Committee evaluated, it mainly found studies that focused on the risk of overall mortality (regardless of cause of death) and cardiovascular disease and its subtypes. It did not find any research into other chronic diseases associated with atherosclerosis, such as dementia, or other common chronic diseases such as cancer. The Committee considers it important that more research is done into the association between diet and the occurrence and course of these health outcomes in people with atherosclerotic cardiovascular disease. The Committee also believes that perceived health and quality of life could be relevant aspects to cover in future research in this population.

Long-term effects of products containing plant sterols and/or stanols

It is not known whether the use of products fortified with plant sterols and/or stanols lowers the risk of cardiovascular disease or whether these products have other long-term health effects. Some cohort studies and genetic studies indicate that relatively higher blood levels of plant sterols are associated with a higher risk of cardiovascular disease, although these findings are inconsistent.⁸³⁻⁸⁹ However, these studies do not say enough about long-term effects of the use of products fortified with plant sterols. One of the reasons for this is that the associations found cannot be separated from those of cholesterol (for a more detailed explanation see the background document *Foods fortified with plant sterols and stanols*⁴⁹). These observations do give cause for further research into long-term effects of these products.

Products fortified with plant sterols and/or stanols have a targeted effect on LDL cholesterol and thus approximate the function of medicines. In the European Union, these products are classified as food and assessed as such, because plant sterols and/or stanols occur naturally in food. For this reason, the Committee has evaluated research into these products as research into foods. On the basis of its methodology, the Committee has found convincing evidence that products fortified with plant sterols and/or stanols lower LDL cholesterol. Nevertheless, research into the long-term effects of these products on hard health outcomes is desirable. The Committee is aware that this type of research is challenging, but it



certainly does not consider it impossible. Possibilities include research into long-term effects on vascular structure or function, such as on the thickness of the inner layers of an artery wall or the degree of dilation of an artery on increasing blood flow. These outcomes do not fall under the Committee's current definition of cardiovascular disease but, in the absence of studies, may be a first step in gaining insight into whether the use of these products can potentially reduce the risk of cardiovascular disease. The Committee is aware of some studies that address such outcomes.⁵¹ These studies are small in scale and often of short duration, and do not yet provide sufficient insight into the effects on such outcomes.

Alcohol consumption in a broader context

The Committee notes that it is relevant to view alcohol consumption in a broader context than merely the prevention of chronic diseases. It advocates broad advice on alcohol consumption that also takes into account the psychosocial aspects and direct social consequences of excessive alcohol consumption, such as labour participation, undesirable behaviour and road accidents.

6.3.5 Target groups

The Committee mainly found studies carried out in people with coronary heart disease or cardiovascular disease in general (a combination of different types of cardiovascular disease patients) and very few studies carried out in people with a stroke or peripheral vascular disease. Based

on this research, the Committee sees no strong evidence that the associations between food and health outcomes differ for people with coronary vascular disease, stroke or peripheral vascular disease. Since atherosclerosis has a similar underlying mechanism, the Committee also sees no immediate cause to believe that the associations would be different for these groups. However, it cannot rule this out. That is why research in people with a stroke or peripheral vascular disease is important. For the time being, the Committee assumes that the guidelines issued can apply to all people with atherosclerotic cardiovascular disease (provided they do not already receive specific dietary advice for other conditions).

Based on the studies found, it is generally impossible to clearly establish whether the health effects of dietary factors are different in people who use certain cardiovascular medication compared to people who do not use this medication. On the basis of the available research, the Committee also cannot state whether the health effects identified differ depending on other individual characteristics such as age or presence of other chronic diseases. Research is needed in these areas to ensure that more specific recommendations can be issued in the future where necessary.

6.3.6 Gender differences

Based on its findings, the Committee assumes that the dietary guidelines described apply to both men and women. It notes, however, that the



research is largely based on males. The Committee therefore emphasises the importance of further research in women and gender-stratified analyses in studies that included both men and women to confirm (or disprove) that the guidelines also apply to women.

6.3.7 Integration in cardiac rehabilitation programmes

As previously stated, the Committee's dietary recommendations should be part of a multifactorial approach. People with atherosclerotic cardiovascular disease may follow a cardiac rehabilitation programme, for example, that focuses both on medication use and lifestyle improvements. It is advisable to carry out research into such programmes whose dietary component is based on the Committee's recommendations and into their long-term effects in people with atherosclerotic cardiovascular disease.



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Committee and consulted experts^a

Members of the Committee on Nutrition for the advisory report *Dutch dietary guidelines for people with atherosclerotic cardiovascular disease*:

- Prof. M. Visser, Professor of Healthy Aging, Vrije Universiteit Amsterdam, *chairperson*
- Prof. J.W.J. Beulens, Professor of lifestyle and cardiometabolic disease epidemiology, Amsterdam UMC, *vice chairperson* (since 17 January 2022)
- Dr. L. Afman, associate professor molecular nutrition, Wageningen UR
- Prof. S.J.L. Bakker, Professor of Internal Medicine, University Medical Center Groningen
- Dr. K.A.C. Berk, Registered Dietitian and Assistant Professor, Department of Internal Medicine at Erasmus MC, Rotterdam
- Prof. E. Blaak, Professor of the Physiology of Fat Metabolism, Maastricht University
- Prof. H. Boersma, Professor of clinical epidemiology of cardiovascular diseases, Erasmus MC, Rotterdam
- Prof. J.B. van Goudoever, Professor of Paediatrics, Amsterdam UMC
- Prof. M.T.E. Hopman, Professor of Integrative Physiology, Radboud University Medical Center, Nijmegen
- Prof. R.P. Mensink, Professor of Molecular Nutrition, Maastricht University
- Dr. N. de Roos, assistant professor nutrition and health, Wageningen UR
- Prof. C.D.A. Stehouwer, Professor of Internal Medicine, Maastricht University Medical Center+
- Dr. J. Verkaik-Kloosterman, nutritionist, National Institute of Public Health and the Environment, Bilthoven
- Prof. E. de Vet, Professor of Consumption and Healthy Lifestyles, Wageningen University

Observers^a

- ir. J.M. van Delft, Ministry of Health, Welfare and Sport, The Hague
- Dr. E. Brink, The Netherlands Nutrition Centre, The Hague

Scientific secretaries

- Dr. I. Sluijs, Health Council of the Netherlands, The Hague
- Dr. L.M. Hengeveld, Health Council of the Netherlands, The Hague
- Dr. J. de Goede, Health Council of the Netherlands, The Hague

Members of the Cardiovascular disease working group

- Prof. J.W.J. Beulens, Professor of lifestyle and cardiometabolic disease epidemiology, Amsterdam UMC, *chairperson from May 2021*
- Prof. M. Visser, Professor of Healthy Aging, Vrije Universiteit Amsterdam, *chairperson until May 2021*
- Prof. S.J.L. Bakker, Professor of Internal Medicine, University Medical Center Groningen
- Dr. K.A.C. Berk, Registered Dietitian and Postdoc Researcher, Department of Internal Medicine at Erasmus MC, Rotterdam
- Prof. H. Boersma, Professor of clinical epidemiology of cardiovascular diseases, Erasmus MC, Rotterdam

^a Consulted experts are consulted by the committee because of their expertise. Consulted experts and observers are entitled to speak during the meeting. They do not have any voting rights and do not bear any responsibility for the content of the committee's advisory report.



- Prof. M.T.E. Hopman, Professor of Integrative Physiology, Radboud University Medical Center, Nijmegen
- Prof. R.P. Mensink, Professor of Molecular Nutrition, Maastricht University
- Prof. C.D.A. Stehouwer, Professor of Internal Medicine, Maastricht University Medical Center+
- Dr. R.G. Voortman, Principal Investigator of Nutrition and Lifestyle Epidemiology, Erasmus MC, Rotterdam and Wageningen University, *structurally consulted expert**

Incidentally consulted experts^a

Consulted because of clinical expertise in the field of cardiovascular diseases:

- Drs. T.T. van Loenhout, cardiologist, Gelderse Vallei Hospital, Ede
- Prof. F.L.J. Visseren, Professor in Vascular Medicine, University Medical Center Utrecht

Consulted on the topic of plant sterols and/or stanols, and Mendelian randomisation studies on this matter in particular:

- Prof. J. Plat, professor in physiology of nutrition with special attention for sterol metabolism, Maastricht University
- Dr. S. Burgess, medical statistician, University of Cambridge (United Kingdom)

Observers^a

- ir. M. Kunst, Ministry of Health, Welfare and Sport, The Hague
- Dr. E. Brink, The Netherlands Nutrition Centre, The Hague



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