

Saturated fatty acid and *trans*-fatty acid intake for adults and children

WHO guideline



World Health
Organization

Saturated fatty acid and *trans*-fatty acid intake for adults and children

WHO guideline

Saturated fatty acid and trans-fatty acid intake for adults and children: WHO guideline

ISBN 978-92-4-007363-0 (electronic version)

ISBN 978-92-4-007364-7 (print version)

© **World Health Organization 2023**

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: “This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition”.

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization (<http://www.wipo.int/amc/en/mediation/rules/>).

Suggested citation. Saturated fatty acid and trans-fatty acid intake for adults and children: WHO guideline. Geneva: World Health Organization; 2023. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

Sales, rights and licensing. To purchase WHO publications, see <https://www.who.int/publications/book-orders>. To submit requests for commercial use and queries on rights and licensing, see <https://www.who.int/copyright>.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

Designed by minimum graphics

Cover illustration by Adele Jackson

Contents

Acknowledgements	v
Abbreviations and acronyms	vi
Executive summary	vii
Introduction	1
Background	1
Rationale	2
Scope	2
Objective	3
Target audience	3
How this guideline was developed	4
Contributors to development of this guideline	4
Management of conflicts of interest	5
Guideline development process	6
Summary of evidence	9
Evidence to recommendations	26
Recommendations and supporting information	30
Uptake of the guideline and future work	37
References	41
Annexes	49
Annex 1: Members of the WHO steering group	51
Annex 2: Members of the guideline development group (NUGAG Subgroup on Diet and Health)	52
Annex 3: External peer review group	54
Annex 4: Summary and management of declarations of interests	55
Annex 5: Key questions in PICO format	59
Annex 6: GRADE evidence profiles	63
Annex 7: Evidence to recommendations table	102
Annex 8: Ruminant TFA intake and consumption of dairy: a modelling exercise	111

Acknowledgements

This guideline was prepared by the Department of Nutrition and Food Safety of the World Health Organization (WHO) under the overall leadership of Francesco Branca, Director of the Department of Nutrition and Food Safety, and the coordination of Chizuru Nishida. Jason Montez was the responsible technical officer. WHO gratefully acknowledges the contributions that many individuals and organizations have made to the development of this guideline.

WHO Steering Group: Ayoub Al-Jawaldeh, Anshu Banerjee, Hana Bekele, Fabio Da Silva Gomes, Jason Montez, Chizuru Nishida, Padmini Angela De Silva, Juliawati Untoro, Cherian Varghese, Kremlin Wickramasinghe

Guideline Development Group (WHO Nutrition Guidance Expert Advisory Group – Subgroup on Diet and Health): Hayder Al-Domi (University of Jordan, Jordan), John H Cummings (University of Dundee, United Kingdom of Great Britain and Northern Ireland), Ibrahim Elmadfa (University of Vienna, Austria), Lee Hooper (University of East Anglia, United Kingdom of Great Britain and Northern Ireland), Shiriki Kumanyika (University of Pennsylvania, United States of America), Mary L'Abbé (University of Toronto, Canada), Pulani Lanerolle (University of Colombo, Sri Lanka), Duo Li (Zhejiang University, China), Jim Mann (University of Otago, New Zealand), Joerg Meerpohl (University of Freiburg, Germany), Carlos Monteiro (University of Sao Paulo, Brazil), Laetitia Ouedraogo Nikiéma (Institut de Recherche en Sciences de la Santé, Burkina Faso), Harshpal Singh Sachdev (Sitaram Bhartia Institute of Science and Research, India), Barbara Schneeman (University of California, Davis, United States of America), Murray Skeaff (University of Otago, New Zealand), Bruno Fokas Sunguya (Muhimbili University of Health and Allied Sciences, United Republic of Tanzania), HH (Esté) Vorster (North-West University, South Africa)

External peer review group: Sohel Reza Choudhury (National Heart Foundation Hospital & Research Institute, Bangladesh), Rod Jackson (University of Auckland, New Zealand), Aamos Laar (University of Ghana, Ghana), Louis Levy (Department of Health and Social Care, and University of Chester, United Kingdom of Great Britain and Northern Ireland), Lara Nasreddine (American University of Beirut, Lebanon), Frank Sacks (Harvard Medical School, United States of America), Caroline Van Rossum (National Institute for Public Health and the Environment, Netherlands [Kingdom of the]), Susanne Westenbrink (National Institute for Public Health and the Environment, Netherlands [Kingdom of the])

WHO would like to acknowledge the important contributions made by members of the systematic review teams (see pages 4–5). Special thanks to Murray Skeaff for conducting the modelling exercise on ruminant *trans*-fatty acid intake and consumption of dairy. Additional thanks are also due to former interns of the Department of Nutrition and Food Safety: Angela Amico, Grace Carroll, Katharina da Silva Lopes and Yvonne Teng, for feedback on the draft guideline and various technical inputs.

WHO gratefully acknowledges the financial support provided by the Ministry of Health, Labour and Welfare of the Government of Japan for the guideline development work, including the systematic reviews, and by Qingdao University in China for hosting the 13th meeting of the WHO Nutrition Guidance Expert Advisory Group – Subgroup on Diet and Health in December 2019.

Abbreviations and acronyms

CI	confidence interval
CLA	conjugated linoleic acid
CVDs	cardiovascular diseases
eLENA	WHO e-Library of Evidence for Nutrition Actions
FAO	Food and Agriculture Organization of the United Nations
GINA	WHO Global database on the Implementation of Nutrition Action
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HDL	high-density lipoprotein
HOMA-IR	homeostasis model assessment of insulin resistance
kJ	kilojoules
LDL	low-density lipoprotein
MD	mean difference
NCD	noncommunicable disease
NUGAG	WHO Nutrition Guidance Expert Advisory Group
PICO	population, intervention, comparator and outcome
RCT	randomized controlled trial
RR	relative risk
SFA	saturated fatty acids
SMD	standardized mean difference
TFA	<i>trans</i> -fatty acids
UN	United Nations
WHO	World Health Organization

Executive summary

Background

Cardiovascular diseases (CVDs) are the leading cause of mortality in the world. Modifiable risk factors such as unhealthy diets, physical inactivity, tobacco use and harmful use of alcohol are major risk factors. Among other dietary factors, the amounts of saturated fatty acids (SFA) and *trans*-fatty acids (TFA) in the diet have been explored as possible contributors to the development of CVDs.

SFA are found primarily in foods from animal sources and in some plant-derived oils and fats. TFA can be produced industrially by the partial hydrogenation of vegetable and fish oils, but also occur naturally in meat and dairy products from ruminant animals (e.g. cattle, sheep, goats, camels). Because the role of SFA and TFA in the development of CVDs continues to be debated, it was considered important to review the evidence in a systematic manner, and update current World Health Organization (WHO) guidance on these fatty acids through the WHO guideline development process.

Objective, scope and methods

The objective of this guideline is to provide updated guidance on the intake of SFA and TFA, to be used by policy-makers, programme managers, health professionals and other stakeholders in efforts to promote healthy diets. The guideline was developed following the WHO guideline development process, as outlined in the *WHO handbook for guideline development*. This process includes a review of systematically gathered evidence by an international, multidisciplinary group of experts; assessment of the quality of that evidence via the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework; and consideration of additional, potentially mitigating factors¹ when translating the evidence into recommendations. The guidance in this guideline replaces previous WHO guidance on SFA and TFA intake, including that from the 1989 WHO Study Group on Diet, Nutrition and the Prevention of Chronic Diseases and the 2002 Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases.

The evidence

SFA

Evidence from recent systematic reviews of randomized controlled trials (RCTs) and prospective observational studies conducted in adults suggests the following.

- ▶ Lowering SFA intake reduces low-density lipoprotein (LDL) cholesterol (*high* certainty evidence) and CVD risk (*moderate* certainty evidence), and may be associated with reduced risk of all-cause mortality (i.e. death from any cause) and coronary heart disease (both *very low* certainty evidence).
- ▶ Consuming 10% or less of daily calories (i.e. total energy intake) as SFA reduces LDL cholesterol (*high* certainty evidence), is associated with reduced risk of all-cause mortality (*low* certainty evidence), and may be associated with reduced risk of coronary heart disease (*very low* certainty evidence).
- ▶ Replacing SFA with unsaturated fatty acids and carbohydrates lowers LDL cholesterol (*high* certainty evidence) and is associated with reduced risk of all-cause mortality (*low to moderate* certainty evidence).

¹ These include desirable and undesirable effects of the intervention, priority of the problem that the recommendation addresses, values and preferences related to the recommendation in different settings, the cost of the options available to public health officials and programme managers in different settings, feasibility and acceptability of implementing the recommendation in different settings, and the potential impact on equity and human rights.

- ▶ Replacing SFA with polyunsaturated fatty acids, monounsaturated fatty acids from plant-based foods, and carbohydrates from foods containing naturally occurring dietary fibre (e.g. whole grains, vegetables, fruits, pulses) is associated with additional health benefits including reduced risk of coronary heart disease (*very low to low* certainty evidence).
- ▶ Replacing SFA with mixed protein or animal protein (but not plant protein) is associated with an increase in risk of coronary heart disease (*very low to low* certainty evidence).

Although beneficial effects of lowering SFA intake were not observed for all outcomes assessed, there was no indication that lower SFA intake increased risk for any critical outcome (except when SFA were replaced by mixed or animal protein), nor were there any other significant undesirable effects identified in the systematic reviews.

Evidence from a systematic review of RCTs conducted in children found that reducing SFA intake reduced total cholesterol, LDL cholesterol and diastolic blood pressure (*high* certainty evidence). A small number of trials suggest that the effect was strongest when SFA were replaced primarily with polyunsaturated fatty acids or a mixture of polyunsaturated fatty acids and monounsaturated fatty acids, and when SFA intake was reduced to a level less than 10% of total energy intake (*high* certainty evidence). Significant effects were not observed for other outcomes, and there were no indications of any adverse effects from reduced SFA intake.

TFA

Evidence from recent systematic reviews of RCTs and prospective observational studies conducted in adults suggests the following.

- ▶ Lowering TFA intake reduces LDL cholesterol (*high* certainty evidence), and is associated with reduced risk of all-cause mortality, CVDs and coronary heart disease (*low to moderate* certainty evidence).
- ▶ Consuming 1% or less of total energy intake as TFA reduces LDL cholesterol (*high* certainty evidence), is associated with reduced risk of CVDs and coronary heart disease (*low* certainty evidence), and may be associated with reduced risk of all-cause mortality (*very low* certainty evidence).
- ▶ Replacing TFA with unsaturated fatty acids and carbohydrates lowers LDL cholesterol (*high* certainty evidence) and is associated with reduced risk of all-cause mortality. Replacing TFA with monounsaturated fatty acids from plant-based foods is associated with reduced risk of coronary heart disease (*low* certainty evidence).
- ▶ Replacing TFA with either carbohydrates or polyunsaturated fatty acids is associated with reduced risk of type 2 diabetes (*moderate* and *very low* certainty evidence, respectively).

There were no indications of any adverse effects from reduced TFA intake.

No studies were identified that met the inclusion criteria established for the systematic review of TFA intake in children.

Recommendations and supporting information

All recommendations for SFA and TFA should be considered in the context of other WHO guidelines on healthy diets, including those on total fat, polyunsaturated fatty acids, sugars, sodium, potassium and carbohydrates.

SFA recommendations

1. WHO recommends that adults and children reduce saturated fatty acid intake to 10% of total energy intake (*strong recommendation*).
2. WHO suggests further reducing saturated fatty acid intake to less than 10% of total energy intake (*conditional recommendation*).
3. WHO recommends replacing saturated fatty acids in the diet with polyunsaturated fatty acids (*strong recommendation*), monounsaturated fatty acids from plant sources (*conditional recommendation*), or carbohydrates from foods containing naturally occurring dietary fibre, such as whole grains, vegetables, fruits and pulses (*conditional recommendation*).

Rationale for SFA recommendations 1 and 2

- ▶ Recommendations 1 and 2 are based on evidence from four systematic reviews that assessed the effects of lower compared with higher SFA intake. These systematic reviews found that lower SFA intake reduced the risk of all-cause mortality and CVDs. The overall certainty in the evidence for recommendation 1 was *moderate*, and for recommendation 2 was *very low*.
- ▶ Specific findings from the reviews supporting these recommendations include the following:
 - As assessed in RCTs, reducing SFA intake reduced the risk of CVDs in adults (*moderate* certainty evidence); greater reductions in SFA intake resulted in greater reduction in risk. No effect, or effects that trended towards reduced risk of CVDs, were observed for other critical outcomes; none suggested increased risk. All but one of the trials included in the analyses reported SFA intakes of more than 10% of total energy intake at baseline, and although stepwise testing of thresholds of intake did not find a clear effect on any cardiovascular or mortality outcome at SFA intakes of less than 10% of total energy intake, significant reductions in risk of CVDs and CVD mortality were observed with SFA intakes of less than 9% of total energy intake. Consequently, there is ample evidence supporting reduction of SFA intake to 10% of total energy, but only limited evidence supporting a reduction to below 10% of total energy intake.
 - As assessed in prospective observational studies, lower SFA intake compared with higher intake (*very low* certainty evidence) and consuming SFA at a level of less than 10% of total energy intake compared with intakes greater than 10% (*low* certainty evidence) were associated with reduced risk of all-cause mortality in adults.
 - As assessed in RCTs and strictly controlled feeding trials, replacing SFA with polyunsaturated fatty acids, monounsaturated fatty acids and carbohydrates all resulted in reductions in low-density lipoprotein (LDL) cholesterol in adults (*high* certainty evidence). The LDL cholesterol-lowering effects of replacing saturated fatty acids with other nutrients are cumulative – that is, the more SFA intake is reduced, the more LDL cholesterol is lowered. The effects were observed down to SFA intakes of 2% of total energy intake (effects were observed across a wide range of SFA intakes, from 2% to 24% of total energy intake).
 - Reducing SFA intake, as assessed in RCTs conducted in children, resulted in reduced LDL cholesterol and blood pressure (both *high* certainty evidence). All but one of the trials included in the analyses reported SFA intakes of more than 10% of total energy intake at baseline, and very limited evidence suggests that reducing SFA intake to less than 10% of total energy intake reduces LDL cholesterol to a greater extent than reducing intake to a level greater than 10% of total energy intake (*moderate* certainty evidence).
- ▶ Evidence from RCTs did not suggest undesirable effects in adults from reduced SFA intake with respect to any of the critical outcomes, cancer incidence or mortality, serum lipids, blood pressure, measures of body fatness, or quality of life. Rather, the evidence suggested small benefits or no effect. Evidence from RCTs further suggested a slight increase in triglycerides and a reduction in high-density lipoprotein

(HDL) cholesterol when SFA are replaced by carbohydrates of mixed composition. However, the clinical relevance of such changes is not clear. This finding was therefore not an influential consideration in the balance of desirable and undesirable effects, given the evidence for disease and mortality outcomes, and taking into account recommendation 3 on replacement nutrients for SFA. Evidence from the systematic review conducted in children indicates that reducing SFA intake does not compromise children's linear growth, micronutrient status, cognitive development or sexual development. No other data on undesirable effects in adults or children were identified.

- ▶ Recommendation 1 was assessed as *strong* because evidence of *moderate* certainty overall from different study types assessing both risk factors and incidence of CVDs suggested reduced risk of CVDs with lower SFA intake. No undesirable effects or other mitigating factors were identified that would argue against a lower SFA intake.
- ▶ Recommendation 2 was assessed as *conditional* because, although evidence from different study types from each of the systematic reviews suggested reduced risk of CVDs with SFA intakes of less than 10% of total energy intake, the evidence is much more limited than for intakes greater than 10% of total energy intake and therefore there is less confidence in it (*very low* certainty evidence overall). No undesirable effects or other mitigating factors were identified that would argue against reducing SFA intake to less than 10% of total energy intake. A conservative approach was therefore taken, leading to a *conditional* recommendation.

Rationale for SFA recommendation 3

- ▶ Recommendation 3 is based on *moderate* certainty evidence overall for replacing SFA with polyunsaturated fatty acids and *low* certainty evidence overall for replacing SFA with monounsaturated fatty acids or carbohydrates. Evidence comes from four systematic reviews that assessed the effects of lower compared with higher SFA intake via replacement nutrient analysis. These reviews found that lower SFA intake reduced the risk of all-cause mortality, CVDs and coronary heart disease.

Specific findings from the reviews supporting this recommendation include the following.

- Subgroup analysis of RCTs showed a reduction in risk of CVDs and coronary heart disease when SFA were replaced with polyunsaturated fatty acids (*moderate* certainty evidence), but not when SFA were replaced by carbohydrates, monounsaturated fatty acids (for which there was insufficient evidence to allow an adequate assessment) or protein.¹
- As assessed in prospective observational studies, replacing SFA with polyunsaturated fatty acids (*low* certainty evidence overall) or plant-based monounsaturated fatty acids (*moderate* certainty evidence overall) was associated with reductions in risk of CVDs, coronary heart disease and all-cause mortality. More limited evidence shows that replacing SFA with carbohydrates, particularly those from whole grains and foods described by the authors of the individual studies as having a low glycaemic index, was associated with small reductions in risk of CVDs and all-cause mortality (*very low* certainty evidence).
- As assessed in RCTs and strictly controlled feeding trials, replacing SFA with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates² all resulted in reductions in LDL cholesterol (*high* certainty evidence). The greatest reduction in LDL cholesterol was observed for polyunsaturated fatty acids, followed by monounsaturated fatty acids and then carbohydrates.
- Very limited evidence from RCTs conducted in children suggests that replacing SFA with polyunsaturated fatty acids or monounsaturated fatty acids reduces LDL cholesterol to a greater extent than replacing SFA with other nutrients (*moderate* certainty evidence).
- ▶ The evidence for the health benefits of replacing SFA with carbohydrates from whole grains, vegetables, fruits and pulses is based on studies in which the composition of the carbohydrates was either unspecified

¹ In these studies, polyunsaturated fatty acids were primarily from plant-based oils, rich in linoleic acid; carbohydrates were of largely unknown, and likely mixed, composition; and little to no data were available for nature of the protein.

² In this review, polyunsaturated fatty acids were predominantly linoleic acid and α -linolenic acid; monounsaturated fatty acids were predominantly oleic acid; and carbohydrates were of largely unknown, and likely mixed, composition.

and therefore likely a mixture, or were reported as coming from whole grains or foods described by the authors of the individual studies as having a low glycaemic index. Although the evidence from the systematic reviews that informed the development of this recommendation did not specifically assess the replacement of SFA with carbohydrates from vegetables, fruits or pulses (whole grains were assessed directly), robust evidence from systematic reviews informing WHO recommendations on carbohydrate intake indicates that consuming whole grains, vegetables, fruits and pulses is associated with health benefits, and therefore that carbohydrates in the diet should primarily come from these foods.

- ▶ The recommendation for replacing SFA with polyunsaturated fatty acids from plant sources was assessed as *strong* because evidence of *moderate* certainty overall from different study types that assessed both risk factors and disease incidence suggested that such replacement reduces the risk of CVDs and all-cause mortality.
- ▶ The recommendations for replacing SFA with monounsaturated fatty acids from plant sources or carbohydrates from whole grains, vegetables, fruits and pulses was assessed as *conditional* because they are primarily based on evidence from observational studies, and also because vegetables, fruits and pulses were not directly assessed in the prospective cohort studies assessing replacement (whole grains were assessed directly).

Remarks for Recommendation 3

- ▶ To facilitate implementing this recommendation, replacing SFA can be achieved via a single recommended nutrient or a combination of nutrients.
- ▶ For further guidance on consumption of whole grains, vegetables, fruits and pulses, see the WHO guideline on carbohydrate intake.
- ▶ The guidance on replacement nutrients is relevant for a state of energy balance, in which total energy consumed is balanced by total energy expended. For energy balance, when the intake of one nutrient is reduced, the resulting energy deficit must be compensated for by intake of another nutrient. In cases of positive energy balance, and where a reduction in total energy intake is desired, SFA intake may be reduced in part or entirely without the need for a replacement nutrient.

Remarks for all SFA recommendations

- ▶ The recommendations as they apply to children are based on the totality of evidence, including both results of the review conducted in children and extrapolation of the results obtained from the reviews conducted in adults.¹
- ▶ The systematic review of prospective observational studies identified studies in which SFA exposures were assessed either by self-reported dietary intakes or measurement of SFA in tissues (e.g. plasma phospholipids, red blood cells, fat biopsies). The results for some outcomes differed between the two methods of exposure assessment: significant reductions in risk were observed for coronary heart disease and type 2 diabetes in studies where SFA intake was assessed by measuring SFA content of tissues, whereas no or non-significant results were observed for all outcomes in studies where SFA intake was assessed by self-reported dietary intakes, when replacement is not considered. Although assessment of SFA in tissues can be a relatively reliable indicator of dietary intake, the potential contribution of endogenous synthesis cannot be consistently estimated. Therefore, although the results for SFA tissue levels in the systematic review provide evidence of benefit of lower SFA tissue levels and generally support the evidence from other studies and analyses, the evidence from tissue levels was not formally assessed or included in the evidence base supporting the recommendations for SFA intake.
- ▶ Although there is evidence for differential effects of individual SFA, it is insufficient to inform the development of specific recommendations. SFA found naturally in foods are generally mixtures; consequently, intakes of individual SFA tend to be highly correlated with one another. Therefore, recommendations

¹ The results from the systematic reviews conducted in adults were not downgraded for indirectness when assessing the evidence via Grading of Recommendations Assessment, Development and Evaluation (GRADE) as there is no evidence that the physiological effects of reducing SFA on risk of disease and mortality would be significantly different between adults and children.

for individual SFA may be of limited utility to end users and difficult to implement – for example, in developing food-based dietary guidelines. Before recommendations can be made for individual SFA, further research is needed into their health effects and how such recommendations might be effectively used.

- ▶ These recommendations do not preclude consumption of particular foods. However, foods containing high levels of SFA should be consumed sparingly to meet the recommended level of intake.

TFA recommendations

1. WHO recommends that adults and children reduce *trans*-fatty acid intake to 1% of total energy intake (*strong recommendation*).
2. WHO suggests further reducing *trans*-fatty acid intake to less than 1% of total energy intake (*conditional recommendation*).
3. WHO recommends replacing *trans*-fatty acids in the diet with polyunsaturated fatty acids or monounsaturated fatty acids primarily from plant sources (*conditional recommendation*).

Rationale for TFA recommendations 1 and 2

- ▶ Recommendations 1 and 2 are based on evidence from two systematic reviews that assessed the effects of lower compared with higher TFA intake. These systematic reviews found that lower TFA intake reduced the risk of CVDs. The overall certainty in the evidence for recommendation 1 was *moderate* and for recommendation 2 was *low*.
- ▶ Specific findings from the reviews supporting these recommendations include the following.
 - As assessed in prospective observational studies, lower TFA intake compared with higher intake (*moderate* certainty evidence overall) and consuming TFA at a level of less than 1% of total energy intake compared with intakes greater than 1% (*low* certainty evidence overall) were associated with reduced risk of all-cause mortality, CVDs and coronary heart disease. Greater reductions in TFA intake resulted in greater reductions in risk of all-cause mortality and coronary heart disease (i.e. dose–response relationships).
 - As assessed in RCTs, replacing TFA with polyunsaturated fatty acids, monounsaturated fatty acids and carbohydrates all resulted in reductions in LDL cholesterol (*high* certainty evidence) and overall improvements in blood lipid profile. The LDL cholesterol–lowering effects of replacing TFA with other nutrients are cumulative – that is, the more TFA intake is reduced, the more LDL cholesterol is lowered. These effects were observed across a wide range of TFA intakes, from 0% to 10.9% of total energy intake.
- ▶ Recommendation 1 was assessed as *strong* because evidence of overall *moderate* certainty from different study types assessing both risk factors and incidence of CVDs suggested reduced risk of all-cause mortality, CVDs and coronary heart disease with lower TFA intake (in a dose-dependent manner with respect to all-cause mortality and coronary heart disease). No undesirable effects or other mitigating factors were identified that would argue against a lower TFA intake.
- ▶ Recommendation 2 was assessed as *conditional* because, although there is evidence from different study types from each of the systematic reviews suggesting reduced risk of all-cause mortality, CVDs and coronary heart disease with TFA intakes of less than 1% of total energy intake, the evidence is more limited than for intakes greater than 1% of total energy intake and therefore there is less confidence in it (*low* certainty evidence overall). No undesirable effects or other mitigating factors were identified that would argue against reducing TFA intake to less than 1% of total energy intake. A conservative approach was therefore taken, leading to a *conditional recommendation*.

Rationale for TFA recommendation 3

- ▶ Recommendation 3 is based on *very low* certainty evidence overall for replacing TFA with polyunsaturated fatty acids and *moderate* certainty evidence overall for replacing TFA with monounsaturated fatty acids from plant sources. Evidence comes from two systematic reviews that assessed the effects of lower compared with higher TFA intake via replacement nutrient analysis. These reviews found that lower TFA intake reduced the risk of all-cause mortality, CVDs, coronary heart disease and type 2 diabetes.
- ▶ Specific findings from the reviews supporting this recommendation include the following.
 - As assessed in prospective observational studies, replacing TFA with polyunsaturated fatty acids was associated with reduced risk of type 2 diabetes (*very low* certainty evidence), and replacing TFA with monounsaturated fatty acids from plant sources was associated with reduced risk of all-cause mortality, CVDs and coronary heart disease (*moderate* certainty evidence overall).
 - As assessed in RCTs, replacing TFA with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates resulted in reductions in LDL cholesterol (*high* certainty evidence) and overall improvements in blood lipid profile. The greatest reduction in LDL cholesterol was observed for polyunsaturated fatty acids, followed by monounsaturated fatty acids and then carbohydrates.
- ▶ Recommendation 3 was assessed as *conditional* because evidence for disease outcomes comes only from a limited number of observational studies; most of the evidence is from RCTs with LDL cholesterol as an outcome. The evidence for LDL cholesterol is of *high* certainty. However, although LDL cholesterol is a well-established biomarker for measuring the effects of interventions on CVD risk, and is considered by many to be a causal factor for atherosclerosis and coronary heart disease, it is not a physical manifestation or confirmation of disease. Therefore, a conservative approach was taken, leading to a *conditional* recommendation.

Remarks for TFA recommendation 3

- ▶ The recommendation to replace TFA with polyunsaturated fatty acids or monounsaturated fatty acids from plant sources does not preclude replacing TFA with carbohydrates, as replacement with carbohydrates significantly lowered LDL cholesterol in the analysis of RCTs that assessed blood lipids. However, polyunsaturated fatty acids and monounsaturated fatty acids had greater effects on LDL cholesterol when used as replacements for TFA, and replacement of TFA with monounsaturated fatty acids from plant sources reduced the risk of coronary heart disease and all-cause mortality in prospective observational studies. Limited evidence suggests that replacing TFA with carbohydrates of unspecified composition also reduces the risk of type 2 diabetes, but that replacing TFA with free sugars or carbohydrates described by study authors as refined carbohydrates has little effect on risk of coronary heart disease. Therefore, a conclusive interpretation of the results for carbohydrate replacement of TFA in the analyses supporting the recommendations in this guideline was not possible.
- ▶ Replacement of TFA with saturated fatty acids did not improve disease outcomes or blood lipids in the two systematic reviews. Saturated fatty acids are therefore not a preferred replacement for TFA.
- ▶ To facilitate implementing this recommendation, replacing TFA can be achieved via polyunsaturated fatty acids or monounsaturated fatty acids alone, or a combination of the two.
- ▶ This guidance on replacement nutrients is relevant for a state of energy balance, in which total energy consumed is balanced by total energy expended. For energy balance, when the intake of one nutrient is reduced, the resulting energy deficit must be compensated for by intake of another nutrient. In cases of positive energy balance, and where a reduction in total energy intake is desired, TFA intake may be reduced in part or entirely without the need for a replacement nutrient.

Remarks for all TFA recommendations

- ▶ Because there weren't any relevant studies identified in a systematic review of TFA intake in children, the recommendations as they apply to children are based on extrapolation of the results obtained from the reviews conducted in adults.¹
- ▶ For the purposes of these recommendations, TFA includes all fatty acids with a double bond in the *trans* configuration, regardless of whether the TFA come from ruminant sources or are produced industrially.²
- ▶ These recommendations do not preclude consumption of particular foods. However, foods containing high levels of industrially produced TFA should largely be avoided.

¹ The results from the reviews conducted in adults were not downgraded for indirectness when assessing the evidence via GRADE as there is no evidence that the physiological effects of reducing or increasing TFA on risk of disease and mortality would be significantly different between adults and children.

² This definition includes conjugated linoleic acid.

Introduction

Background

Noncommunicable diseases (NCDs) are the world's leading cause of death, responsible for an estimated 41 million of the 55 million deaths in 2019 (1). Nearly half of these deaths were premature (i.e. in people aged less than 70 years) and occurred in low- and middle-income countries. Of the major NCDs, cardiovascular diseases (CVDs)¹ were the leading cause of mortality in 2019, responsible for more than 18 million deaths (2). Modifiable risk factors such as unhealthy diets, physical inactivity, tobacco use and harmful use of alcohol are major risk factors for CVDs. Dietary saturated fatty acids (SFA) and *trans*-fatty acids (TFA) are of particular concern because high levels of intake have been correlated with increased risk of CVDs (3).

SFA are fatty acids containing only single carbon-carbon bonds (i.e. no double bonds). They are found primarily in foods from animal sources (e.g. dairy foods, meat, egg yolks, hard fats), as well as in some plant-derived fats and oils.

TFA are unsaturated fatty acids with at least one double carbon-carbon bond in the *trans* configuration. TFA can be produced industrially by the partial hydrogenation of vegetable and fish oils, but also occur naturally in meat and dairy products from ruminant animals (e.g. cattle, sheep, goats, camels) as a result of the conversion of *cis* double bonds in unsaturated fatty acids to the *trans* position by bacterial enzymes in the stomach (rumen) of the animals. Although the sources are different, the individual isomers in industrially produced and ruminant TFA are largely the same, but present in differing proportions (4-6). Industrially produced TFA are the predominant source of dietary TFA in many populations. They can be found in partially hydrogenated cooking oils and fats which are often used at home, in restaurants, or in the informal sector (e.g. street vendors), and in ready-made baked and fried foods (e.g. doughnuts, cookies, crackers and pies) and other pre-packaged snacks and foods. Although current intakes of ruminant TFA are generally low, ruminant TFA may become the predominant dietary source of TFA in populations where industrially produced TFA are being phased out of the food supply (7-9).

Reduced intake of SFA has been associated with a significant reduction in the risk of coronary heart disease when SFA are replaced with polyunsaturated fatty acids or carbohydrates from whole grains (10-13). However, an apparent lack of effect is often observed in studies in which the macronutrients replacing SFA are unknown, are not accounted for or consist largely of refined carbohydrates (10, 13-15). Studies have also demonstrated that high intakes of industrially produced TFA are strongly associated with increased risk of coronary heart disease and related mortality (16, 17). Few studies have identified an association between intake of ruminant TFA and CVDs; however, to date, ruminant TFA intake in most study populations has been very low (18). Efforts to understand the effects of SFA intake in greater detail have shown that individual SFA may have differing effects on blood lipids (19). In addition, growing evidence has led to the suggestion that different SFA-containing foods, such as dairy foods, may have differential effects on risk of CVDs and type 2 diabetes, as a result of either differing compositions of SFAs across foods, other constituents of the foods (i.e. the "food matrix") or a combination of the two (20-26).

The reduction in CVD risk observed with decreased intake of SFA and TFA is believed to occur primarily through an effect on blood lipids, because intakes of both are associated with increases in levels of total cholesterol and low-density lipoprotein (LDL) cholesterol (19, 27), and decreases in high-density lipoprotein (HDL) cholesterol in the case of TFA (27). Other physiological mechanisms, such as inflammation, may also

¹ Cardiovascular diseases include coronary heart disease, cerebrovascular disease (e.g. stroke), structural abnormalities of the heart at birth or damage resulting from rheumatic fever, peripheral arterial disease, and deep vein thrombosis and pulmonary embolism.

play a role (28, 29). Increased total cholesterol is associated with increased risk of coronary heart disease (30). LDL cholesterol is a well-established surrogate end-point (i.e. biomarker) for measuring the effects of interventions on CVD risk (31, 32), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (33). Other lipid measures – such as non-HDL cholesterol, triglycerides, cholesterol ratios and cholesterol particle number – have also been suggested as possible predictors of CVD risk.

Although CVDs typically present later in life, preclinical signs of atherosclerosis in the form of atherosclerotic lesions in the aorta and coronary arteries can begin to appear in childhood (34, 35), and are positively associated with abnormal blood lipid levels and other CVD risk factors (36, 37). Elevated total and LDL cholesterol in childhood are associated with an increase in CVD risk factors in adulthood (38), including thickening of the carotid artery intima-media (39–41), which is a marker of subclinical atherosclerosis and a predictor of future cardiovascular events (42). Dietary intervention studies conducted in children have demonstrated significant reductions in total or LDL cholesterol when SFA were replaced with polyunsaturated fatty acids (43–48). Despite the positive effect of such replacement on blood lipids, concern has been raised about the possible negative impact of a reduced-fat diet or a diet intended to reduce blood lipids on normal growth and development in children (49, 50), although the primary concern has generally been the potential for inadequate caloric or micronutrient intake rather than any effects related to SFA itself.

Studies of TFA intake in children are limited; nevertheless, there is no evidence to suggest that the effects on blood lipids would be different from those observed in adults, and intake may therefore lead to preclinical signs of atherosclerosis (34–37), as described in the preceding paragraph.

Despite longstanding dietary advice to limit SFA intake and a limited number of focused efforts to reduce intake at the population level, SFA intake remains high in many parts of the world (51). And while more consistent efforts to reduce the level of industrially produced TFA in the food supply at the local to national levels have led to decreased intake in some countries (52), the global average intake of TFA in 2010 (51) was estimated to exceed the population nutrient intake goal of 1% of total energy intake established by the 1989 World Health Organization (WHO) Study Group on Diet, Nutrition and the Prevention of Chronic Diseases (53) and updated by the 2002 Joint WHO/Food and Agriculture Organization of the United Nations (FAO) Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases (3). Efforts to reduce the level of industrially produced TFA in the food supply received a boost in 2018, when their elimination was identified as one of the priority targets in the WHO 13th General Programme of Work. The WHO REPLACE action package was launched in 2018 to help countries eliminate industrially produced TFA from their food supplies.¹

Rationale

Following the work of the 1989 WHO Study Group on Diet, Nutrition and the Prevention of Chronic Diseases (53), the 2002 Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases updated guidance on SFA and TFA intake as part of the guidance on population nutrient intake goals for the prevention of NCDs (3). Since then, new data and analyses have become available leading to differing interpretations and conclusions regarding the role of SFA intake in health, particularly the risk of CVDs. Consequently, the debate has intensified about whether current evidence supports a link between SFA intake and CVDs, and therefore whether efforts to limit SFA intake as a means of reducing CVD risk are warranted. Also, although there is increasing scientific consensus about the adverse health effects of intake of industrially produced TFA, discussion continues regarding the role that consumption of ruminant TFA may play in the development of NCDs. Therefore, it was considered important to review the evidence in a systematic manner, and update WHO guidance on SFA and TFA intake through the WHO guideline development process.

Scope

This guideline is part of the larger effort to update the population nutrient intake goals for the prevention of NCDs established by the 2002 Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases (3). The focus of this guideline is on the health effects of SFA and TFA intake. Considering

¹ <https://www.who.int/teams/nutrition-and-food-safety/replace-trans-fat>

the effects of specific foods or classes of foods is beyond the scope of this guideline. The guidance in this guideline is intended for the general adult and child population, and replaces previous WHO guidance on SFA and TFA intake, including that from the 1989 WHO Study Group on Diet, Nutrition and the Prevention of Chronic Diseases (53) and the 2002 Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases (3).

Objective

The objective of this guideline is to provide evidence-informed guidance on intake of SFA and TFA. The recommendations in this guideline can be used by policy-makers and programme managers to address SFA and TFA intake in their populations through a range of policy actions and public health interventions.

Updating the WHO recommendations for SFA and TFA intake is an important element of WHO's efforts in implementing the NCD agenda and achieving the "triple billion" targets set by the 13th General Programme of Work (2019–2023), including 1 billion more people enjoying better health and well-being. In addition, the recommendations and other elements of this guideline will support:

- ▶ implementation of the political declarations of the United Nations (UN) high-level meetings on the prevention and control of NCDs held in New York in 2011 and 2018, and the outcome document of the high-level meeting of the UN General Assembly on NCDs (A/RES/68/300) held in New York in July 2014;
- ▶ implementation of the WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2030, which was adopted by the 66th World Health Assembly held in May 2013 (the timeline was extended to 2030 at the 72nd World Health Assembly held in May 2019);
- ▶ implementation of the recommendations of the high-level Commission on Ending Childhood Obesity established by the WHO Director-General in May 2014;
- ▶ Member States in implementing the commitments of the Rome Declaration on Nutrition and recommended actions in the Framework for Action, including a set of policy options and strategies to promote diversified, safe and healthy diets at all stages of life – these were adopted by the Second International Conference on Nutrition (ICN2) in 2014 and endorsed by the 136th Session of the WHO Executive Board held in January 2015 and the 68th World Health Assembly held in May 2015, which called on Member States to implement the commitments of the Rome Declaration across multiple sectors;
- ▶ achievement of the goals of the UN Decade of Action on Nutrition (2016–2025), declared by the UN General Assembly in April 2016, which include increased action at the national, regional and global levels to achieve the commitments of the Rome Declaration, through implementing policy options included in the Framework for Action and evidence-informed programme actions; and
- ▶ the 2030 Agenda on Sustainable Development and achieving the Sustainable Development Goals, particularly Goal 2 (Zero hunger) and Goal 3 (Good health and well-being).

Target audience

This guideline is intended for a wide audience involved in the development, design and implementation of policies and programmes in nutrition and public health. The end users for this guideline are thus:

- ▶ policy-makers at the national, local and other levels;
- ▶ managers and implementers of programmes relating to nutrition and NCD prevention;
- ▶ nongovernmental and other organizations, including professional societies, involved in managing and implementing programmes relating to nutrition and NCD prevention;
- ▶ health professionals in all settings;
- ▶ scientists and others involved in nutrition and NCD-related research;
- ▶ educators teaching nutrition and prevention of NCDs at all levels; and
- ▶ representatives of the food industry and related associations.

How this guideline was developed

This guideline was developed in accordance with the WHO evidence-informed process for guideline development outlined in the *WHO handbook for guideline development* (54). Because of the complex nature of the guideline topic and evolving evidence base, the guideline was developed over several meetings of the WHO Nutrition Guidance Expert Advisory Group (NUGAG) Subgroup on Diet and Health, beginning in 2012.¹

Contributors to the development of this guideline

This guideline was developed by the WHO Department of Nutrition and Food Safety (formerly the Department of Nutrition for Health and Development). Several groups contributed to the development of this guideline, and additional feedback was received from interested stakeholders via public consultation, as described below.

WHO steering group

The work was guided by an internal steering group, which included technical staff from WHO with varied perspectives and an interest in the provision of scientific advice on healthy diets ([Annex 1](#)).

Guideline development group

The guideline development group – the NUGAG Subgroup on Diet and Health – was convened to support the development of this guideline ([Annex 2](#)). This group included experts who had previously participated in various WHO expert consultations or were members of WHO expert advisory panels, and others identified through open calls for experts. In forming the group, the WHO Secretariat took into consideration the need for expertise in multiple disciplinary areas, representation from all WHO regions and a balanced gender mix. Efforts were made to include subject matter experts (e.g. in nutrition, epidemiology, paediatrics, physiology); experts in systematic review, programme evaluation and Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologies; and representatives of potential stakeholders (e.g. programme managers, policy advisers, other health professionals involved in the health-care process). Professor Shiriki Kumanyika served as the chair at the meetings of the NUGAG Subgroup on Diet and Health. The names, institutional affiliations and summary background information of the members of the NUGAG Subgroup on Diet and Health are available on the WHO website,¹ along with information on each meeting of the group.

External peer review group

External experts with diverse perspectives and backgrounds relevant to the topic of this guideline were invited to review the draft guideline to identify any factual errors, and comment on the clarity of the language, contextual issues and implications for implementation ([Annex 3](#)).

Systematic review teams

Systematic review teams with expertise in both systematic review methodologies and the subject matter were identified.

¹ For a complete list of meetings and information on members of the NUGAG Subgroup on Diet and Health, see [https://www.who.int/groups/nutrition-guidance-expert-advisory-group-\(nugag\)/diet-and-health](https://www.who.int/groups/nutrition-guidance-expert-advisory-group-(nugag)/diet-and-health).

- ▶ A team from the University of East Anglia and University College London in the United Kingdom of Great Britain and Northern Ireland (the United Kingdom), consisting of Lee Hooper, Nicole Martin, Oluseyi Jimoh, Christian Kirk, Eve Foster and Asmaa Abdelhamid completed a systematic review on SFA intake and risk of NCDs in adults as assessed in randomized controlled trials (RCTs) (55).
- ▶ A team from Otago University in New Zealand, the University of Oxford in the United Kingdom and McMaster University in Canada, consisting of Andrew Reynolds, Leanne Hodson, Russell de Souza, Huyen Tran Diep Pham, Lara Vlietstra, and Jim Mann completed a systematic review on SFA and TFA intake and risk of NCDs in adults as assessed in prospective observational studies (56). This review is an update of a systematic review commissioned in 2015 (57) to inform the work of the NUGAG Subgroup on Diet and Health in developing the guidelines on SFA and TFA intake.
- ▶ Ronald Mensink of Maastricht University in Netherlands (Kingdom of the) conducted a systematic review and regression analysis on SFA intake and risk factors for NCDs (i.e. blood lipids) in adults as assessed in RCTs and strictly controlled feeding trials (58).
- ▶ Ingeborg Brouwer of Vrije Universiteit in Netherlands (Kingdom of the) conducted a systematic review and regression analysis on TFA intake and risk factors for NCDs (i.e. blood lipids) in adults as assessed in RCTs and strictly controlled feeding trials (59).
- ▶ Lisa Te Morenga of Otago University in New Zealand and Jason Montez of WHO conducted a systematic review on SFA and TFA intake and risk of NCDs in children as assessed in RCTs and prospective observational studies (60).

Teams consulted frequently with the WHO Secretariat to ensure that the reviews met the needs of the WHO guideline development process.

Stakeholder feedback via public consultation

Two public consultations were held during the development of this guideline: one at the scoping phase of the process in 2012 (feedback was received from a total of 39 individuals and organizational stakeholders) and one on the draft guideline in May 2018 (feedback was received from a total of 48 individuals and organizational stakeholders). Stakeholders and others with an interest in the guideline were invited to provide feedback on overall clarity, any potentially missing information, setting-specific or contextual issues, considerations and implications for adaptation and implementation of the guideline, and additional gaps in the evidence to be addressed by future research. The consultation was open to everyone. Declaration of interest forms were collected from all those submitting comments, which were assessed by the WHO Secretariat, following the procedures for management of interests described in the next section. Comments were summarized, and together with WHO responses to the summary comments, posted on the WHO website.¹ Comments that helped to focus the scope of the guideline or improve clarity and usability of the draft guideline were considered in finalizing the scope and the guideline document.

Management of conflicts of interest

Financial and intellectual interests of the members of the NUGAG Subgroup on Diet and Health, those serving as external peer reviewers, and individuals who prepared systematic reviews or contributed other analyses were reviewed by members of the WHO Secretariat, in consultation with the WHO Department of Compliance and Risk Management and Ethics, where necessary. Declared interests of members of the NUGAG Subgroup on Diet and Health and of the systematic review teams were reviewed before their original engagement in the guideline development process and before every meeting. In addition, each member of the NUGAG Subgroup on Diet and Health (and members of the systematic review teams, if present) verbally declared their interests, if required, at the start of each meeting of the group. Declared interests of external reviewers were assessed before they were invited to review the draft guideline. In addition to reviewing interests declared by the individuals themselves, an internet search was conducted for each contributor to independently assess financial and intellectual interests for the 4 years before their engagement in the

¹ [https://www.who.int/groups/nutrition-guidance-expert-advisory-group-\(nugag\)/diet-and-health](https://www.who.int/groups/nutrition-guidance-expert-advisory-group-(nugag)/diet-and-health)

development of the guideline, which was repeated as necessary. The overall procedures for management of interests outlined in the *WHO handbook for guideline development (54)* were followed.

Interests declared by members of the NUGAG Subgroup on Diet and Health, external reviewers and members of the systematic review teams, and the process for managing any identified conflicts of interest are summarized in [Annex 4](#).

Guideline development process

Scoping of the guideline

The scientific literature was reviewed to identify important populations, outcomes and other topics relevant to the health effects of SFA and TFA intake. Existing systematic reviews on the topic were identified. The information gathered was compiled and used to generate the key questions and outcomes that would guide the selection of existing systematic reviews or the undertaking of new systematic reviews.

Defining key questions and prioritizing outcomes

The questions were based on the needs of Member States and international partners for policy and programme guidance. The population, intervention, comparison and outcome (PICO) format was used in generating the questions ([Annex 5](#)). The PICO questions were first discussed and reviewed by the WHO Secretariat and the NUGAG Subgroup on Diet and Health, and were then made available for public comment in 2012.

Intakes of SFA and TFA have been shown to be associated with similar health outcomes, and a goal of setting recommendations for these nutrients is to include quantitative targets of intake wherever possible. As a result, the PICO questions developed for each nutrient are nearly identical in terms of population, interventions (i.e. types of studies and interventions employed), comparators and outcomes.

The flow of assessing the evidence for both SFA and TFA was as follows:

- ▶ Assess evidence of higher versus lower intake of either nutrient.
- ▶ Where possible, test different thresholds of intake to establish a target level of intake for both nutrients.
- ▶ Assess the effects of replacing SFA or TFA with other nutrients. This is because, in most cases (particularly for SFA), when intake of SFA or TFA is reduced, other nutrients need to be consumed to replace the resulting deficit in energy intake.
- ▶ Assess the available evidence for differences in subtypes (i.e. individual SFA, or ruminant TFA compared with industrially produced TFA).

The key questions that guided the systematic reviews undertaken are therefore as follows.

What is the effect on prioritised health outcomes in adults and children of:

- ▶ lower intake of SFA or TFA compared with higher intake;
- ▶ SFA intake below 10% of total energy intake compared with intake above 10%, and TFA intake below 1% of total energy intake compared with intake above 1%;
- ▶ replacement of SFA or TFA in the diet with polyunsaturated fatty acids, monounsaturated fatty acids, carbohydrates or protein;
- ▶ lower intake of individual SFA¹ compared with higher intake; and
- ▶ lower intake of ruminant TFA compared with higher intake, and lower intake of industrially produced TFA compared with higher intake.

¹ SFA comprise many different, individual SFA molecules that vary in chain length (i.e. the number of carbon atoms in the carbon backbone of the fatty acid). Common SFA found in the diet of humans include lauric acid (12 carbons), myristic acid (14 carbons), pentadecanoic acid (15 carbons), palmitic acid (16 carbons), heptadecanoic acid (17 carbons) and stearic acid (18 carbons).

Priority health outcomes are identical for SFA and TFA. Those considered for adults were all-cause mortality, coronary heart disease (incidence, mortality), CVDs (incidence, mortality), stroke (incidence, mortality), blood lipids¹ and type 2 diabetes incidence. Priority health outcomes considered for children were blood lipids, weight and measures of adiposity, blood pressure, type 2 diabetes incidence and insulin resistance, linear growth, and potential adverse effects.

Evidence gathering and review

SFA

Four systematic reviews were conducted to assess the relationship between lower SFA intake and health outcomes of interest in adults and children.

- ▶ A systematic review of RCTs that assessed the effects of reducing intake of SFA on risk of mortality, CVDs and type 2 diabetes in adults. This review was most recently updated in 2020 (55).
- ▶ A systematic review of prospective observational studies that assessed associations between intake of SFA and risk of mortality, CVDs and type 2 diabetes in adults. This review was most recently updated in 2021 (56).
- ▶ A systematic review of RCTs of specific design (i.e. strictly controlled feeding studies) that assessed the effects of replacing SFA with other nutrients on blood lipid profiles in adults. This review was most recently updated in 2016 (58). The review was not further updated because it had previously been updated in 2003 (19), and the results from the original 1994 review (61) and the updates in 2003 and 2016 were all similar. In addition, RCTs assessing behaviour change interventions (including those in the review in the first bullet point of this list) and observational studies have almost unanimously come to the same conclusions regarding the effects of SFA on blood lipids, particularly for LDL cholesterol. Because the relationship between SFA intake and LDL cholesterol is so well established that many consider elevated LDL cholesterol a causal factor for atherosclerosis and coronary heart disease (33), and robust data show an association between SFA intake and CVDs (for which LDL cholesterol is considered a risk factor), further updating of this systematic review was deemed unnecessary.
- ▶ A systematic review of RCTs and prospective observational studies that assessed the effects of reducing intake of SFA on risk factors for CVDs, type 2 diabetes, and adverse effects on growth and development in children, which was published in 2017 (60). A subsequent scan of the literature was conducted, covering the period from when the literature was searched for the original review to June 2021; no studies were identified that would significantly change the results or conclusions of the original review. Therefore, this systematic review was not formally updated.

TFA

Three systematic reviews were conducted to assess the relationship between lower TFA intake and health outcomes of interest in adults and children.

- ▶ A systematic review of prospective observational studies that assessed associations between intake of TFA and risk of mortality, CVDs and type 2 diabetes in adults. This review was most recently updated in 2021 (56).
- ▶ A systematic review of RCTs of specific design (i.e. strictly controlled feeding studies) that assessed the effects of replacing TFA with other nutrients on blood lipid profiles in adults. This review was most recently updated in 2016 (59), and the results from the original 2010 review (27) and the 2016 update were similar. Further updating of this systematic review for total TFA was deemed unnecessary because evidence from other sources has almost unanimously come to the same conclusions regarding the

¹ Blood lipids are indirect measures of patient-important CVD outcomes. Total cholesterol is a relevant indicator of CVD risk (30). LDL cholesterol is a well-established biomarker for measuring the effects of interventions on CVD risk (31, 32) and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (33). Therefore, LDL was included as a critical outcome (54) in the formulation of recommendations on SFA and TFA intake, and was not downgraded for indirectness when determining the certainty in the evidence within the GRADE framework. Total cholesterol, HDL cholesterol, triglycerides and blood lipid ratios were also considered when formulating the recommendations; however, noting that the evidence supporting their use to measure effects of interventions on CVD risk was less certain, they were classified as important outcomes.

effects of TFA on blood lipids, particularly for LDL cholesterol, and the evidence for an association between TFA intake and CVDs (for which LDL is considered a risk factor) is very robust. Because relatively little data were available for ruminant TFA at the time the systematic review was conducted, a scan of the literature was conducted, covering the period from when the literature was searched in the original review (September 2014) to June 2021; no studies were identified that would significantly change the results or conclusions of the original review. Therefore, this systematic review was not formally updated.

- ▶ A systematic review of RCTs and prospective observational studies that assessed the effects of reducing intake of TFA on risk factors for CVDs, type 2 diabetes and adverse effects on growth and development in children, which was published in 2017 (60). A scan of the literature was conducted, covering the period from when the literature was searched for the original review (July 2016) to June 2021; no additional studies meeting the inclusion/exclusion criteria were identified, and the systematic review was not formally updated.

Assessment of certainty in the evidence

GRADE¹ methodology was used to assess the certainty of (i.e. confidence in) the evidence identified in the systematic reviews. GRADE assessments assigned by the systematic review teams were discussed by the NUGAG Subgroup on Diet and Health and the systematic review teams, and refined as necessary under the guidance of an expert with extensive expertise in GRADE methodology.² A summary of GRADE assessments, together with further information on how GRADE assessments were conducted, can be found in [Annex 6](#).

Formulation of the recommendations

In formulating the recommendations and determining their strength, the NUGAG Subgroup on Diet and Health assessed the evidence in the context of the certainty of the evidence, desirable and undesirable effects of the intervention, the priority of the problem that the intervention would address, values and preferences related to the effects of the intervention in different settings, the cost of the options available to public health officials and programme managers in different settings, the feasibility and acceptability of implementing the intervention in different settings, and the potential impact on equity and human rights ([Annex 7](#)).

Because much of the evidence that NUGAG Subgroup on Diet and Health reviewed came from assessment of individuals, and dose–response relationships were observed for many outcomes, the decision was made to formulate the recommendations such that the recommended levels of intake of SFA and TFA are targets for individuals to achieve, not population goals. NUGAG Subgroup on Diet and Health further concluded that individual targets would be easier to implement, particularly in terms of updating food-based dietary guidelines, education/awareness campaigns, and other interventions aimed at eliciting desired behavioural change at the individual level. Because neither SFA nor TFA are essential nutrients, and some studies included in the reviews included obese individuals and those at risk for disease without observed differences in effects or associations, the recommendations were formulated for all individuals regardless of health status.

Based on the evidence and additional factors, the NUGAG Subgroup on Diet and Health developed the recommendations and associated remarks by consensus.

¹ <http://www.gradeworkinggroup.org/>

² Because the NUGAG Subgroup on Diet and Health, under the guidance of the GRADE methodological expert, occasionally came to different assessments to those of the systematic reviewers in published (or in press) reviews, the final assessment for a small number of outcomes used by the NUGAG Subgroup on Diet and Health in formulating recommendations as found in this guideline differs slightly from that found in the published reviews.

Summary of evidence

The flow of assessing the evidence for both SFA and TFA is summarized in the section *Defining key questions and prioritizing outcomes*. Results for CVDs and coronary heart disease from RCTs and observational studies for SFA and TFA intake include fatal and non-fatal events. In addition, results for CVD mortality and coronary heart disease mortality only are reported from RCTs for SFA intake.

SFA

Four systematic reviews were commissioned to assess the effects of reducing SFA intake, or a lower SFA intake, on risk of mortality and CVDs in adults and children.

Systematic review characteristics

Review 1

A systematic review of RCTs that assessed the effects of reducing the intake of SFA on risk of mortality, CVDs and type 2 diabetes in adults identified 15 trials (16 comparisons) with more than 56 000 participants (55). The review included:

- ▶ trials with a stated intention to reduce intake of SFA; and
- ▶ trials with a general dietary aim (e.g. improving heart health, reducing total fat intake) that achieved a statistically significant reduction in SFA intake ($P < 0.05$) in the intervention group compared with the control group.

Interventions included dietary advice or provision of food (e.g. fats, oils, modified or lower-fat foods, complete diet), or a combination of the two. Outcomes assessed included all-cause mortality, CVD mortality, CVDs, coronary heart disease mortality, coronary heart disease, myocardial infarction and stroke. Only trials in which the dietary intervention lasted at least 2 years were included in the review (trial duration ranged from 2 to >8 years, with a mean duration of 4.7 years).¹ Trials were conducted in Australia, Netherlands (Kingdom of the), New Zealand, Norway, the United Kingdom and the United States of America (the United States). Of the 16 comparisons, six included only people at high risk of CVDs, four included people at moderate risk, five included people at low risk, and one included people with both low and high risk. Seven studies included only men, three only women, and five both men and women. SFA intake ranged from 6% to 18.5% of total energy intake across intervention and control groups.

Review 2

A systematic review of prospective observational studies that assessed the effects of higher intake of SFA compared with lower intake on risk of mortality, CVDs and type 2 diabetes in adults identified 112 publications involving 3 696 568 participants (56). Many publications reported on the same cohorts (but different outcomes, such that there were no duplicate datasets included in the review), on both exposures of SFA intake and TFA intake, and on multiple relevant outcomes. Study locations were geographically

¹ The selection of a minimum study duration of 2 years as a criterion for study inclusion was based on recognition that the effects of changes in diet on the development of mortality and disease outcomes may not be observed with short-term follow-up. In selecting a minimum study duration, consideration was given to what is known regarding statin use as an example of an intervention that is known to have a significant effect on LDL cholesterol levels and cardiovascular outcomes. An ongoing meta-analysis of statin efficacy trials including a large number of participants has established a minimum treatment duration of 2 years as an inclusion criterion (31, 62–64). Dietary changes are generally anticipated to have a less robust physiological impact than statins; therefore, 2 years was selected as a conservative estimate for physiological effects of dietary changes in the review of Hooper et al. (55).

diverse (38% North America, 28% Europe, 16% Asia, 4% Australia, 4% United Kingdom and the remainder from the eastern Mediterranean region or multinational cohorts). SFA intake across studies ranged from 6% to 18.5% of total energy intake.¹

Review 3

A systematic review and multiple regression analysis of RCTs that assessed the effects of modifying intake of fatty acids on blood lipids identified 84 trials with 2363 participants (58). Of these, 74 trials provided 177 data points² that were used to assess the effects of different classes of fatty acids on blood lipids, and 52 trials provided 134 data points that were used to assess the effects of individual SFA on blood lipids. SFA intake ranged from 1.6% to 24.4% of total energy intake across the included trials. The RCTs included in the review were all strictly controlled dietary trials, of 13–91 days duration, in which cholesterol, protein and alcohol intake were held constant, and dietary fat or carbohydrate intake was varied. Outcomes assessed included total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, LDL cholesterol to HDL cholesterol ratio, total cholesterol to HDL cholesterol ratio, triglyceride to HDL cholesterol ratio, apolipoprotein A-I (ApoA-I) and apolipoprotein B (ApoB). Trials were primarily conducted in the United States, but also in Austria, Canada, Denmark, Finland, Germany, Israel, Italy, Malaysia, Netherlands (Kingdom of the), New Zealand, Norway, Spain, Sweden and the United Kingdom. Using multiple regression analysis – in which the intake of SFA, polyunsaturated fatty acids, monounsaturated fatty acids and carbohydrates as a percentage of total energy intake served as the independent variables, and the mean concentration of a given blood lipid or lipid ratio as the dependent variable – four models were developed that provide an estimate of the effect (i.e. regression coefficient) on a given blood lipid when 1% of total energy intake as SFA was isocalorically³ exchanged with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates. A fifth model was developed to estimate the effects of individual SFA.

Review 4

A systematic review of RCTs that assessed the effects of reducing intake of SFA on CVD risk factors, and growth and development in children identified a total of eight trials with 2430 participants (60). The trials included children and adolescents aged from 2 to 19 years⁴ with either normal or elevated cholesterol levels. Interventions included dietary advice or provision of food in which the fatty acid content had been modified, or a combination of the two. Outcomes assessed included total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride and associated blood lipid ratios; height; body weight, body mass index and other measures of adiposity; systolic blood pressure; diastolic blood pressure; insulin resistance and incidence of impaired glucose tolerance, impaired fasting glycaemia or type 2 diabetes; and potential adverse effects. Trials were conducted in Australia, China, Finland, Spain and the United States. Trial duration ranged from 5 weeks to approximately 19 years. SFA intake ranged from 9% to 16.6% of total energy intake across intervention and control groups.

Results of systematic reviews

Lower compared with higher intake of SFA

Results for adults and children are summarized in **Table 1**.

¹ Studies included both those that assessed SFA intake via self-reporting (e.g. 24-hour recall, food diaries, food frequency questionnaires) and tissue measurements (e.g. plasma phospholipids, red blood cells, fat biopsies). Only results for studies with self-reported SFA intakes are included in the main evidence summary and **Tables 1–3**.

² Data points consisted of the fatty acid (i.e. SFA, polyunsaturated fatty acids and monounsaturated fatty acids) and carbohydrate composition of a particular diet, and the mean serum lipid concentration of intervention and control groups, as measured at the end of the intervention period in all included trials.

³ The amount of polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates used as a replacement for SFA was identical in terms of calories to that of the SFA being replaced.

⁴ One trial recruited infants at 7 months of age and followed up the participants for approximately 19 years.

Table 1. Summary of results from RCTs and observational studies for lower compared with higher intake of SFA

Outcome	Pooled estimate (95%CI)	No. studies	No. participants	Certainty
Adults				
All-cause mortality				
RCT	RR 0.96 (0.90 to 1.03)	12	55 858	Moderate
Observational	RR 0.93 (0.86 to 1.00)	21	1 211 729	Low
CVD mortality				
RCT	RR 0.94 (0.78 to 1.13)	11	53 421	Low
CVDs				
RCT	RR 0.83 (0.70 to 0.98)	13	53 758	Moderate
Observational	RR 0.93 (0.86 to 1.02)	16	1 088 501	Very low
CHD mortality				
RCT	RR 0.97 (0.82 to 1.16)	9	53 159	Low
CHD				
RCT	RR 0.83 (0.68 to 1.01)	11	53 199	Very low
Observational	RR 0.96 (0.90 to 1.03)	18	570 326	Very low
Stroke				
RCT	RR 0.92 (0.68 to 1.25)	7	50 952	Very low
Observational	RR 1.02 (0.90 to 1.16)	9	402 847	Very low
Type 2 diabetes				
Observational	RR 0.98 (0.91 to 1.06)	13	351 134	Low
LDL cholesterol (mmol/L per 1% energy exchange)				
RCT	-0.055 (-0.061 to -0.050) ^a	69	1 973	High
Children				
LDL cholesterol (mmol/L)				
RCT	MD -0.13 (-0.22 to -0.03)	7	2 048	High

CHD: coronary heart disease; CI: confidence interval; CVDs: cardiovascular diseases; LDL: low-density lipoprotein; MD: mean difference; RCT: randomized controlled trial; RR: relative risk.

^a The amount of reduction in LDL cholesterol (mmol/L) for every 1% of SFA (as total energy intake) replaced.

The systematic review and meta-analysis of RCTs that assessed the effects of reducing the intake of SFA on risk of CVDs and mortality in adults (55) found that reducing SFA intake without considering replacement nutrients reduced the risk of CVDs and coronary heart disease by 17%, although the latter was not statistically significant. Reducing SFA intake did not appear to have an effect on risk of all-cause mortality, CVD mortality, coronary heart disease mortality or stroke, as assessed in RCTs.

The effect observed on CVDs persisted in various sensitivity analyses, which included only trials that aimed to reduce SFA, statistically significantly reduced SFA intake, achieved a reduction in total or LDL cholesterol, or excluded the largest trial (65). Subgroup and meta-regression analyses suggested that the degree of reduction in risk of CVDs was positively correlated with the degree of reduction in serum total cholesterol – that is, greater reductions in total cholesterol were associated with greater reductions in risk. Subgroup analysis further suggested a greater reduction in risk of CVDs with greater reductions in SFA intake.

The systematic review and meta-analysis of prospective observational studies that assessed the effects of lower compared with higher intake of SFA on risk of CVDs, type 2 diabetes and mortality in adults (56) found that, without considering replacement nutrients, lower intake of SFA was associated with a 7% reduction in risk of all-cause mortality; however, the effect was not statistically significant. No associations were observed for other outcomes.

The systematic review of RCTs and multiple regression analyses that assessed the effects on blood lipids of replacing SFA with other nutrients (58) found that reducing SFA intake resulted in reduced LDL cholesterol and general improvement in blood lipid profile.

The overall certainty in the available evidence for an effect of lower compared with higher SFA intake on outcomes in adults was based on disease and mortality outcomes and was assessed as *moderate*.¹ GRADE assessments for each outcome can be found in [Annex 6](#) – GRADE evidence profile 1.

Children

A systematic review of RCTs that assessed the effects of reducing intake of SFA on CVD risk factors and growth and development in children found that reducing SFA intake lowered LDL cholesterol by 0.13 mmol/L (**Table 1**), total cholesterol by 0.16 mmol/L (95% confidence interval [CI]: -0.25 to -0.07; seven trials, 2372 participants) and diastolic blood pressure by 1.45 mmHg (95% CI: -2.34 to -0.56; two trials, 1106 participants).² Significant effects of reducing SFA intake were not observed for HDL cholesterol, triglycerides or systolic blood pressure. Additionally, reduced SFA intake had no effect on anthropometric measures, including height (standardized mean difference [SMD] 0.09; 95% CI: -0.03 to 0.21; three trials, 1287 participants), body weight (SMD -0.03; 95% CI: -0.13 to 0.07; four trials, 1419 participants), body mass index (mean difference [MD] -0.10 kg/m²; 95% CI: -0.32 to 0.12; three trials, 1189 participants) or waist circumference (MD -0.20 cm; 95% CI: -1.38 to 0.98; two trials, 576 participants). One study reported improvements in insulin sensitivity as measured by the homeostasis model assessment of insulin resistance (HOMA-IR)³ at 9 years of age (66), and again between 15 and 20 years of age, during which HOMA-IR was on average 7.5% lower in the intervention group than in the control group (67). Two trials reported on micronutrient intake and cognitive development in children with reduced SFA intake (68-72), and one further reported on sexual maturation (73); however, data were not suitable for pooling. Neither study reported any significant difference in any of these outcomes between children with reduced SFA intake and those consuming usual levels of SFA.

The overall certainty in the available evidence for an effect of lower compared with higher SFA intake on outcomes in children was assessed as *high*. GRADE assessments for each outcome can be found in [Annex 6](#) – GRADE evidence profile 2.

SFA intake of less than 10% of total energy intake

Results for adults and children are summarized in **Table 2**.

Adults

To assess the effect of different levels of SFA intake on cardiovascular and mortality outcomes in RCTs, trials that assessed these outcomes were grouped by SFA intake achieved in the intervention group. The threshold for SFA intake achieved was stepped down in increments of 1% of total energy intake, from 13% to 7%,⁴ and each group was assessed for possible effect on outcomes via meta-analysis (55). Results of this analysis were difficult to interpret, and confidence intervals for pooled effect estimates were wide. As shown in **Table 2**, no clear effect on any cardiovascular or mortality outcome was observed when reducing SFA intake to less than 10% of total energy intake. However, significant reductions in risk of CVD mortality (RR 0.69; 95% CI: 0.51 to 0.94) and CVDs (RR 0.79; 95% CI: 0.62 to 0.99) were observed in meta-analysis of two trials with 979 participants in which SFA intake was reduced to less than 9% of total energy intake (55).

¹ Based on the grades of evidence set by the GRADE Working Group. *High* certainty means that we are very confident that the true effect lies close to that of the estimate of the effect; *moderate* certainty means that we are moderately confident in the effect estimate – the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; *low* certainty means that our confidence in the effect estimate is limited – the true effect may be substantially different from the estimate of the effect; and *very low* certainty means that we have very little confidence in the effect estimate – the true effect is likely to be substantially different from the estimate of the effect (54).

² Similar results were obtained when one study at high risk of reporting bias was excluded via sensitivity analyses: LDL cholesterol was reduced by 0.16 mmol/L (95% CI: -0.25 to -0.08; six trials, 1622 participants) and total cholesterol by 0.18 mmol/L (95% CI: -0.28 to -0.09; six trials, 1990 participants).

³ HOMA-IR is the combined outcome of serum insulin and glucose levels, and is a proxy measure of insulin sensitivity that is often used in epidemiological studies.

⁴ For example, trials were included in the 10% group if they had an intervention group that achieved an SFA intake of less than 10% of total energy intake and a control group with intake greater than 10%. Thus, the 10% group would also contain all trials included in the 9%, 8% and 7% groups.

Table 2. Summary of results from RCTs and observational studies for intake of SFA at levels less than 10% of total energy intake compared with more than 10%

Outcome	Pooled estimate (95%CI)	No. studies	No. participants	Certainty
Adults				
All-cause mortality				
RCT	RR 0.99 (0.90 to 1.09)	5	50 327	Low
Observational	RR 0.92 (0.85 to 0.99)	13	1 095 528	Low
CVD mortality				
RCT	RR 0.95 (0.67 to 1.35)	5	50 327	Very low
CVDs				
RCT	RR 0.88 (0.66 to 1.18)	5	50 327	Very low
Observational	RR 0.91 (0.82 to 1.01)	11	969 859	Very low
CHD mortality				
RCT	RR 1.05 (0.77 to 1.43)	3	50 139	Very low
CHD				
RCT	RR 0.82 (0.60 to 1.13)	3	47 936	Very low
Observational	RR 1.00 (0.87 to 1.14)	5	268 221	Low
Stroke				
RCT	RR 0.87 (0.58 to 1.33)	3	47 936	Low
Observational	RR 1.10 (0.81 to 1.50)	3	172 688	Very low
Type 2 diabetes				
Observational	RR 0.99 (0.81 to 1.21)	5	118 400	Very low
LDL cholesterol (mmol/L per 1% energy exchange)				
RCT	-0.055 (-0.061 to -0.050) ^a	69	1 973	High
Children				
LDL cholesterol (mmol/L)				
RCT	MD -0.29 (-0.38 to -0.20)	1	268	Moderate

CHD: coronary heart disease; CI: confidence interval; CVDs: cardiovascular diseases; LDL: low-density lipoprotein; MD: mean difference; RCT: randomized controlled trial; RR: relative risk.

^a The amount of reduction in LDL cholesterol (mmol/L) for every 1% of SFA (as total energy intake) replaced.

To assess the effects of consuming SFA at a level less than 10% of total energy intake compared with more than 10% in prospective observational studies, meta-analyses were limited to studies in which a comparison between those consuming less than 10% and those consuming more than 10% was reported. Meta-analyses of this subset of studies found that intake of SFA at a level of less than 10% compared with more than 10% was associated with an 8% decrease in risk of all-cause mortality and a reduction in risk of CVDs of 9%, although the latter was not statistically significant. No association was observed for other outcomes.

Effects of modifying SFA intake on blood lipids in multiple regression analyses of RCTs were observed across a wide range of SFA intakes (1.6–24.4% of total energy intake) (58). Of the 177 data points used in the multiple regression, 113 included an SFA intake component of 10% of total energy or less, including 65 data points with intakes of less than 8%. Analysis of the residuals of the regression line for LDL cholesterol indicates that the relationship between reducing SFA intake and effects on blood lipids is consistent across the entire range of SFA intakes reported in the included trials and is cumulative, and therefore suggests benefit in reducing intake to below 10% of total energy intake.

The overall certainty in the available evidence for an effect of consuming SFA at a level less than 10% of total energy intake compared with more than 10% on outcomes in adults was based on disease and mortality outcomes, and was assessed as *low*. GRADE assessments for each outcome can be found in [Annex 6](#) – GRADE evidence profile 3.

Children

The intervention group in one trial achieved a reduction in SFA intake to 9% of total energy intake, and demonstrated greater reductions in total cholesterol (MD -0.29 mmol/L; 95% CI: -0.40 to -0.18) and LDL cholesterol (MD -0.29 mmol/L; 95% CI: -0.38 to -0.20) than in the remaining trials, in which the intake achieved was above 10% of total energy intake, and which showed mean reductions in total cholesterol of -0.15 mmol/L (95% CI: -0.23 to -0.06) and LDL cholesterol of -0.13 mmol/L (95% CI: -0.19 to -0.06). A non-significant effect was observed for body weight.

The overall certainty in the available evidence for an effect of consuming SFA at a level less than 10% of total energy intake compared with more than 10% on outcomes in children was assessed as *high*. GRADE assessments for each outcome can be found in [Annex 6](#) – GRADE evidence profile 4.

Replacement of SFA with other macronutrients

Results for adults and children are summarized in [Table 3](#).

Adults

Subgroup analysis was used to assess the effects of replacing SFA with polyunsaturated fatty acids, monounsaturated fatty acids, carbohydrates or protein on cardiovascular and mortality outcomes (55). Trials were grouped based on whether the difference between the intervention and control groups achieved statistical significance ($P < 0.05$), regardless of whether or not the replacement macronutrient constituted the main replacement for SFA.¹

Subgroup analysis found that replacing SFA with polyunsaturated fatty acids reduced the risk of CVDs by 21% and the risk of coronary heart disease by 24%, although the latter was not statistically significant. Replacing SFA with polyunsaturated fatty acids did not appear to have an effect on risk of all-cause mortality, CVD mortality, coronary heart disease mortality or stroke as assessed in RCTs. No significant effect on any cardiovascular or mortality outcome was observed when replacing SFA with monounsaturated fatty acids, carbohydrates or protein; however, only one small trial with olive oil as an intervention was included in the monounsaturated fatty acids subgroup. Furthermore, there was insufficient information on the composition of carbohydrates used as replacements in the trials included in the carbohydrate subgroup to assess whether different types of carbohydrates might have differentially affected pooled effect estimates for cardiovascular or mortality outcomes.

The systematic review and meta-analysis of prospective observational studies assessed the effects of replacing SFA with other macronutrients on risk of CVD, type 2 diabetes and mortality in adults via modelling (56) found the following.

- ▶ Replacing SFA with polyunsaturated fatty acids was associated with a 15% reduction in risk of all-cause mortality, a 10% reduction in risk of CVDs and an 11% reduction in risk of coronary heart disease, although the association observed with CVDs was not statistically significant.
- ▶ Replacing SFA with monounsaturated fatty acids from plant-based sources was associated with a 15% reduction in risk of all-cause mortality, a 10% reduction in risk of CVDs and a 17% reduction in risk of coronary heart disease, although the association observed with coronary heart disease was not statistically significant. A 16% reduction in risk of all-cause mortality was also observed when replacing SFA with monounsaturated fatty acids from unspecified sources. No associations were observed between replacing SFA with monounsaturated fatty acids from animal-based sources and all-cause mortality or coronary heart disease (the only two outcomes for which data were identified).
- ▶ Replacing SFA with carbohydrates from unspecified sources was associated with an 8% reduction in risk of all-cause mortality, and replacing SFA with whole grains or foods described by the authors of the individual studies as having a low glycaemic index was associated with a 6% reduction in risk of coronary heart disease. Replacing SFA with free sugars or foods described by the authors of the individual studies as having a high glycaemic index was associated with an 8% increase in risk of coronary heart disease, although the association was not statistically significant.

¹ Trials in which SFA were replaced by more than one nutrient at statistically significant levels are therefore included in more than one subgroup.

- ▶ Replacing SFA with protein from unspecified or animal sources was associated with a 26% and 31% increase, respectively, in the risk of coronary heart disease. No association was observed between replacing SFA with protein from plant sources and coronary heart disease.

Table 3. Summary of results from RCTs and observational studies for replacing SFA in the diet with other macronutrients^a

Outcome	Pooled estimate (95%CI)	No. studies	No. participants	Certainty
REPLACEMENT WITH POLYUNSATURATED FATTY ACIDS				
Adults				
All-cause mortality				
RCT	RR 0.96 (0.82 to 1.13)	7	4 328	Low
Observational	RR 0.85 (0.75 to 0.97)	5	606 552	Low
CVD mortality				
RCT	RR 0.95 (0.73 to 1.25)	7	4 251	Very low
CVDs				
RCT	RR 0.79 (0.62 to 1.00)	8	4 353	Low
Observational	RR 0.90 (0.81 to 1.00)	5	600 850	Very low
CHD mortality				
RCT	RR 0.98 (0.74 to 1.28)	7	4 298	Low
CHD				
RCT	RR 0.76 (0.57 to 1.00)	7	3 895	Low
Observational	RR 0.89 (0.81 to 0.98)	17	448 921	Low
Stroke				
RCT	RR 0.68 (0.37 to 1.27)	4	1 706	Low
Observational	No studies identified			
LDL cholesterol (mmol/L per 1% energy exchange)				
RCT	-0.055 (-0.061 to -0.050) ^b	69	1 973	High
Children				
LDL cholesterol (mmol/L)				
RCT	MD -0.29 (-0.38 to -0.20)	1	268	Moderate
REPLACEMENT WITH MONOUNSATURATED FATTY ACIDS				
Adults				
All-cause mortality				
RCT (olive oil)	RR 3.0 (0.33 to 26.99)	1	52	Very low
Observational (plant)	RR 0.85 (0.82 to 0.88)	4	628 803	Moderate
Observational (animal)	RR 1.00 (0.83 to 1.20)	2	535 425	Very low
Observational	RR 0.84 (0.75 to 0.95)	5	606 552	Low
CVD mortality				
RCT (olive oil)	RR 3.0 (0.33 to 26.99)	1	52	Very low
CVDs				
RCT (olive oil)	RR 3.0 (0.33 to 26.99)	1	52	Very low
Observational (plant)	RR 0.90 (0.84 to 0.96)	3	614 498	Moderate
Observational	RR 0.94 (0.87 to 1.02)	5	600 850	Very low
CHD mortality				
RCT (olive oil)	RR 3.0 (0.33 to 26.99)	1	52	Very low

Outcome	Pooled estimate (95%CI)	No. studies	No. participants	Certainty
CHD				
RCT (olive oil)	RR 3.0 (0.33 to 26.99)	1	52	Very low
Observational (plant)	RR 0.83 (0.69 to 1.01)	2	93 384	Very low
Observational (animal)	RR 1.06 (0.80 to 1.41)	2	93 385	Very low
Observational	RR 1.00 (0.82 to 1.21)	4	167 855	Very low
Stroke				
	No studies identified			
LDL cholesterol (mmol/L per 1% energy exchange)				
RCT	-0.042 (-0.047 to -0.037) ^b	69	1 973	High
Children				
LDL cholesterol (mmol/L)				
RCT	MD -0.26 (-0.41 to -0.11)	7	176	Moderate
REPLACEMENT WITH CARBOHYDRATES				
Adults				
All-cause mortality				
RCT	RR 0.97 (0.90 to 1.04)	6	53 669	Moderate
Observational	RR 0.92 (0.86 to 0.99)	5	277 553	Low
CVD mortality				
RCT	RR 0.99 (0.85 to 1.14)	5	51 232	Low
CVDs				
RCT	RR 0.84 (0.67 to 1.06)	5	51 232	Low
Observational	RR 0.98 (0.90 to 1.07)	6	274 970	Very low
CHD mortality				
RCT	RR 0.99 (0.85 to 1.16)	2	50 868	Low
CHD				
RCT	RR 0.93 (0.78 to 1.11)	4	51 104	Low
Observational	RR 0.98 (0.88 to 1.09)	6	313 066	Very low
Observational (SDC)	RR 0.94 (0.89 to 0.99)	7	225 278	Low
Observational (MDC)	RR 1.03 (0.79 to 1.33)	3	93 963	Very low
Observational (RDC)	RR 1.08 (0.99 to 1.17)	7	225 278	Very low
Stroke				
RCT	RR 0.73 (0.29 to 1.87)	3	49 066	Low
Observational	No studies identified			
LDL cholesterol (mmol/L per 1% energy exchange)				
RCT	-0.033 (-0.039 to -0.027) ^b	69	1 973	High
Children				
LDL cholesterol				
	No studies identified			
REPLACEMENT WITH PROTEIN				
Adults				
All-cause mortality				
RCT	RR 0.97 (0.90 to 1.04)	5	53 614	Moderate
Observational	No studies identified			
CVD mortality				
RCT	RR 0.99 (0.86 to 1.14)	4	51 177	Low

Outcome	Pooled estimate (95%CI)	No. studies	No. participants	Certainty
CVDs				
RCT	RR 0.97 (0.91 to 1.03)	4	51 177	Moderate
Observational	No studies identified			
CHD mortality				
RCT	RR 0.99 (0.85 to 1.16)	2	50 868	Low
CHD				
RCT	RR 0.96 (0.88 to 1.05)	3	51 044	Moderate
Observational	RR 1.26 (1.06 to 1.50)	2	40 319	Very low
Observational (plant)	RR 0.83 (0.61 to 1.12)	2	40 319	Very low
Observational (animal)	RR 1.31 (1.14 to 1.50)	2	40 319	Low
Stroke				
RCT	RR 0.65 (0.15 to 2.75)	2	49 011	Very low
Observational	No studies identified			
LDL cholesterol				
	No studies identified ^c			
Children				
LDL cholesterol				
	No studies identified			

CHD: coronary heart disease; CI: confidence interval; CVDs: cardiovascular diseases; LDL: low-density lipoprotein; MD: mean difference; MDC: moderately digestible carbohydrates (moderate glycaemic index); RCT: randomized controlled trial; RDC: rapidly digestible carbohydrates (free sugars and high glycaemic index); RR: relative risk; SDC: slowly digestible carbohydrates (whole grains and low glycaemic index).

^a Unless otherwise specified (i.e. plant, animal, SDC, MDC, RDC), replacement macronutrients were of unspecified origin, although polyunsaturated fatty acids were predominantly plant-based for all outcomes, as were monounsaturated fatty acids for LDL cholesterol.

^b The amount of reduction in LDL cholesterol (mmol/L) for every 1% of SFA (as total energy intake) replaced.

^c Because studies were included in the blood lipids analyses (58) only if protein intakes were held constant, assessment of possible effects on the blood lipid profile of replacing SFA with protein intake was not possible.

Multiple regression analysis of data from RCTs assessing blood lipids found that, for every 1% of total energy intake as SFA replaced with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates, LDL cholesterol was significantly lowered by 0.055 mmol/L (95% CI: -0.061 to -0.050), 0.042 mmol/L (95% CI: -0.047 to -0.037) and 0.033 mmol/L (95% CI: -0.039 to -0.027), respectively (58). Replacing SFA with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates also lowered total cholesterol; replacing SFA with polyunsaturated fatty acids or monounsaturated fatty acids additionally lowered triglycerides, the total cholesterol to HDL cholesterol ratio and the LDL cholesterol to HDL cholesterol ratio. Replacement with polyunsaturated fatty acid had the greatest effect on all outcomes. HDL cholesterol was slightly reduced with all replacements, and a small increase in triglycerides was observed when SFA were replaced with carbohydrates.

The overall certainty in the available evidence for an effect of replacing SFA with various macronutrients was based on disease and mortality outcomes, and was assessed as *moderate* for replacement with plant-based monounsaturated fatty acids; *low* for replacement with polyunsaturated fatty acids, monounsaturated fatty acids from unspecified sources, whole grains or foods described by the authors of the individual studies as having a low glycaemic index, carbohydrates from unspecified sources, or animal-based protein; and *very low* for replacement with free sugars or foods described by the authors of the individual studies as having a high glycaemic index and protein from unspecified sources. GRADE assessments for each outcome for each replacement nutrient can be found in [Annex 6](#) – GRADE evidence profiles 5, 7, 9 and 10.

Children

Complete dietary information was not available for all RCTs, but two trials reported replacement of SFA with unsaturated fatty acids. In one trial in which SFA were replaced almost entirely with polyunsaturated fatty acids, LDL cholesterol was reduced by 0.29 mmol/L (95% CI: -0.38 to -0.20) and total cholesterol by 0.29 mmol/L (95% CI: -0.40 to -0.18); there was a non-significant effect on body weight. In the second trial in which SFA were replaced predominantly with monounsaturated fatty acids (80% monounsaturated fatty acids, 20% polyunsaturated fatty acids), LDL cholesterol was reduced by 0.26 mmol/L (95% CI: -0.52 to -0.14) and total cholesterol by 0.33 mmol/L (95% CI: -0.41 to -0.11). In subgroup analysis, these two trials when combined showed stronger reductions in LDL cholesterol (MD -0.28 mmol/L; 95% CI: -0.36 to -0.20) and total cholesterol (MD -0.30 mmol/L; 95% CI: -0.39 to -0.21) than in the remaining trials, which, when pooled, showed mean reductions in LDL cholesterol of -0.07 mmol/L (95% CI: -0.15 to 0.01) and total cholesterol of -0.10 mmol/L (95% CI: -0.15 to -0.04) (60). No studies were identified that allowed assessment of the effects of replacing SFA with carbohydrates or protein directly in children. Therefore, results were extrapolated from adults without downgrading for indirectness.

The overall certainty in the available evidence for an effect on outcomes in children of replacing SFA with polyunsaturated fatty acids or monounsaturated fatty acids was assessed as *high*. GRADE assessments for replacing SFA with polyunsaturated fatty acids or monounsaturated fatty acids can be found in [Annex 6](#) – GRADE evidence profiles 6 and 8.

Additional evidence reviewed

Additional evidence was reviewed and is summarized below, although the NUGAG Subgroup on Diet and Health did not use it to support the formulation of recommendations for the reasons given in the section *Interpreting the evidence for SFA*.

Tissue measurements of SFA intake

In addition to studies in which SFA intake was self-reported (via 24-hour recall, food diaries, food frequency questionnaires, etc.), the systematic review of observational studies (56) also identified studies in which intake was assessed by measuring total SFA in tissues of the body (e.g. plasma phospholipids, red blood cells, fat biopsies). Meta-analyses of observational studies assessing total SFA intake via tissue measurements found that lower intake is associated with a 31% reduction in the risk of coronary heart disease (95% CI: 0.51 to 0.91) and a 23% reduction in the risk of type 2 diabetes (95% CI: 0.63 to 0.94). Several studies also assessed the intake of individual SFA via tissue measurement, as described below.

Individual SFA intake

The systematic review and meta-analyses of observational studies identified studies that assessed individual SFA intake via tissue measurement (56), including lauric acid (12:0), myristic acid (14:0), pentadecanoic acid (15:0), palmitic acid (16:0), heptadecanoic acid (17:0), stearic acid (18:0) and very long chain fatty acids (i.e. longer than 18 carbons) of different length. Data for all-cause mortality and CVDs were limited, and consistent associations were not observed between individual SFA and these outcomes. Increased intake of pentadecanoic acid, heptadecanoic acid and very long chain SFA were strongly associated with reduced risk of type 2 diabetes, whereas increased intake of palmitic acid was strongly associated with increased risk of type 2 diabetes.

The effects of individual SFA (lauric acid, myristic acid, palmitic acid and stearic acid) on blood lipids were also assessed in the systematic review and multiple regression analyses of blood lipids, as the effects of isocalorically replacing a mixture of carbohydrates with these individual SFA (58). Replacement of carbohydrates with lauric acid, myristic acid or palmitic acid all significantly raised total, LDL and HDL cholesterol (with the magnitude of effect decreasing in the order myristic > palmitic > lauric), and lowered triglyceride levels and the triglyceride to HDL cholesterol ratio. Lauric acid lowered the total cholesterol to HDL cholesterol ratio and the LDL cholesterol to HDL cholesterol ratio. Stearic acid did not have a significant effect on any outcome assessed. Although differences were observed in effects of the individual SFA on the lipid profile, reported intakes of lauric acid and myristic acid in the individual trials included in the regression analysis were low (mean of 1.2% of total energy intake), which may have influenced the results.

Interpreting the evidence for SFA

Several observations were made in interpreting the results of the systematic reviews, some based directly on data from the review and others supported by background questions and information that helps to establish the context for the recommendation (54). They are summarized below.

Replacement nutrients. The NUGAG Subgroup on Diet and Health reaffirmed what has been previously noted in the literature, that is, associations between lower SFA intake and relevant health outcomes are limited or generally not observed when the nutrients replacing SFA are not specified. In the systematic reviews assessed for this guideline, the only effect observed when replacement nutrients were not accounted for was on CVDs as assessed in RCTs; no effects were seen for other disease outcomes. Only when specific replacement nutrients were assessed were significant associations observed. This suggests that, in studies where no association is observed between lower SFA intake and reduced risk of disease, the nutrients replacing SFA may themselves increase the risk of disease and therefore may mask any benefit of reducing SFA intake. Consequently, choice of replacement nutrient is key to obtaining a health benefit from reducing SFA intake.

Extrapolating results from adults to children. Although ample evidence was available from studies in children, the NUGAG Subgroup on Diet and Health considered the available evidence for cardiovascular, mortality and blood lipid outcomes from adults to also be relevant to children, given that preclinical signs of atherosclerosis in the form of atherosclerotic lesions in the aorta and coronary arteries can begin to appear in childhood (34, 35); these changes are positively associated with abnormal blood lipid levels and other CVD risk factors (36, 37). Therefore, in formulating recommendations for children, the NUGAG Subgroup on Diet and Health considered not only the evidence from direct assessments in children but also the evidence for adults, without downgrading for indirectness.

Tissue measurement of SFA intake. Although data were available for both self-reported intakes of SFA and estimates of intake based on tissue levels of SFA, there were more studies that included self-reported data on total SFA intake, and these data were generally more robust. In addition, although assessment of SFA in tissues can be a fairly reliable indicator of dietary intake, the potential contribution of endogenous synthesis cannot be consistently estimated. Therefore, using a conservative approach, the evidence from tissue levels was not included in the evidence base supporting the recommendations for SFA intake, even though these results are in line with the results and conclusions from self-reported intakes, as well as the other reviews assessed for these guidelines.

Individual SFA. Significant associations were observed between certain individual SFA (as assessed by tissue levels) and type 2 diabetes, and differences were observed between individual SFA with respect to their effects on blood lipids, with the exception of stearic acid (which showed little effect on blood lipids). However, results observed for associations between individual SFA and disease outcomes were consistent with the results observed for total SFA – that is, none of the statistically non-significant effects observed for individual SFA suggested benefit with increased intake, but some suggested harm. In addition, as noted above, the NUGAG Subgroup on Diet and Health had concerns with tissue measurements because of the inability to ensure consistent measurement of endogenous synthesis of SFA, as well as with the low reported intakes of lauric acid and myristic acid in the blood lipids analyses. Finally, there was no evidence available from RCTs assessing the effects of consuming individual SFA on disease outcomes. It was therefore concluded that further research is needed before recommendations on the intake of individual SFA can be made.

TFA

Three systematic reviews were commissioned to assess the effects of reducing or lower TFA intake on risk of mortality and CVDs in adults and children.

Systematic review characteristics

Review 1

A systematic review of prospective observational studies that assessed the effects of higher compared with lower intake of TFA on risk of mortality, CVDs and type 2 diabetes in adults identified 112 publications involving 3 696 568 participants (56). Many publications reported on the same cohorts, on both SFA intake and TFA intake, and on multiple relevant outcomes. The majority of studies reported on “total” TFA intake, which is the total amount of TFA consumed from both industrially produced sources (e.g. partially hydrogenated oils) and ruminant sources (i.e. TFA from meat or dairy products from ruminant animals). A small number of studies assessed the health effects of industrially produced and ruminant TFA separately. Study locations were geographically diverse (38% North America, 28% Europe, 16% Asia, 4% Australia, 4% UK, and the remainder from the eastern Mediterranean region or multinational cohorts). Total TFA intake across studies ranged from 0.7% to 2.9% of total energy intake. The highest weighted mean intakes observed for industrially produced and ruminant TFA were 1.9% and 0.9% of total energy intake, respectively.

Review 2

A systematic review and meta-regression of RCTs that assessed the effects of modifying intake of TFA on blood lipids in adults identified 16 RCTs with 680 participants (59). Sixteen trials contributed to an analysis of the effects of TFA, 13 to the effects of industrially produced TFA, and four to the effects of ruminant TFA.¹ The RCTs included in this review were all strictly controlled dietary trials, 14–56 days in duration, in which protein and cholesterol intakes were held constant, and intervention groups received food enriched in industrially produced or ruminant TFA, compared with a control group with low TFA intake. Outcomes assessed included total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, LDL cholesterol to HDL cholesterol ratio, total cholesterol to HDL cholesterol ratio, ApoB and ApoA-I. Trials were conducted in Canada, Denmark, Finland, Netherlands (Kingdom of the), Norway, the United Kingdom and the United States. Intake of TFA ranged from 0% to 10.9% of total energy intake across the included trials. Using regression analysis – in which the change in TFA intake served as the independent variable and the change in a given blood lipid or lipid ratio as the dependent variable – a model was developed that provides an estimate of the effect (i.e. regression coefficient) on a given blood lipid when 1% of total energy intake as total, industrially produced or ruminant TFA is isocalorically exchanged with polyunsaturated fatty acids, monounsaturated fatty acids, carbohydrates or SFA.

Review 3

A systematic review of RCTs and prospective observational studies that assessed the effects of reducing or lower intake of TFA on CVD risk factors and growth and development in children did not identify any studies meeting the inclusion/exclusion criteria (60).

Results of systematic reviews

Because no studies conducted in children were identified, results from adults were extrapolated for all questions, without downgrading for indirectness.

Lower compared with higher intake of TFA

Results are summarized in **Table 4**.

¹ One trial assessed the effects of both industrially produced and ruminant TFA.

Table 4. Summary of results for lower compared with higher intake of TFA^a

Outcome	Pooled estimate (95%CI)	No. studies	No. participants	Certainty
All-cause mortality				
Total TFA	RR 0.90 (0.83 to 0.98)	6	673 830	Moderate
Industrially produced TFA ^b	RR 0.70 (0.34 to 1.43)	3	5 427	Very low
Ruminant TFA ^b	RR 0.81 (0.58 to 1.15)	3	5 427	Very low
CVDs				
Total TFA	RR 0.88 (0.80 to 0.96)	6	675 673	Low
Industrially produced TFA ^b	RR 1.92 (0.53 to 7.01)	2	3 439	Very low
Ruminant TFA ^b	RR 2.08 (0.64 to 6.74)	2	3 439	Very low
CHD				
Total TFA	RR 0.86 (0.79 to 0.92)	7	185 664	Moderate
Industrially produced TFA	RR 0.78 (0.67 to 0.91)	3	177 090	Low
Ruminant TFA	RR 1.08 (0.87 to 1.33)	4	177 659	Very low
Stroke				
Total TFA	RR 0.92 (0.68 to 1.25)	3	257 437	Very low
Type 2 diabetes				
Total TFA	RR 0.95 (0.86 to 1.05)	3	275 402	Low
LDL cholesterol (units)				
Total TFA	-0.048 (-0.055 to -0.041) ^c	16	1 338	High

CHD: coronary heart disease; CI: confidence interval; CVDs: cardiovascular disease; LDL: low-density lipoprotein; RR: relative risk; TFA: *trans*-fatty acids.

^a All results are from observational studies except for LDL cholesterol, which is from RCTs.

^b Dietary intake assessed by tissue measurements.

^c The reduction in the amount of LDL cholesterol (mmol/L) for every 1% of TFA (as total energy intake) replaced.

The systematic review and meta-analysis of prospective observational studies that assessed the effects of lower compared with higher intake of TFA on risk of CVDs, type 2 diabetes and mortality in adults (56) found that, without considering replacement nutrients, lower intake of total TFA was associated with a 10% reduction in risk of all-cause mortality, a 12% reduction in risk of CVDs and a 14% reduction in risk of coronary heart disease. Statistically significant dose–response relationships were observed between total TFA intake and all-cause mortality and coronary heart disease: for every 2% increase in total TFA intake as a percentage of total energy, the risk of all-cause mortality increased by 14% (95% CI: 1.04 to 1.26) and the risk of coronary heart disease increased by 25% (95% CI: 1.15 to 1.36). In the relatively small number of studies that assessed the effects of industrially produced TFA separately from ruminant TFA, the only association observed was between industrially produced TFA and coronary heart disease, where a 22% reduction in risk was observed with lower intake.¹ The systematic review of RCTs and multiple regression analyses that assessed the effects on blood lipids of replacing TFA with different nutrients (59) found that reducing TFA intake resulted in reduced LDL cholesterol and general improvement in blood lipid profile.

The overall certainty in the available evidence for an effect of lower compared with higher total TFA intake in adults on critical outcomes was based on disease and mortality outcomes and was assessed as *moderate*. GRADE assessments for each outcome can be found in [Annex 6](#) – GRADE evidence profile 11.

TFA intake of less than 1% of total energy intake

Results are summarized in [Table 5](#).

¹ Results for effects of industrially produced and ruminant TFA on all-cause mortality and CVDs came from studies in which dietary intake was assessed by tissue measurements. Results for all other analyses in observational studies (including for effects of industrially produced and ruminant TFA on coronary heart disease) came from studies in which dietary intake was self-reported.

Table 5. Summary of results for intake of total TFA at levels less than 1% of total energy intake compared with more than 1%^a

Outcome	Pooled estimate (95% CI)	No. studies	No. participants	Certainty
All-cause mortality	RR 0.90 (0.81 to 1.00)	3	127 159	Very low
CVDs	RR 0.83 (0.75 to 0.93)	2	126 233	Low
CHD	RR 0.88 (0.80 to 0.96)	4	67 739	Low
Stroke	No studies identified			
Type 2 diabetes	RR 0.98 (0.82 to 1.18)	3	81 231	Low
LDL cholesterol (units)	-0.048 (-0.055 to -0.041) ^b	16	1 338	High

CHD: coronary heart disease; CI: confidence interval; CVDs: cardiovascular diseases; LDL, low-density lipoprotein; RR: relative risk.

^a All results are for total TFA from observational studies except for LDL cholesterol, which is from RCTs.

^b The reduction in the amount of LDL cholesterol (mmol/L) for every 1% of TFA (as total energy intake) replaced.

To assess the effects of consuming TFA at a level less than 1% of total energy intake compared with more than 1% in prospective observational studies, meta-analyses were limited to studies in which a comparison between those consuming less than 1% and those consuming more than 1% was reported. Meta-analyses of this subset of studies found that intake of TFA at a level of less than 1% compared with more than 1% was associated with a 10% decrease in risk of all-cause mortality, a 17% reduction in risk of CVDs and a 12% reduction in risk of coronary heart disease. No association was observed for type 2 diabetes, and no studies meeting the threshold requirements were identified for stroke. Data were too limited from studies reporting separately on industrially produced TFA and ruminant TFA to be able to assess threshold effects in a meaningful way.

Effects of modifying TFA intake on blood lipids in meta-regression analysis were observed across a wide range of TFA intakes (0–10.9% of total energy intake) (59). Analysis of the residuals of the regression line for LDL cholesterol indicates that the relationship between reducing or increasing TFA intake and effects on blood lipids is consistent across the entire range of TFA intakes reported in the included studies and is cumulative, and therefore suggests benefit in reducing intake to below 1% of total energy intake.

The overall certainty in the available evidence for an effect on critical outcomes of consuming TFA at a level less than 1% of total energy intake compared with more than 1% in adults was based on disease and mortality outcomes, and was assessed as *low*. GRADE assessments for each outcome can be found in [Annex 6](#) – GRADE evidence profile 12.

Replacement of TFA with other macronutrients

Results are summarized in **Table 6**.

The systematic review and meta-analysis of prospective observational studies assessed the effects of replacing TFA with other macronutrients on risk of CVD, type 2 diabetes and mortality in adults via modelling (56) found the following.

- ▶ Replacing TFA with polyunsaturated fatty acids was associated with a 28% reduction in risk of type 2 diabetes.
- ▶ Replacing TFA with monounsaturated fatty acids from plant-based sources was associated with a 10% reduction in risk of all-cause mortality, and a 20% reduction in risk of coronary heart disease. No associations were observed between replacing TFA with monounsaturated fatty acids from animal-based sources and coronary heart disease (the only outcome for which data were identified).
- ▶ Replacing TFA with carbohydrates from unspecified sources was associated with a 29% reduction in risk of type 2 diabetes.
- ▶ No associations were observed between replacing TFA with SFA and risk of all-cause mortality, CVDs or coronary heart disease.

Table 6. Summary of results for replacing TFA in the diet with other macronutrients^a

Outcome	Pooled estimate (95%CI)	No. studies	No. participants	Certainty
REPLACEMENT WITH POLYUNSATURATED FATTY ACIDS				
Type 2 diabetes	RR 0.72 (0.52 to 0.99)	2	295 726	Very low
LDL cholesterol (units)	-0.048 (-0.055 to -0.041) ^b	16	669	High
REPLACEMENT WITH MONOUNSATURATED FATTY ACIDS				
All-cause mortality				
Plant-based	RR 0.90 (0.85 to 0.96)	2	93 378	Low
CVDs				
Plant-based	RR 0.97 (0.71 to 1.32)	2	93 378	Very low
CHD				
Plant-based	RR 0.80 (0.70 to 0.92)	2	93 384	Low
Animal-based	RR 0.89 (0.78 to 1.03)	2	93 384	Very low
LDL cholesterol (units)	-0.035 (-0.042 to -0.028) ^b	16	669	High
REPLACEMENT WITH CARBOHYDRATES				
All-cause mortality	No studies identified			
CVDs	No studies identified			
CHD				
RDC	RR 0.95 (0.80 to 1.13)	2	127 536	Very low
Type 2 diabetes	RR 0.71 (0.60 to 0.84)	2	106 543	Moderate
LDL cholesterol (units)	-0.026 (-0.033 to -0.019) ^b	16	669	High
REPLACEMENT WITH PROTEIN				
No studies identified for any outcome				
REPLACEMENT WITH SATURATED FATTY ACIDS				
All-cause mortality	RR 0.92 (0.82 to 1.03)	2	647 353	Very low
CVDs	RR 0.93 (0.83 to 1.04)	2	647 353	Very low
CHD	RR 0.97 (0.86 to 1.09)	2	127 536	Very low
Stroke	No studies identified			
LDL cholesterol (units)	0.010 (0.003 to 0.017) ^b	16	669	High

CHD: coronary heart disease; CI: confidence interval; CVDs: cardiovascular diseases; LDL: low-density lipoprotein; RDC: rapidly digestible carbohydrates (free sugars and high glycaemic index); RR: relative risk.

^a All results are for total TFA from observational studies except for LDL cholesterol, which is from RCTs. Unless otherwise noted (i.e. plant-based, animal-based, RDC), macronutrients used as replacements were of unspecified origin.

^b The reduction in the amount of LDL cholesterol (mmol/L) for every 1% of TFA (as total energy intake) replaced.

It was not possible to assess threshold effects for industrially produced TFA and ruminant TFA separately because the available data were too limited.

Regression analysis of RCTs found that, for every 1% of total energy intake as TFA replaced with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates, LDL cholesterol was significantly lowered, by 0.048 mmol/L (95% CI: -0.055 to -0.041), 0.035 mmol/L (95% CI: -0.042 to -0.028) and 0.026 mmol/L (95% CI: -0.033 to -0.019), respectively. Replacing TFA with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates also lowered total cholesterol. Replacing TFA with SFA resulted in raised LDL cholesterol (0.010 mmol/L; 95% CI: 0.003 to 0.017) and total cholesterol. Replacing TFA with polyunsaturated fatty acids or monounsaturated fatty acids also lowered triglycerides. Replacing TFA with polyunsaturated fatty acids, monounsaturated fatty acids, carbohydrates or SFA lowered the total cholesterol to HDL cholesterol ratio and the LDL cholesterol to HDL cholesterol ratio, and raised HDL cholesterol; replacement with polyunsaturated fatty acids had the greatest effect on all outcomes (59).

The overall certainty in the available evidence for an effect of replacing TFA with various macronutrients was based on disease and mortality outcomes and was assessed as *moderate* for replacement with carbohydrates; *low* for replacement with plant-based monounsaturated fatty acids; and *very low* for replacement with polyunsaturated fatty acids, animal-based monounsaturated fatty acids, free sugars and foods described by the authors of the individual studies as having a high glycaemic index, and SFA. GRADE assessments for each outcome for each replacement nutrient can be found in [Annex 6](#) – GRADE evidence profiles 13–16.

Interpreting the evidence for TFA

Several observations were made in interpreting the results of the systematic reviews, some based directly on data from the review and others supported by background questions and information that helps to establish the context for the recommendations (54). They are summarized below.

Total, industrially produced and ruminant TFA. As per the original PICO questions, results were generated for total TFA intake,¹ and separately for industrially produced and ruminant TFA intake for both the meta-analyses of observational studies and regression analyses of RCTs and blood lipids. In the meta-analyses of prospective observational studies, results for total and industrially produced TFA intake were similar for risk of coronary heart disease, but not for all-cause mortality or CVDs, for which only total TFA intake demonstrated a significant association between reduced intake and reduced risk. No associations were observed for the analysis of studies reporting effects of ruminant TFA intake.² In the regression analysis of RCTs, reduced intake of total TFA or industrially produced TFA was associated with a beneficial effect on the blood lipid profile, regardless of which nutrient was used as a replacement. A significant effect of reducing ruminant TFA intake on lowering LDL cholesterol was only observed when ruminant TFA were replaced with polyunsaturated fatty acids. For all other blood lipid outcomes, results were not statistically significant; however, they were similar to those for total and industrially produced TFA in both direction and magnitude.³

Intake of ruminant TFA in the studies included in the analyses of both prospective observational studies and RCTs was very low relative to intake of industrially produced TFA, and the difference between lower and higher intakes was very small. The available evidence suggests that differences in effects on health outcomes between ruminant, industrially produced and total TFA observed in many studies may be due to differences in the amount of TFA being consumed rather than differences between types of TFA. To further assess the nature of the observed differences, post hoc analyses were conducted in which the intakes observed in the studies of ruminant TFA were approximated in the studies of total TFA, such that the highest intakes of total TFA were limited to 0.7–1.3% of total energy intake and then compared with the lowest intakes. When total TFA intake was assessed in this manner, the associations and dose–response relationships originally observed between lower TFA intake and reduced risk of all-cause mortality remained, but those for CVDs and coronary heart disease were no longer present. Based on these observations, the NUGAG Subgroup on Diet and Health concluded that, at the low levels of ruminant TFA intake in the small number of studies, the difference between the lowest and highest intakes was not large enough to allow reliable comparisons. It was further noted that in the very few studies assessing LDL cholesterol in which the highest levels of ruminant TFA intake were closer to those observed for industrially produced and total TFA, the effects of

¹ For the meta-analysis of prospective cohort studies, separate analyses were performed for total, industrially produced and ruminant TFA, because most studies did not differentiate between industrially produced and ruminant TFA and only reported results for total TFA intake. For the regression analysis of total TFA, all trials that assessed either total, industrially produced or ruminant TFA intake were included in a single analysis.

² Results for effects of industrially produced and ruminant TFA on all-cause mortality and CVDs came from studies in which dietary intake was assessed by tissue measurements. Although the NUGAG Subgroup on Diet and Health expressed concerns with the assessment of dietary intake of SFA via tissue measurements, the correlation between TFA measured in tissue and dietary intake has generally been shown to be stronger (74). Results for effects of industrially produced and ruminant TFA on coronary heart disease came from studies in which dietary intake was self-reported.

³ The two trials that reported ruminant TFA intakes at levels more similar to the intakes reported for industrially produced TFA (i.e. >2% of total energy intake) reported greater reductions in LDL cholesterol (75, 76).

ruminant TFA intake were similar to, or more pronounced than, those observed for industrially produced and total TFA.¹

It was therefore determined that the available evidence did not support making a distinction between industrially produced and ruminant TFA. Because the vast majority of studies included in the systematic reviews reported results for total TFA intake (which includes intake from industrially produced and ruminant sources), it was considered appropriate to consider only evidence from total TFA when formulating the recommendations on TFA intake.

Conjugated linoleic acid (CLA). CLA is found in fat from ruminant animals and represents several isomers of linoleic acid in which the two double bonds are conjugated (i.e. separated by a single bond), resulting in a three-dimensional shape that is different from most other TFA isomers. As CLA contains both *cis* and *trans* configurations, RCTs assessing CLA as it naturally occurs in foods (i.e. not from supplements) were included in the systematic review and regression analyses of blood lipids,² although the number of such trials was limited and intakes of CLA were very low. Nevertheless, results of these trials provided no indication that CLA had an effect on blood lipids that was significantly different from other TFA when consumed at similar levels. The NUGAG Subgroup on Diet and Health therefore concluded that, because CLA contributes to total TFA intake, it should be included in the definition of TFA as used in the recommendations on TFA.

¹ This approach is further supported by results of several studies that were identified in the informal updating of the literature search, which were unpublished at the time the evidence was reviewed for this guideline (and thus have not been included in the systematic review of RCTs assessing blood lipid outcomes). These studies included two RCTs in which diets enriched with ruminant TFA were shown to significantly raise LDL cholesterol not only compared with a control diet but also compared with a diet enriched with industrially produced TFA (77, 78). A 2020 systematic review of RCTs also concluded that ruminant TFA caused greater increases in LDL cholesterol than industrially produced TFA (79).

² Although a large number of studies on the health effects of CLA supplements have been published, the amounts provided in supplements are generally well above what is consumed naturally in foods. Assessment of this separate body of evidence was considered to be beyond the scope of this guideline.

Evidence to recommendations

In translating the evidence into recommendations, the NUGAG Subgroup on Diet and Health assessed the evidence in the context of the certainty in the evidence, desirable and undesirable effects of the interventions, the priority of the problem that the interventions would address, values and preferences related to the effects of the interventions in different settings, the feasibility and acceptability of implementing the interventions in different settings, the potential impact on equity and human rights, and the cost of the options available to public health officials and programme managers in different settings.

Because the recommended “interventions” in this guideline are in fact dietary goals, they can be translated into policies and actions in a number of ways, including behaviour change interventions, fiscal policies, regulation of marketing, labelling schemes and reformulation of manufactured products, among others. Because each of these interventions has its own substantial evidence base (which was not reviewed by the NUGAG Subgroup on Diet and Health) and requires individual consideration of the additional evidence to recommendation factors, a detailed discussion of these factors for each of the possible interventions is beyond the scope of this guideline. However, forthcoming WHO guidelines will provide specific guidance on nutrition labelling policies, policies on marketing of food and non-alcoholic beverages to children, fiscal and pricing policies, and school food and nutrition policies, which will enable policy-makers to translate dietary goals into evidence-informed policies.¹ Therefore, in assessing the factors relevant to translating the evidence into recommendations for this guideline, the NUGAG Subgroup on Diet and Health primarily considered each recommendation in the context of achieving the recommended dietary goals.

Evidence for this process was gathered via comprehensive searches of relevant scientific databases and identification of high-quality studies, including recent systematic reviews, where available. An evidence to recommendations table can be found in [Annex 7](#).

Overall certainty in the evidence

Because evidence for children was extrapolated from adults in all cases, the overall certainties in the evidence reported below come from adult data.

SFA

The overall certainty in the available evidence for lower compared with higher SFA intake (SFA recommendation 1) was assessed as *moderate*. For consuming SFA at a level less than 10% of total energy intake compared with more than 10% (SFA recommendation 2), the certainty was assessed as *low*. For replacing SFA with different nutrients (SFA recommendation 3), the certainty was assessed as:

- ▶ *moderate* for plant-based monounsaturated fatty acids;
- ▶ *low* for polyunsaturated fatty acids, monounsaturated fatty acids from unspecified sources, whole grains or foods described by the authors of the individual studies as having a low glycaemic index, carbohydrates from unspecified sources, and animal-based protein; and
- ▶ *very low* for free sugars or foods described by the authors of the individual studies as having a high glycaemic index, and protein from unspecified sources.

¹ [https://www.who.int/groups/nutrition-guidance-expert-advisory-group-\(nugag\)/policy-actions](https://www.who.int/groups/nutrition-guidance-expert-advisory-group-(nugag)/policy-actions)

TFA

The overall certainty in the available evidence for lower compared with higher TFA intake (TFA recommendation 1) was assessed as *moderate*. For consuming TFA at a level less than 1% of total energy intake compared with more than 1% (TFA recommendation 2), the certainty was assessed as *low*. For replacing TFA with different nutrients (TFA recommendation 3), the certainty was assessed as:

- ▶ *moderate* for carbohydrates;
- ▶ *low* for plant-based monounsaturated fatty acids; and
- ▶ *very low* for polyunsaturated fatty acids, animal-based monounsaturated fatty acids, free sugars and foods described by the authors of the individual studies as having a high glycaemic index, and SFA.

Balance of desirable and undesirable effects

There was robust evidence for a cardiovascular benefit of reducing SFA and TFA intake across many study types and outcomes, and evidence for reduced risk of all-cause mortality from prospective observational studies. There were no adverse effects of any kind associated with reducing intake of SFA or TFA when assessed in aggregate. Although increased risk of type 2 diabetes was associated with reduced consumption of two individual odd chain SFA – pentadecanoic acid and heptadecanoic acid – intake of these SFA was assessed by tissue measurements, which may not consistently distinguish between dietary intake and endogenous synthesis. Furthermore, because SFA are found as mixtures in foods and not in isolation, pentadecanoic acid and heptadecanoic acid as found in foods will be accompanied by other SFA and, as noted, reducing intake of SFA as a whole is associated with reduced risk of all-cause mortality and CVDs. Therefore, until more is known about how potential health effects of individual SFA might be interpreted in the context of health effects of SFA as a class of molecules, the desirable effects of reducing both SFA and TFA intake strongly outweigh the undesirable effects.

Concerns have been raised about the potential negative impact of reducing or limiting the intake of dietary fat on nutritional adequacy and resulting growth and development of children (49, 50), particularly in the context of limiting intake of dairy intake and other animal-source foods. The systematic review supporting this guideline did not identify undesirable effects related to linear growth and development in children who reduced their SFA intake (60). A primary focus of two large studies included in the review – the Dietary Intervention Study in Children (DISC) (73) and the Special Turku Coronary Risk Factor Intervention Project (STRIP) (80) – was to assess the safety of reducing SFA in the diet of children. Authors of both trials concluded that a diet low in SFA did not affect normal growth and development of children, and was therefore safe. The STRIP study, in particular, demonstrated the long-term safety of a diet low in SFA: it implemented a low-SFA diet beginning at 7 months of age and followed up participants regularly for more than 20 years, during which no adverse effects on growth, neurological or sexual development, or psychosocial wellbeing were noted (81).

Although no evidence was identified for effects of reducing TFA intake in children, concerns regarding potential adverse effects of limiting ruminant TFA found in dairy foods and meat from ruminant animals were addressed in modelling analyses (Annex 8) that assessed ruminant TFA content of various dairy foods in the context of SFA content and the WHO recommendations on SFA intake.

The WHO recommendations on SFA and TFA intake allow adequate consumption of dairy foods, particularly reduced-fat versions of these foods, and are compatible with many national guidelines on dairy intake. Because reducing SFA and TFA intake in children reduces CVD risk without any identified adverse effects, the desirable effects of reducing both SFA and TFA intake strongly outweigh the undesirable effects (none identified).

Evidence from the systematic review by Mensink (58) suggested a slight increase in triglycerides and reduction in HDL cholesterol when SFA are replaced by carbohydrates of mixed composition. However, the clinical relevance of such changes is not clear (82), and this was not considered an influential consideration in the balance of desirable and undesirable effects, given the evidence for disease and mortality outcomes, and in light of recommendation 3 on replacement nutrients for SFA.

Priority of the problem, and values and preferences

These recommendations address both CVDs and all-cause mortality. CVDs are the leading cause of disease burden globally (2), and therefore interventions and programmes targeting reduction in risk of CVDs are valuable in all contexts and are a high priority for many countries. Despite the global burden of CVDs, the priority placed on this problem by authorities at different levels may vary depending on the real or perceived magnitude of the problem within a particular country or region.

The recommendations in this guideline place a high value on reducing the risk of CVDs; however, individuals affected by the recommendations may place a different value on the benefit of reducing CVD risk. Because CVDs are a high-profile public health topic, including in many low- and middle-income countries where these diseases represent a growing threat (83), it is expected that most individuals would value efforts to reduce risk. However, in real-world settings, perception of the risk varies considerably (84–87), and outreach and communication efforts may be needed to improve understanding.

Feasibility

In settings where efforts to reduce SFA and TFA intake are planned or are already under way, feasibility should be much higher than in settings where plans are not yet in place. Regardless, feasibility will be influenced by the existing relevant infrastructure (for different interventions) and the available resources. In implementing interventions to bring about the desired change in SFA and TFA intake (e.g. behaviour change and education campaigns, fiscal policies, marketing and labelling policies, reformulation), feasibility will vary widely and detailed discussion of feasibility for each type of intervention is beyond the scope of this guideline. Relevant to all interventions, widespread use and availability of certain food items high in SFA and/or TFA may pose challenges in decreasing consumption to meet the recommended intake. Regardless of which interventions are employed to realize the recommended intakes, some amount of behaviour change at the individual level will be required. This may be challenging with respect to SFA in certain settings, particularly those in which some medical professionals and academic researchers question the link between SFA intake and CVDs (88), and where popular opinion has recently been shaped to view high SFA intakes as part of a healthy, natural diet (89).

That large-scale reduction in SFA intake is feasible has been demonstrated in North Karelia in eastern Finland where, from 1972 to 2007, population intake of SFA was reduced from 20% to 12% of total energy intake, and total cholesterol decreased on average by more than 20% (90). Although there is evidence of real-world success, SFA intake has slightly increased in North Karelia since 2007 (91), and other unsuccessful approaches such as the Danish tax on SFA which was abandoned after a little more than a year (despite resulting in a small reduction in population SFA intake) (92) are reminders that, although feasible, large-scale reduction of SFA intake depends on a number of contextual factors that vary across settings. Interventions may well be challenging and will require multisectoral cooperation in many settings to be successful.

Global efforts to eliminate industrially produced TFA are already well under way, supported by the WHO REPLACE action package launched in May 2018. As of September 2022, 60 countries had implemented mandatory TFA limits; of these, 43 countries had implemented a best-practice TFA policy that either virtually eliminates industrially produced TFA or bans partially hydrogenated oils (93), demonstrating that global reduction in TFA intake may be an achievable goal. In addition, in light of the strong evidence base and growing public awareness of the undesirable health effects associated with TFA intake, several companies have voluntarily reformulated their products to remove TFA (94).

Acceptability

The recommendations in this guideline are in line with many existing national policies, however, acceptability may vary across different countries and cultural contexts.

Acceptability may be influenced by:

- ▶ how the recommendations are translated into policies and actions (e.g. nutrition labelling policies, marketing policies, fiscal policies, reformulation) – some may be more acceptable than others;

- ▶ level of awareness of the health problem that CVDs pose – interventions may be less acceptable in settings where awareness is low;
- ▶ potential impact on national economies; and
- ▶ compatibility with existing policies.

At an individual level, for people who acknowledge the evidence linking SFA and TFA intake to risk of CVDs and value reducing this risk, acceptability should be high because CVDs are a significant, recognized global health problem. As noted with respect to feasibility, however, there are many for whom the recommendation may not be acceptable, based on the current, popular perception that diets high in SFA do not pose a health risk (89). Because the health risks of consuming large amounts of industrially produced TFA are already generally accepted and TFA are already being phased out in many settings, the recommendations on TFA intake should be acceptable to many.

Equity and human rights

The recommendations in this guideline have the potential to reduce health inequity by improving the health of people of lower socioeconomic status, who are generally disproportionately affected by CVDs (95) and NCDs in general (96). For example, modelling studies and real-world assessments of bans and other policies targeting elimination of industrially produced TFA in high-income countries suggest that reducing TFA intake could reduce coronary heart disease–related health inequity stemming from differences in socioeconomic status (94, 97). However, effects on equity and human rights would likely depend on how the recommendations are translated into policies and actions (e.g. fiscal policies, reformulation). The impact of interventions on the pricing of manufactured foods would require careful consideration, as any increase in costs borne by manufacturers might be passed on to the consumer; this would likely disproportionately affect people of lower socioeconomic status.

Resource implications

Costs of translating the recommendations into policies and actions will vary widely, depending on which approaches are taken, but may be associated with long-term savings in costs of health care, particularly when implemented as part of a coherent package of interventions (98). The extent of these savings and resource use depend on strategies chosen for implementation and the time scale for evaluation. Implementation of the recommendations will likely require consumer education and public health communications, some or all of which can be incorporated into existing public health nutrition education campaigns and other nutrition programmes at the global, regional, national and subnational levels.

Specific evidence for resource implications of reducing SFA and/or TFA intake is limited; however, a small number of modelling studies have been published. Simulations in high-income countries suggest that reducing SFA and TFA intake through various means, including reformulation of conventional oils (and bans in the case of industrially produced TFA) could result in savings of hundreds of millions to billions of US dollar equivalents from reduced health-care costs (94, 97, 99–102).

Recommendations and supporting information

All recommendations for SFA and TFA should be considered in the context of other WHO guidelines on healthy diets, including those on total fat (103), polyunsaturated fatty acids (3),¹ sugars (104), sodium (105), potassium (106) and carbohydrates (107). An explanation of the strength of WHO recommendations can be found in **Box 1**.

SFA recommendations

1. WHO recommends that adults and children reduce saturated fatty acid intake to 10% of total energy intake (*strong recommendation*).
2. WHO suggests further reducing saturated fatty acid intake to less than 10% of total energy intake (*conditional recommendation*).
3. WHO recommends replacing saturated fatty acids in the diet with polyunsaturated fatty acids (*strong recommendation*); monounsaturated fatty acids from plant sources (*conditional recommendation*); or carbohydrates from foods containing naturally occurring dietary fibre, such as whole grains, vegetables, fruits and pulses (*conditional recommendation*).

Rationale and remarks

The following provides the reasoning (rationale) behind the formulation of the recommendations, as well as remarks designed to provide context for the recommendations and facilitate their interpretation and implementation.

Rationale for SFA recommendations 1 and 2

- ▶ Recommendations 1 and 2 are based on evidence from four systematic reviews that assessed the effects of lower compared with higher SFA intake. These systematic reviews found that lower SFA intake reduced the risk of all-cause mortality and CVDs. The overall certainty in the evidence for recommendation 1 was *moderate*, and for recommendation 2 was *very low*.
- ▶ Specific findings from the reviews supporting these recommendations include the following.
 - As assessed in RCTs in the systematic review by Hooper et al. (55), reducing SFA intake reduced the risk of CVDs in adults (*moderate* certainty evidence); greater reductions in SFA intake resulted in greater reduction in risk. No effect, or effects that trended towards reduced risk of CVDs, were observed for other critical outcomes; none suggested increased risk. All but one of the trials included in the analyses reported SFA intakes of more than 10% of total energy intake at baseline, and although stepwise testing of thresholds of intake did not find a clear effect on any cardiovascular or mortality outcome at SFA intakes of less than 10% of total energy intake, significant reductions in risk of CVDs and CVD mortality were observed with SFA intakes of less than 9% of total energy intake. Consequently, there is ample evidence supporting reduction of SFA intake to 10% of total energy, but only limited evidence supporting a reduction to below 10% of total energy intake.

¹ WHO guidance on polyunsaturated fatty acids is currently being updated.

Box 1. Strength of WHO recommendations

WHO recommendations can either be *strong* or *conditional*, based on a number of factors including overall certainty in the supporting scientific evidence, balance of desirable and undesirable consequences, and others as described in the *Evidence to recommendations* section of the guideline.

Strong recommendations are those recommendations for which the WHO guideline development group is confident that the desirable consequences of implementing the recommendation outweigh the undesirable consequences. *Strong* recommendations can be adopted as policy in most situations.

Conditional recommendations are those recommendations for which the WHO guideline development group is less certain that the desirable consequences of implementing the recommendation outweigh the undesirable consequences or when the anticipated net benefits are very small. Therefore, substantive discussion amongst policy-makers may be required before a *conditional* recommendation can be adopted as policy.

The reasoning behind the strength of recommendations in this guideline is provided in the rationale for each recommendation. Additional information on assessing the strength of WHO recommendations can be found in the *WHO handbook for guideline development* (54).

- As assessed in prospective observational studies in the systematic review by Reynolds et al. (56), lower SFA intake compared with higher intake (*very low* certainty evidence) and consuming SFA at a level of less than 10% of total energy intake compared with intakes greater than 10% (*low* certainty evidence) are associated with reduced risk of all-cause mortality in adults.
- As assessed in RCTs and strictly controlled feeding trials in the systematic review by Mensink (58), replacing SFA with polyunsaturated fatty acids, monounsaturated fatty acids and carbohydrates all resulted in reductions in low-density lipoprotein (LDL) cholesterol in adults (*high* certainty evidence). The LDL cholesterol-lowering effects of replacing saturated fatty acids with other nutrients are cumulative – that is, the more SFA intake is reduced, the more LDL cholesterol is lowered. The effects were observed down to SFA intakes of 2% of total energy intake (effects were observed across a wide range of SFA intakes, from 2% to 24% of total energy intake).
- Reducing SFA intake, as assessed in RCTs conducted in children (60), resulted in reduced LDL cholesterol and blood pressure (both *high* certainty evidence). All but one of the trials included in the analyses reported SFA intakes of more than 10% of total energy intake at baseline and very limited evidence suggests that reducing SFA intake to less than 10% of total energy intake reduces LDL cholesterol to a greater extent than reducing intake to a level higher than 10% of total energy intake (*moderate* certainty evidence).
- ▶ Evidence from the systematic review by Hooper et al. (55) did not suggest undesirable effects in adults from reduced SFA intake with respect to any of the critical outcomes, cancer incidence or mortality, serum lipids, blood pressure, measures of body fatness, or quality of life. Rather, the evidence suggested small benefits or no effect. Evidence from the systematic review by Mensink (58) suggested a slight increase in triglycerides and a reduction in high-density lipoprotein (HDL) cholesterol when SFA are replaced by carbohydrates of mixed composition. However, the clinical relevance of such changes is not clear (82). This finding was therefore not an influential consideration in the balance of desirable and undesirable effects, given the evidence for disease and mortality outcomes, and taking into account recommendation 3 on replacement nutrients for SFA. Evidence from the systematic review conducted in children indicates that reducing SFA intake does not compromise children’s linear growth, micronutrient status, cognitive development or sexual development (60). No other data on undesirable effects in adults or children were identified.
- ▶ Recommendation 1 was assessed as *strong* because evidence of *moderate* certainty overall from different study types assessing both risk factors and incidence of CVDs suggested reduced risk of CVDs with lower SFA intake. No undesirable effects or other mitigating factors were identified that would argue against a lower SFA intake.

- ▶ Recommendation 2 was assessed as *conditional* because, although evidence from different study types from each of the systematic reviews suggested reduced risk of CVDs with SFA intakes of less than 10% of total energy intake, the evidence is much more limited than for intakes greater than 10% of total energy intake and therefore there is less confidence in it (*very low* certainty evidence overall). No undesirable effects or other mitigating factors were identified that would argue against reducing SFA intake to less than 10% of total energy intake. A conservative approach was therefore taken, leading to a *conditional* recommendation.

Rationale for SFA recommendation 3

- ▶ Recommendation 3 is based on *moderate* certainty evidence overall for replacing SFA with polyunsaturated fatty acids and *low* certainty evidence overall for replacing SFA with monounsaturated fatty acids or carbohydrates. Evidence comes from four systematic reviews that assessed the effects of lower compared with higher SFA intake via replacement nutrient analysis. These reviews found that lower SFA intake reduced the risk of all-cause mortality, CVDs and coronary heart disease.
- ▶ Specific findings from the reviews supporting this recommendation include the following.
 - Subgroup analysis of RCTs in the systematic review by Hooper et al. (55) showed a reduction in risk of CVDs and coronary heart disease when SFA were replaced with polyunsaturated fatty acids (*moderate* certainty evidence), but not when SFA were replaced by carbohydrates, monounsaturated fatty acids (for which there was insufficient evidence to allow an adequate assessment) or protein.¹
 - As assessed in prospective observational studies in the systematic review by Reynolds et al. (56), replacing SFA with polyunsaturated fatty acids (*low* certainty evidence overall) or plant-based monounsaturated fatty acids (*moderate* certainty evidence overall) was associated with reductions in risk of CVDs, coronary heart disease and all-cause mortality. More limited evidence shows that replacing SFA with carbohydrates, particularly those from whole grains and foods described by the authors of the individual studies as having a low glycaemic index, was associated with small reductions in risk of CVDs and all-cause mortality (*very low* certainty evidence).
 - As assessed in RCTs and strictly controlled feeding studies in the systematic review by Mensink (58), replacing SFA with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates² all resulted in reductions in LDL cholesterol (*high* certainty evidence). The greatest reduction in LDL cholesterol was observed for polyunsaturated fatty acids, followed by monounsaturated fatty acids and then carbohydrates.
 - Very limited evidence from RCTs conducted in children (60) suggests that replacing SFA with polyunsaturated fatty acids or monounsaturated fatty acids reduces LDL cholesterol to a greater extent than replacing SFA with other nutrients (*moderate* certainty evidence).
- ▶ The evidence for the health benefits of replacing SFA with carbohydrates from whole grains, vegetables, fruits and pulses is based on studies in which the composition of the carbohydrates was either unspecified and therefore likely a mixture, or were reported as coming from whole grains or foods described by the authors of the individual studies as having a low glycaemic index. Although the evidence from the systematic reviews that informed the development of this recommendation did not specifically assess the replacement of SFA with carbohydrates from vegetables, fruits or pulses (whole grains were assessed directly), robust evidence from systematic reviews informing WHO recommendations on carbohydrate intake (108–113) indicates that consuming whole grains, vegetables, fruits and pulses is associated with health benefits, and therefore that carbohydrates in the diet should primarily come from these foods (107).
- ▶ The recommendation for replacing SFA with polyunsaturated fatty acids from plant sources was assessed as *strong* because evidence of *moderate* certainty overall from different study types that

¹ In this review, polyunsaturated fatty acids were primarily from plant-based oils, rich in linoleic acid; carbohydrates were of largely unknown, and likely mixed, composition; and little to no data were available for nature of the protein.

² In this review, polyunsaturated fatty acids were predominantly linoleic acid and α -linolenic acid; monounsaturated fatty acids were predominantly oleic acid; and carbohydrates were of largely unknown, and likely mixed, composition.

assessed both risk factors and disease incidence suggested that such replacement reduces the risk of CVDs and all-cause mortality.

- ▶ The recommendations for replacing SFA with monounsaturated fatty acids from plant sources or carbohydrates from whole grains, vegetables, fruits and pulses was assessed as *conditional* because they are primarily based on evidence from observational studies, and also because vegetables, fruits and pulses were not directly assessed in the prospective cohort studies assessing replacement (whole grains were assessed directly).

Remarks for Recommendation 3

- ▶ To facilitate implementing this recommendation, replacing SFA can be achieved via a single recommended nutrient or a combination of nutrients.
- ▶ For further guidance on consumption of whole grains, vegetables, fruits and pulses, see the WHO guideline on carbohydrate intake (107).
- ▶ The guidance on replacement nutrients is relevant for a state of energy balance, in which total energy consumed is balanced by total energy expended. For energy balance, when the intake of one nutrient is reduced, the resulting energy deficit must be compensated for by intake of another nutrient. In cases of positive energy balance, and where a reduction in total energy intake is desired, SFA intake may be reduced in part or entirely without the need for a replacement nutrient.

Remarks for all SFA recommendations

- ▶ The recommendations as they apply to children are based on the totality of evidence, including both results of the review conducted in children and extrapolation of the results obtained from the reviews conducted in adults.¹
- ▶ The systematic review of prospective observational studies by Reynolds et al. (56) identified studies in which SFA exposures were assessed either by self-reported dietary intakes or measurement of SFA in tissues (e.g. plasma phospholipids, red blood cells, fat biopsies). The results for some outcomes differed between the two methods of exposure assessment: significant reductions in risk were observed for coronary heart disease and type 2 diabetes in studies where SFA intake was assessed by measuring SFA content of tissues, whereas no or non-significant results were observed for all outcomes in studies where SFA intake was assessed by self-reported dietary intakes, when replacement is not considered. Although assessment of SFA in tissues can be a relatively reliable indicator of dietary intake, the potential contribution of endogenous synthesis cannot be consistently estimated. Therefore, although the results for SFA tissue levels in the systematic review provide evidence of benefit of lower SFA tissue levels and generally support the evidence from other studies and analyses, the evidence from tissue levels was not formally assessed or included in the evidence base supporting the recommendations for SFA intake.
- ▶ Although there is evidence for differential effects of individual SFA, it is insufficient to inform the development of specific recommendations. SFA found naturally in foods are generally mixtures; consequently, intakes of individual SFA tend to be highly correlated with one another (114). Therefore, recommendations for individual SFA may be of limited utility to end users and difficult to implement – for example, in developing food-based dietary guidelines. Before recommendations can be made for individual SFA, further research is needed into their health effects and how such recommendations might be effectively used.
- ▶ These recommendations do not preclude consumption of particular foods. However, foods containing high levels of SFA should be consumed sparingly to meet the recommended level of intake.

¹ The results from the systematic reviews conducted in adults were not downgraded for indirectness when assessing the evidence via GRADE as there is no evidence that the physiological effects of reducing SFA on risk of disease and mortality would be significantly different between adults and children.

TFA recommendations

1. WHO recommends that adults and children reduce *trans*-fatty acid intake to 1% of total energy intake (*strong recommendation*).
2. WHO suggests further reducing *trans*-fatty acid intake to less than 1% of total energy intake (*conditional recommendation*).
3. WHO recommends replacing *trans*-fatty acids in the diet with polyunsaturated fatty acids or monounsaturated fatty acids primarily from plant sources (*conditional recommendation*).

Rationale for TFA recommendations 1 and 2

- ▶ Recommendations 1 and 2 are based on evidence from two systematic reviews that assessed the effects of lower compared with higher TFA intake. These systematic reviews found that lower TFA intake reduced the risk of CVDs. The overall certainty in the evidence for recommendation 1 was *moderate* and for recommendation 2 was *low*.
- ▶ Specific findings from the reviews supporting these recommendations include the following.
 - As assessed in prospective observational studies in the systematic review by Reynolds et al. (56), lower TFA intake compared with higher intake (*moderate* certainty evidence overall) and consuming TFA at a level of less than 1% of total energy intake compared with intakes greater than 1% (*low* certainty evidence overall) were associated with reduced risk of all-cause mortality, CVDs and coronary heart disease. Greater reductions in TFA intake resulted in greater reductions in risk of all-cause mortality and coronary heart disease (i.e. dose–response relationships).
 - As assessed in RCTs in the systematic review by Brouwer (59), replacing TFA with polyunsaturated fatty acids, monounsaturated fatty acids and carbohydrates all resulted in reductions in LDL cholesterol (*high* certainty evidence) and overall improvements in blood lipid profile. The LDL cholesterol-lowering effects of replacing TFA with other nutrients are cumulative – that is, the more TFA intake is reduced, the more LDL cholesterol is lowered. These effects were observed across a wide range of TFA intakes, from 0% to 10.9% of total energy intake.
- ▶ Recommendation 1 was assessed as *strong* because evidence of overall *moderate* certainty from different study types assessing both risk factors and incidence of CVDs suggested reduced risk of all-cause mortality, CVDs and coronary heart disease with lower TFA intake (in a dose-dependent manner with respect to all-cause mortality and coronary heart disease). No undesirable effects or other mitigating factors were identified that would argue against a lower TFA intake.
- ▶ Recommendation 2 was assessed as *conditional* because, although there is evidence from different study types from each of the systematic reviews suggesting reduced risk of all-cause mortality, CVDs and coronary heart disease with TFA intakes of less than 1% of total energy intake, the evidence is more limited than for intakes greater than 1% of total energy intake and therefore there is less confidence in it (*low* certainty evidence overall). No undesirable effects or other mitigating factors were identified that would argue against reducing TFA intake to less than 1% of total energy intake. A conservative approach was therefore taken, leading to a *conditional* recommendation.

Rationale for TFA recommendation 3

- ▶ Recommendation 3 is based on *very low* certainty evidence overall for replacing TFA with polyunsaturated fatty acids and *moderate* certainty evidence overall for replacing TFA with monounsaturated fatty acids from plant sources. Evidence comes from two systematic reviews that assessed the effects of lower compared with higher TFA intake via replacement nutrient analysis. These reviews found that lower TFA intake reduced the risk of all-cause mortality, CVDs, coronary heart disease and type 2 diabetes.
- ▶ Specific findings from the reviews supporting this recommendation include the following.
 - As assessed in prospective observational studies in the systematic review by Reynolds et al. (56), replacing TFA with polyunsaturated fatty acids was associated with reduced risk of type 2 diabetes (*very low* certainty evidence), and replacing TFA with monounsaturated fatty acids from plant sources was associated with reduced risk of all-cause mortality, CVDs and coronary heart disease (*moderate* certainty evidence overall).
 - As assessed in RCTs in the systematic review by Brouwer (59), replacing TFA with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates resulted in reductions in LDL cholesterol (*high* certainty evidence) and overall improvements in blood lipid profile. The greatest reduction in LDL cholesterol was observed for polyunsaturated fatty acids, followed by monounsaturated fatty acids and then carbohydrates.
- ▶ Recommendation 3 was assessed as *conditional* because evidence for disease outcomes comes only from a limited number of observational studies; most of the evidence is from RCTs with LDL cholesterol as an outcome. The evidence for LDL cholesterol is of *high* certainty. However, although LDL cholesterol is a well-established biomarker for measuring the effects of interventions on CVD risk, and is considered by many to be a causal factor for atherosclerosis and coronary heart disease, it is not a physical manifestation or confirmation of disease. Therefore, a conservative approach was taken, leading to a *conditional* recommendation.

Remarks for TFA recommendation 3

- ▶ The recommendation to replace TFA with polyunsaturated fatty acids or monounsaturated fatty acids from plant sources does not preclude replacing TFA with carbohydrates, as replacement with carbohydrates significantly lowered LDL cholesterol in the analysis of RCTs that assessed blood lipids. However, polyunsaturated fatty acids and monounsaturated fatty acids had greater effects on LDL cholesterol when used as replacements for TFA, and replacement of TFA with monounsaturated fatty acids from plant sources reduced the risk of coronary heart disease and all-cause mortality in prospective observational studies. Limited evidence suggests that replacing TFA with carbohydrates of unspecified composition also reduces the risk of type 2 diabetes, but that replacing TFA with free sugars or carbohydrates described by study authors as refined carbohydrates has little effect on risk of coronary heart disease. Therefore, a conclusive interpretation of the results for carbohydrate replacement of TFA in the analyses supporting the recommendations in this guideline was not possible.
- ▶ Replacement of TFA with saturated fatty acids did not improve disease outcomes or blood lipids in the two systematic reviews. Saturated fatty acids are therefore not a preferred replacement for TFA.
- ▶ To facilitate implementing this recommendation, replacing TFA can be achieved via polyunsaturated fatty acids or monounsaturated fatty acids alone, or a combination of the two.
- ▶ This guidance on replacement nutrients is relevant for a state of energy balance, in which total energy consumed is balanced by total energy expended. For energy balance, when the intake of one nutrient is reduced, the resulting energy deficit must be compensated for by intake of another nutrient. In cases of positive energy balance, and where a reduction in total energy intake is desired, TFA intake may be reduced in part or entirely without the need for a replacement nutrient.

Remarks for all TFA recommendations

- ▶ Because there weren't any relevant studies identified in a systematic review of TFA intake in children (60), the recommendations as they apply to children are based on extrapolation of the results obtained from the reviews conducted in adults.¹
- ▶ For the purposes of these recommendations, TFA includes all fatty acids with a double bond in the *trans* configuration, regardless of whether the TFA come from ruminant sources or are produced industrially.²
- ▶ These recommendations do not preclude consumption of particular foods. However, foods containing high levels of industrially produced TFA should largely be avoided.

¹ The results from the reviews conducted in adults were not downgraded for indirectness when assessing the evidence via GRADE as there is no evidence that the physiological effects of reducing or increasing TFA on risk of disease and mortality would be significantly different between adults and children.

² This definition includes conjugated linoleic acid.

Uptake of the guideline and future work

Dissemination

The guideline will be disseminated through:

- ▶ the WHO e-Library of Evidence for Nutrition Actions (eLENA),¹ which is an online library of evidence-informed guidance for nutrition interventions that provides policy-makers, programme managers, health workers, partners, stakeholders and other interested actors with access to the latest nutrition guidelines and recommendations, as well as complementary documents, such as systematic reviews, and biological, behavioural and contextual rationales for the effectiveness of nutrition actions;
- ▶ relevant nutrition webpages on the WHO website, including a summary of the guideline in all six official WHO languages;
- ▶ the electronic mailing lists of the WHO Department of Nutrition and Food Safety, and the UN Standing Committee on Nutrition;
- ▶ the network of the six WHO regional offices and country offices; and
- ▶ the WHO collaborating centres.

The guideline will also be disseminated at various relevant WHO meetings, as well as at global and regional scientific meetings.

Translation and implementation

The recommendations in this guideline should be considered in conjunction with other WHO guidance on healthy diets – in particular, guidelines on total fat (103), polyunsaturated fatty acids (3),² carbohydrates (107) and free sugars (104), as well as sodium (105) and potassium (106), to guide effective policy actions and intervention programmes to promote healthy diets and nutrition, and prevent diet-related NCDs.

The recommendations in this and related WHO guidelines acknowledge that both quantity and quality of fat consumed are important for maintaining health. Public health interventions should therefore aim to reduce total fat intake where necessary (103), while reducing SFA and TFA intake, through replacement with unsaturated fatty acids and/or carbohydrates, without increasing free sugars intake (104).

A detailed discussion of how the recommendations on SFA and TFA intake might be implemented is beyond the scope of this guideline, however they can be considered by policy-makers and programme managers when discussing possible measures, including:

- ▶ assessing current intake of SFA and TFA in their populations relative to benchmarks;
- ▶ developing policy measures to reduce intake of SFA and/or TFA, where necessary, through a range of public health interventions, many of which are already being implemented by countries, including:
 - nutrition labelling (i.e. mandatory nutrient declaration) and front-of-pack labelling systems
 - regulation of marketing of foods and non-alcoholic beverages that are high in SFA and/or TFA, including bans on marketing of foods that contain industrially produced TFA

¹ <https://www.who.int/tools/elena>

² WHO guidance on polyunsaturated fatty acids is currently being updated.

- restriction of the sale and promotion of foods and beverages that are high in SFA and/or TFA in and around schools
 - implementation of fiscal policies targeting foods and beverages that are high in SFA and/or TFA
 - consumer education;
- ▶ developing strategies to reformulate food products; and
 - ▶ translating the recommendations at the country-level into culturally and contextually specific food-based dietary guidelines that take into account locally available foods and dietary customs.

Elimination of industrially produced TFA is among the priority actions identified by WHO in its 13th General Programme of Work, which will guide the work of WHO in 2019–2023. Industrially produced TFA are the predominant source of dietary TFA in many populations. They can be found in baked and fried foods (e.g. doughnuts, cookies, crackers, pies), pre-packaged snacks and food, and partially hydrogenated cooking oils and fats, which are often used in homes, in restaurants and in the informal sector (e.g. by street vendors). Therefore, removing industrially produced TFA from the food supply through legislation or regulatory action represents a well-defined mechanism for translating the recommendations in this guideline into action and achieving significant reductions in TFA intake at the population level.

In 2018, WHO released the REPLACE action package, which provides support for implementing the WHO recommendations on TFA and is a roadmap for countries to achieve prompt, complete and sustained elimination of industrially produced TFA from the food supply. In 2019, WHO released six REPLACE modules, which provide practical, step-by-step implementation guidance to support governments. WHO recommends that countries adopt and implement one of two best-practice policy options for eliminating industrially produced TFA from the food supply. Before the release of REPLACE, industrially produced TFA had already largely been removed or were in the process of being removed from the food supply at the national and subnational levels in many countries (9, 115, 116). As of September 2022, 60 countries had implemented mandatory TFA limits; of these, 43 countries had implemented a best-practice TFA policy that either virtually eliminates industrially produced TFA or bans partially hydrogenated oils (93), demonstrating that global reduction in TFA intake may be an achievable goal.

Providing comprehensive dietary guidance is beyond the scope of these guidelines, because such guidance should be based on overall dietary goals that consider all required nutrients. However, it is feasible to achieve the recommendations in this guideline while respecting national dietary customs, because a wide variety of fresh foods are naturally low in SFA and TFA, and reduced-fat versions of whole foods (e.g. reduced-fat dairy foods, lean cuts of meat) are available.

Monitoring and evaluation

The impact of this guideline can be evaluated by assessing its adoption and adaptation across countries. Evaluation at the global level will be through the WHO Global database on the Implementation of Nutrition Action (GINA)¹ – a centralized platform developed by the WHO Department of Nutrition and Food Safety for sharing information on nutrition actions in public health practice implemented around the world. GINA currently contains information on thousands of policies (including laws and legislation), nutrition actions and programmes in more than 190 countries. GINA includes data and information from many sources, including the first and second WHO global nutrition policy reviews conducted in 2010–2011 and 2016–2017, respectively (117, 118). By providing programmatic implementation details, specific country adaptations and lessons learned, GINA serves as a platform for monitoring and evaluating how nutrition-relevant WHO guidelines are being translated into policy actions and intervention programmes.

¹ <https://extranet.who.int/nutrition/gina/en>

Research gaps and future initiatives

Based on the results of the systematic reviews and discussions with the NUGAG Subgroup on Diet and Health, a number of questions and gaps in the current evidence that should be addressed by future research were identified, as outlined below.

Research needed on SFA.

- ▶ Further assess the health effects of replacing SFA with different macronutrients in populations from different geographical regions, particularly low- and middle-income countries.
- ▶ Further assess the health effects of different types and different sources (i.e. plant, animal) of polyunsaturated fatty acids, monounsaturated fatty acids, carbohydrates and proteins used as replacements for SFA.
- ▶ Assess how effects of reducing SFA intake may vary with different background diets (i.e. diets with differing macronutrient compositions) and different profiles of other modifiable risk factors (e.g. physical activity level, alcohol and tobacco use).
- ▶ Assess long-term health effects of different established dietary patterns containing different amounts of SFA.
- ▶ Compare the health effects of SFA from different food sources (e.g. plant, animal, dairy, specific oils), taking into consideration the nature of the replacement nutrient(s) or food(s).
- ▶ Assess the health effects of thresholds lower than 10% of total energy intake in settings with currently low SFA intake.
- ▶ Assess the health effects of a natural increase in SFA intake in populations in which intake was previously low.
- ▶ Explore potential genetic and epigenetic contributions to variations between individuals in response to changes in dietary fatty acid intake with respect to LDL cholesterol (119) and other markers of CVD risk.
- ▶ Further explore the health effects of individual SFA and how this information may be used in the development of dietary guidance.

Research needed on TFA.

- ▶ Assess the health effects of TFA intake in children, with long-term follow-up to assess the effects on CVD risk and inflammation.
- ▶ Undertake further research to better understand potential differential effects on health of industrially produced and ruminant TFA.
- ▶ Undertake research on methods to more accurately differentiate between intake of industrially produced and ruminant TFA.
- ▶ Undertake basic research and epidemiological studies to better understand the physiological pathways through which TFA intake affects mortality and cardiovascular outcomes, including effects on inflammation and the immune response.
- ▶ Further assess the current levels of TFA intake in different countries, particularly in developing countries.

Research needed relevant to both SFA and TFA.

- ▶ Assess the health effects of modifying SFA or TFA intake in individuals at different risk for CVDs, including those who are on lipid-lowering medication.
- ▶ Harmonize reporting of CVD end-points in studies to improve the ability to compare across studies and synthesize data.
- ▶ When assessing lipid end-points, include non-HDL cholesterol and apolipoproteins (in addition to LDL cholesterol, HDL cholesterol, ratios, triglycerides etc.).

- ▶ Explore ways of combining information from self-reported dietary intakes and fatty acid biomarkers for more robust dietary exposure assessments.
- ▶ Improve methods of analysis for assessing fatty acid intakes in individuals, including further development of robust biomarkers.

Updating the guideline

WHO regularly updates its guidelines and recommendations to reflect the latest scientific and medical knowledge. This guideline will therefore be updated as part of the ongoing efforts of WHO to update existing dietary goals and nutrition guidance for promoting healthy diets, nutrition and the prevention of NCDs. It is planned that the recommendations in this guideline will be reviewed when new data and information become available. At that time, any new evidence will be evaluated, and formal updates will be made, if necessary. The WHO Department of Nutrition and Food Safety, together with partners in other departments within the WHO Secretariat, will be responsible for coordinating the updating of the guideline, following the formal procedure described in the *WHO handbook for guideline development* (54). At the time the guideline is due for review, WHO will welcome suggestions for additional questions that could be addressed in a potential update of the guideline.

References

1. Global Health Observatory data. Noncommunicable diseases mortality and morbidity. Geneva: World Health Organization; 2021 (http://www.who.int/gho/ncd/mortality_morbidity/en/, accessed 1 January 2023).
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol.* 2020;76(25):2982–3021.
3. Diet, nutrition and the prevention of chronic diseases: report of a Joint WHO/FAO expert consultation. Geneva: World Health Organization; 2003 (<https://apps.who.int/iris/handle/10665/42665>, accessed 1 January 2023).
4. Yoshinaga K, Asanuma M, Mizobe H, Kojima K, Nagai T, Beppu F, et al. Characterization of cis- and trans-octadecenoic acid positional isomers in edible fat and oil using gas chromatography–flame ionisation detector equipped with highly polar ionic liquid capillary column. *Food Chem.* 2014;160:39–45.
5. Ratnayake WM, Chen ZY. *Trans*, n-3, and n-6 fatty acids in Canadian human milk. *Lipids.* 1996;31(Suppl):S279–82.
6. Stender S, Astrup A, Dyerberg J. Ruminant and industrially produced *trans* fatty acids: health aspects. *Food Nutr Res.* 2008;52.
7. Jakobsen MU, Bysted A, Andersen NL, Heitmann BL, Hartkopp HB, Leth T, et al. Intake of ruminant *trans* fatty acids in the Danish population aged 1–80 years. *Eur J Clin Nutr.* 2006;60(3):312–18.
8. Craig-Schmidt MC. World-wide consumption of *trans* fatty acids. *Atheroscler Suppl.* 2006;7(2):1–4.
9. Eliminating *trans* fats in Europe: a policy brief. Copenhagen: World Health Organization Regional Office for Europe; 2015 (<https://apps.who.int/iris/handle/10665/363877>, accessed 1 January 2023).
10. Jakobsen MU, O’Reilly EJ, Heitmann BL, Pereira MA, Balter K, Fraser GE, et al. Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. *Am J Clin Nutr.* 2009;89(5):1425–32.
11. Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. *PLoS Med.* 2010;7(3):e1000252.
12. Farvid MS, Ding M, Pan A, Sun Q, Chiuve SE, Steffen LM, et al. Dietary linoleic acid and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies. *Circulation.* 2014;130(18):1568–78.
13. Li Y, Hruby A, Bernstein AM, Ley SH, Wang DD, Chiuve SE, et al. Saturated fats compared with unsaturated fats and sources of carbohydrates in relation to risk of coronary heart disease: a prospective cohort study. *J Am Coll Cardiol.* 2015;66(14):1538–48.
14. Jakobsen MU, Dethlefsen C, Joensen AM, Stegger J, Tjønneland A, Schmidt EB, et al. Intake of carbohydrates compared with intake of saturated fatty acids and risk of myocardial infarction: importance of the glycemic index. *Am J Clin Nutr.* 2010;91(6):1764–8.

15. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *Am J Clin Nutr.* 2010;91(3):535–46.
16. Bendsen NT, Christensen R, Bartels EM, Astrup A. Consumption of industrial and ruminant *trans* fatty acids and risk of coronary heart disease: a systematic review and meta-analysis of cohort studies. *Eur J Clin Nutr.* 2011;65(7):773–83.
17. Mozaffarian D, Clarke R. Quantitative effects on cardiovascular risk factors and coronary heart disease risk of replacing partially hydrogenated vegetable oils with other fats and oils. *Eur J Clin Nutr.* 2009;63(Suppl 2):S22–33.
18. Brouwer IA, Wanders AJ, Katan MB. *Trans* fatty acids and cardiovascular health: research completed? *Eur J Clin Nutr.* 2013;67(5):541–7.
19. Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr.* 2003;77(5):1146–55.
20. Forouhi NG, Koulman A, Sharp SJ, Imamura F, Kroger J, Schulze MB, et al. Differences in the prospective association between individual plasma phospholipid saturated fatty acids and incident type 2 diabetes: the EPIC-InterAct case-cohort study. *Lancet Diabetes Endocrinol.* 2014;2(10):810–18.
21. Guo J, Astrup A, Lovegrove JA, Gijsbers L, Givens DI, Soedamah-Muthu SS. Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. *Eur J Epidemiol.* 2017;32(4):269–87.
22. de Goede J, Soedamah-Muthu SS, Pan A, Gijsbers L, Geleijnse JM. Dairy consumption and risk of stroke: a systematic review and updated dose-response meta-analysis of prospective cohort studies. *J Am Heart Assoc.* 2016;5(5):e002787.
23. Gijsbers L, Ding EL, Malik VS, de Goede J, Geleijnse JM, Soedamah-Muthu SS. Consumption of dairy foods and diabetes incidence: a dose-response meta-analysis of observational studies. *Am J Clin Nutr.* 2016;103(4):1111–24.
24. Pimpin L, Wu JH, Haskelberg H, Del Gobbo L, Mozaffarian D. Is butter back? A systematic review and meta-analysis of butter consumption and risk of cardiovascular disease, diabetes, and total mortality. *PLoS One.* 2016;11(6):e0158118.
25. Steur M, Johnson L, Sharp SJ, Imamura F, Sluijs I, Key TJ, et al. Dietary fatty acids, macronutrient substitutions, food sources and incidence of coronary heart disease: findings from the EPIC-CVD case-cohort study across nine European countries. *J Am Heart Assoc.* 2021;10(23):e019814.
26. Trieu K, Bhat S, Dai Z, Leander K, Gigante B, Qian F, et al. Biomarkers of dairy fat intake, incident cardiovascular disease, and all-cause mortality: a cohort study, systematic review, and meta-analysis. *PLoS Med.* 2021;18(9):e1003763.
27. Brouwer IA, Wanders AJ, Katan MB. Effect of animal and industrial *trans* fatty acids on HDL and LDL cholesterol levels in humans: a quantitative review. *PLoS One.* 2010;5(3):e9434.
28. Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. *Trans* fatty acids and cardiovascular disease. *N Engl J Med.* 2006;354(15):1601–13.
29. Santos S, Oliveira A, Lopes C. Systematic review of saturated fatty acids on inflammation and circulating levels of adipokines. *Nutr Res.* 2013;33(9):687–95.
30. Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, Halsey J, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet.* 2007;370(9602):1829–39.
31. Fulcher J, O’Connell R, Voysey M, Emberson J, Blackwell L, Mihaylova B, et al. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. *Lancet.* 2015;385(9976):1397–405.

32. Committee on Qualification of Biomarkers and Surrogate Endpoints in Chronic Disease, Board on Health Sciences Policy, Food and Nutrition Board, Institute of Medicine. Evaluation of biomarkers and surrogate endpoints in chronic disease. Washington DC: National Academies Press; 2010.
33. Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J*. 2017;38(32):2459–72.
34. Berenson GS, Wattigney WA, Tracy RE, Newman WP 3rd, Srinivasan SR, Webber LS, et al. Atherosclerosis of the aorta and coronary arteries and cardiovascular risk factors in persons aged 6 to 30 years and studied at necropsy (the Bogalusa Heart Study). *Am J Cardiol*. 1992;70(9):851–8.
35. Strong JP, Malcom GT, McMahan CA, Tracy RE, Newman WP 3rd, Herderick EE, et al. Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. *JAMA*. 1999;281(8):727–35.
36. Berenson GS, Srinivasan SR, Bao W, Newman WP 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults: the Bogalusa Heart Study. *N Engl J Med*. 1998;338(23):1650–6.
37. McGill HC Jr, McMahan CA, Malcom GT, Oalmann MC, Strong JP. Effects of serum lipoproteins and smoking on atherosclerosis in young men and women. The PDAY Research Group. Pathobiological Determinants of Atherosclerosis in Youth. *Arterioscler Thromb Vasc Biol*. 1997;17(1):95–106.
38. Srinivasan SR, Frontini MG, Xu J, Berenson GS. Utility of childhood non-high-density lipoprotein cholesterol levels in predicting adult dyslipidemia and other cardiovascular risks: the Bogalusa Heart Study. *Pediatrics*. 2006;118(1):201–6.
39. Davis PH, Dawson JD, Riley WA, Lauer RM. Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: the Muscatine Study. *Circulation*. 2001;104(23):2815–19.
40. Raitakari OT, Juonala M, Kahonen M, Taittonen L, Laitinen T, Maki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA*. 2003;290(17):2277–83.
41. Li S, Chen W, Srinivasan SR, Bond MG, Tang R, Urbina EM, et al. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study. *JAMA*. 2003;290(17):2271–6.
42. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. *Circulation*. 2007;115(4):459–67.
43. Stein EA, Shapero J, McNerney C, Glueck CJ, Tracy T, Gartside P. Changes in plasma lipid and lipoprotein fractions after alteration in dietary cholesterol, polyunsaturated, saturated, and total fat in free-living normal and hypercholesterolemic children. *Am J Clin Nutr*. 1982;35(6):1375–90.
44. Vartiainen E, Puska P, Pietinen P, Nissinen A, Leino U, Uusitalo U. Effects of dietary fat modifications on serum lipids and blood pressure in children. *Acta Paediatr Scand*. 1986;75(3):396–401.
45. Stein EA, Mendelsohn D, Fleming M, Barnard GD, Carter KJ, du Toit PS, et al. Lowering of plasma cholesterol levels in free-living adolescent males; use of natural and synthetic polyunsaturated foods to provide balanced fat diets. *Am J Clin Nutr*. 1975;28(11):1204–16.
46. Kaufmann RL, Assal J, Soeldner JS, Wilmschurst EG, Lemaire JR, Gleason RE, et al. Plasma lipid levels in diabetic children: effect of diet restricted in cholesterol and saturated fats. *Diabetes*. 1975;24(7):672–9.
47. McGandy RB, Hall B, Ford C, Stare FJ. Dietary regulation of blood cholesterol in adolescent males: a pilot study. *Am J Clin Nutr*. 1972;25(1):61–6.

48. Ford CH, McGandy RB, Stare FJ. An institutional approach to the dietary regulation of blood cholesterol in adolescent males. *Prev Med.* 1972;1(3):426–45.
49. Kaplan RM, Toshima MT. Does a reduced fat diet cause retardation in child growth? *Prev Med.* 1992;21(1):33–52.
50. Mauer AM. Should there be intervention to alter serum lipids in children? *Annu Rev Nutr.* 1991;11:375–91.
51. Micha R, Khatibzadeh S, Shi P, Fahimi S, Lim S, Andrews KG, et al. Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys. *BMJ.* 2014;348:g2272.
52. Wanders AJ, Zock PL, Brouwer IA. *Trans* fat intake and its dietary sources in general populations worldwide: a systematic review. *Nutrients.* 2017;9(8):840.
53. Diet, nutrition and the prevention of chronic diseases: report of a WHO Study Group. Geneva: World Health Organization; 1990 (<https://apps.who.int/iris/handle/10665/39426>, accessed 1 January 2023).
54. WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014 (<https://apps.who.int/iris/handle/10665/145714>, accessed 1 January 2023).
55. Hooper L, Martin N, Jimoh OF, Kirk C, Foster E, Abdelhamid AS. Reduction in saturated fat intake for cardiovascular disease. *Cochrane Database Syst Rev.* 2020;5(5):CD011737.
56. Reynolds AN, Hodson L, De Souza R, Pham HTD, Vlietstra L, Mann J. Saturated fat and trans-fat intakes and their replacement with other macronutrients: a systematic review and meta-analysis of prospective observational studies. Geneva: World Health Organization; 2022 (<https://apps.who.int/iris/handle/10665/366301>, accessed 1 January 2023).
57. de Souza RJ, Mente A, Maroleanu A, Cozma AI, Ha V, Kishibe T, et al. Intake of saturated and *trans* unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ.* 2015;351:h3978.
58. Mensink RP. Effects of saturated fatty acids on serum lipids and lipoproteins: a systematic review and regression analysis. Geneva: World Health Organization; 2016 (<https://apps.who.int/iris/handle/10665/246104>, accessed 1 January 2023).
59. Brouwer I. Effect of *trans*-fatty acid intake on blood lipids and lipoproteins: a systematic review and meta-regression analysis. Geneva: World Health Organization; 2016 (<https://apps.who.int/iris/handle/10665/246109>, accessed 1 January 2023).
60. Te Morenga L, Montez JM. Health effects of saturated and *trans*-fatty acid intake in children and adolescents: systematic review and meta-analysis. *PLoS One.* 2017;12(11):e0186672.
61. Katan MB, Zock PL, Mensink RP. Effects of fats and fatty acids on blood lipids in humans: an overview. *Am J Clin Nutr.* 1994;60(6 Suppl):1017s–22s.
62. Cholesterol Treatment Trialists' Collaboration. Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials. *Lancet.* 2019;393(10170):407–415.
63. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet.* 2005;366(9493):1267–78.
64. Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhalra N, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet.* 2010;376(9753):1670–81.
65. Prentice RL, Aragaki AK, Van Horn L, Thomson CA, Beresford SA, Robinson J, et al. Low-fat dietary pattern and cardiovascular disease: results from the Women's Health Initiative randomized controlled trial. *Am J Clin Nutr.* 2017;106(1):35–43.

66. Kaitosaari T, Ronnema T, Viikari J, Raitakari O, Arffman M, Marniemi J, et al. Low-saturated fat dietary counseling starting in infancy improves insulin sensitivity in 9-year-old healthy children: the Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) study. *Diabetes Care*. 2006;29(4):781–5.
67. Oranta O, Pahkala K, Ruottinen S, Niinikoski H, Lagstrom H, Viikari JS, et al. Infancy-onset dietary counseling of low-saturated-fat diet improves insulin sensitivity in healthy adolescents 15–20 years of age: the Special Turku Coronary Risk Factor Intervention Project (STRIP) study. *Diabetes Care*. 2013;36(10):2952–9.
68. Rask-Nissila L, Jokinen E, Terho P, Tammi A, Lapinleimu H, Ronnema T, et al. Neurological development of 5-year-old children receiving a low-saturated fat, low-cholesterol diet since infancy: a randomized controlled trial. *JAMA*. 2000;284(8):993–1000.
69. Tarmi-Mattsson M, Keskinen S, Korhonen TT, Lapinleimu H, Tuominen J, Niinikoski H, et al. Behavior of 3-year old children in a prospective randomized trial of reduced saturated fat and cholesterol diet since infancy: the STRIP baby project. *Int J Behav Med*. 1997;4(4):310–22.
70. Lavigne JV, Brown KM, Gidding S, Evans M, Stevens VJ, von Almen TK, et al. A cholesterol-lowering diet does not produce adverse psychological effects in children: three-year results from the dietary intervention study in children. *Health Psychol*. 1999;18(6):604–13.
71. Niinikoski H, Koskinen P, Punnonen K, Seppanen R, Viikari J, Ronnema T, et al. Intake and indicators of iron and zinc status in children consuming diets low in saturated fat and cholesterol: the STRIP baby study. Special Turku Coronary Risk Factor Intervention Project for Babies. *Am J Clin Nutr*. 1997;66(3):569–74.
72. Lauer RM, Obarzanek E, Hunsberger SA, Van Horn L, Hartmuller VW, Barton BA, et al. Efficacy and safety of lowering dietary intake of total fat, saturated fat, and cholesterol in children with elevated LDL cholesterol: the Dietary Intervention Study in Children. *Am J Clin Nutr*. 2000;72(5 Suppl):1332S–42S.
73. Writing Group for the DISC Collaborative Research Group. Efficacy and safety of lowering dietary intake of fat and cholesterol in children with elevated low-density lipoprotein cholesterol: the Dietary Intervention Study in Children (DISC). *JAMA*. 1995;273(18):1429–35.
74. Hodson L, Skeaff CM, Fielding BA. Fatty acid composition of adipose tissue and blood in humans and its use as a biomarker of dietary intake. *Prog Lipid Res*. 2008;47(5):348–80.
75. Desroches S, Chouinard PY, Galibois I, Corneau L, Delisle J, Lamarche B, et al. Lack of effect of dietary conjugated linoleic acids naturally incorporated into butter on the lipid profile and body composition of overweight and obese men. *Am J Clin Nutr*. 2005;82(2):309–19.
76. Motard-Belanger A, Charest A, Grenier G, Paquin P, Chouinard Y, Lemieux S, et al. Study of the effect of *trans* fatty acids from ruminants on blood lipids and other risk factors for cardiovascular disease. *Am J Clin Nutr*. 2008;87(3):593–9.
77. Gebauer SK, Destailats F, Dionisi F, Krauss RM, Baer DJ. Vaccenic acid and *trans* fatty acid isomers from partially hydrogenated oil both adversely affect LDL cholesterol: a double-blind, randomized controlled trial. *Am J Clin Nutr*. 2015;102(6):1339–46.
78. Radtke T, Schmid A, Trepp A, Dähler F, Coslovsky M, Eser P, et al. Short-term effects of *trans* fatty acids from ruminant and industrial sources on surrogate markers of cardiovascular risk in healthy men and women: a randomized, controlled, double-blind trial. *European J Prev Cardiol*. 2017;24(5):534–43.
79. Verneque BJB, Machado AM, de Abreu Silva L, Lopes ACS, Duarte CK. Ruminant and industrial *trans*-fatty acids consumption and cardiometabolic risk markers: a systematic review. *Crit Rev Food Sci Nutr*. 2020:1–11.
80. Lapinleimu H, Viikari J, Jokinen E, Salo P, Routi T, Leino A, et al. Prospective randomised trial in 1062 infants of diet low in saturated fat and cholesterol. *Lancet*. 1995;345(8948):471–6.

81. Pahkala K, Laitinen TT, Niinikoski H, Kartiosuo N, Rovio SP, Lagström H, et al. Effects of 20-year infancy-onset dietary counselling on cardiometabolic risk factors in the Special Turku Coronary Risk Factor Intervention Project (STRIP): 6-year post-intervention follow-up. *Lancet Child Adolesc Health*. 2020;4(5):359–69.
82. Xiang AS, Kingwell BA. Rethinking good cholesterol: a clinicians' guide to understanding HDL. *Lancet Diabetes Endocrinol*. 2019;7(7):575–82.
83. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr Probl Cardiol*. 2010;35(2):72–115.
84. Wekesah FM, Kyobutungi C, Grobbee DE, Klipstein-Grobusch K. Understanding of and perceptions towards cardiovascular diseases and their risk factors: a qualitative study among residents of urban informal settings in Nairobi. *BMJ Open*. 2019;9(6):e026852.
85. Negesa LB, Magarey J, Rasmussen P, Hendriks JML. Patients' knowledge on cardiovascular risk factors and associated lifestyle behaviour in Ethiopia in 2018: a cross-sectional study. *PLoS One*. 2020;15(6):e0234198.
86. Oli N, Vaidya A, Subedi M, Krettek A. Experiences and perceptions about cause and prevention of cardiovascular disease among people with cardiometabolic conditions: findings of in-depth interviews from a peri-urban Nepalese community. *Glob Health Action*. 2014;7:24023.
87. Erhardt L, Hobbs FD. Public perceptions of cardiovascular risk in five European countries: the react survey. *Int J Clin Pract*. 2002;56(9):638–44.
88. Malhotra A. Saturated fat is not the major issue. *BMJ*. 2013;347:f6340.
89. Teicholz N. *The big fat surprise: why butter, meat and cheese belong in a healthy diet*. Simon & Schuster; 2014.
90. Jousilahti P, Laatikainen T, Peltonen M, Borodulin K, Männistö S, Jula A, et al. Primary prevention and risk factor reduction in coronary heart disease mortality among working aged men and women in eastern Finland over 40 years: population based observational study. *BMJ*. 2016;352:i721.
91. Vartiainen E, Laatikainen T, Tapanainen H, Puska P. Changes in serum cholesterol and diet in North Karelia and all Finland. *Glob Heart*. 2016;11(2):179–84.
92. Smed S, Scarborough P, Rayner M, Jensen JD. The effects of the Danish saturated fat tax on food and nutrient intake and modelled health outcomes: an econometric and comparative risk assessment evaluation. *Eur J Clin Nutr*. 2016;70(6):681–6.
93. Countdown to 2023: WHO report on global trans-fat elimination 2022. Geneva: World Health Organization; 2023 (<https://apps.who.int/iris/handle/10665/365617>, accessed 1 January 2023).
94. Downs SM, Bloem MZ, Zheng M, Catterall E, Thomas B, Veerman L, et al. The impact of policies to reduce *trans* fat consumption: a systematic review of the evidence. *Curr Dev Nutr*. 2017;1(12):cdn.117.000778.
95. Schultz WM, Kelli HM, Lisko JC, Varghese T, Shen J, Sandesara P, et al. Socioeconomic status and cardiovascular outcomes: challenges and interventions. *Circulation*. 2018;137(20):2166–78.
96. Allen L, Williams J, Townsend N, Mikkelsen B, Roberts N, Foster C, et al. Socioeconomic status and non-communicable disease behavioural risk factors in low-income and lower-middle-income countries: a systematic review. *Lancet Glob Health*. 2017;5(3):e277–e89.
97. Marklund M, Zheng M, Veerman JL, Wu JHY. Estimated health benefits, costs, and cost-effectiveness of eliminating industrial *trans*-fatty acids in Australia: a modelling study. *PLoS Med*. 2020;17(11):e1003407.
98. Bertram MY, Sweeny K, Lauer JA, Chisholm D, Sheehan P, Rasmussen B, et al. Investing in non-communicable diseases: an estimation of the return on investment for prevention and treatment services. *Lancet*. 2018;391(10134):2071–8.

99. Dall TM, Fulgoni VL 3rd, Zhang Y, Reimers KJ, Packard PT, Astwood JD. Potential health benefits and medical cost savings from calorie, sodium, and saturated fat reductions in the American diet. *Am J Health Promot.* 2009;23(6):412–22.
100. Meier T, Senftleben K, Deumelandt P, Christen O, Riedel K, Langer M. Healthcare costs associated with an adequate intake of sugars, salt and saturated fat in Germany: a health econometrical analysis. *PLoS One.* 2015;10(9):e0135990.
101. Malla S, Hobbs JE, Perger O. Estimating the health care savings from *trans* fat-free canola in Canada. *Acta Agric Scand C Food Econ.* 2005;2(3–4):175–84.
102. Abdullah MM, Jew S, Jones PJ. Health benefits and evaluation of healthcare cost savings if oils rich in monounsaturated fatty acids were substituted for conventional dietary oils in the United States. *Nutr Rev.* 2017;75(3):163–74.
103. Total fat intake for the prevention of unhealthy weight gain in adults and children: WHO guideline. Geneva: World Health Organization; 2023 (<https://www.who.int/publications/i/item/9789240073654>, accessed 25 May 2023).
104. Guideline: sugars intake for adults and children. Geneva: World Health Organization; 2015 (<https://apps.who.int/iris/handle/10665/149782>, accessed 1 January 2023).
105. Guideline: sodium intake for adults and children. Geneva: World Health Organization; 2012 (<https://apps.who.int/iris/handle/10665/77985>, accessed 1 January 2023).
106. Guideline: potassium intake for adults and children. Geneva: World Health Organization; 2012 (<https://apps.who.int/iris/handle/10665/77986>, accessed 1 January 2023).
107. Carbohydrate intake for adults and children: WHO guideline. Geneva: World Health Organization; 2023 (<https://www.who.int/publications/i/item/9789240073593>, accessed 25 May 2023).
108. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. *Lancet.* 2019;393(10170):434–45.
109. Aune D, Giovannucci E, Boffetta P, Fadnes LT, Keum N, Norat T, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality: a systematic review and dose–response meta-analysis of prospective studies. *Int J Epidemiol.* 2017;46(3):1029–56.
110. Marventano S, Izquierdo Pulido M, Sánchez-González C, Godos J, Speciani A, Galvano F, et al. Legume consumption and CVD risk: a systematic review and meta-analysis. *Public Health Nutr.* 2017;20(2):245–54.
111. Afshin A, Micha R, Khatibzadeh S, Mozaffarian D. Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis. *Am J Clin Nutr.* 2014;100(1):278–88.
112. Mytton OT, Nnoaham K, Eyles H, Scarborough P, Ni Mhurchu C. Erratum to: systematic review and meta-analysis of the effect of increased vegetable and fruit consumption on body weight and energy intake. *BMC Public Health.* 2017;17(1):662.
113. Mytton OT, Nnoaham K, Eyles H, Scarborough P, Ni Mhurchu C. Systematic review and meta-analysis of the effect of increased vegetable and fruit consumption on body weight and energy intake. *BMC Public Health.* 2014;14:886.
114. Zong G, Li Y, Wanders AJ, Alsema M, Zock PL, Willett WC, et al. Intake of individual saturated fatty acids and risk of coronary heart disease in US men and women: two prospective longitudinal cohort studies. *BMJ.* 2016;355:i5796.
115. Downs SM, Thow AM, Leeder SR. The effectiveness of policies for reducing dietary *trans* fat: a systematic review of the evidence. *Bull World Health Organ.* 2013;91(4):262–9H.
116. L'Abbe MR, Stender S, Skeaff CM, Ghafoorunissa, Tavella M. Approaches to removing *trans* fats from the food supply in industrialized and developing countries. *Eur J Clin Nutr.* 2009;63(S2):S50–S67.

117. Global Nutrition Policy Review 2016–2017: country progress in creating enabling policy environments for promoting healthy diets and nutrition. Geneva: World Health Organization; 2018 (<https://apps.who.int/iris/handle/10665/275990>, accessed 1 January 2023).
118. Global Nutrition Policy Review: what does it take to scale up nutrition action? Geneva: World Health Organization; 2013 (<https://apps.who.int/iris/handle/10665/84408>, accessed 1 January 2023).
119. Griffin BA, Mensink RP, Lovegrove JA. Does variation in serum LDL-cholesterol response to dietary fatty acids help explain the controversy over fat quality and cardiovascular disease risk? *Atherosclerosis*. 2021;328:108–13.

Annexes

Annex 1

Members of the WHO steering group

Dr Ayoub Al-Jawaldeh,

Regional Adviser in Nutrition
WHO Regional Office for the Eastern
Mediterranean
Egypt

Dr Anshu Banerjee

Director
Maternal, Newborn, Child & Adolescent Health &
Ageing
WHO headquarters
Switzerland

Dr Hana Bekele

Nutrition Adviser
WHO Regional Office for Africa/Intercountry
Support Team for East and Southern Africa
Congo

Dr Fabio Da Silva Gomes

Nutrition and Physical Activity Adviser
WHO Regional Office for the Americas
United States of America

Dr Padmini Angela De Silva

Regional Adviser in Nutrition
WHO Regional Office for South-East Asia
India

Dr Jason Montez

Scientist, Standards and Scientific Advice on Food
and Nutrition
Department of Nutrition and Food Safety
WHO headquarters
Switzerland

Dr Chizuru Nishida

Unit Head, Safe, Healthy and Sustainable Diets
Department of Nutrition and Food Safety
WHO headquarters
Switzerland

Dr Juliawati Untoro

Regional Adviser in Nutrition
WHO Regional Office for the Western Pacific
Philippines

Dr Cherian Varghese

Cross-cutting lead, Noncommunicable Diseases
Department of Noncommunicable Diseases
WHO headquarters
Switzerland

Dr Kremlin Wickramasinghe

Nutrition Adviser
WHO European Office for the Prevention and
Control of NCDs
Russian Federation

Annex 2

Members of the guideline development group (NUGAG Subgroup on Diet and Health)

Professor Hayder Al-Domi

Division of Nutrition and Dietetics
Department of Nutrition and Food Technology
School of Agriculture
University of Jordan
Jordan
Areas of expertise: dietetics, human nutrition, diet and health, obesity biomarkers, diabetogenic dietary proteins

Professor John H Cummings (member until 2018)

Division of Cancer Research, Medical Research Institute
Ninewells Hospital & Medical School
University of Dundee
United Kingdom of Great Britain and Northern Ireland
Areas of expertise: carbohydrates, dietary fibre

Emeritus Professor Ibrahim Elmadfa

Department of Nutritional Sciences
Faculty of Life Sciences
University of Vienna
Austria
Areas of expertise: human nutrition, nutrient requirements, fats and fatty acids, diet and health, dietary diversity

Dr Lee Hooper

Norwich Medical School
University of East Anglia
United Kingdom of Great Britain and Northern Ireland
Areas of expertise: systematic review and research methods, dietetics, human nutrition, hydration, frail older adults and long-term care

Emeritus Professor Shiriki Kumanyika

(Chairperson)
Perelman School of Medicine
University of Pennsylvania
United States of America
Areas of expertise: human nutrition, epidemiology, obesity, salt/sodium

Professor Mary L'Abbé

Department of Nutritional Sciences
Temerty Faculty of Medicine
University of Toronto
Canada
Areas of expertise: nutrition science, *trans*-fatty acids, sodium, risk assessment/risk management, food regulation, diet and health

Professor Pulani Lanerolle

Department of Biochemistry and Molecular Biology
Faculty of Medicine
University of Colombo
Sri Lanka
Areas of expertise: nutrition and health, body composition, nutrition education

Professor Duo Li

Institute of Nutrition & Health
Qingdao University
Department of Food Science and Nutrition
Zhejiang University
China
Areas of expertise: nutritional epidemiology, fats and fatty acids

Professor Jim Mann

Departments of Medicine and Human Nutrition
University of Otago
New Zealand
Areas of expertise: carbohydrates, sugars, diabetes, fats and fatty acids

Professor Joerg Meerpohl

Institute for Evidence in Medicine
Medical Center, University of Freiburg
Germany
Areas of expertise: systematic review methods, GRADE methodology, paediatrics, paediatric haematology and oncology

Professor Carlos Monteiro

Department of Nutrition, School of Public Health
University of Sao Paulo
Brazil

Areas of expertise: nutritional epidemiology, diet and all forms of malnutrition, obesity, food-based dietary guidelines

Dr Laetitia Ouedraogo Nikièma (member until 2020)

Institut de Recherche en Sciences de la Santé
Burkina Faso

Areas of expertise: nutritional epidemiology, maternal and child health and nutrition, all forms of malnutrition, diet-related noncommunicable diseases

Professor Harshpal Singh Sachdev

Sitaram Bhartia Institute of Science and Research
India

Areas of expertise: developmental origins of adult cardiometabolic disease, nutrition in children and mothers in low- and middle-income countries, childhood obesity, systematic review methods

Dr Barbara Schneeman

Departments of Nutrition/Food Science and Technology
University of California, Davis
United States of America

Areas of expertise: carbohydrates, dietary fibre, nutrition, diet and health, Codex Alimentarius, food regulation

Emeritus Professor Murray Skeaff

Department of Human Nutrition
University of Otago
New Zealand

Areas of expertise: fats and fatty acids, biomarkers, diet and health, human nutrition

Professor Bruno Fokas Sunguya

School of Public Health and Social Sciences
Muhimbili University of Health and Allied Sciences
United Republic of Tanzania

Areas of expertise: public health nutrition, research methods, systematic review methodology, human nutrition, nutrition epidemiology

Professor HH (Esté) Vorster (member until 2020)

Faculty of Health Sciences
North-West University
South Africa

Areas of expertise: nutrition physiology, public health nutrition, food-based dietary guidelines, nutrition transition in Africa

Annex 3

External peer review group

Professor Sohel Reza Choudhury

Professor and Head, Department of Epidemiology and Research
National Heart Foundation Hospital & Research Institute
Bangladesh

Professor Rod Jackson

Professor, Medical and Health Sciences, Epidemiology and Biostatistics
University of Auckland
New Zealand

Dr Amos Laar

Associate Professor of Public Health
Department of Population, Family & Reproductive Health, School of Public Health
University of Ghana
Ghana

Professor Louis Levy

Expert Advisor, Department of Health and Social Care
Honorary Visiting Professor, University of Chester
United Kingdom of Great Britain and Northern Ireland

Professor Lara Nasreddine

Department of Nutrition and Food Sciences
Faculty of Agricultural and Food Sciences
American University of Beirut
Lebanon

Professor Frank Sacks

Professor of Cardiovascular Disease Prevention, Departments of Nutrition and Molecular Metabolism, Harvard TH Chan School of Public Health
Professor of Medicine, Harvard Medical School
United States of America

Dr Caroline Van Rossum (co-reviewed with Dr Westenbrink)

National Institute for Public Health and the Environment (RIVM)
Centre for Nutrition, Prevention and Health Services
Netherlands (Kingdom of the)

Dr Susanne Westenbrink (co-reviewed with Dr Van Rossum)

National Institute for Public Health and the Environment (RIVM)
Centre for Nutrition, Prevention and Health Services
Netherlands (Kingdom of the)

Annex 4

Summary and management of declarations of interests

Members of the guideline development group (NUGAG Subgroup on Diet and Health)

Interests declared or otherwise identified independently for the following members during the development of this guideline are summarized below.

Member	Interests declared/identified	Action taken
Mary L'Abbé	<ul style="list-style-type: none"> ▶ Iodine Global Network: member, Board of Directors (2020–2021) ▶ WHO: Director, WHO Collaborating Centre on Nutrition Policy for NCD Prevention (2015–2021) ▶ Pan American Health Organization (PAHO): Chair, PAHO Technical Advisory Group to Mobilize Cardiovascular Disease Prevention through Dietary Salt/Sodium Control Policies and Interventions (2015–2021) ▶ PAHO: member/Chair of PAHO consultation meetings for setting sodium reduction targets, and other sodium-related work (2012–2021) ▶ Resolve to Save Lives, Vital Strategies: technical adviser on trans-fatty acids (2018–2019) ▶ Heart and Stroke Foundation of Canada: member, Council on Mission: Priorities, Advice, Science and Strategy Advisory Panel (CoMPASS) (2013–2021) ▶ World Obesity, World Federation of Public Health Associations: delegate representative to Codex Committee on Nutrition and Foods for Special Dietary Uses, and to Codex Committee on Food Labelling (2018–2021) ▶ National Nutrient Databank Conference: Steering Committee member (2017–2021) ▶ Nestle Nutrition: external peer reviewer for two research proposals; attended peer review meeting (2018) ▶ US National Academies of Sciences, Engineering, and Medicine (NASEM): member, NASEM Panel on Global Harmonization of DRIs (2017–2018) ▶ World Obesity: member, Scientific and Technical Advisory Network (2014–2021) ▶ International Network for Food and Obesity/NCDs Research, Monitoring and Action Support (INFORMAS): member, International Network for Food and Obesity/NCD Research (2012–2021) ▶ Marketing to Kids Coalition: member and technical adviser, Health Canada discussion on policy options regarding marketing to children (2016–2021) 	<p>Each engagement was assessed in the context of the topic of this guideline. While meeting expenses were often covered by the relevant agencies listed, no income or honorariums were paid. The engagements have been on a variety of nutrition topics, none of which were determined to be directly relevant to the objective of this guideline, and were therefore not considered to represent a conflict of interest.</p> <p>The sources of research funds were not considered to represent a conflict of interest for this guideline. Nor were the topics covered by the research funds which focused primarily on assessing dietary quality, ways of promoting healthy diets (including sodium reduction strategies), and food labelling.</p> <p>Because none of the interests were directly relevant to the objective of this guideline, it was determined that they would not impact the ability of this expert to serve as a member of the NUGAG Subgroup</p>

Member	Interests declared/identified	Action taken
	<ul style="list-style-type: none"> ▶ Statistics Canada and Health Canada: technical adviser on analysis of dietary intake patterns for 2015 Canadian Community Health Survey (2015–2021) ▶ Health Canada: technical adviser on various projects – nutrient profiling for front-of-pack labelling, restricting marketing to children, updating Canada’s Food Guide, developing a Canada Food Guide Adherence Tool on “what to eat” (2016–2021) ▶ Received research funding from various agencies: Canadian Institute of Health Research, Institute for the Advancement of Food and Nutrition Sciences, Alberta Innovates and Alberta Health Services, Health Canada, Sanofi-Pasteur – University of Toronto – Université Paris – Descartes International Collaborative Research Pilot and Feasibility Program, International Development Research Centre – NCD Prevention Program, Burroughs Wellcome Foundation, Fonds de recherche Société et culture Québec, Heart and Stroke Foundation of Canada (2012–2021) 	<p>on Diet and Health in an objective manner, and the expert was allowed to participate fully as a member of the NUGAG Subgroup on Diet and Health throughout the guideline development process.</p>
<p>Barbara Schneeman</p>	<ul style="list-style-type: none"> ▶ US Agency for International Development (USAID): employed as higher education coordinator from 2015 to 2016, where she worked with the higher education community to increase engagement with USAID ▶ US Food and Drug Administration (FDA): employed through 2012 (retired in 2013) ▶ Head of the US delegate to the Codex Committee on Nutrition and Foods for Special Dietary Uses, and Codex Committee on Food Labelling; she presented the positions of the United States in these Codex forums (up to 2012) ▶ Monsanto: member of advisory committee discussing role of agriculture in addressing climate change, and improving food and nutrition security (2014–2017) ▶ McCormick Science Institute: member of advisory committee reviewing research proposals on spices and herbs (2014–2021) ▶ Ocean Spray: temporary adviser on health claim petitions that are submitted to US FDA related to cranberries (2014–2015) ▶ Genera Mills: temporary adviser on labelling requirements for nutrition declarations in the United States (2014–2016, and 2018) ▶ DSM: temporary adviser on Codex Alimentarius processes (2014–2015) ▶ Hampton Creek: temporary adviser on labelling standards for mayonnaise (2014–2015) ▶ Washington DC law firm: temporary adviser on labelling of genetically modified foods (2014–2015) ▶ NASEM: member of the National Academies and member/Chair of the Dietary Guidelines Advisory Committee, involved in reviewing the evidence for developing the Dietary Guidelines for Americans 	<p>Each engagement was assessed in the context of the topic of this guideline. Meeting expenses and honorariums were paid in some instances.</p> <p>With the exception of membership on the US Dietary Guidelines Advisory Committee, the engagements have all been on topics unrelated to the objective of this guideline, primarily providing expert advice on US regulatory issues, such as food labelling (i.e. nutrient declarations, health claims, other types of labelling), or presenting the process for developing the dietary guidelines for the US, <i>Dietary Guidelines for Americans</i>. Regarding her membership on the US Dietary Guidelines Advisory Committee, although the nature of the work was similar to the work being carried out for this guideline, the work was done for</p>

Member	Interests declared/identified	Action taken
	<ul style="list-style-type: none"> — Nominated to the Dietary Guidelines Advisory Committee of the USA by representatives from the North American Branch of the International Life Sciences Institute; American Beverage Association; American Bakers Association, Grain Chain; Grocery Manufacturers Association USA Dry Pea & Lentil Council, American Pulse Association — Received honorariums for presentations on the process to develop the Dietary Guidelines for Americans and policies for food labelling in the United States at various scientific meetings organized by PMK Associates (Institute of Food Technologists and American Oil Chemists' Society), McCormick Science Institute, Fiber Association Japan, and Mushroom Council ▶ International Food Information Council (IFIC): member, Board of Trustees, which ensures that IFIC upholds its responsibilities as a 501(c)(3) non-profit organization (2021) ▶ International Life Science Institute North America: government liaison, and evaluating research and organizing webinars on the microbiome (2018) ▶ International Dairy Foods Association: presented webinar on the work of the 2020 Dietary Guideline Advisory Committee, for which she received no remuneration (2020) 	<p>a national authority and therefore was not considered a conflict of interest. With respect to her nomination to the US Dietary Guidelines Advisory Committee by various industry groups, there is no relationship or affiliation between nominator and nominee.</p> <p>Because none of the interests were directly relevant to the objective of this guideline or were otherwise determined not to represent a conflict of interest, it was concluded that the interests would not impact the ability of this expert to serve as a member of the NUGAG Subgroup on Diet and Health in an objective manner. The expert was allowed to participate fully as a member of the NUGAG Subgroup on Diet and Health throughout the guideline development process.</p>

No other members of the NUGAG Subgroup on Diet and Health declared any interests (or the declared interests clearly did not represent a conflict of interest), nor were any interests independently identified (see [Annex 2](#) for the list of members of the NUGAG Subgroup on Diet and Health).

Members of the external peer review group

Member	Interests declared/identified	Action taken
Amos Laar	<ul style="list-style-type: none"> ▶ International Development Research Center, Canada: research support to study the food environments of Ghanaian children to prevent obesity and NCDs (MEALS4NCDs) 	Given the nature and topic of the research funding, it was not considered to represent a conflict of interest for serving as an external reviewer of this guideline.
Louis Levy	<ul style="list-style-type: none"> ▶ Public Health England and Department of Health and Social Care (England): Head of Nutrition Science (until 2019) and an expert adviser to the diet and obesity team responsible for oversight of nutrition science evidence, including the work of the Scientific Advisory Committee on Nutrition 	Given the nature and topic of the engagement, it was not considered to represent a conflict of interest for serving as an external reviewer of this guideline.
Frank Sacks	<ul style="list-style-type: none"> ▶ National Institute on Aging, National Institutes of Health: research funding for a clinical trial of a diet similar to DASH or Mediterranean diet to prevent age-related cognitive decline ▶ American Heart Association (AHA): Chair of the writing group on AHA scientific statement on dietary fats (2017) 	Given the nature and topic of the engagement and research funding, it was not considered to represent a conflict of interest for serving as an external reviewer of this guideline.

No other members of the external peer review group declared any interests, nor were any interests independently identified (see [Annex 3](#) for the list of external peer reviewers).

Members of the systematic review teams

No members of the systematic review teams declared any interests, nor were any interests independently identified.

Annex 5

Key questions in PICO format (population, intervention, comparator, outcome)

SFA

What is the effect on prioritized health outcomes in adults and children of:

- ▶ lower intake of SFA compared with higher intake;
- ▶ SFA intake below 10% of total energy intake compared with intake above 10%;
- ▶ replacement of SFA in the diet with polyunsaturated fatty acids, monounsaturated fatty acids, carbohydrates or protein; and
- ▶ lower intake of individual SFA¹ compared with higher intake.

Adults

Population	<p>Apparently healthy adults in low-, middle- and high-income countries</p> <ul style="list-style-type: none"> ▶ In each, consider population characteristics, such as age, gender, ethnicity, country/region (urban/rural), socioeconomic status, demographic factors, sanitation, health background and health status, including baseline risk of CVDs
Intervention/exposure	<p>Definitions</p> <ul style="list-style-type: none"> ▶ SFA/saturated fat ▶ % energy intake from SFA ▶ Dietary fatty acids/dietary fat
Control	<ul style="list-style-type: none"> ▶ Comparison of levels ▶ Continuous or categorical ▶ Adherence to recommendations ▶ Appropriately matched to intervention group by randomization
Confounders/effect modifiers/intermediates	<ul style="list-style-type: none"> ▶ Baseline level of SFA intake ▶ Energy intake ▶ Energy expenditure; fitness and physical activity ▶ Consider other interventions in design, dietary and non-dietary (protocol to specify) ▶ Consider influence of other aspects of diet/dietary patterns ▶ Consider effects of nutrients used to replace SFA <p>Intermediates</p> <ul style="list-style-type: none"> ▶ Take into account effect of energy density ▶ Blood lipids as an intermediate between SFA and cardiovascular outcomes

¹ SFA comprise many different, individual SFA molecules that vary in chain length (i.e. the number of carbon atoms in the carbon backbone of fatty acids). Common SFA found in the diet of humans include lauric acid (12 carbons), myristic acid (14 carbons), pentadecanoic acid (15 carbons), palmitic acid (16 carbons), heptadecanoic acid (17 carbons) and stearic acid (18 carbons).

Outcome	<ul style="list-style-type: none"> ▶ All-cause mortality ▶ Cardiovascular outcomes <ul style="list-style-type: none"> – CVDs: events, mortality – Coronary heart disease: events, mortality – Stroke ▶ Type 2 diabetes ▶ LDL cholesterol
Time frame	<ul style="list-style-type: none"> ▶ For studies where the intervention is advisory or provision of food, and outcomes are CVD events and mortality, minimum study duration is 2 years (24 months) ▶ For controlled feeding studies with blood lipid outcomes, minimum study duration is 13 days, which is the minimum time necessary for blood lipids to reach a new steady state in response to changes in diet

Children

Population	<p>Apparently healthy children in low-, middle- and high-income countries</p> <ul style="list-style-type: none"> ▶ In each, consider population characteristics, such as age, gender, ethnicity, country/region (urban/rural), socioeconomic status/ demographic factors/sanitation health background and health status
Intervention/exposure	<p>Definitions</p> <ul style="list-style-type: none"> ▶ SFA/saturated fat ▶ % energy intake from SFA ▶ Dietary fatty acids/dietary fat ▶ Dairy fat
Control	<ul style="list-style-type: none"> ▶ Comparison of levels ▶ Continuous or categorical ▶ Adherence to recommendations ▶ Appropriately matched to intervention group by randomization
Confounders/effect modifiers/ intermediates	<ul style="list-style-type: none"> ▶ Baseline level of SFA intake ▶ Energy intake ▶ Energy expenditure; fitness and physical activity ▶ Consider other interventions in design, dietary and non-dietary (protocol to specify) ▶ Consider influence of other aspects of diet/dietary patterns ▶ Consider effects of nutrients used to replace SFA <p>Intermediates</p> <ul style="list-style-type: none"> ▶ Take into account effect of energy density ▶ Blood lipids as an intermediate between SFA and cardiovascular outcomes
Outcome	<ul style="list-style-type: none"> ▶ LDL cholesterol ▶ Measures of body weight, adiposity ▶ Measures of growth and development ▶ Type 2 diabetes incidence, insulin resistance ▶ Adverse effects
Time frame	<ul style="list-style-type: none"> ▶ For studies where the intervention is advisory or provision of food and outcomes are blood lipids, minimum study duration is 13 days, which is the minimum time necessary for blood lipids to reach a new steady state in response to changes in diet

TFA

What is the effect on prioritized health outcomes in adults and children of:

- ▶ lower intake of total TFA compared with higher intake;
- ▶ total TFA intake below 1% of total energy intake compared with intake above 1%;
- ▶ lower intake of ruminant TFA compared with higher intake, or lower intake of industrially produced TFA compared with higher intake; and
- ▶ replacement of total TFA in the diet with polyunsaturated fatty acids, monounsaturated fatty acids, SFA, carbohydrates or protein?

Adults

Population	<p>Apparently healthy adults in low-, middle- and high-income countries</p> <ul style="list-style-type: none"> ▶ In each, consider population characteristics, such as age, gender, ethnicity, country/region (urban/rural), socioeconomic status/ demographic factors/sanitation health background and health status, including baseline risk of CVDs
Intervention/exposure	<p>Definitions</p> <ul style="list-style-type: none"> ▶ TFA/<i>trans</i> fats ▶ Industrially produced TFA ▶ Ruminant TFA ▶ % energy intake from TFA ▶ Dietary fatty acids/dietary fat
Control	<ul style="list-style-type: none"> ▶ Comparison of levels ▶ Continuous or categorical ▶ Adherence to recommendations ▶ Appropriately matched to intervention group by randomization
Confounders/effect modifiers/intermediates	<ul style="list-style-type: none"> ▶ Baseline level of TFA intake ▶ Energy intake ▶ Energy expenditure; fitness and physical activity ▶ Consider other interventions in design, dietary and non-dietary (protocol to specify) ▶ Consider influence of other aspects of diet/dietary patterns ▶ Consider effects of nutrients used to replace TFA <p>Intermediates</p> <ul style="list-style-type: none"> ▶ Take into account effect of energy density ▶ Blood lipids as an intermediate between TFA and cardiovascular outcomes
Outcome	<ul style="list-style-type: none"> ▶ All-cause mortality ▶ Cardiovascular outcomes <ul style="list-style-type: none"> — CVDs: events, mortality — Coronary heart disease: events, mortality — Stroke ▶ Type 2 diabetes ▶ LDL cholesterol

Time frame	<ul style="list-style-type: none"> ▶ No minimum duration for prospective observational studies with CVD events, mortality and type 2 diabetes outcomes ▶ For controlled feeding studies with blood lipid outcomes, minimum study duration is 13 days, which is the minimum time necessary for blood lipids to reach a new steady state in response to changes in diet
-------------------	---

Children

Population	<p>Apparently healthy children in low-, middle- and high-income countries</p> <ul style="list-style-type: none"> ▶ In each, consider population characteristics, such as age, gender, ethnicity, country/region (urban/rural), socioeconomic status/ demographic factors/sanitation health background and health status, including baseline risk of CVDs
Intervention/exposure	<p>Definitions</p> <ul style="list-style-type: none"> ▶ TFA/<i>trans</i> fats ▶ Industrially produced TFA ▶ Ruminant TFA ▶ % energy intake from TFA ▶ Dietary fatty acids/dietary fat ▶ Dairy fat
Control	<ul style="list-style-type: none"> ▶ Comparison of levels ▶ Continuous or categorical ▶ Adherence to recommendations ▶ Appropriately matched to intervention group by randomization
Confounders/effect modifiers/intermediates	<ul style="list-style-type: none"> ▶ Baseline level of TFA intake ▶ Energy intake ▶ Energy expenditure; fitness and physical activity ▶ Consider other interventions in design, dietary and non-dietary (protocol to specify) ▶ Consider influence of other aspects of diet/dietary patterns ▶ Consider effects of nutrients used to replace TFA <p>Intermediates</p> <ul style="list-style-type: none"> ▶ Take into account effect of energy density ▶ Blood lipids as an intermediate between TFA and cardiovascular outcomes
Outcome	<ul style="list-style-type: none"> ▶ LDL cholesterol ▶ Measures of body weight, adiposity ▶ Measures of growth and development ▶ Type 2 diabetes incidence, insulin resistance ▶ Adverse effects
Time frame	<ul style="list-style-type: none"> ▶ For studies where the intervention is advisory or provision of food and outcomes are blood lipids, minimum study duration is 13 days, which is the minimum time necessary for blood lipids to reach a new steady state in response to changes in diet

Annex 6

GRADE evidence profiles

For details on how GRADE assessments were carried out, see the end of this Annex.

GRADE evidence profile 1

Question: What is the effect of lower compared with higher intake of SFA in adults?

Population: General adult population

No. of studies	Study design	Assessment					No. of events/participants (study event rate)		Effect		Certainty ⁴
		Risk of bias	Inconsistency	Indirectness ¹	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ² (95% CI)	Absolute – per 1000 ³ (95% CI)	
All-cause mortality											
12	RCT	Not serious ⁵	Not serious	Not serious	Serious ⁶	None ⁷	1 465/22 819 (6.4%)	2 053/33 039 (6.2%)	RR 0.96 (0.90 to 1.03)	2 fewer (from 6 fewer to 2 more)	⊕⊕⊕⊕ Moderate
21	Observational	Not serious ⁸	Serious ⁹	Not serious	Not serious	None ⁷	213 579/1 211 729 (17.6%)		RR 0.93 (0.86 to 1.00)	12 fewer (from 25 fewer to 0)	⊕⊙⊙⊙ Very low
Cardiovascular disease mortality											
11	RCT	Not serious ⁵	Not serious	Not serious	Very serious ¹⁰	None ⁷	483/21 844 (2.2%)	613/31 577 (1.9%)	RR 0.94 (0.78 to 1.13)	1 fewer (from 4 fewer to 2 more)	⊕⊕⊙⊙ Low
Cardiovascular diseases											
13	RCT	Serious ^{5,11}	Not serious ¹²	Not serious	Not serious	None ¹³	1 853/22 012 (8.4%)	2 685/31 746 (8.5%)	RR 0.83 (0.70 to 0.98)	15 fewer (from 25 fewer to 2 fewer)	⊕⊕⊕⊙ Moderate
16	Observational	Not serious ⁸	Serious ⁹	Not serious	Not serious	None ⁷	68 232/1 088 501 (6.3%)		RR 0.93 (0.86 to 1.02)	4 fewer (from 9 fewer to 1 more)	⊕⊙⊙⊙ Very low
Coronary heart disease mortality											
9	RCT	Not serious ⁵	Not serious	Not serious	Very serious ¹⁰	None ⁷	415/21 714 (1.9%)	512/31 445 (1.6%)	RR 0.97 (0.82 to 1.16)	1 fewer (from 3 fewer to 3 more)	⊕⊕⊙⊙ Low

		Assessment					No. of events/participants (study event rate)		Effect		Certainty ⁴
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness ¹	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ² (95% CI)	Absolute – per 1000 ³ (95% CI)	
Coronary heart disease (fatal and non-fatal)											
11	RCT	Serious ^{5,11}	Serious ⁹	Not serious	Serious ⁶	None ⁷	936/21 743 (4.3%)	1 325/31 456 (4.2%)	RR 0.83 (0.68 to 1.01)	7 fewer (from 14 fewer to 0)	⊕⊕○○ Very low
18	Observational	Not serious ⁸	Serious ⁹	Not serious	Not serious	None ⁷	19 263/570 326 (3.4%)		RR 0.96 (0.90 to 1.03)	1 fewer (from 3 fewer to 1 more)	⊕○○○ Very low
Stroke¹⁴											
7	RCT	Serious ^{5,11}	Not serious	Not serious	Very serious ¹⁰	None ⁷	454/20 602 (2.2%)	664/30 350 (2.2%)	RR 0.92 (0.68 to 1.25)	2 fewer (from 7 fewer to 6 more)	⊕○○○ Very low
9	Observational	Not serious ⁸	Not serious	Not serious	Not serious	None ⁷	6 400/402 847 (1.6%)		RR 1.02 (0.90 to 1.16)	0 more (from 2 fewer to 3 more)	⊕⊕○○ Low
Type 2 diabetes¹⁵											
13	Observational	Not serious ⁸	Not serious	Not serious	Not serious	None ⁷	15 727/351 134 (4.5%)		RR 0.98 (0.91 to 1.06)	1 fewer (from 4 fewer to 3 more)	⊕⊕○○ Low
LDL cholesterol (mmol/L per 1% energy exchange)											
13 (18) ¹⁶	RCT	Not serious ¹⁷	Not serious ¹⁸	Not serious ¹⁹	Not serious ²⁰	None ²¹	1 973 ²²		-0.055 (-0.061 to -0.050) ²³		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk; SFA: saturated fatty acids.

¹ All studies were conducted in the population of interest and employed appropriate interventions to assess the effect of lower SFA intake compared with higher intake, or assessed effects of appropriate exposures in observational studies on priority health outcomes decided upon prior to initiating the reviews. The RCTs were primarily conducted in populations from Australia, Europe, New Zealand and the United States, and observational studies in North America, Europe, Asia, Australia, the United Kingdom and multinational cohorts. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. For outcomes other than LDL cholesterol, a small number of the RCTs included in the corresponding systematic review (1) employed one or more dietary interventions in addition to SFA reduction (i.e. multifactorial dietary interventions). However, all studies either explicitly or implicitly aimed to reduce SFA intake, did achieve a reduction in SFA intake, or both.

² For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

³ Based on the event rate in the studies (in the control group for RCTs and the total cohort for prospective observational studies) – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁴ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

- 5 These large RCTs of relatively long duration (minimum 24 months) all appeared to use appropriate methods of random sequence generation, and about half had good allocation concealment (allocation concealment in the remaining studies was unclear). Incomplete outcome reporting was variable across studies, and most included studies had systematic differences in care (i.e. intervention group had more time or attention than the control group). Most studies were not blinded, as blinding in dietary trials is generally very difficult. No other biases were noted. Not downgraded for bias, but it is noted that the level of compliance with interventions involving long-term behaviour change, such as those used in these studies, can vary widely. This is likely to attenuate the pooled effect and bias it towards the null.
- 6 The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- 7 Visual inspection of the funnel plot, comparison of fixed- and random-effects meta-analyses, or other assessment did not suggest publication bias. No indication of a dose-response relationship in observational studies.
- 8 These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- 9 $I^2 > 50\%$, indicating a significant level of heterogeneity that was not explained by sensitivity and/or subgroup analyses, where conducted. Downgraded once.
- 10 The 95% CI crosses thresholds of both important benefit and harm. Downgraded twice.
- 11 Limiting trials to those at low summary risk of bias via sensitivity analyses moved the relative risk either closer to the null (CVDs and coronary heart disease) or away from the null (stroke). Downgraded once as a conservative measure.
- 12 Although $I^2 > 50\%$, indicating a significant level of heterogeneity, this was mostly explained by the degree of cholesterol lowering assessed by subgroup and meta-regression analyses.
- 13 The funnel plot did not suggest publication bias, but comparison of fixed- and random-effects meta-analyses suggested possible publication bias. Downgraded once (together with serious risk of bias) as a conservative measure.
- 14 For RCTs, this outcome includes any type of stroke; for observational studies, it includes ischaemic stroke only.
- 15 Additional evidence on the relationship between SFA intake and type 2 diabetes comes from a single, large RCT in which 3342 participants developed diabetes (RR 0.96; 95% CI: 0.90 to 1.02; 48 835 participants; not assessed via GRADE) (3).
- 16 The number of data points is provided in parentheses. Each data point contains dietary information on SFA, polyunsaturated fatty acid, monounsaturated fatty acid and carbohydrate intake, as well as an associated change in LDL cholesterol for each study group (i.e. intervention and control groups) at the end of a dietary treatment period. Each data point was extracted for all treatment groups within studies included in the multiple regression analysis of blood lipids.
- 17 All studies were strictly controlled dietary trials lasting from 13 to 91 days, in which protein and cholesterol intakes were held constant. Some of the studies with parallel design were assessed as having unclear risk of bias in terms of randomization, because the randomization procedure was not fully described. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated if participants were randomized, because all participants were intended to receive all treatments, and thus it was unlikely that any differences at baseline would have had a significant, systematic effect on study results. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it is possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means, so the risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal. Overall, the studies were judged as having a low risk of bias.
- 18 This analysis was conducted as a multiple regression in which data points were directly extracted from each study, rather than mean differences extracted between groups within each included study. As a result, directly measuring between-study variability in a quantitative manner was not feasible. Qualitative assessment of the included studies and the strength and consistency of the results of the multiple regression, however, suggest that any inconsistency was likely to be minor and was therefore not considered to be serious.
- 19 LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- 20 Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing SFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of irrelevant benefit or important harm.

²¹ Publication bias was not formally assessed but, given the large number and nature of the studies included in the analysis (i.e. interventions were not limited to those modifying SFA intake but also included studies in which other dietary fats were modified), risk of publication bias is likely to be low.

²² Total number of participants.

²³ The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as SFA is replaced with an isocaloric amount of polyunsaturated fatty acids. Reductions in LDL cholesterol were also observed when SFA were replaced with monounsaturated fatty acids (-0.042 mmol/L; 95% CI: -0.047 to -0.037) (*high certainty evidence*) or carbohydrates (-0.033 mmol/L; 95% CI: -0.039 to -0.027) (*high certainty evidence*).

GRADE evidence profile 2

Question: What is the effect of lower compared with higher intake of SFA in children?¹

Population: General child population

No. of studies	Study design	Risk of bias	Assessment				No. of participants ²		Relative effect (95% CI)	Certainty ⁵
			Inconsistency	Indirectness ³	Imprecision	Other ⁴	Lower SFA intake	Higher SFA intake		
LDL cholesterol (mmol/L)⁶										
7	RCT	Not serious ⁷	Not serious ⁸	Not serious	Not serious	None	945	1 059	MD 0.13 lower (0.22 lower to 0.03 lower)	⊕⊕⊕⊕ High
Diastolic blood pressure (mmHg)⁹										
2	RCT	Not serious ⁷	Not serious	Not serious	Not serious	None	549	557	MD 1.45 lower (2.34 lower to 0.56 lower)	⊕⊕⊕⊕ High
BMI (kg/m²)¹⁰										
3	RCT	Not serious ⁷	Not serious	Not serious	Serious ¹¹	None	590	599	MD 0.10 lower (0.32 lower to 0.12 higher)	⊕⊕⊕⊕ Moderate
Height (SMD)										
3	RCT	Not serious ⁷	Not serious	Not serious	Serious ¹¹	None	664	623	SMD 0.09 higher (0.03 lower to 0.21 higher)	⊕⊕⊕⊕ Moderate
Insulin resistance (measured as HOMA-IR)¹²										
1	RCT	Serious ¹³	Not serious ¹⁴	Not serious	Not serious	None	245	275	MD 7.5% lower P = 0.0051	⊕⊕⊕⊕ Moderate
Adverse effects										
2	RCT						Outcomes reported varied across studies that reported adverse events; not suitable for pooling but no serious adverse effects identified ¹⁵			

BMI: body mass index; CI: confidence interval; HOMA-IR: homeostasis model assessment of insulin resistance; LDL: low-density lipoprotein; MD: mean difference; RCT: randomized controlled trial; SD: standard deviation; SFA: saturated fatty acids; SMD: standardized mean difference.

¹ This GRADE evidence profile provides assessments for outcomes measured directly in children. In formulating recommendations for children, data for disease incidence, mortality and LDL cholesterol from adults were also used, without downgrading for indirectness. Although adverse clinical cardiovascular outcomes in children are rare, there is no evidence to indicate that the physiological response to a change in SFA intake would be significantly different between adults and children (7-13).

² Participants in crossover trials are counted twice: once in the *Lower SFA intake* column and once in the *Higher SFA intake* column.

³ All studies were conducted in the population of interest, all comparisons were made directly with an appropriate control group, and all outcomes were priority outcomes that were decided upon prior to initiating the review. Studies were conducted in populations from Australia, China, Finland, Spain and the United States. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6).

- ⁴ Too few studies to conduct funnel plot analysis, but no suggestion of publication bias.
- ⁵ All outcomes in this evidence profile are critical outcomes except “height” and “adverse effects”, which are important outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation. Evidence profiles for additional important outcomes can be found in the systematic review of studies conducted in children (14).
- ⁶ Additional evidence on the relationship between SFA intake and blood lipids came from meta-analysis of six studies conducted in children with total cholesterol as an outcome: MD -0.16 mmol/L (95% CI: -0.25 to -0.07; seven trials, 2372 participants) (*high* certainty evidence).
- ⁷ Potential sources of bias were identified in some of the studies included in the meta-analyses, but none of the studies was assessed as having serious risk of bias overall. The following potential sources of bias were noted: two studies had systematic differences in care in terms of frequency of participant interaction with study personnel (i.e. dietary counselling sessions), one study did not report effects for all predefined outcomes, and one study employed cluster randomization based on ability of study centres to implement the intervention (food modification). Only one study was at high risk of bias in several areas and thus considered to be at high risk of bias overall (15); however, results of sensitivity analyses in which this study was removed do not differ significantly from original analyses for critical outcomes.
- ⁸ $I^2 > 50\%$, indicating a significant level of heterogeneity, but point estimates were similar, and virtually all the heterogeneity could be explained by study design and/or the nature of the nutrient replacing SFA in the studies, as assessed by subgroup analysis. Two crossover studies, in which SFA were replaced primarily with polyunsaturated fatty acids and/or monounsaturated fatty acids, achieved greater reductions in total cholesterol and LDL cholesterol than in studies in which the nature of the replacement nutrients was less clear. The outcome was therefore not downgraded for serious inconsistency.
- ⁹ Additional evidence on the relationship between SFA intake and blood pressure comes from meta-analysis of two studies with systolic blood pressure as an outcome (MD -0.68 mmHg; 95% CI: -1.71 to 0.35) (*moderate* certainty evidence).
- ¹⁰ Additional evidence on the relationship between reduced SFA intake and adiposity comes from meta-analysis of four studies with body weight as an outcome (SMD 0.03; 95% CI: -0.13 to 0.07) (*high* certainty evidence) and two studies with waist circumference as an outcome (MD -0.20 cm; 95% CI: -1.38 to 0.98) (*moderate* certainty evidence).
- ¹¹ The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- ¹² HOMA-IR is a composite measure of insulin resistance, incorporating both glucose and insulin, and is calculated as follows: HOMA-IR = fasting glucose (mmol/L) × fasting insulin (mU/L)/22.5.
- ¹³ Possible confounding by dietary fibre intakes, which were higher in intervention children than in control children. Dietary fibre was significantly associated with HOMA-IR in girls. Downgraded once.
- ¹⁴ Only one study included, reporting a small *P* value for effect on HOMA-IR.
- ¹⁵ In addition to no observed effects on growth (i.e. height and weight), there was no evidence of adverse effects of reducing SFA intake in children on micronutrient intakes, cognitive development or sexual maturation in the two studies reporting these outcomes.

GRADE evidence profile 3

Question: What is the effect in adults of consuming less than 10% of total energy intake as SFA compared with consuming more than 10% of total energy intake as SFA?

Population: General adult population

No. of studies	Study design	Certainty assessment					No. of events/participants (study event rate)		Relative ² (95% CI)	Effect Absolute – per 1000 ³ (95% CI)	Certainty ⁴
		Risk of bias	Inconsistency	Indirectness ¹	Imprecision	Other	Lower SFA intake	Higher SFA intake			
All-cause mortality											
5	RCT	Not serious ⁵	Not serious	Not serious	Very serious ⁶	None ⁷	1 204/20 279 (5.9%)	1 730/30 048 (5.8%)	RR 0.99 (0.90 to 1.09)	1 fewer (from 6 fewer to 5 more)	⊕⊕○○ Low
13	Observational	Not serious ⁸	Not serious	Not serious	Not serious	None ⁷	194 456/1 095 528 (17.7%)		RR 0.92 (0.85 to 0.99)	14 fewer (from 27 fewer to 2 fewer)	⊕⊕○○ Low
Cardiovascular disease mortality											
5	RCT	Not serious ⁵	Serious ⁹	Not serious	Very serious ⁶	None ⁷	308/20 279 (1.5%)	431/30 048 (1.4%)	RR 0.95 (0.67 to 1.35)	1 fewer (from 5 fewer to 5 more)	⊕○○○ Very low
Cardiovascular diseases											
5	RCT	Not serious ⁵	Serious ⁹	Not serious	Very serious ⁶	None ⁷	1 541/20 279 (7.5%)	2 314/30 048 (7.7%)	RR 0.88 (0.66 to 1.18)	9 fewer (from 26 fewer to 14 more)	⊕○○○ Very low
11	Observational	Not serious ⁸	Serious ⁹	Not serious	Not serious	None ⁷	61 329/969 859 (6.3%)		RR 0.91 (0.82 to 1.01)	6 fewer (from 11 fewer to 1 more)	⊕○○○ Very low
Coronary heart disease mortality											
3	RCT	Not serious ⁵	Serious ⁹	Not serious	Very serious ⁶	None ⁷	248/20 186 (1.2%)	334/29 953 (1.1%)	RR 1.05 (0.77 to 1.43)	1 more (from 3 fewer to 5 more)	⊕○○○ Very low
Coronary heart disease											
3	RCT	Not serious ⁵	Serious ⁹	Not serious	Very serious ⁶	None ⁷	653/19 992 (3.3%)	1 001/29 744 (3.4%)	RR 0.82 (0.60 to 1.13)	6 fewer (from 14 fewer to 4 more)	⊕○○○ Very low
5	Observational	Not serious ⁸	Not serious	Not serious	Not serious	None ⁷	10 538/268 221 (3.9%)		RR 1.00 (0.87 to 1.14)	0 fewer (from 5 fewer to 6 more)	⊕⊕○○ Low

		Certainty assessment					No. of events/participants (study event rate)			Effect		Certainty ⁴
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness ¹	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ² (95% CI)	Absolute – per 1000 ³ (95% CI)		
Stroke¹⁰												
3	RCT	Not serious ⁵	Not serious	Not serious	Very serious ⁶	None ⁷	448/19 992 (2.2%)	657/29 744 (2.2%)	RR 0.87 (0.58 to 1.33)	3 fewer (from 9 fewer to 7 more)	⊕⊕○○ Low	
3	Observational	Not serious ⁸	Serious ⁹	Not serious	Serious ¹¹	None ⁷	3 048/172 688 (1.8%)		RR 1.10 (0.81 to 1.50)	2 more (from 1 fewer to 9 more)	⊕○○○ Very low	
Type 2 diabetes												
5	Observational	Not serious ⁸	Serious ⁹	Not serious	Serious ¹¹	None ⁷	7 294/118 400 (6.2%)		RR 0.99 (0.81 to 1.21)	1 fewer (from 12 fewer to 13 more)	⊕○○○ Very low	
LDL cholesterol (mmol/L per 1% energy exchange)¹²												
13 (18) ¹³	RCT	Not serious ¹⁴	Not serious ¹⁵	Not serious ¹⁶	Not serious ¹⁷	None ¹⁸	1 973 ¹⁹		-0.055 (-0.061 to -0.050) ²⁰		⊕⊕⊕⊕ High	

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk; SFA: saturated fatty acids.

¹ All studies were conducted in the population of interest and employed appropriate interventions to assess the effect of lower SFA intake compared with higher intake, or assessed effects of appropriate exposures in observational studies on priority health outcomes decided upon prior to initiating the reviews. The RCTs were primarily conducted in populations from Australia, Europe, New Zealand and the United States, and observational studies in North America, Europe, Asia, Australia, the United Kingdom and multinational cohorts. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. For outcomes other than LDL cholesterol, a small number of the RCTs included in the corresponding systematic review (1) employed one or more dietary interventions in addition to SFA reduction (i.e. multifactorial dietary interventions). However, all studies either explicitly or implicitly aimed to reduce SFA intake, did achieve a reduction in SFA intake, or both.

² For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

³ Based on the event rate in the studies (in the control group for RCTs and the total cohort for prospective observational studies) – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁴ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

⁵ These large RCTs of relatively long duration (minimum 24 months) all appeared to use appropriate methods of random sequence generation, and about half had good allocation concealment (allocation concealment in the remaining studies was unclear). Incomplete outcome reporting was variable across studies, and most included studies had systematic differences in care (i.e. intervention group had more time or attention than the control group). Most studies were not blinded, as blinding in dietary trials is generally very difficult. No other biases were noted. Not downgraded for bias, but it is noted that the level of compliance with interventions involving long-term behaviour change, such as those used in these studies, can vary widely. This is likely to attenuate the pooled effect and bias it towards the null.

⁶ The 95% CI crosses thresholds of both important benefit and harm. Downgraded twice.

⁷ Visual inspection of the funnel plot, comparison of fixed- and random-effects meta-analyses, or other assessment did not suggest publication bias. Where there were too few studies to conduct funnel plot analysis, it was assumed that, because the studies were a subset of the larger group of studies for which there was no indication of publication bias, there was no indication of publication bias in the subsets of studies. No indication of a dose-response relationship in observational studies.

- ⁸ These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- ⁹ $I^2 > 50\%$, indicating a significant level of heterogeneity that was not explained by sensitivity and/or subgroup analyses, where conducted. Downgraded once.
- ¹⁰ For RCTs, this outcome includes any type of stroke; for observational studies, it includes ischaemic stroke only.
- ¹¹ The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- ¹² Effects of decreasing SFA intake on blood lipids by replacement with polyunsaturated fatty acids, monounsaturated fatty acids or carbohydrates, as obtained from regression analysis, were observed across a wide range of SFA intakes, from 1.6% to 24.4% of total energy intake. Of the 177 total data points used in the multiple regression, 113 included an SFA intake of less than 10% of total energy intake; 65 data points included intakes of less than 8%. Residuals analysis indicates that the relationship between SFA intake and effect on blood lipids is linear across the entire range of SFA intakes, including above and below 10% of total energy intake.
- ¹³ The number of data points is provided in parentheses. Each data point contains dietary information on SFA, polyunsaturated fatty acid, monounsaturated fatty acid and carbohydrate intake, as well as an associated change in LDL cholesterol for each study group (i.e. intervention and control groups) at the end of a dietary treatment period. Each data point was extracted for all treatment groups within studies included in the multiple regression analysis of blood lipids.
- ¹⁴ All studies were strictly controlled dietary trials lasting from 13 to 91 days, in which protein and cholesterol intakes were held constant. Some of the studies with parallel design were assessed as having unclear risk of bias in terms of randomization, because the randomization procedure was not fully described. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated if participants were randomized, because all participants were intended to receive all treatments, and thus it was unlikely that any differences at baseline would have had a significant, systematic effect on study results. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it is possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means, so the risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal. Overall, the studies were judged as having a low risk of bias.
- ¹⁵ This analysis was conducted as a multiple regression in which data points were directly extracted from each study, rather than mean differences extracted between groups within each included study. As a result, directly measuring between-study variability in a quantitative manner was not feasible. Qualitative assessment of the included studies and the strength and consistency of the results of the multiple regression, however, suggest that any inconsistency was likely to be minor and was therefore not considered to be serious.
- ¹⁶ LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- ¹⁷ Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing SFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of irrelevant benefit or important harm.
- ¹⁸ Publication bias was not formally assessed but, given the large number and the nature of the studies included in the analysis (i.e. interventions were not limited to those modifying SFA but also included studies in which other dietary fats were modified), risk of publication bias is likely to be low.
- ¹⁹ Total number of participants.
- ²⁰ The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as SFA is replaced with an isocaloric amount of polyunsaturated fatty acids. Reductions in LDL cholesterol were also observed when SFA were replaced with monounsaturated fatty acids (-0.042 mmol/L; 95% CI: -0.047 to -0.037) (high certainty evidence) or carbohydrates (-0.033 mmol/L; 95% CI: -0.039 to -0.027) (high certainty evidence).

GRADE evidence profile 4

Question: What is the effect in children of consuming less than 10% of total energy intake as SFA compared with consuming more than 10% of total energy intake as SFA?¹

Setting: General child population

No. of studies	Study design	Risk of bias	Assessment					No. of participants ²		Relative effect (95% CI)	Certainty ³
			Inconsistency	Indirectness	Imprecision	Other	Lower SFA intake	Higher SFA intake			
1	RCT	Not serious ⁵	Not serious ⁶	Not serious ⁷	Not serious ⁸	None ⁹	134	134	MD 0.29 lower (0.38 lower to 0.20 lower)	⊕⊕⊕⊕ High	

CI: confidence interval; LDL: low-density lipoprotein; MD: mean difference; RCT: randomized controlled trial; SFA: saturated fatty acids.

¹ This GRADE evidence profile provides assessments for outcomes measured directly in children. In formulating recommendations for children, data for disease incidence, mortality and LDL cholesterol from adults were also used, without downgrading for indirectness. Although adverse clinical cardiovascular outcomes in children are rare, there is no evidence to indicate that the physiological response to a change in SFA intake would be significantly different between adults and children (7–13).

² Participants in crossover trials are counted twice: once in the *Lower SFA intake* column and once in the *Higher SFA intake* column.

³ LDL cholesterol is a critical outcome. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation. Additional evidence on the relationship between SFA intake and blood lipids comes from results of one study in children with total cholesterol as an outcome (MD –0.29 mmol/L; 95% CI: –0.40 to –0.18) (*high certainty evidence*).

⁵ No serious risk of bias in the included study.

⁶ Only one study included.

⁷ This study was conducted in the population of interest, all comparisons were made directly with an appropriate control group, and LDL cholesterol is a priority outcome that was decided on before initiating the review. This study was conducted in a population from the USA. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.

⁸ The 95% CI does not cross a threshold of relevant benefit or harm.

⁹ Too few studies to conduct funnel plot analysis.

GRADE evidence profile 5

Question: What is the effect of replacing some SFA in the diet of adults with polyunsaturated fatty acids?¹

Population: General adult population

No. of studies	Assessment							No. of events/participants (study event rate)		Effect		Certainty ⁵
	Study design	Risk of bias	Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)		
All-cause mortality												
7	RCT	Not serious ⁶	Not serious	Not serious	Very serious ⁷	None ⁸	406/2 123 (19.1%)	418/2 115 (19.8%)	RR 0.96 (0.82 to 1.13)	8 fewer (from 36 fewer to 26 more)	⊕⊕○○ Low	
5	Observational	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	Dose–response ^{8,11}	165 011/606 552 (27.2%)		RR 0.85 (0.75 to 0.97)	41 fewer (from 68 fewer to 8 fewer)	⊕⊕○○ Low	
Cardiovascular disease mortality												
7	RCT	Not serious ⁶	Serious ¹⁰	Not serious	Very serious ⁷	None ⁸	266/2 123 (12.5%)	287/2 128 (13.5%)	RR 0.95 (0.73 to 1.25)	7 fewer (from 36 fewer to 34 more)	⊕○○○ Very low	
Cardiovascular diseases												
8	RCT	Not serious ⁶	Serious ¹⁰	Not serious	Serious ¹²	None ⁸	427/2 174 (19.6%)	519/2 179 (23.8%)	RR 0.79 (0.62 to 1.00)	50 fewer (from 91 fewer to 0)	⊕⊕○○ Low	
5	Observational	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	None ^{8,13}	43 892/600 850 (7.3%)		RR 0.90 (0.81 to 1.00)	7 fewer (from 14 fewer to 0)	⊕○○○ Very low	
Coronary heart disease mortality												
7	RCT	Not serious ⁶	Not serious	Not serious	Very serious ⁷	None ⁸	240/2 147 (11.2%)	251/2 151 (11.7%)	RR 0.98 (0.74 to 1.28)	2 fewer (from 30 fewer to 33 more)	⊕⊕○○ Low	
Coronary heart disease												
7	RCT	Not serious ⁶	Serious ¹⁰	Not serious	Serious ¹²	None ⁸	329/1 953 (16.8%)	408/1 942 (21.0%)	RR 0.76 (0.57 to 1.00)	50 fewer (from 90 fewer to 0)	⊕⊕○○ Low	
17	Observational	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	Dose–response ^{8,11}	22 320/448 921 (5.0%)		RR 0.89 (0.81 to 0.98)	5 fewer (from 9 fewer to 1 fewer)	⊕⊕○○ Low	

		Assessment					No. of events/participants (study event rate)		Effect		Certainty ⁵
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)	
Stroke⁴											
4	RCT	Not serious ⁹	Not serious	Not serious	Very serious ⁷	None ⁸	17/856 (2%)	24/850 (2.8%)	RR 0.68 (0.37 to 1.27)	9 fewer (from 18 fewer to 8 more)	⊕⊕○○ Low
Type 2 diabetes											
16	Observational	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	None ¹⁵	20 908/139 771 (15.0%)		RR 0.96 (0.85 to 1.08)	6 fewer (from 22 fewer to 12 more)	⊕○○○ Very low
LDL cholesterol (mmol/L per 1% energy exchange)											
13 (18) ¹⁶	RCT	Not serious ¹⁷	Not serious ¹⁸	Not serious ¹⁹	Not serious ²⁰	None ²¹	1 973 ²²		-0.055 (-0.061 to -0.050) ²³		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk; SFA: saturated fatty acids.

¹ For RCT outcomes other than LDL cholesterol, the polyunsaturated fatty acids used as replacement for SFA in the studies included in the analysis were predominantly of plant origin. For the LDL cholesterol outcome, the polyunsaturated fatty acids used as replacement for SFA in the studies included in the regression analysis were predominantly linoleic acid and α -linolenic acid. For observational studies, the polyunsaturated fatty acids were mixed. For observational studies, the effects reported are for replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of polyunsaturated fatty acids.

² All studies were conducted in the population of interest and employed appropriate interventions to assess the effect of lower SFA intake compared with higher intake, or assessed effects of appropriate exposures in observational studies on priority health outcomes decided upon prior to initiating the reviews. The RCTs were primarily conducted in populations from Australia, Europe, New Zealand and the United States, and observational studies in North America, Europe, Asia, Australia, the United Kingdom and multinational cohorts. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. For outcomes other than LDL cholesterol, a small number of the RCTs included in the corresponding systematic review (1) employed one or more dietary interventions in addition to SFA reduction (i.e. multifactorial dietary interventions). However, all studies either explicitly or implicitly aimed to reduce SFA intake, did achieve a reduction in SFA intake, or both.

³ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁴ Based on the event rate in the studies (in the control group for RCTs and the total cohort for prospective observational studies) – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁵ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

⁶ These large RCTs of relatively long duration (minimum 24 months) all appeared to use appropriate methods of random sequence generation, and about half had good allocation concealment (allocation concealment in the remaining studies was unclear). Incomplete outcome reporting was variable across studies, and most included studies had systematic differences in care (i.e. intervention group had more time or attention than the control group). Most studies were not blinded, as blinding in dietary trials is generally very difficult. No other biases were noted. Not downgraded for bias, but it is noted that the level of compliance with interventions involving long-term behaviour change, such as those used in these studies, can vary widely. This is likely to attenuate the pooled effect and bias it towards the null.

⁷ The 95% CI crosses thresholds of both important benefit and harm. Downgraded twice.

- ⁸ Visual inspection of the funnel plot or other assessment did not suggest publication bias. Where there were too few studies to conduct funnel plot analysis, it was assumed that, because the studies were a subset of the larger group of studies for which there was no indication of publication bias, there was no indication of publication bias in the subsets of studies.
- ⁹ These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- ¹⁰ $I^2 > 50\%$, indicating a significant level of heterogeneity that was not explained by sensitivity, subgroup or meta-regression analyses, where conducted. Downgraded once. (For observational studies, the observed I^2 may be due to statistical rather than clinical heterogeneity; however, downgraded once as a conservative measure.)
- ¹¹ A dose-response relationship was observed when replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of polyunsaturated fatty acids. Upgraded once.
- ¹² The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- ¹³ Although the pooled result of this analysis indicated a significant dose-response association, there was sufficient uncertainty in the calculation that the outcome was not upgraded.
- ¹⁴ This outcome includes any type of stroke.
- ¹⁵ There was no indication of publication bias or a dose-response relationship.
- ¹⁶ The number of data points is provided in parentheses. Each data point contains dietary information on SFA, polyunsaturated fatty acid, monounsaturated fatty acid and carbohydrate intake, as well as an associated change in LDL cholesterol for each study group (i.e. intervention and control groups) at the end of a dietary treatment period. Each data point was extracted for all treatment groups within studies included in the multiple regression analysis of blood lipids.
- ¹⁷ All studies were strictly controlled dietary trials lasting from 13 to 91 days, in which protein and cholesterol intakes were held constant. Some of the studies with parallel design were assessed as having unclear risk of bias in terms of randomization, because the randomization procedure was not fully described. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated if participants were randomized, because all participants were intended to receive all treatments, and thus it was unlikely that any differences at baseline would have had a significant, systematic effect on study results. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it is possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means, so the risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was assessed as low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal. Overall, the studies were judged as having a low risk of bias.
- ¹⁸ This analysis was conducted as a multiple regression in which data points were directly extracted from each study, rather than mean differences extracted between groups within each included study. As a result, directly measuring between-study variability in a quantitative manner was not feasible. Qualitative assessment of the included studies and the strength and consistency of the results of the multiple regression, however, suggest that any inconsistency was likely to be minor and was therefore not considered to be serious.
- ¹⁹ LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- ²⁰ Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing SFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of irrelevant benefit or important harm.
- ²¹ Publication bias was not formally assessed but, given the large number and nature of the studies included in the analysis (i.e. interventions were not limited to those modifying SFA intake but also included studies in which other dietary fats were modified), risk of publication bias is likely to be low.
- ²² Total number of participants.
- ²³ The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as SFA is replaced with an isocaloric amount of polyunsaturated fatty acids.

GRADE evidence profile 6

Question: What is the effect of replacing some SFA in the diet of children with polyunsaturated fatty acids?¹

Setting: General child population

No. of studies	Study design	Risk of bias	Assessment				No. of participants ²		Relative effect (95% CI)	Certainty ³
			Inconsistency	Indirectness	Imprecision	Other	Lower SFA intake	Higher SFA intake		
LDL cholesterol (mmol/L)⁴										
1	RCT	Not serious ⁵	Not serious ⁶	Not serious ⁷	Not serious	None ⁸	134	134	MD 0.29 lower (0.38 lower to 0.20 lower)	⊕⊕⊕⊕ High
Body weight (kg)										
1	RCT	Not serious ⁵	Not serious ⁶	Not serious ⁷	Serious ⁹	None ⁸	134	134	MD 0.20 lower (0.63 lower to 0.23 higher)	⊕⊕⊕○ Moderate

CI: confidence interval; LDL: low-density lipoprotein; MD: mean difference; RCT: randomized controlled trial; SFA: saturated fatty acids.

¹ This GRADE evidence profile provides assessments for outcomes measured directly in children. In formulating recommendations for children, data for disease incidence, mortality and LDL cholesterol from adults were also used, without downgrading for indirectness. Although adverse clinical cardiovascular outcomes in children are rare, there is no evidence to indicate that the physiological response to a change in SFA intake would be significantly different between adults and children (7-13). In the included study, polyunsaturated fatty acids were the predominant replacement for SFA.

² Participants in crossover trials are counted twice: once in the *Lower SFA intake* column and once in the *Higher SFA intake* column.

³ LDL cholesterol is a critical outcome, and body weight is an important outcome. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

⁴ Additional evidence on the relationship between SFA intake and blood lipids comes from results of one study in children with total cholesterol as an outcome (MD -0.29 mmol/L; 95% CI: -0.40 to -0.18) (*high* certainty evidence).

⁵ No serious risk of bias in the included study.

⁶ Only one study included.

⁷ This study was conducted in the population of interest, all comparisons were made directly with an appropriate control group, and LDL cholesterol is a priority outcome that was decided on before initiating the review. The study was conducted in a population from the United States. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6).

⁸ Too few studies to conduct funnel plot analysis.

⁹ The 95% CI crosses a threshold of important benefit or harm. Downgraded once.

GRADE evidence profile 7

Question: What is the effect of replacing some SFA in the diet of adults with monounsaturated fatty acids?¹

Population: General adult population

No. of studies	Study design	Risk of bias	Assessment					No. of events/participants (study event rate)		Effect		Certainty ⁵
			Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)		
All-cause mortality												
16	RCT (plant MUFA)	Serious ⁶	Not serious	Not serious	Very serious ⁷	None	3/26 (1.5%)	1/26 (0.4%)	RR 3.00 (0.33 to 26.99)	77 more (from 26 fewer to 1000 more)	⊕○○○ Very low	
4	Observational (plant MUFA)	Not serious ⁸	Not serious	Not serious	Dose-response ⁹	Dose-response ⁹	151 006/628 803 (24.0%)		RR 0.85 (0.82 to 0.88)	36 fewer (from 43 fewer to 29 fewer)	⊕⊕⊕○ Moderate	
2	Observational (animal MUFA)	Serious ¹⁰	Serious ¹¹	Not serious	None ¹²	None ¹²	130 334/535 425 (24.3%)		RR 1.00 (0.83 to 1.20)	0 fewer (from 41 fewer to 49 more)	⊕○○○ Very low	
5	Observational (mixed MUFA)	Not serious ⁸	Serious ¹¹	Not serious	Dose-response ⁹	Dose-response ⁹	165 011/606 552 (27.2%)		RR 0.84 (0.75 to 0.95)	44 fewer (from 68 fewer to 14 fewer)	⊕⊕○○ Low	
Cardiovascular disease mortality												
16	RCT (plant MUFA)	Serious ⁶	Not serious	Not serious	Very serious ⁷	None	3/26 (1.5%)	1/26 (0.4%)	RR 3.00 (0.33 to 26.99)	77 more (from 26 fewer to 1000 more)	⊕○○○ Very low	
Cardiovascular diseases												
16	RCT (plant MUFA)	Serious ⁶	Not serious	Not serious	Very serious ⁷	None	3/26 (1.5%)	1/26 (0.4%)	RR 3.00 (0.33 to 26.99)	77 more (from 26 fewer to 1000 more)	⊕○○○ Very low	
3	Observational (plant MUFA)	Not serious ⁸	Not serious	Not serious	Dose-response ⁹	Dose-response ⁹	43 335/614 498 (7.1%)		RR 0.90 (0.84 to 0.96)	7 fewer (from 11 fewer to 3 fewer)	⊕⊕⊕○ Moderate	
5	Observational (mixed MUFA)	Not serious ⁸	Serious ¹¹	Not serious	None ¹²	None ¹²	43 892/600 850 (7.3%)		RR 0.94 (0.87 to 1.02)	4 fewer (from 9 fewer to 1 more)	⊕○○○ Very low	

		Assessment					No. of events/participants (study event rate)			Effect		Certainty ⁵
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)		
Coronary heart disease mortality												
16	RCT (plant MUFA)	Serious ⁶	Not serious	Not serious	Very serious ⁷	None	3/26 (1.5%)	1/26 (0.4%)	RR 3.00 (0.33 to 26.99)	77 more (from 26 fewer to 1000 more)	⊕○○○ Very low	
Coronary heart disease												
16	RCT (plant MUFA)	Serious ⁶	Not serious	Not serious	Very serious ⁷	None	3/26 (1.5%)	1/26 (0.4%)	RR 3.00 (0.33 to 26.99)	77 more (from 26 fewer to 1000 more)	⊕○○○ Very low	
2	Observational (plant MUFA)	Serious ¹⁰	Not serious	Serious ¹⁰	Serious ¹³	None ¹²	4 419/93 384 (4.7%)		RR 0.83 (0.69 to 1.01)	8 fewer (from 15 fewer to 0 fewer)	⊕○○○ Very low	
2	Observational (animal MUFA)	Serious ¹⁰	Not serious	Serious ¹⁰	Serious ¹³	None ¹²	4 419/93 385 (4.7%)		RR 1.06 (0.80 to 1.41)	3 more (from 9 fewer to 19 more)	⊕○○○ Very low	
4	Observational (mixed MUFA)	Not serious ⁸	Serious ¹¹	Not serious	Serious ¹³	None ¹²	10 133/167 855 (6.0%)		RR 1.00 (0.82 to 1.21)	0 fewer (from 11 fewer to 13 more)	⊕○○○ Very low	
LDL cholesterol (mmol/L per 1% energy exchange)												
13 (18) ¹⁴	RCT (mixed MUFA)	Not serious ¹⁵	Not serious ¹⁶	Not serious ¹⁷	Not serious ¹⁸	None ¹⁹	1 973 ²⁰		-0.042 (-0.047 to -0.037) ²¹		⊕⊕⊕⊕ High	

CI: confidence interval; LDL: low-density lipoprotein; MUFA: monounsaturated fatty acids; RCT: randomized controlled trial; RR: relative risk; SFA: saturated fatty acids.

¹ For RCT outcomes other than LDL cholesterol, the monounsaturated fatty acids used as replacement for SFA in the included study were from olive oil. For the LDL cholesterol outcome, the monounsaturated fatty acids used as replacement for SFA in studies included in the regression analysis were predominantly oleic acid. For observational studies, results were available for mixed monounsaturated fatty acids, and monounsaturated fatty acids from plant and animal sources individually. For observational studies, the effects reported are for replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of monounsaturated fatty acids. No studies were identified that reported on stroke for this question.

² Unless otherwise noted, all studies were conducted in the population of interest and employed appropriate interventions to assess the effect of lower SFA intake compared with higher intake, or assessed effects of appropriate exposures in observational studies on priority health outcomes decided upon prior to initiating the reviews. The RCTs were primarily conducted in populations from Australia, Europe, New Zealand and the United States, and observational studies in North America, Europe, Asia, Australia, the United Kingdom and multinational cohorts. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. For outcomes other than LDL cholesterol, a small number of the RCTs included in the corresponding systematic review (1) employed one or more dietary interventions in addition to SFA reduction (i.e. multifactorial dietary interventions). However, all studies either explicitly or implicitly aimed to reduce SFA intake, did achieve a reduction in SFA intake, or both.

³ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁴ Based on the event rate in the studies (in the control group for RCTs and the total cohort for prospective observational studies) – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

- 5 All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.
- 6 This single, very small RCT of relatively long duration was well randomized, but had an unclear risk of bias in terms of allocation concealment and incomplete outcome data, and lacked participant blinding. Downgraded once.
- 7 The 95% CI crosses thresholds of both important benefit and harm. Downgraded twice.
- 8 These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- 9 There was no evidence of publication bias. A dose-response relationship was observed when replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of monounsaturated fatty acids. Upgraded once.
- 10 Both cohorts included in the analysis for this outcome were similar populations of health professionals, and the same or very similar questionnaires and instruments were used to assess dietary intake. Because of concerns about potential risk of bias via the use of very similar assessment tools and concerns about indirectness resulting from the very specific study populations, the outcome was conservatively downgraded once across risk of bias and indirectness.
- 11 $I^2 > 50\%$, indicating a significant level of heterogeneity that was not explained by sensitivity, subgroup or meta-regression analyses, where conducted. Downgraded once. (The observed I^2 may be due to statistical rather than clinical heterogeneity; however, downgraded once as a conservative measure.)
- 12 There was no indication of publication bias or a dose-response relationship.
- 13 The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- 14 The number of data points is provided in parentheses. Each data point contains dietary information on SFA, polyunsaturated fatty acid and carbohydrate intake, as well as an associated change in LDL cholesterol for each study group (i.e. intervention and control groups) at the end of a dietary treatment period. Each data point was extracted for all treatment groups within studies included in the multiple regression analysis of blood lipids.
- 15 All studies were strictly controlled dietary trials lasting from 13 to 91 days, in which protein and cholesterol intakes were held constant. Some of the studies with parallel design were assessed as having unclear risk of bias in terms of randomization, because the randomization procedure was not fully described. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated if participants were randomized, because all participants were intended to receive all treatments, and thus it was unlikely that any differences at baseline would have had a significant, systematic effect on study results. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it is possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means, so the risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal. Overall, the studies were judged as having a low risk of bias.
- 16 This analysis was conducted as a multiple regression in which data points (see note 16) were directly extracted from each study, rather than mean differences extracted between groups within each included study. As a result, directly measuring between-study variability in a quantitative manner was not feasible. Qualitative assessment of the included studies and the strength and consistency of the results of the multiple regression, however, suggest that any inconsistency was likely to be minor and was therefore not considered to be serious.
- 17 LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- 18 Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing SFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of irrelevant benefit or important harm.
- 19 Publication bias was not formally assessed but, given the large number and the nature of the studies included in the analysis (i.e. interventions were not limited to those modifying SFA intake but also included studies in which other dietary fats were modified), risk of publication bias is likely to be low.
- 20 Total number of participants.
- 21 The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as SFA is replaced with an isocaloric amount of monounsaturated fatty acids.

GRADE evidence profile 8

Question: What is the effect of replacing some SFA in the diet of children with monounsaturated fatty acids?¹

Setting: General child population

No. of studies	Study design	Risk of bias	Assessment					No. of participants ²		Relative effect (95% CI)	Certainty ³
			Inconsistency	Indirectness	Imprecision	Other	Lower SFA intake	Higher SFA intake			
1	RCT	Not serious ⁵	Not serious ⁶	Not serious ⁷	Not serious	None ⁸	88	88	MD 0.26 lower (0.41 lower to 0.11 lower)	⊕⊕⊕⊕ High	

CI: confidence interval; LDL: low-density lipoprotein; MD: mean difference; RCT: randomized controlled trial; SFA: saturated fatty acids.

¹ This GRADE evidence profile provides assessments for outcomes measured directly in children. In formulating recommendations for children, data for disease incidence, mortality and LDL cholesterol from adults were also used, without downgrading for indirectness. Although adverse clinical cardiovascular outcomes in children are rare, there is no evidence to indicate that the physiological response to a change in SFA intake would be significantly different between adults and children (7–13). In the included study, SFA were replaced with a mixture of unsaturated fatty acids consisting of 80% monounsaturated fatty acids and 20% polyunsaturated fatty acids.

² Participants in crossover trials are counted twice: once in the *Lower SFA intake* column and once in the *Higher SFA intake* column.

³ LDL cholesterol is a critical outcome. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

⁴ Additional evidence on the relationship between SFA intake and blood lipids comes from results of one study with total cholesterol as an outcome (MD -0.33 mmol/L; 95% CI: -0.52 to -0.14) (*high certainty evidence*).

⁵ No serious risk of bias in the included study.

⁶ Only one study included.

⁷ This study was conducted in the population of interest, all comparisons were made directly with an appropriate control group, and LDL cholesterol is a priority outcome that was decided on before initiating the review. This study was conducted in a population from Spain. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6).

⁸ Too few studies to conduct funnel plot analysis.

GRADE evidence profile 9

Question: What is the effect of replacing some SFA in the diet of adults with carbohydrates?¹

Population: General adult population

No. of studies		Assessment							No. of events/participants (study event rate)			Effect		Certainty ⁵
		Study design	Risk of bias	Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)			
All-cause mortality														
6	RCT	Not serious ⁶	Not serious	Not serious	Serious ⁷	None ⁸	1 168/21 715 (5.4%)	1 751/3 1954 (5.5%)	RR 0.97 (0.90 to 1.04)	2 fewer (from 5 fewer to 2 more)	⊕⊕⊕○ Moderate			
5	Observational	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	Dose–response ^{8,11}	40 141/277 553 (14.5%)		RR 0.92 (0.86 to 0.99)	12 fewer (from 20 fewer to 1 fewer)	⊕⊕○○ Low			
Cardiovascular disease mortality														
5	RCT	Not serious ⁶	Not serious	Not serious	Very serious ¹²	None ⁸	316/20 740 (1.5%)	429/30 492 (1.4%)	RR 0.99 (0.85 to 1.14)	0 fewer (from 2 fewer to 2 more)	⊕⊕○○ Low			
Cardiovascular diseases														
5	RCT	Not serious ⁶	Serious ¹⁰	Not serious	Serious ⁷	None ⁸	1 554/20 740 (7.5%)	2 330/30 492 (7.6%)	RR 0.84 (0.67 to 1.06)	12 fewer (from 25 fewer to 5 more)	⊕⊕○○ Low			
6	Observational	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	None ¹³	13 284/274 970 (4.8%)		RR 0.98 (0.90 to 1.07)	1 fewer (from 5 fewer to 3 more)	⊕○○○ Very low			
Coronary heart disease mortality														
2	RCT	Not serious ⁶	Not serious	Not serious	Very serious ¹²	None ⁸	269/20 559 (1.3%)	358/30 309 (1.2%)	RR 0.99 (0.85 to 1.16)	0 fewer (from 2 fewer to 2 more)	⊕⊕○○ Low			
Coronary heart disease														
4	RCT	Not serious ⁶	Not serious	Not serious	Very serious ¹²	None ⁸	730/20 677 (3.5%)	1 070/30 427 (3.5%)	RR 0.93 (0.78 to 1.11)	3 fewer (from 8 fewer to 4 more)	⊕⊕○○ Low			

		Assessment							No. of events/participants (study event rate)		Effect		Certainty ⁵
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)			
6	Observational (mixed)	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	None ¹³	10 458/313 066 (3.3%)		RR 0.98 (0.88 to 1.09)	1 fewer (from 4 fewer to 3 more)	⊕○○○ Very low		
7	Observational (SDC)	Not serious ⁹	Not serious	Not serious	Not serious	None ^{8,14}	12 641/225 278 (5.6%)		RR 0.94 (0.89 to 0.99)	3 fewer (from 6 fewer to 1 fewer)	⊕⊕○○ Low		
3	Observational (MDC)	Not serious ⁹	Serious ¹⁰	Not serious	Serious ⁷	None ¹³	4 409/93 963 (4.7%)		RR 1.03 (0.79 to 1.33)	1 more (from 10 fewer to 15 more)	⊕○○○ Very low		
7	Observational (RDC)	Not serious ⁹	Serious ¹⁰	Not serious	Not serious	None ¹³	12 641/225 278 (5.6%)		RR 1.08 (0.99 to 1.17)	4 more (from 1 fewer to 10 more)	⊕○○○ Very low		
Stroke¹⁵													
3	RCT	Not serious ⁶	Not serious	Not serious	Very serious ¹²	None ⁸	436/19 656 (2.2%)	640/29 410 (2.2%)	RR 0.73 (0.29 to 1.87)	6 fewer (from 16 fewer to 19 more)	⊕⊕○○ Low		
Type 2 diabetes													
15	Observational	Not serious ⁹	Not serious	Not serious	Not serious	None ¹³	20 015/102 350 (19.6%)		RR 1.05 (0.99 to 1.11)	10 more (from 2 fewer to 22 more)	⊕⊕○○ Low		
LDL cholesterol (mmol/L per 1% energy exchange)													
13 (18) ¹⁶	RCT	Not serious ¹⁷	Not serious ¹⁸	Not serious ¹⁹	Not serious ²⁰	None ²¹	1 973 ²²		-0.033 (-0.039 to -0.027) ²³		⊕⊕⊕⊕ High		

CI: confidence interval; LDL: low-density lipoprotein; MDC: moderately digestible carbohydrates; RCT: randomized controlled trial; RDC: rapidly digestible carbohydrates; RR: relative risk; SDC: slowly digestible carbohydrates; SFA: saturated fatty acids.

¹ Unless otherwise noted, there was insufficient information across all studies included in the analyses to make any determination about the composition or types of carbohydrate used as replacement for SFA. For observational studies, in addition to carbohydrates of unknown or mixed composition, data were available for different types of carbohydrates: rapidly digestible (free sugars and foods described by the authors of the individual studies as having a high glycaemic index), moderately digestible (foods described by the authors of the individual studies as having a moderate glycaemic index) and slowly digestible (wholegrains and foods described by the authors of the individual studies as having a low glycaemic index). For observational studies, the effects reported are for replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of carbohydrates. No studies conducted in children were identified that reported on outcomes relevant for this question.

- 2 All studies were conducted in the population of interest and employed appropriate interventions to assess the effect of lower SFA intake compared with higher intake, or assessed effects of appropriate exposures in observational studies on priority health outcomes decided upon prior to initiating the reviews. The RCTs were primarily conducted in populations from Australia, Europe, New Zealand and the United States, and observational studies in North America, Europe, Asia, Australia, the United Kingdom and multinational cohorts. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. For outcomes other than LDL cholesterol, a small number of the RCTs included in the corresponding systematic review (1) employed one or more dietary interventions in addition to SFA reduction (i.e. multifactorial dietary interventions). However, all studies either explicitly or implicitly aimed to reduce SFA intake, did achieve a reduction in SFA intake, or both.
- 3 For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).
- 4 Based on the event rate in the studies (in the control group for RCTs and the total cohort for prospective observational studies) – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = $1000 \times [\text{event rate} \times (1 - \text{RR})]$. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.
- 5 All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.
- 6 These large RCTs of relatively long duration (minimum 24 months) all appeared to use appropriate methods of random sequence generation, and about half had good allocation concealment (allocation concealment in the remaining studies was unclear). Incomplete outcome reporting was variable across studies, and most included studies had systematic differences in care (i.e. intervention group had more time or attention than the control group). Most studies were not blinded, as blinding in dietary trials is generally very difficult. No other biases were noted. Not downgraded for bias, but it is noted that the level of compliance with interventions involving long-term behaviour change, such as those used in these studies, can vary widely. This is likely to attenuate the pooled effect and bias it towards the null.
- 7 The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- 8 Visual inspection of the funnel plot or other assessments did not suggest publication bias. Where there were too few studies to conduct funnel plot analysis, it was assumed that, because the studies were a subset of the larger group of studies for which there was no indication of publication bias, there was no indication of publication bias in the subsets of studies.
- 9 These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- 10 $I^2 > 50\%$, indicating a significant level of heterogeneity that was not explained by sensitivity, subgroup or meta-regression analyses, where conducted. Downgraded once. (The observed I^2 may be due to statistical rather than clinical heterogeneity; however, downgraded once as a conservative measure.)
- 11 A dose-response relationship was observed when replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of specified nutrient. Upgraded once.
- 12 The 95% CI crosses thresholds of both important benefit and harm. Downgraded twice.
- 13 There was no indication of publication bias or a dose-response relationship.
- 14 Although the pooled result of this analysis indicated a significant dose-response association, there was sufficient uncertainty in the calculation that the body of evidence was not upgraded.
- 15 This outcome includes any type of stroke.
- 16 The number of data points is provided in parentheses. Each data point contains dietary information on SFA, polyunsaturated fatty acid, monounsaturated fatty acid and carbohydrate intake, as well as an associated change in LDL cholesterol for each study group (i.e. intervention and control groups) at the end of a dietary treatment period. Each data point was extracted for all treatment groups within studies included in the multiple regression analysis of blood lipids.

- ¹⁷ All studies were strictly controlled dietary trials lasting from 13 to 91 days, in which protein and cholesterol intakes were held constant. Some of the studies with parallel design were assessed as having unclear risk of bias in terms of randomization, because the randomization procedure was not fully described. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated if participants were randomized, because all participants were intended to receive all treatments, and thus it was unlikely that any differences at baseline would have had a significant, systematic effect on study results. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it is possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means, so the risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal. Overall, the studies were judged as having a low risk of bias.
- ¹⁸ This analysis was conducted as a multiple regression in which data points (see note 16) were directly extracted from each study, rather than mean differences extracted between groups within each included study. As a result, directly measuring between-study variability in a quantitative manner was not feasible. Qualitative assessment of the included studies and the strength and consistency of the results of the multiple regression, however, suggest that any inconsistency was likely to be minor and was therefore not considered to be serious.
- ¹⁹ LDL cholesterol is an indirect measure of patient-important cardiovascular outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- ²⁰ Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing SFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of irrelevant benefit or important harm.
- ²¹ Publication bias was not formally assessed but, given the large number and the nature of the studies included in the analysis (i.e. interventions were not limited to those modifying SFA intake but also included studies in which other dietary fats were modified), risk of publication bias is likely to be low.
- ²² Total number of participants.
- ²³ The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as SFA is replaced with an isocaloric amount of carbohydrates.

GRADE evidence profile 10

Question: What is the effect of replacing some SFA in the diet of adults with protein?¹

Population: General adult population

No. of studies	Assessment							No. of events/participants (study event rate)		Effect		Certainty ⁵
	Study design	Risk of bias	Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake	Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)		
All-cause mortality												
5	RCT	Not serious ⁶	Not serious	Not serious	Serious ⁷	None ⁸	1 167/21 688 (5.4%)	1 748/31 926 (5.5%)	RR 0.97 (0.90 to 1.04)	2 fewer (from 5 fewer to 2 more)	⊕⊕⊕○ Moderate	
Cardiovascular disease mortality												
4	RCT	Not serious ⁶	Not serious	Not serious	Very serious ⁹	None ⁸	315/20 713 (1.5%)	426/30 464 (1.4%)	RR 0.99 (0.86 to 1.14)	0 fewer (from 2 fewer to 2 more)	⊕⊕○○ Low	
Cardiovascular diseases												
4	RCT	Not serious ⁶	Not serious	Not serious	Serious ⁷	None ⁸	1 546/20 713 (7.5%)	2 310/30 464 (7.6%)	RR 0.97 (0.91 to 1.03)	2 fewer (from 8 fewer to 4 more)	⊕⊕⊕○ Moderate	
Coronary heart disease mortality												
2	RCT	Not serious ⁶	Not serious	Not serious	Very serious ⁹	None ⁸	269/20 559 (1.3%)	358/30 309 (1.2%)	RR 0.99 (0.85 to 1.16)	0 fewer (from 2 fewer to 2 more)	⊕⊕○○ Low	
Coronary heart disease												
3	RCT	Not serious ⁶	Not serious	Not serious	Serious ⁷	None ⁸	727/20 647 (3.5%)	1 060/30 397 (3.5%)	RR 0.96 (0.88 to 1.05)	1 fewer (from 4 fewer to 2 more)	⊕⊕⊕○ Moderate	
2	Observational (mixed)	Not serious ¹⁰	Not serious	Serious ¹¹	Not serious	None ¹²	2 466/40 319 (6.1%)		RR 1.26 (1.06 to 1.50)	16 more (from 4 more to 31 more)	⊕○○○ Very low	
2	Observational (plant)	Not serious ¹⁰	Not serious	Serious ¹¹	Serious ⁷	None ¹²	2 466/40 319 (6.1%)		RR 0.83 (0.61 to 1.12)	10 fewer (from 24 fewer to 7 more)	⊕○○○ Very low	

Assessment				No. of events/participants (study event rate)			Effect		Certainty ⁵		
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness ²	Imprecision	Other	Lower SFA intake	Higher SFA intake		Relative ³ (95% CI)	Absolute – per 1000 ⁴ (95% CI)
2	Observational (animal)	Not serious ¹⁰	Not serious	Serious ¹¹	Not serious	Dose–response ^{8,13}	2 466/40 319 (6.1%)	639/29 382 (2.2%)	RR 1.31 (1.14 to 1.50)	19 more (from 9 more to 31 more)	⊕⊕○○○ Low
Stroke¹⁴											
2	RCT	Not serious ⁵	Serious ¹⁵	Not serious	Very serious ⁹	None ⁸	436/19 629 (2.2%)	639/29 382 (2.2%)	RR 0.65 (0.15 to 2.75)	2 more (from 24 fewer to 33 more)	⊕○○○○ Very low

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk; SFA: saturated fatty acids.

- Unless otherwise noted, protein used as replacement for SFA was of mixed plant and animal origin. For observational studies, results were available for mixed protein, and protein from plant and animal sources individually. For observational studies, the effects reported are for replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of protein. Because studies were included in the blood lipids analyses (16) only if protein intakes were held constant, assessment of possible effects on the blood lipid profile of replacing SFA with protein intake was not possible, and therefore no values for the effect on LDL cholesterol of replacing some SFA in the diet of adults and children with protein are reported. No studies conducted in children were identified that reported on outcomes relevant for this question.
- Unless otherwise noted, all studies were conducted in the population of interest and employed appropriate interventions to assess the effect of lower SFA intake compared with higher intake, or assessed effects of appropriate exposures in observational studies on priority health outcomes decided upon before initiating the reviews. The RCTs were primarily conducted in populations from Australia, Europe, New Zealand and the United States, and observational studies in North America, Europe, Asia, Australia, the United Kingdom and multinational cohorts. Significant differences in the basic physiological responses to SFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated. For outcomes other than LDL cholesterol, a small number of the RCTs included in the corresponding systematic review (1) employed one or more dietary interventions in addition to SFA reduction (i.e. multifactorial dietary interventions). However, all studies either explicitly or implicitly aimed to reduce SFA intake, did achieve a reduction in SFA intake, or both.
- For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).
- Based on the event rate in the studies (in the control group for RCTs and the total cohort for prospective observational studies) – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.
- All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.
- These large RCTs of relatively long duration (minimum 24 months) all appeared to use appropriate methods of random sequence generation, and about half had good allocation concealment (allocation concealment in the remaining studies was unclear). Incomplete outcome reporting was variable across studies, and most included studies had systematic differences in care (i.e. intervention group had more time or attention than the control group). Most studies were not blinded, as blinding in dietary trials is generally very difficult. No other biases were noted. Not downgraded for bias, but it is noted that the level of compliance with interventions involving long-term behaviour change, such as those used in these studies, can vary widely. This is likely to attenuate the pooled effect and bias it towards the null.
- The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- Visual inspection of the funnel plot did not suggest publication bias. Where there were too few studies to conduct funnel plot analysis, it was assumed that, because the studies were a subset of the larger group of studies for which there was no indication of publication bias, there was no indication of publication bias in the subsets of studies.
- The 95% CI crosses thresholds of both important benefit and harm. Downgraded twice.

- ¹⁰ These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- ¹¹ Both cohorts included in the analysis for this outcome were Dutch populations. Although there is no evidence that the physiological response to a change in SFA intake would be significantly different across different populations, the outcome was conservatively downgraded once.
- ¹² There was no indication of publication bias or a dose-response relationship.
- ¹³ A dose-response relationship was observed when replacing 5% of energy intake as SFA with the equivalent (i.e. isocaloric) amount of protein. Upgraded once.
- ¹⁴ This outcome includes any type of stroke.
- ¹⁵ $I^2 > 50\%$, indicating a significant level of heterogeneity that was not explained by sensitivity, subgroup or meta-regression analyses, where conducted. Downgraded once.

GRADE evidence profile 11

Question: What is the effect of lower compared with higher intake of TFA¹ in adults?²

Population: General adult population

No. of studies	Assessment					No. of events/ participants (study event rate)	Effect		Certainty ⁶	
	Study design	Risk of bias	Inconsistency	Indirectness ³	Imprecision		Other	Relative ⁴ (95% CI)		Absolute – per 1000 ⁵ (95% CI)
All-cause mortality										
6	Observational	Not serious ⁷	Not serious	Not serious	Not serious	Dose–response ⁸	164 951/673 830 (24.5%)	RR 0.90 (0.83 to 0.98)	25 fewer (from 42 fewer to 5 fewer)	⊕⊕⊕○ Moderate
Cardiovascular diseases										
6	Observational	Not serious ⁷	Not serious	Not serious	Not serious	None ⁹	47 406/675 673 (7.0%)	RR 0.88 (0.80 to 0.96)	8 fewer (from 14 fewer to 3 fewer)	⊕⊕○○ Low
Coronary heart disease										
7	Observational	Not serious ⁷	Not serious	Not serious	Not serious	Dose–response ⁸	10 311/185 664 (5.6%)	RR 0.86 (0.79 to 0.92)	8 fewer (from 12 fewer to 5 fewer)	⊕⊕⊕○ Moderate
Stroke										
3	Observational	Not serious ⁷	Serious ¹⁰	Not serious	Serious ¹¹	None ⁹	1 889/257 437 (0.7%)	RR 0.92 (0.68 to 1.25)	1 fewer (from 2 fewer to 2 more)	⊕○○○ Very low
Type 2 diabetes										
9	Observational	Not serious ⁷	Not serious	Not serious	Not serious	None ⁹	11 049/275 402 (4.0%)	RR 0.95 (0.86 to 1.05)	2 fewer (from 6 fewer to 2 more)	⊕⊕○○ Low
LDL cholesterol (mmol/L per 1% energy exchange)										
13 (18) ¹²	RCT	Not serious ¹³	Not serious ¹⁴	Not serious ¹⁵	Not serious ¹⁶	None ¹⁷	669 ¹⁸	-0.048 (-0.055 to -0.041) ¹⁹		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk.

¹ TFA include all fatty acids with a carbon–carbon double bond in the *trans* configuration.

² No studies meeting the inclusion criteria for children were identified in the systematic review.

³ All studies were conducted in the adult population of interest to assess the effects of lower TFA intake compared with higher intake on priority health outcomes decided upon prior to initiating the reviews. Studies were mainly conducted in North America and Europe, as well as the UK, Australia and Asia. Significant differences in the basic physiological responses to TFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated.

⁴ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁵ Based on the event rate in the studies – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

- 6 All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.
- 7 These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- 8 There was no indication of publication bias, and a dose-response relationship was observed between increased intake of TFA and increased risk of the outcome. Upgraded once.
- 9 There was no indication of publication bias or a dose-response relationship.
- 10 $I^2 > 50\%$, indicating a significant level of heterogeneity.
- 11 The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- 12 The number of comparisons is provided in parentheses.
- 13 All studies included in this analysis were strictly controlled, relatively short-term dietary trials. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated that participants were randomized, because all participants were intended to receive all treatments, and it is thus unlikely that any differences at baseline would have a significant, systematic effect on study results. The two studies with parallel design were assessed as having an unclear risk of bias in terms of randomization because it was not specified whether participants were randomized. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it was possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means; hence, risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be very low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal.
- 14 Qualitative assessment of the included studies shows that point estimates across individual studies were similar and 95% CIs overlapped, suggesting that any inconsistency is not serious.
- 15 LDL cholesterol is an indirect measure of patient-important CVD outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- 16 Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing TFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of important benefit or harm.
- 17 Visual inspection of the funnel plot did not suggest publication bias.
- 18 Total number of participants.
- 19 The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as TFA is replaced with an isocaloric amount of polyunsaturated fatty acids. Effects on LDL cholesterol were also observed when TFA were replaced with monounsaturated fatty acids (-0.035 mmol/L; 95% CI: -0.042 to -0.028) (high certainty evidence), carbohydrates (-0.026 mmol/L; 95% CI: -0.033 to -0.019) (high certainty evidence) or SFA (0.010 mmol/L; 95% CI: 0.003 to 0.017) (high certainty evidence).

GRADE evidence profile 12

Question: What is the effect in adults and children of consuming less than 1% of total energy intake as TFA¹ compared with consuming more than 1% of total energy intake as TFA?²

Population: General adult population

No. of studies	Study design	Assessment					No. of events/ participants (study event rate)	Effect		Certainty ⁶
		Risk of bias	Inconsistency	Indirectness ³	Imprecision	Other		Relative ⁴ (95% CI)	Absolute – per 1000 ⁵ (95% CI)	
All-cause mortality										
3	Observational	Not serious ⁷	Serious ⁸	Not serious	Not serious	None ⁹	33 637/127 159 (26.5%)	RR 0.90 (0.81 to 1.00)	27 fewer (from 50 fewer to 0 fewer)	⊕⊕⊕⊕ Very low
Cardiovascular diseases										
2	Observational	Serious ¹⁰	Not serious	Serious ¹⁰	Not serious	None ⁹	7 878/126 233 (6.2%)	RR 0.83 (0.75 to 0.93)	11 fewer (from 16 fewer to 4 fewer)	⊕⊕⊕⊕ Low
Coronary heart disease										
4	Observational	Not serious ⁷	Not serious	Not serious	Not serious	None ⁹	6 575/67 739 (9.7%)	RR 0.88 (0.80 to 0.96)	12 fewer (from 19 fewer to 4 fewer)	⊕⊕⊕⊕ Low
Type 2 diabetes										
3	Observational	Not serious ⁷	Not serious	Not serious	Not serious	None ⁹	3 286/81 231 (4.0%)	RR 0.98 (0.82 to 1.18)	1 fewer (from 7 fewer to 7 more)	⊕⊕⊕⊕ Low
LDL cholesterol (mmol/L per 1% energy exchange)¹¹										
13 (18) ¹²	RCT	Not serious ¹³	Not serious ¹⁴	Not serious ¹⁵	Not serious ¹⁶	None ¹⁷	669 ¹⁸	-0.048 (-0.055 to -0.041) ¹⁹		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk.

¹ TFA include all fatty acids with a carbon-carbon double bond in the *trans* configuration.

² No studies meeting the inclusion criteria for children were identified in the systematic review. No studies were identified that reported on stroke for this question.

³ All studies were conducted in the adult population of interest to assess the effects of lower TFA intake compared with higher intake on priority health outcomes decided upon prior to initiating the reviews. Studies were mainly conducted in North America and Europe, as well as the UK, Australia and Asia. Significant differences in the basic physiological responses to TFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated.

⁴ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁵ Based on the event rate in the studies – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁶ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

- 7 These large prospective observational studies included populations that were well balanced in terms of participant characteristics, with no major differences between those exposed and those unexposed, and were well controlled for potential confounders (although the possibility of residual confounding always exists). Cohorts were followed up sufficiently to assess outcomes of interest (up to 32 years of follow-up). Influence analyses were conducted on the studies for each outcome (where each study is removed one at a time to consider its individual effect on the pooled result) to assess the potential of any individual study to unduly influence the pooled result. No one study significantly changed the magnitude or direction of the pooled results. Baseline diet was assessed differently across included studies, typically via a food frequency questionnaire, diet record or 24-hour recall at least once at baseline. These self-reported methods of dietary intake are likely to result in different assessments of exposure; however, many of the dietary assessment tools have been validated, and the overall contribution to interstudy differences in assessment of exposure was not considered to be a significant source of bias.
- 8 $I^2 > 50\%$, indicating a significant level of heterogeneity. Downgraded once.
- 9 There was no indication of publication bias or a dose-response relationship.
- 10 Both cohorts included in the analysis for this outcome were similar populations of health professionals, and the same or very similar questionnaires and instruments were used to assess dietary intake. Because of concerns about potential risk of bias via the use of very similar assessment tools and concerns about indirectness resulting from the very specific study populations, the outcome was conservatively downgraded once across risk of bias and indirectness.
- 11 Effects of decreasing TFA intake on blood lipids by replacement with polyunsaturated fatty acids, monounsaturated fatty acids, carbohydrates or saturated fatty acids, as obtained from regression analysis, were observed across a wide range of TFA intakes, from 0% to 11% of total energy intake. Residuals analysis indicates that the relationship between TFA intake and effect on blood lipids is linear across the entire range of TFA intakes, including above and below 1% of total energy intake.
- 12 The number of comparisons is provided in parentheses.
- 13 All studies included in this analysis were strictly controlled, relatively short-term dietary trials. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated that participants were randomized, because all participants were intended to receive all treatments, and it is thus unlikely that any differences at baseline would have a significant, systematic effect on study results. The two studies with parallel design were assessed as having an unclear risk of bias in terms of randomization because it was not specified whether participants were randomized. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it was possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means; hence, risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be very low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal.
- 14 Qualitative assessment of the included studies shows that point estimates across individual studies were similar and 95% CIs overlapped, suggesting that any inconsistency is not serious.
- 15 LDL cholesterol is an indirect measure of patient-important CVD outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- 16 Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing TFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of important benefit or harm.
- 17 Visual inspection of the funnel plot did not suggest publication bias.
- 18 Total number of participants.
- 19 The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as TFA is replaced with an isocaloric amount of polyunsaturated fatty acids. Effects on LDL cholesterol were also observed when TFA were replaced with monounsaturated fatty acids (-0.035 mmol/L; 95% CI: -0.042 to -0.028) (high certainty evidence), carbohydrates (-0.026 mmol/L; 95% CI: -0.033 to -0.019) (high certainty evidence) or SFA (0.010 mmol/L; 95% CI: 0.003 to 0.017) (high certainty evidence).

GRADE evidence profile 13

Question: What is the effect of replacing some TFA¹ in the diet of adults with polyunsaturated fatty acids?²

Population: General adult population

		Assessment				No. of events/ participants (study event rate)	Effect		Certainty ⁶
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness ³	Imprecision		Other	Relative ⁴ (95% CI)	
Type 2 diabetes									
2	Observational	Serious ⁷	Serious ⁸	Serious ⁷	Not serious	Dose-response ⁹	RR 0.72 (0.52 to 0.99)	20 fewer (from 34 fewer to 1 fewer)	⊕○○○ Very low
LDL cholesterol (mmol/L per 1% energy exchange)									
13 (18) ¹⁰	RCT	Not serious ¹¹	Not serious ¹²	Not serious ¹³	Not serious ¹⁴	None ¹⁵	-0.048 (-0.055 to -0.041) ¹⁷		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk.

¹ TFA include all fatty acids with a carbon-carbon double bond in the *trans* configuration.

² For observational studies, the effects reported are for replacing 2% of energy intake as TFA with the equivalent (i.e. isocaloric) amount of polyunsaturated fatty acids. No studies meeting the inclusion criteria for children were identified in the systematic review. No studies were identified that reported on all-cause mortality, CVDs, coronary heart disease or stroke for this question.

³ All studies were conducted in the adult population of interest to assess the effects of lower TFA intake compared with higher intake on priority health outcomes decided upon prior to initiating the reviews. Studies were mainly conducted in North America and Europe, as well as the UK, Australia and Asia. Significant differences in the basic physiological responses to TFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated.

⁴ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁵ Based on the event rate in the studies – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁶ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

⁷ Both cohorts included in the analysis for this outcome were similar populations of health professionals, and the same or very similar questionnaires and instruments were used to assess dietary intake. Because of concerns about potential risk of bias via the use of very similar assessment tools and concerns about indirectness resulting from the very specific study populations, the outcome was conservatively downgraded once across risk of bias and indirectness.

⁸ $I^2 > 50\%$, indicating a significant level of heterogeneity. Downgraded once.

⁹ There was no indication of publication bias, and a dose-response relationship was observed when replacing 2% of energy intake as TFA with the equivalent (i.e. isocaloric) amount of polyunsaturated fatty acids. Upgraded once.

¹⁰ The number of comparisons is provided in parentheses.

- ¹¹ All studies included in this analysis were strictly controlled, relatively short-term dietary trials. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated that participants were randomized, because all participants were intended to receive all treatments, and it is thus unlikely that any differences at baseline would have a significant, systematic effect on study results. The two studies with parallel design were assessed as having an unclear risk of bias in terms of randomization because it was not specified whether participants were randomized. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it was possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means; hence, risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be very low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal.
- ¹² Qualitative assessment of the included studies shows that point estimates across individual studies were similar and 95% CIs overlapped, suggesting that any inconsistency is not serious.
- ¹³ LDL cholesterol is an indirect measure of patient-important CVD outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- ¹⁴ Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing TFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of important benefit or harm.
- ¹⁵ Visual inspection of the funnel plot did not suggest publication bias.
- ¹⁶ Total number of participants.
- ¹⁷ The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as TFA is replaced with an isocaloric amount of polyunsaturated fatty acids.

GRADE evidence profile 14

Question: What is the effect of replacing some TFA¹ in the diet of adults with monounsaturated fatty acids?²

Population: General adult population

No. of studies		Assessment					No. of events/ participants (study event rate)	Effect		Certainty ⁶
		Study design	Risk of bias	Inconsistency	Indirectness ³	Imprecision		Other	Relative ⁴ (95% CI)	
All-cause mortality										
2	Observational (plant MUFA)	Serious ⁷	Not serious	Serious ⁷	Not serious	Dose–response ⁸	41 344/93 378 (44.3%)	RR 0.90 (0.85 to 0.96)	44 fewer (from 66 fewer to 18 fewer)	⊕⊕○○ Low
Cardiovascular diseases										
2	Observational (plant MUFA)	Serious ⁷	Serious ⁹	Serious ⁷	Serious ¹⁰	None ¹¹	4 588/93 378 (4.9%)	RR 0.97 (0.71 to 1.32)	1 fewer (from 14 fewer to 16 more)	⊕○○○ Very low
Coronary heart disease										
2	Observational (plant MUFA)	Serious ⁷	Not serious	Serious ⁷	Not serious	Dose–response ⁸	4 419/93 384 (4.7%)	RR 0.80 (0.70 to 0.92)	9 fewer (from 14 fewer to 4 fewer)	⊕⊕○○ Low
2	Observational (animal MUFA)	Serious ⁷	Not serious	Serious ⁷	Serious ¹⁰	None ¹¹	4 419/93 384 (4.7%)	RR 0.89 (0.78 to 1.03)	5 fewer (from 10 fewer to 1 more)	⊕○○○ Very low
LDL cholesterol (mmol/L per 1% energy exchange)										
13 (18) ¹²	RCT	Not serious ¹³	Not serious ¹⁴	Not serious ¹⁵	Not serious ¹⁶	None ¹⁷	669 ¹⁸	-0.035 (-0.042 to -0.028) ¹⁹		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk.

¹ TFA include all fatty acids with a carbon–carbon double bond in the *trans* configuration.

² For observational studies, results were available for monounsaturated fatty acids from plant and animal sources individually. For observational studies, the effects reported are for replacing 2% of energy intake as TFA with the equivalent (i.e. isocaloric) amount of monounsaturated fatty acids. No studies meeting the inclusion criteria for children were identified in the systematic review. No studies were identified that reported on stroke or type 2 diabetes for this question.

³ All studies were conducted in the adult population of interest to assess the effects of lower TFA intake compared with higher intake on priority health outcomes decided upon prior to initiating the reviews. Studies were mainly conducted in North America and Europe, as well as the UK, Australia and Asia. Significant differences in the basic physiological responses to TFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated.

⁴ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁵ Based on the event rate in the studies – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁶ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

- 7 Both cohorts included in the analysis for this outcome were similar populations of health professionals, and the same or very similar questionnaires and instruments were used to assess dietary intake. Because of concerns about potential risk of bias via the use of very similar assessment tools and concerns about indirectness resulting from the very specific study populations, the outcome was conservatively downgraded once across risk of bias and indirectness.
- 8 There was no indication of publication bias, and a dose–response relationship was observed when replacing 2% of energy intake as TFA with the equivalent (i.e. isocaloric) amount of monounsaturated fatty acids. Upgraded once.
- 9 $I^2 > 50\%$, indicating a significant level of heterogeneity. Downgraded once.
- 10 The 95% CI crosses a threshold of important benefit or harm. Downgraded once.
- 11 There was no indication of publication bias or a dose–response relationship.
- 12 The number of comparisons is provided in parentheses.
- 13 All studies included in this analysis were strictly controlled, relatively short-term dietary trials. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated that participants were randomized, because all participants were intended to receive all treatments, and it is thus unlikely that any differences at baseline would have a significant, systematic effect on study results. The two studies with parallel design were assessed as having an unclear risk of bias in terms of randomization because it was not specified whether participants were randomized. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it was possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means; hence, risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be very low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal.
- 14 Qualitative assessment of the included studies shows that point estimates across individual studies were similar and 95% CIs overlapped, suggesting that any inconsistency is not serious.
- 15 LDL cholesterol is an indirect measure of patient-important CVD outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- 16 Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing TFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of important benefit or harm.
- 17 Visual inspection of the funnel plot did not suggest publication bias.
- 18 Total number of participants.
- 19 The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as TFA is replaced with an isocaloric amount of monounsaturated fatty acids.

GRADE evidence profile 15

Question: What is the effect of replacing some TFA¹ in the diet of adults with carbohydrates?²

Population: General adult population

No. of studies		Assessment					No. of events/ participants (study event rate)	Effect		Certainty ⁶
		Study design	Risk of bias	Inconsistency	Indirectness ³	Imprecision		Other	Relative ⁴ (95% CI)	
Coronary heart disease										
2	Observational (RDC)	Serious ⁷	Serious ⁸	Serious ⁷	Not serious	None ⁹	7 667/127 536 (6.0%)	RR 0.95 (0.80 to 1.13)	3 fewer (from 12 fewer to 8 more)	⊕○○○ Very low
Type 2 diabetes										
2	Observational	Not serious ¹⁰	Not serious	Not serious	Not serious	Dose–response ⁸	3 604/106 543 (3.4%)	RR 0.71 (0.60 to 0.84)	10 fewer (from 14 fewer to 5 fewer)	⊕⊕⊕○ Moderate
LDL cholesterol (mmol/L per 1% energy exchange)										
13 (18) ¹¹	RCT	Not serious ¹²	Not serious ¹³	Not serious ¹⁴	Not serious ¹⁵	None ¹⁶	6 69 ¹⁷	-0.026 (-0.033 to -0.019) ¹⁸		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RDC: rapidly digestible carbohydrates; RR: relative risk.

¹ TFA include all fatty acids with a carbon–carbon double bond in the *trans* configuration.

² For coronary heart disease, the carbohydrate exposure was free sugars and foods described by the authors of the individual studies as having a high glycaemic index (“rapidly digestible carbohydrates”). For type 2 diabetes, the exposure was carbohydrates of unknown or mixed composition. For observational studies, the effects reported are for replacing 2% of energy intake as TFA with the equivalent (i.e. isocaloric) amount of carbohydrates. No studies meeting the inclusion criteria for children were identified in the systematic review. No studies were identified that reported on all-cause mortality, CVDs or stroke for this question.

³ All studies were conducted in the adult population of interest to assess the effects of lower TFA intake compared with higher intake on priority health outcomes decided upon prior to initiating the reviews. Studies were mainly conducted in North America and Europe, as well as the UK, Australia and Asia. Significant differences in the basic physiological responses to TFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated.

⁴ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁵ Based on the event rate in the studies – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁶ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

⁷ Both cohorts included in the analysis for this outcome were similar populations of health professionals, and the same or very similar questionnaires and instruments were used to assess dietary intake. Because of concerns about potential risk of bias via the use of very similar assessment tools and concerns about indirectness resulting from the very specific study populations, the outcome was conservatively downgraded once across risk of bias and indirectness.

⁸ $I^2 > 50\%$, indicating a significant level of heterogeneity. Downgraded once.

⁹ There was no indication of publication bias or a dose–response relationship.

¹⁰ Although this outcome included only two cohorts, they were different populations, and therefore the outcome was not downgraded.

- ¹¹ The number of comparisons is provided in parentheses.
- ¹² All studies included in this analysis were strictly controlled, relatively short-term dietary trials. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated that participants were randomized, because all participants were intended to receive all treatments, and it is thus unlikely that any differences at baseline would have a significant, systematic effect on study results. The two studies with parallel design were assessed as having an unclear risk of bias in terms of randomization because it was not specified whether participants were randomized. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it was possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means; hence, risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be very low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal.
- ¹³ Qualitative assessment of the included studies shows that point estimates across individual studies were similar and 95% CIs overlapped, suggesting that any inconsistency is not serious.
- ¹⁴ LDL cholesterol is an indirect measure of patient-important CVD outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- ¹⁵ Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing TFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of important benefit or harm.
- ¹⁶ Visual inspection of the funnel plot did not suggest publication bias.
- ¹⁷ Total number of participants.
- ¹⁸ The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as TFA is replaced with an isocaloric amount of carbohydrates.

GRADE evidence profile 16

Question: What is the effect of replacing some TFA¹ in the diet of adults with SFA?²

Population: General adult population

No. of studies		Assessment						No. of events/ participants (study event rate)	Effect		Certainty ⁶
		Study design	Risk of bias	Inconsistency	Indirectness ³	Imprecision	Other		Relative ⁴ (95% CI)	Absolute – per 1000 ⁵ (95% CI)	
All-cause mortality											
2	Observational	Not serious ⁷	Not serious ⁸	Serious ⁸	Not serious	Not serious	None ⁹	46 625/647 353 (7.2%)	RR 0.92 (0.82 to 1.03)	6 fewer (from 13 fewer to 2 more)	⊕○○○ Very low
Cardiovascular diseases											
2	Observational	Not serious ⁷	Not serious ⁸	Serious ⁸	Not serious	Not serious	None ⁹	46 625/647 353 (7.2%)	RR 0.93 (0.83 to 1.04)	5 fewer (from 12 fewer to 3 more)	⊕○○○ Very low
Coronary heart disease											
2	Observational	Serious ¹⁰	Not serious	Not serious	Serious ¹⁰	Not serious	None ⁹	7 667/127 536 (6.0%)	RR 0.97 (0.86 to 1.09)	2 fewer (from 8 fewer to 5 more)	⊕○○○ Very low
LDL cholesterol (mmol/L per 1% energy exchange)											
13 (18) ¹¹	RCT	Not serious ¹²	Not serious ¹³	Not serious ¹⁴	Not serious ¹⁵	Not serious ¹⁶	None ¹⁶	669 ¹⁷	0.010 (0.003 to 0.017) ¹⁸		⊕⊕⊕⊕ High

CI: confidence interval; LDL: low-density lipoprotein; RCT: randomized controlled trial; RR: relative risk.

¹ TFA include all fatty acids with a carbon-carbon double bond in the *trans* configuration.

² For observational studies, the effects reported are for replacing 2% of energy intake as TFA with the equivalent (i.e. isocaloric) amount of SFA. No studies meeting the inclusion criteria for children were identified in the systematic review. No studies were identified that reported on stroke or type 2 diabetes for this question.

³ All studies were conducted in the adult population of interest to assess the effects of lower TFA intake compared with higher intake on priority health outcomes decided upon prior to initiating the reviews. Studies were mainly conducted in North America and Europe, as well as the UK, Australia and Asia. Significant differences in the basic physiological responses to TFA intake across different ethnic groups and/or populations in different geographic settings are not anticipated.

⁴ For observational studies, relative effects are most-adjusted multivariate estimates (i.e. the multivariate association measure with the highest number of covariates as reported in individual studies).

⁵ Based on the event rate in the studies – that is, the number of people with events divided by the total number of people. The absolute effect (per 1000 people) is calculated using the following equation: absolute effect = 1000 × [event rate × (1 – RR)]. The magnitude of absolute effect in “real world” settings depends on baseline risk, which can vary across different populations.

⁶ All outcomes in this evidence profile are critical outcomes. Outcomes can be assessed as either not important, important or critical for decision-making in the guideline development process (2). Generally, only important and critical outcomes are considered when formulating recommendations, and only critical outcomes are used in designating an overall certainty in the body of evidence supporting a recommendation.

⁷ Although this outcome included only two cohorts, they were different populations and included a very large number of participants; therefore, the outcome was not downgraded.

⁸ *I* > 50%, indicating a significant level of heterogeneity. Downgraded once.

⁹ There was no indication of publication bias or a dose-response relationship.

- ¹⁰ Both cohorts included in the analysis for this outcome were similar populations of health professionals, and the same or very similar questionnaires and instruments were used to assess dietary intake. Because of concerns about potential risk of bias via the use of very similar assessment tools and concerns about indirectness resulting from the very specific study populations, the outcome was conservatively downgraded once across risk of bias and indirectness.
- ¹¹ The number of comparisons is provided in parentheses.
- ¹² All studies included in this analysis were strictly controlled, relatively short-term dietary trials. Studies with crossover and Latin-square designs were deemed to be at low risk of bias for randomization, whether or not it was specifically indicated that participants were randomized, because all participants were intended to receive all treatments, and it is thus unlikely that any differences at baseline would have a significant, systematic effect on study results. The two studies with parallel design were assessed as having an unclear risk of bias in terms of randomization because it was not specified whether participants were randomized. Blinding was not deemed to be a significant source of bias because all interventions consisted of food provision and, although it was possible that participants in some studies may have been able to distinguish between intervention and control diets, this was not expected to alter compliance, given the study design and conduct. All outcomes were objectively measured by chemical and mathematical means; hence, risk of detection bias (i.e. bias resulting from unblinded outcome assessment) was considered to be very low. There was no indication of widespread attrition bias or selective reporting, and other sources of bias were minimal.
- ¹³ Qualitative assessment of the included studies shows that point estimates across individual studies were similar and 95% CIs overlapped, suggesting that any inconsistency is not serious.
- ¹⁴ LDL cholesterol is an indirect measure of patient-important CVD outcomes. However, LDL cholesterol is a well-established biomarker for assessing the effects of interventions on CVD risk (4, 5), and is considered by many to be a causal factor for atherosclerosis and coronary heart disease (6). Therefore not downgraded for indirectness.
- ¹⁵ Imprecision was assessed using the 95% CI of the regression coefficient as a proxy for the 95% CI of a pooled estimate of effect. The rationale was that the regression coefficient provides an estimate of the effect of reducing TFA intake on LDL cholesterol, and the 95% CI is a measure of variability of that effect. The 95% CI does not cross a threshold of important benefit or harm.
- ¹⁶ Visual inspection of the funnel plot did not suggest publication bias.
- ¹⁷ Total number of participants.
- ¹⁸ The relative effect is a regression coefficient that is interpreted as the change in LDL cholesterol when 1% of total energy intake as TFA is replaced with an isocaloric amount of SFA.

Annex 6 references

1. Hooper L, Martin N, Jimoh OF, Kirk C, Foster E, Abdelhamid AS. Reduction in saturated fat intake for cardiovascular disease. *Cochrane Database Syst Rev*. 2020;5(5):CD011737.
2. WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014 (<https://apps.who.int/iris/handle/10665/145714>, accessed 1 January 2023).
3. Assaf AR, Beresford SA, Risica PM, Aragaki A, Brunner RL, Bowen DJ, et al. Low-fat dietary pattern intervention and health-related quality of life: the Women's Health Initiative randomized controlled dietary modification trial. *J Acad Nutr Diet*. 2016;116(2):259–71.
4. Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, Halsey J, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet*. 2007;370(9602):1829–39.
5. Committee on Qualification of Biomarkers and Surrogate Endpoints in Chronic Disease, Board on Health Sciences Policy, Food and Nutrition Board, Institute of Medicine. Evaluation of biomarkers and surrogate endpoints in chronic disease. Washington DC: National Academies Press; 2010.
6. Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J*. 2017;38(32):2459–72.
7. Berenson GS, Srinivasan SR, Bao W, Newman WP 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults: the Bogalusa Heart Study. *N Engl J Med*. 1998;338(23):1650–6.
8. McGill HC Jr, McMahan CA, Malcom GT, Oalmann MC, Strong JP. Effects of serum lipoproteins and smoking on atherosclerosis in young men and women. The PDAY Research Group. Pathobiological Determinants of Atherosclerosis in Youth. *Arterioscler Thromb Vasc Biol*. 1997;17(1):95–106.
9. Srinivasan SR, Frontini MG, Xu J, Berenson GS. Utility of childhood non-high-density lipoprotein cholesterol levels in predicting adult dyslipidemia and other cardiovascular risks: the Bogalusa Heart Study. *Pediatrics*. 2006;118(1):201–6.
10. Davis PH, Dawson JD, Riley WA, Lauer RM. Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: the Muscatine Study. *Circulation*. 2001;104(23):2815–19.
11. Raitakari OT, Juonala M, Kahonen M, Taittonen L, Laitinen T, Maki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA*. 2003;290(17):2277–83.
12. Li S, Chen W, Srinivasan SR, Bond MG, Tang R, Urbina EM, et al. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study. *JAMA*. 2003;290(17):2271–6.
13. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. *Circulation*. 2007;115(4):459–67.
14. Te Morenga L, Montez JM. Health effects of saturated and *trans*-fatty acid intake in children and adolescents: systematic review and meta-analysis. *PloS One*. 2017;12(11):e0186672.
15. Zhu WL, Feng NP, Ma J, Wang Y, Ye GJ. [The effect of dietary intervention on lipidemia in school-aged children]. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2003;24(9):794–7 (in Chinese).
16. Mensink RP. Effects of saturated fatty acids on serum lipids and lipoproteins: a systematic review and regression analysis. Geneva: World Health Organization; 2016 (<https://apps.who.int/iris/handle/10665/246104>, accessed 1 January 2023).

Notes on how GRADE assessment was conducted

Because GRADE assessments were carried out by each systematic review team for each systematic review, there were originally different approaches in assessing some of the domains (bias, inconsistency, indirectness, imprecision). However, under the guidance of the GRADE methodologist, the approaches were largely harmonized. Nevertheless, because of inherent differences in study design between RCTs and prospective observational studies, the approach in assessing imprecision was slightly different, as noted below. The principles used in assessing the domains were as follows.

- ▶ For inconsistency, an $I^2 > 50\%$ was considered to be moderate to significant heterogeneity. Unless explained by subgroup or similar analyses, this was downgraded.
- ▶ For imprecision, a slightly different approach was used between RCTs and prospective observational studies.

For RCTs:

1. Downgrade if the RR for the main meta-analysis crosses 1.0 and includes at least two categories (e.g. harm and little or no effect).
2. Downgrade twice if either the main or sensitivity analyses include both major benefit and major harm.
 - Definition of effect or harm: $RR < 0.92$ or $RR > 1.08$ (therefore little to no effect or harm for RR 0.92 to 1.08).
 - Definition of major benefit: $RR < 0.80$. Definition of major harm: $RR > 1.20$.

For prospective observational studies:

1. If the 95% CI crosses the null (i.e. RR of 1.0 or no effect) but does not contain a strong effect (< 0.8 or > 1.2), not downgraded for imprecision.
2. If the 95% CI crosses the null and includes a strong effect (< 0.8 or > 1.2), downgraded for imprecision.

For both RCTs and prospective observational studies in adults, sample size was also taken into consideration, and an outcome was downgraded if it had a very small sample size.

- ▶ For prospective observational studies, when a dose–response relationship was observed for an outcome that had already been downgraded in another domain, provided it was clear that the dose–response relationship was not dependent or otherwise influenced by the existing downgrade in one or more domains, the outcome was also upgraded.
- ▶ When assessing the overall certainty in the evidence, critical outcomes were considered. Because the effects and associations observed for all critical outcomes were consistent (i.e. all showed the same direction of effect or association, or showed no effect or association), the highest certainty assessed for all outcomes was taken as the overall certainty of the evidence.

Annex 7

Evidence to recommendations table

Background

Intervention: lower SFA intake or lower TFA intake

Comparison: usual diet or higher SFA intake, or usual diet or higher TFA intake

Main outcomes: CVDs, all-cause mortality

Setting: healthy individuals; RCTs, strictly controlled feeding trials, prospective cohort studies

Assessment

	Judgement	Research evidence	Additional considerations
Problem	<p>Is the problem a priority?</p> <p>SFA and TFA</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Probably no</p> <p><input type="checkbox"/> Probably yes</p> <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p>	<p>NCDs are the world's leading cause of death, responsible for an estimated 41 million of the 55 million deaths in 2019 (1). Nearly half of these deaths were premature (i.e. under the age of 70 years) and occurred in low- and middle-income countries. Of the major NCDs, CVDs were the leading cause of mortality in 2019, responsible for more than 18 million deaths (2). Modifiable risk factors such as unhealthy diets, physical inactivity, tobacco use and harmful use of alcohol are major risk factors for CVDs. Dietary SFA and TFA are of particular concern because high levels of intake have been correlated with increased risk of CVDs (3).</p>	<p>Rates of CVDs are growing rapidly in low- and middle-income countries.</p>
Desirable effects	<p>How substantial are the desirable anticipated effects?</p> <p>SFA</p> <p><input type="checkbox"/> Trivial</p> <p><input type="checkbox"/> Small</p> <p><input checked="" type="checkbox"/> Moderate</p> <p><input type="checkbox"/> Large</p> <p><input type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p> <p>TFA</p> <p><input type="checkbox"/> Trivial</p> <p><input type="checkbox"/> Small</p> <p><input checked="" type="checkbox"/> Moderate</p> <p><input type="checkbox"/> Large</p> <p><input type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p>	<p>Because evidence for children was extrapolated from evidence for adults in all cases, the assessment of the magnitude of desirable effects come from adult data.</p> <p>SFA</p> <p>The desirable effects are as follows.</p> <p>Lower vs higher SFA intake:</p> <p>CVDs: RR 0.83 (95% CI: 0.70 to 0.98) (adults) LDL cholesterol: MD -0.13 mmol/L (95% CI: -0.22 to -0.03) (children)</p> <p>10% of total energy intake compared with more than 10%</p> <p>CVDs: RR 0.83 (95% CI: 0.70 to 0.98) (adults) LDL cholesterol: MD -0.29 mmol/L (95% CI: -0.38 to -0.20) (children)</p> <p>Replacing SFA with the following:</p> <p><i>Polyunsaturated fatty acids</i></p> <p>All-cause mortality: RR 0.85 (95% CI: 0.75 to 0.97) (adults) Coronary heart disease: RR 0.89 (95% CI: 0.81 to 0.98) (adults) LDL cholesterol: -0.055 mmol/L* (95% CI: -0.061 to -0.050) (adults) LDL cholesterol: MD -0.29 mmol/L (95% CI: -0.38 to -0.20) (children)</p>	

	Judgement	Research evidence	Additional considerations
Desirable effects		<p><i>Monounsaturated fatty acids</i> All-cause mortality: RR 0.84 (95% CI: 0.75 to 0.95) (adults) LDL cholesterol: -0.042 mmol/L* (95% CI: -0.047 to -0.037) (adults) LDL cholesterol: MD -0.26 mmol/L (95% CI: -0.41 to -0.11) (children)</p> <p><i>Monounsaturated fatty acids (plant-based only)</i> All-cause mortality: RR 0.85 (95% CI: 0.82 to 0.88) (adults) CVDs: RR 0.90 (95% CI: 0.84 to 0.96) (adults)</p> <p><i>Carbohydrates</i> All-cause mortality: RR 0.92 (95% CI: 0.86 to 0.99) (adults) LDL cholesterol: -0.033 mmol/L* (95% CI: -0.039 to -0.027) (adults)</p> <p><i>Carbohydrates (whole grains or low glycaemic index)</i> Coronary heart disease: RR 0.94 (95% CI: 0.89 to 0.99) (adults)</p> <p>* The amount of LDL cholesterol was reduced (mmol/L) for every 1% of SFA (as total energy intake) replaced.</p> <p>Overall, the desirable effects of lower SFA intake are <i>moderate</i>.</p> <p>TFA</p> <p>The desirable effects are as follows (all for adults, all total TFA).</p> <p>Lower vs higher TFA intake</p> <p>All-cause mortality: RR 0.90 (95% CI: 0.83 to 0.98) CVDs: RR 0.88 (95% CI: 0.80 to 0.96) Coronary heart disease: RR 0.86 (95% CI: 0.79 to 0.92)</p> <p>1% of total energy intake compared with more than 1%</p> <p>CVDs: RR 0.83 (95% CI: 0.75 to 0.93) Coronary heart disease: RR 0.88 (95% CI: 0.80 to 0.96)</p> <p>Replacing TFA with the following:</p> <p><i>Polyunsaturated fatty acids</i> Type 2 diabetes: RR 0.72 (95% CI: 0.52 to 0.99) LDL cholesterol: -0.048 mmol/L* (95% CI: -0.055 to -0.041)</p> <p><i>Monounsaturated fatty acids</i> LDL cholesterol: -0.035 mmol/L* (95% CI: -0.042 to -0.028)</p> <p><i>Monounsaturated fatty acids (plant-based only)</i> All-cause mortality: RR 0.90 (95% CI: 0.85 to 0.96) Coronary heart disease: RR 0.80 (95% CI: 0.70 to 0.92)</p> <p><i>Carbohydrates</i> LDL cholesterol: -0.026 mmol/L* (95% CI: -0.033 to -0.019)</p> <p>* The amount of LDL cholesterol was reduced (mmol/L) for every 1% of TFA (as total energy intake) replaced.</p> <p>Overall, the desirable effects of lower TFA intake are <i>moderate</i>.</p>	

	Judgement	Research evidence	Additional considerations
Undesirable effects	<p>How substantial are the undesirable anticipated effects?</p> <p>SFA</p> <p><input type="checkbox"/> Trivial <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large <input type="checkbox"/> Varies <input checked="" type="checkbox"/> None identified/don't know</p> <p>TFA</p> <p><input type="checkbox"/> Trivial <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large <input type="checkbox"/> Varies <input checked="" type="checkbox"/> None identified/don't know</p>	<p>There were no identified adverse effects of any kind associated with reducing intake of SFA or TFA when assessed in aggregate.</p> <p>Although increased risk of type 2 diabetes was associated with reduced consumption of two individual odd chain SFA – pentadecanoic acid and heptadecanoic acid – intake of these SFA was assessed by tissue measurements, which may not consistently distinguish between dietary intake and endogenous synthesis. Furthermore, because SFA are found as mixtures in foods and not in isolation, pentadecanoic acid and heptadecanoic acid as found in foods will be accompanied by other SFA and, as noted, reducing intake of SFA as a whole is associated with reduced risk of all-cause mortality and CVDs.</p>	
Certainty of evidence	<p>What is the overall certainty in the evidence of effects?</p> <p>See adjacent column</p> <p><input type="checkbox"/> Very low <input type="checkbox"/> Low <input type="checkbox"/> Moderate <input type="checkbox"/> High <input type="checkbox"/> No included studies</p>	<p>Because evidence for children was extrapolated from evidence for adults in all cases, the overall certainties in the evidence reported below come from adult data.</p> <p>SFA</p> <p>The overall certainty in the available evidence for lower compared with higher SFA intake (recommendation 1) was assessed as moderate. For consuming SFA at a level less than 10% of total energy intake compared with more than 10% (recommendation 2), the certainty was assessed as low. For replacing SFA with different nutrients, the certainty was considered:</p> <ul style="list-style-type: none"> • moderate for plant-based monounsaturated fatty acids; • low for polyunsaturated fatty acids, monounsaturated fatty acids from unspecified sources, whole grains or foods described by the authors of the individual studies as having a low glycaemic index, carbohydrates from unspecified sources, and animal-based protein; and • very low for free sugars or foods described by the authors of the individual studies as having a high glycaemic index, and protein from unspecified sources. <p>TFA</p> <p>The overall certainty in the available evidence for lower compared with higher TFA intake (recommendation 1) was assessed as moderate. For consuming TFA at a level less than 1% of total energy intake compared with more than 1% (recommendation 2) the certainty was assessed as low. For replacing TFA with different nutrients, the certainty was assessed as:</p> <ul style="list-style-type: none"> • moderate for carbohydrates; • low for plant-based monounsaturated fatty acids; and • very low for polyunsaturated fatty acids, animal-based monounsaturated fatty acids, free sugars and foods described by the authors of the individual studies as having a high glycaemic index, and SFA. 	<p>See GRADE evidence profiles for certainty of evidence for all outcomes (Annex 6).</p>

	Judgement	Research evidence	Additional considerations
Values	<p>Is there important uncertainty about, or variability in, how much people value the main outcomes?</p> <p>SFA and TFA</p> <p><input type="checkbox"/> Important uncertainty or variability</p> <p><input type="checkbox"/> Possibly important uncertainty or variability</p> <p><input checked="" type="checkbox"/> Probably no important uncertainty or variability</p> <p><input type="checkbox"/> No important uncertainty or variability</p>	<p>These recommendations address CVDs as well as all-cause mortality. CVDs are the leading cause of disease burden globally (2), and therefore interventions and programmes targeting reduction in risk of CVDs are valuable in all contexts and are a high priority for many countries. Despite the global burden of CVDs, the priority placed on this problem by authorities at different levels may vary depending on the real or perceived magnitude of the problem within a particular country or region.</p> <p>The recommendations in this guideline place a high value on reducing risk of CVDs; however, individuals affected by the recommendations may place a different value on the benefit of reducing CVD risk. Because CVDs are a high-profile public health topic, including in many low- and middle-income countries where these diseases represent a growing threat (4), it is expected that most individuals would value efforts to reduce risk. However, in real-world settings, perception of the risk varies considerably (5–8), and outreach and communication efforts may be needed to improve understanding.</p>	
Balance of effects	<p>Does the balance between desirable and undesirable effects favour the interventions or the comparisons?</p> <p>SFA</p> <p><input checked="" type="checkbox"/> Favours interventions</p> <p><input type="checkbox"/> Probably favours interventions</p> <p><input type="checkbox"/> Does not favour either</p> <p><input type="checkbox"/> Probably favours comparisons</p> <p><input type="checkbox"/> Favours comparisons</p> <p><input type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p> <p>TFA</p> <p><input checked="" type="checkbox"/> Favours interventions</p> <p><input type="checkbox"/> Probably favours interventions</p> <p><input type="checkbox"/> Does not favour either</p> <p><input type="checkbox"/> Probably favours comparisons</p> <p><input type="checkbox"/> Favours comparisons</p> <p><input type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p>	<p>There was abundant evidence for cardiovascular benefit of reducing SFA and TFA intake across many study types and outcomes, and evidence for reduced risk of all-cause mortality from prospective observational studies. There were no adverse effects of any kind associated with reducing intake of SFA or TFA when assessed in aggregate. Although increased risk of type 2 diabetes was associated with reduced consumption of two individual odd chain SFA – pentadecanoic acid and heptadecanoic acid – intake of these SFA was assessed by tissue measurements, which may not consistently distinguish between dietary intake and endogenous synthesis. Furthermore, because SFA are found as mixtures in foods and not in isolation, pentadecanoic acid and heptadecanoic acid as found in foods will be accompanied by other SFA and, as noted, reducing intake of SFA as a whole is associated with reduced risk of all-cause mortality and CVDs. Therefore, until more is known about how potential health effects of individual SFA might be interpreted in the context of health effects of SFA as a class of molecules, the desirable effects of reducing both SFA and TFA intake strongly outweigh the undesirable effects.</p> <p>Concerns have been raised about the potential negative impact of reducing or limiting the intake of dietary fat on nutritional adequacy and resulting growth and development of children (9, 10), particularly in the context of limiting intake of dairy and other animal-source foods. The systematic review supporting this guideline did not identify undesirable effects related to growth and development in children who reduced their SFA intake (11). A primary focus of two large studies included in the review – the Dietary Intervention Study in Children (DISC) (12) and the Special Turku Coronary Risk Factor Intervention Project (STRIP) (13) – was to assess the safety of reducing SFA in the diet of children. Authors of both trials concluded that a diet low in SFA did not affect normal growth and development of children, and was therefore safe. The STRIP study, in particular, demonstrates the long-term safety of a diet low in SFA. It implemented a low-SFA diet beginning at 7 months of age and followed up</p>	

	Judgement	Research evidence	Additional considerations
Balance of effects		<p>participants regularly for more than 20 years, during which no adverse effects on growth, neurological or sexual development, or psychosocial well-being were noted (14).</p> <p>Although no evidence for effects of reducing TFA intake on children was identified, concerns regarding potential adverse effects of limiting ruminant TFA found in dairy foods and meat from ruminant animals were addressed in modelling analyses (Annex 8) that assessed ruminant TFA content of various dairy foods in the context of SFA content and the WHO recommendations on SFA intake.</p> <p>The WHO recommendations on SFA and TFA intake allow for adequate consumption of dairy foods, particularly reduced-fat versions of these foods, and are compatible with many national guidelines on dairy intake. Because reducing SFA and TFA intake in children reduces CVD risk without any identified adverse effects, the desirable effects of reducing both SFA and TFA intake strongly outweigh the undesirable effects (none identified).</p> <p>Evidence from the Mensink systematic review suggests a slight increase in triglycerides and reduction in HDL cholesterol when SFA are replaced by carbohydrates of mixed composition. However, the clinical relevance of such changes is not clear (15), and this was not considered an influential consideration in the balance of desirable and undesirable effects, given the evidence for disease and mortality outcomes, and in light of Recommendation 3 on replacement nutrients for SFA.</p>	
Resources required	<p>How large are the resource requirements of the interventions?</p> <p>SFA and TFA</p> <p><input type="checkbox"/> Large costs</p> <p><input type="checkbox"/> Moderate costs</p> <p><input type="checkbox"/> Negligible costs and savings</p> <p><input type="checkbox"/> Moderate savings</p> <p><input type="checkbox"/> Large savings</p> <p><input checked="" type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p>	<p>Costs of translating the recommendations into policies and actions will vary widely, depending on which approaches are taken, but may be associated with long-term savings in costs of health care, particularly when implemented as part of a coherent package of interventions (16). The extent of these savings and resource use depend on strategies chosen for implementation and the time scale for evaluation. Implementation of the recommendations will likely require consumer education and public health communications, some or all of which can be incorporated into existing public health nutrition education campaigns and other existing nutrition programmes at the global, regional, national and subnational levels.</p>	<p>An assessment of the costs of all possible ways of implementing the recommendation is beyond the scope of this guideline.</p>
Certainty of evidence of required resources	<p>What is the certainty of the evidence of resource requirements (costs)?</p> <p>SFA and TFA</p> <p><input type="checkbox"/> Very low</p> <p><input type="checkbox"/> Low</p> <p><input type="checkbox"/> Moderate</p> <p><input type="checkbox"/> High</p> <p><input checked="" type="checkbox"/> Don't know</p>	<p>No studies assessing the costs of achieving the dietary goals in this guideline were identified.</p>	

	Judgement	Research evidence	Additional considerations
Cost-effectiveness	<p>Does the cost-effectiveness of the intervention favour the intervention or the comparison?</p> <p>SFA and TFA</p> <p><input type="checkbox"/> Favours the intervention</p> <p><input type="checkbox"/> Probably favours the intervention</p> <p><input type="checkbox"/> Does not favour either</p> <p><input type="checkbox"/> Probably favours the comparison</p> <p><input type="checkbox"/> Favours the comparison</p> <p><input type="checkbox"/> Varies</p> <p><input checked="" type="checkbox"/> Don't know</p>	<p>Whether or not implementing the recommendations is cost-effective is not conclusively known, given the various ways that the recommendations can be implemented. However, given the escalating costs of long-term health care for conditions and diseases associated with CVDs, implementing the recommendations may be associated with long-term savings in costs of health care.</p> <p>Specific evidence for resource implications of reducing SFA and/or TFA intake is limited; however, a small number of modelling studies have been published. Simulations in high-income countries suggest that reducing SFA and TFA intake through various means, including reformulation of conventional oils (and bans in the case of industrially produced TFA) could result in savings of hundreds of millions to billions of US dollar equivalents from reduced health-care costs (17, 18, 19–22).</p>	<p>This question cannot be answered with certainty because it requires an assessment of different modes of implementing the recommendations, which is beyond the scope of this guideline.</p>
Equity	<p>What would be the impact on health inequity?</p> <p>SFA and TFA</p> <p><input type="checkbox"/> Reduced</p> <p><input checked="" type="checkbox"/> Probably reduced</p> <p><input type="checkbox"/> Probably no impact</p> <p><input type="checkbox"/> Probably increased</p> <p><input type="checkbox"/> Increased</p> <p><input type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p>	<p>The recommendations in this guideline have the potential to reduce health inequity by improving the health of people of lower socioeconomic status, who are generally disproportionately affected by CVDs (23) and NCDs in general (24). However, effects on equity and human rights would likely be affected by how the recommendations are translated into policies and actions (e.g. fiscal policies, reformulation). The impact of interventions on the pricing of manufactured foods would require careful consideration, as any increase in costs borne by manufacturers might be passed on to the consumer; this would likely disproportionately affect people of lower socioeconomic status.</p> <p>Modelling studies and real-world assessments of bans and other policies targeting elimination of industrially produced TFA in high-income countries suggest that reducing TFA intake could reduce coronary heart disease-related health inequity stemming from differences in socioeconomic status (17, 18).</p>	<p>Limited published evidence is available from which to draw conclusions.</p>

	Judgement	Research evidence	Additional considerations
Acceptability	<p>Is the intervention acceptable to key stakeholders?</p> <p>SFA</p> <p><input type="checkbox"/> No <input type="checkbox"/> Probably no <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> Varies <input type="checkbox"/> Don't know</p> <p>TFA</p> <p><input type="checkbox"/> No <input type="checkbox"/> Probably no <input checked="" type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/> Varies <input type="checkbox"/> Don't know</p>	<p>The recommendations in this guideline are in line with many existing national dietary guidelines and policies. However, acceptability may vary across different countries and cultural contexts.</p> <p>Acceptability may be influenced by:</p> <ul style="list-style-type: none"> • how the recommendations are translated into policies and actions (e.g. nutrition labelling policies, marketing policies, fiscal policies, reformulation) – some may be more acceptable than others; • level of awareness of the health problem that CVDs pose – interventions may be less acceptable in settings where awareness is low; • potential impact on national economies; and • compatibility with existing policies. <p>At an individual level, for people who acknowledge the evidence linking SFA and TFA intake to risk of CVDs and value reducing this risk, acceptability should be high because CVDs are a significant, recognized global health problem. As noted with respect to feasibility, however, there are many for whom the recommendation may not be acceptable, based on the current, popular perception that diets high in SFA do not pose a health risk (25). Because the health risks of consuming large amounts of industrially produced TFA are already generally accepted and TFA are already being phased out in many settings, acceptability of the recommendations on TFA intake should be acceptable to many.</p>	<p>Limited published evidence is available from which to draw conclusions.</p>
Feasibility	<p>Is the intervention feasible to implement?</p> <p>SFA</p> <p><input type="checkbox"/> No <input type="checkbox"/> Probably no <input checked="" type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/> Varies <input type="checkbox"/> Don't know</p> <p>TFA</p> <p><input type="checkbox"/> No <input type="checkbox"/> Probably no <input checked="" type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/> Varies <input type="checkbox"/> Don't know</p>	<p>In settings where efforts to reduce SFA and TFA intake are planned or are already under way, feasibility should be much higher than in settings where plans are not yet in place. Regardless, feasibility will be influenced by the existing relevant infrastructure (for different interventions) and the available resources. In implementing interventions to bring about the desired change in SFA and TFA intake (e.g. behaviour change and education campaigns, fiscal policies, marketing and labelling policies, reformulation), feasibility will vary widely; detailed discussions of feasibility for each type of intervention are beyond the scope of this guideline. Relevant to all interventions, widespread use and availability of certain food items high in SFA and/or TFA may pose challenges in decreasing consumption to meet the recommended intake. Regardless of which interventions are employed to realize the recommended intakes, some amount of behaviour change at the individual level will be required. This may be challenging with respect to SFA in certain settings, particularly those in which some medical professionals and academic researchers question the link between SFA intake and CVDs (26), and popular opinion has currently been shaped to view high SFA intakes as part of a healthy, natural diet (25).</p> <p>That large-scale reduction in SFA intake is feasible has been demonstrated in North Karelia in Eastern Finland where, from 1972 to 2007, population intake of SFA was reduced from 20% to 12% of total energy intake, and total cholesterol decreased by more than 20% (27). Although there is evidence of real-world success, SFA intake has slightly increased in North Karelia since 2007 (28), and other unsuccessful approaches such as the Danish tax on SFA which was abandoned after a little more than a year (despite resulting in a small reduction in population SFA intake) (29) are</p>	

	Judgement	Research evidence	Additional considerations
Feasibility		<p>reminders that, although feasible, large-scale reduction of SFA intake depends on a number of contextual factors that vary across settings. Interventions may well be challenging and will require multisectoral cooperation in many settings to be successful.</p> <p>Global efforts to eliminate industrially produced TFA are already well under way, supported by the WHO REPLACE action package launched in May 2018.^a As of September 2022, 60 countries had implemented mandatory TFA limits; of these, 43 countries had implemented a best-practice TFA policy that either virtually eliminates industrially produced TFA or bans partially hydrogenated oils (30), demonstrating that global reduction in TFA intake may be an achievable goal. In addition, in light of the strong evidence base and growing public awareness of the undesirable health effects associated with TFA intake, several companies have voluntarily reformulated their products to remove TFA (17).</p>	

^a <https://www.who.int/teams/nutrition-and-food-safety/replace-trans-fat>

Annex 7 references

1. Global Health Observatory data. Noncommunicable diseases mortality and morbidity. Geneva: World Health Organization; 2021 (http://www.who.int/gho/ncd/mortality_morbidity/en/, accessed 1 January 2023).
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol.* 2020;76(25):2982–3021.
3. Diet, nutrition and the prevention of chronic diseases: report of a Joint WHO/FAO expert consultation. Geneva: World Health Organization; 2003 (<https://apps.who.int/iris/handle/10665/42665>, accessed 1 January 2023).
4. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr Probl Cardiol.* 2010;35(2):72–115.
5. Wekesah FM, Kyobutungi C, Grobbee DE, Klipstein-Grobusch K. Understanding of and perceptions towards cardiovascular diseases and their risk factors: a qualitative study among residents of urban informal settings in Nairobi. *BMJ Open.* 2019;9(6):e026852.
6. Negesa LB, Magarey J, Rasmussen P, Hendriks JML. Patients' knowledge on cardiovascular risk factors and associated lifestyle behaviour in Ethiopia in 2018: a cross-sectional study. *PloS One.* 2020;15(6):e0234198.
7. Oli N, Vaidya A, Subedi M, Krettek A. Experiences and perceptions about cause and prevention of cardiovascular disease among people with cardiometabolic conditions: findings of in-depth interviews from a peri-urban Nepalese community. *Glob Health Action.* 2014;7:24023.
8. Erhardt L, Hobbs FD. Public perceptions of cardiovascular risk in five European countries: the react survey. *Int J Clin Pract.* 2002;56(9):638–44.
9. Kaplan RM, Toshima MT. Does a reduced fat diet cause retardation in child growth? *Prev Med.* 1992;21(1):33–52.
10. Mauer AM. Should there be intervention to alter serum lipids in children? *Annu Rev Nutr.* 1991;11:375–91.
11. Te Morenga L, Montez JM. Health effects of saturated and *trans*-fatty acid intake in children and adolescents: systematic review and meta-analysis. *PloS One.* 2017;12(11):e0186672.

12. Writing Group for the DISC Collaborative Research Group. Efficacy and safety of lowering dietary intake of fat and cholesterol in children with elevated low-density lipoprotein cholesterol: the Dietary Intervention Study in Children (DISC). *JAMA*. 1995;273(18):1429–35.
13. Lapinleimu H, Viikari J, Jokinen E, Salo P, Routi T, Leino A, et al. Prospective randomised trial in 1062 infants of diet low in saturated fat and cholesterol. *Lancet*. 1995;345(8948):471–6.
14. Pahkala K, Laitinen TT, Niinikoski H, Kartiosuo N, Rovio SP, Lagström H, et al. Effects of 20-year infancy-onset dietary counselling on cardiometabolic risk factors in the Special Turku Coronary Risk Factor Intervention Project (STRIP): 6-year post-intervention follow-up. *Lancet Child Adolesc Health*. 2020;4(5):359–69.
15. Xiang AS, Kingwell BA. Rethinking good cholesterol: a clinicians' guide to understanding HDL. *Lancet Diabetes Endocrinol*. 2019;7(7):575–82.
16. Bertram MY, Sweeny K, Lauer JA, Chisholm D, Sheehan P, Rasmussen B, et al. Investing in non-communicable diseases: an estimation of the return on investment for prevention and treatment services. *Lancet*. 2018;391(10134):2071–8.
17. Downs SM, Bloem MZ, Zheng M, Catterall E, Thomas B, Veerman L, et al. The impact of policies to reduce *trans* fat consumption: a systematic review of the evidence. *Curr Dev Nutr*. 2017;1(12):cdn.117.000778.
18. Marklund M, Zheng M, Veerman JL, Wu JHY. Estimated health benefits, costs, and cost-effectiveness of eliminating industrial *trans*-fatty acids in Australia: a modelling study. *PLoS Med*. 2020;17(11):e1003407.
19. Dall TM, Fulgoni VL 3rd, Zhang Y, Reimers KJ, Packard PT, Astwood JD. Potential health benefits and medical cost savings from calorie, sodium, and saturated fat reductions in the American diet. *Am J Health Promot*. 2009;23(6):412–22.
20. Meier T, Senftleben K, Deumelandt P, Christen O, Riedel K, Langer M. Healthcare costs associated with an adequate intake of sugars, salt and saturated fat in Germany: a health econometrical analysis. *PloS One*. 2015;10(9):e0135990.
21. Malla S, Hobbs JE, Perger O. Estimating the health care savings from *trans* fat-free canola in Canada. *Acta Agric Scand C Food Econ*. 2005;2(3–4):175–84.
22. Abdullah MM, Jew S, Jones PJ. Health benefits and evaluation of healthcare cost savings if oils rich in monounsaturated fatty acids were substituted for conventional dietary oils in the United States. *Nutr Rev*. 2017;75(3):163–74.
23. Schultz WM, Kelli HM, Lisko JC, Varghese T, Shen J, Sandesara P, et al. Socioeconomic status and cardiovascular outcomes: challenges and interventions. *Circulation*. 2018;137(20):2166–78.
24. Allen L, Williams J, Townsend N, Mikkelsen B, Roberts N, Foster C, et al. Socioeconomic status and non-communicable disease behavioural risk factors in low-income and lower-middle-income countries: a systematic review. *Lancet Glob Health*. 2017;5(3):e277–e89.
25. Teicholz N. *The big fat surprise: why butter, meat and cheese belong in a healthy diet*. Simon & Schuster; 2014.
26. Malhotra A. Saturated fat is not the major issue. *BMJ*. 2013;347:f6340.
27. Jousilahti P, Laatikainen T, Peltonen M, Borodulin K, Männistö S, Jula A, et al. Primary prevention and risk factor reduction in coronary heart disease mortality among working aged men and women in eastern Finland over 40 years: population based observational study. *BMJ*. 2016;352:i721.
28. Vartiainen E, Laatikainen T, Tapanainen H, Puska P. Changes in serum cholesterol and diet in North Karelia and all Finland. *Glob Heart*. 2016;11(2):179–84.
29. Smed S, Scarborough P, Rayner M, Jensen JD. The effects of the Danish saturated fat tax on food and nutrient intake and modelled health outcomes: an econometric and comparative risk assessment evaluation. *Eur J Clin Nutr*. 2016;70(6):681–6.
30. Countdown to 2023: WHO report on global *trans*-fat elimination 2022. Geneva: World Health Organization; 2023 (<https://apps.who.int/iris/handle/10665/365617>, accessed 1 January 2023).

Annex 8

Ruminant TFA intake and consumption of dairy: a modelling exercise

Prepared by Emeritus Professor C Murray Skeaff

Executive summary

Background

WHO is currently updating guidance on SFA and TFA intake. Based on the evidence review for TFA, the WHO NUGAG Subgroup on Diet and Health concluded that industrially produced and ruminant TFA behaved in a similar manner with respect to effects on health and therefore formulated recommendations for total TFA (i.e. the total intake from both industrially produced and ruminant TFA). Dairy fat contains both SFA and ruminant TFA, and concerns have been raised about the potential impact of recommendations to limit intake, particularly of ruminant TFA, on dairy consumption.

Aim

To model the potential impact on the consumption of dairy products of the updated WHO recommendations on TFA.

Methods

The amount of milk (3.3% fat) and cheddar cheese (34% fat) providing 1% of total energy intake from TFA was calculated for daily energy intakes ranging from 5 millijoules (MJ) to 13 MJ, and TFA content of dairy fat ranging from 3% to 8% of total fatty acids. Similar calculations were done to estimate the amounts of milk (3.3% fat) and cheddar cheese (34% fat) providing 10% of total energy from SFA. Values for the mean TFA and mean SFA composition of fat in milk, cheese and butter were obtained from published sources.

Results

The mean TFA content of dairy fat was 4.2% of total fatty acids, and the mean SFA content was 67% of total fatty acids. For dairy fat comprising 4.2% TFA and 67% SFA, and for a person with a daily energy intake of 8.7 MJ, 1665 g of milk (3.3% fat) or 162 g of cheddar cheese (34% fat) would provide 1% of total energy as TFA. This compares with 1044 g of milk (3.3% fat) or 101 g of cheddar cheese (34% fat) that would provide 10% of total energy from SFA. At any level of energy intake, and assuming dairy fat composition of 4.2% TFA and 67% SFA, acceptable dairy product consumption would be roughly 60% higher for milk and for cheese ($1665/1044 \times 100$ for milk; and $162/101 \times 100$ for cheese) when adhering to the limit of 1% of energy from TFA compared with the limit of 10% of energy from SFA.

Conclusions

The updated WHO recommendation to limit total TFA intake to 1% or less of total energy intake is in line with the WHO recommendation to limit SFA intake to less than 10% of total energy in terms of potential impact on dairy consumption.

¹ Department of Human Nutrition, University of Otago, Dunedin, New Zealand; member of the NUGAG Subgroup on Diet and Health

Introduction

WHO is currently updating guidance on SFA and TFA intake. Based on the evidence review for TFA, the WHO NUGAG Subgroup on diet and health concluded that industrially produced and ruminant TFA behaved in a similar manner with respect to effects on health and therefore formulated recommendations for total TFA (i.e. the total intake from both industrially produced and ruminant TFA). Dairy fat contains both SFA and ruminant TFA, and concerns have been raised about the potential impact of recommendations to limit intake, particularly of ruminant TFA, on dairy consumption. The concern only needs to be addressed for dairy products that supply reasonable amounts of fat in the diet because dairy products such as skimmed milk that are low in total fat can be consumed in large amounts yet provide virtually no TFA.

The potential of the updated TFA recommendations to restrict dairy food intake was examined in the context of dairy consumption when adhering to the WHO recommendations on SFA intake.

Methods

TFA composition of dairy fat

Information about the total TFA and SFA composition of fat in commonly consumed dairy foods – including milk, cheeses and butter – was obtained from published sources (as shown in **Table A8.1**). The modelling work is based primarily on the TFA composition of milk and cheese; however, information about the TFA composition of butter was included to examine consistency of the TFA composition of dairy fat across dairy products. When extracting results from the relevant articles, total TFA composition of the fat in the dairy foods was calculated by summing the percentage contribution of all fatty acids with one or more double bonds in the *trans* configuration, and is expressed as a percentage of total fatty acids.

Amount of dairy food providing 1% of total energy as TFA

Using the information about the TFA composition of dairy fat, the amount of milk (3.3% fat) or cheese (34% fat) that provides 1% of total energy intake from TFA was estimated across a range of daily energy intakes from 5 MJ to 13 MJ, and a range of TFA content of dairy fat from 3% to 8% of total fatty acids.

Calculations:

Step 1. Amount (g) of TFA providing 1% of total daily energy

$$= (\text{Daily energy intake, kJ} \times 1\%) \div 37.7 \text{ kJ per g fat}$$

Step 2. TFA content of dairy product (g TFA per 100 g edible portion).

$$= \text{Fat content of dairy product (g per 100 g edible portion)} \\ \times \% \text{ TFA composition of dairy fat}$$

Step 3. Amount (g) of dairy product that provides 1% of total daily energy from TFA

$$= [\text{Amount (g) of TFA that provides 1\% of total energy} \\ \div \text{TFA content of dairy product (g per 100 g edible portion)}] \\ \times 100 \text{ g}$$

Example calculation for the amount of milk (3.3% fat) that provides 1% of total daily energy intake:

$$\begin{aligned} \text{Total daily energy intake} &= 8700 \text{ kJ} \\ \text{Total fat content of milk} &= 3.3 \text{ g per 100 g} \\ \text{TFA content of milk fat} &= 4.2\% \text{ of total fatty acids} \\ \text{Amount of milk containing 1\% of total daily energy from TFA} \\ &= \frac{(\text{Amount (g) of TFA providing 1\% of total daily energy}}{\text{TFA content of dairy product (g TFA per 100 g edible portion)}} \times 100 \text{ g} \\ &= \frac{((8700 \text{ kJ} \times 1\%) \div 37.7 \text{ kJ per g})}{(3.3 \text{ g per 100g} \times 4.2\% \text{ TFA}) \times 100 \text{ g}} = 1665 \text{ g} \end{aligned}$$

Amount of dairy food providing 10% of total energy as SFA

The amount of milk (3.3% fat) or cheese (34% fat) that provides 10% of total energy from SFA was estimated across a range of daily energy intakes from 5 MJ to 13 MJ. The SFA composition of milk and cheese fat was taken as 67% of total fatty acids, which was the mean composition of the dairy products listed in [Table 1](#); otherwise, the calculations were similar to those for TFA.

Example calculation for the amount of milk (3.3% fat) that provides 10% of total energy intake from SFA:

$$\begin{aligned} &\text{Total daily energy intake} = 8700 \text{ kJ} \\ &\text{Total fat content of milk} = 3.3 \text{ g per } 100 \text{ g} \\ &\text{SFA content of milk fat} = 67\% \text{ of total fatty acids} \\ &\text{Amount of milk containing } 10\% \text{ of total daily energy from SFA} \\ &\frac{((8700 \text{ kJ} \times 10\%) \div 37.7 \text{ kJ per g})}{(3.3 \text{ g per } 100 \text{ g} \times 67\% \text{ SFA})} \times 100 \text{ g} = 1044 \text{ g} \end{aligned}$$

Results and discussion

TFA composition of dairy products

The TFA composition of a selection of dairy products from a number of countries is shown in [Table A8.1](#) and [Fig. A8.1](#). The TFA composition ranged from 2.9% to 6.8% of total fatty acids in European butters (1), from 6.1% to 6.4% in Canadian dairy products (2), from 4.6% to 5.1% in Portuguese cheeses (3), from 2.5% to 3.5% in New Zealand dairy products (4), and from 4.0% to 4.5% in US dairy products (5). A seasonal comparison of the TFA composition of French (6) and Bulgarian (1) butter showed higher TFA composition in summer than in winter. Overall, the mean TFA composition of fat in various dairy products, across a number of countries, was 4.2% of total fatty acids, ranging from 2.5% to 6.8% of total fatty acids. The SFA composition of the same dairy products ([Table A8.1](#) and [Fig. A8.2](#)) ranged from 57% to 73% of total fatty acids, with a mean of 67%.

Amount of milk (3.3% fat) or cheese (34% fat) that provides 1% of total energy as TFA

The amounts of milk (3.3% fat) or cheddar cheese (34% fat) that provide 1% of total energy as TFA are shown in [Figs. A8.3](#) and [A8.4](#) and are calculated for dairy fat with a TFA content of either 3%, 4%, 5%, 6%, 7% or 8% of total fatty acids. When the TFA composition of milk fat is 3%, 1340 g and 3483 g of milk (3.3% fat) will provide 1% of total energy intake as TFA at daily energy intakes of 5 MJ and 13 MJ, respectively. As the TFA composition of milk fat increases, the amount of milk (3.3% fat) that will provide 1% of total energy intake as TFA decreases. When milk fat contains 8% TFA, 502 g and 1306 g of milk (3.3% fat) will provide 1% of total energy intake as TFA at daily energy intakes of 5 MJ and 13 MJ, respectively. For cheese fat containing 3% TFA, 130 g and 338 g of cheddar cheese will provide 1% of total energy intake as TFA at daily energy intakes of 5 MJ and 13 MJ, respectively. For cheese fat containing 8% TFA, 49 g and 127 g of cheddar cheese will provide 1% of total energy intake as TFA at daily energy intakes of 5 MJ and 13 MJ, respectively.

Based on a typical TFA composition of dairy fat of 4.2% of total fatty acids – the mean across the dairy products shown in [Table A8.1](#) – the amount of milk (3.3% fat) that would supply 1% of total daily energy as TFA ranges from 957 g to 2488 g at daily energy intakes of 5 MJ and 13 MJ, respectively. The amount of cheddar cheese (34% fat) that would supply 1% of total daily energy as TFA ranges from 93 g to 241 g at daily energy intakes of 5 MJ and 13 MJ, respectively. The SFA supplied by these amounts of milk and cheddar cheese (67% SFA) would contribute 16.0% of total energy as SFA, far in excess of the WHO recommendation to limit SFA intake to less than 10% of total energy. Therefore, for dairy products with a typical TFA composition (4.2% of total fatty acids), consumption should not be affected in the context of adhering to the WHO recommendations on SFA intake.

It is only when the TFA composition of dairy fat exceeds 6.7% of total fatty acids – and SFA content is 67% – that an amount of dairy product that provides at least 1% of total energy as TFA will supply less than 10% of total daily energy from SFA, and would therefore affect consumption in the context of adhering to the WHO recommendations on SFA intake. When the TFA content of dairy fat in dairy foods is less than 6.7% of

total fatty acids, consumption of such foods should not be affected in the context of adhering to the WHO recommendations on SFA intake.

A limitation of this analysis is that it includes only a representative sample of dairy foods, none of which come from low- and middle-income countries. Although it is unknown if the SFA content and TFA content is similar in all dairy foods commonly consumed across all populations, it is nevertheless expected that the relationships observed between the fatty acids in this analysis would not vary significantly, and therefore the conclusions derived from this analysis would be generally applicable.

Table A8.1 Total TFA content (% of total fatty acids) of selected dairy products in different countries

	Country	Total TFA ^a	SFA
<i>Marekov et al., 2009 (1)</i>			
Butter	Germany	3.3	69.4
Butter	Austria	2.6	71.0
Butter	Switzerland	2.9	68.8
Butter	Denmark	3.9	66.1
Butter	France	4.0	67.6
Butter	Sweden	4.0	67.6
Butter	Bulgaria (winter)	3.9	68.6
Butter	Bulgaria (summer)	6.8	65.1
<i>Mendis et al., 2008 (2)</i>			
Cheese	Canada	6.3	66.5
Butter	Canada	6.4	67.2
Milk	Canada	6.4	66.7
Cream	Canada	6.1	66.6
All dairy combined	Canada	6.1	66.9
<i>Partidario et al., 2008 (3)</i>			
Ewes cheese (Azeito)	Portugal	4.8	70.9
Ewes cheese (Evora)	Portugal	4.7	73.2
Ewes cheese (Nisa)	Portugal	4.6	69.2
Ewes milk (Azeito)	Portugal	4.0	70.2
Ewes milk (Evora)	Portugal	5.1	69.2
Ewes milk (Nisa)	Portugal	4.6	69.7
<i>New Zealand Food Composition Database (4)</i>			
Edam cheese	New Zealand	3.4	66.4
Colby cheese	New Zealand	3.1	68.7
Cheddar cheese	New Zealand	3.0	67.6
Cottage cheese	New Zealand	3.6	72.7
Milk (3.3% fat)	New Zealand	3.8	66.3
Butter	New Zealand	2.5	68.4
<i>USDA Nutrient Database (5)</i>			
Butter	USA	4.3	68.1
Cheddar cheese	USA	4.0	66.3
Milk (2% fat)	USA	4.5	66.5
<i>Ledoux et al., 2005 (6)</i>			
Butter (winter)	France	2.5	61.3
Butter (spring)	France	3.1	60.0
Butter (summer)	France	3.8	56.5

SFA: saturated fatty acids; TFA: *trans*-fatty acids; USA: United States of America.

^a Total TFA includes monoene, diene and conjugated linoleic acid.

Fig. A8.1 Total TFA content (% of total fatty acids) of selected dairy products in different countries

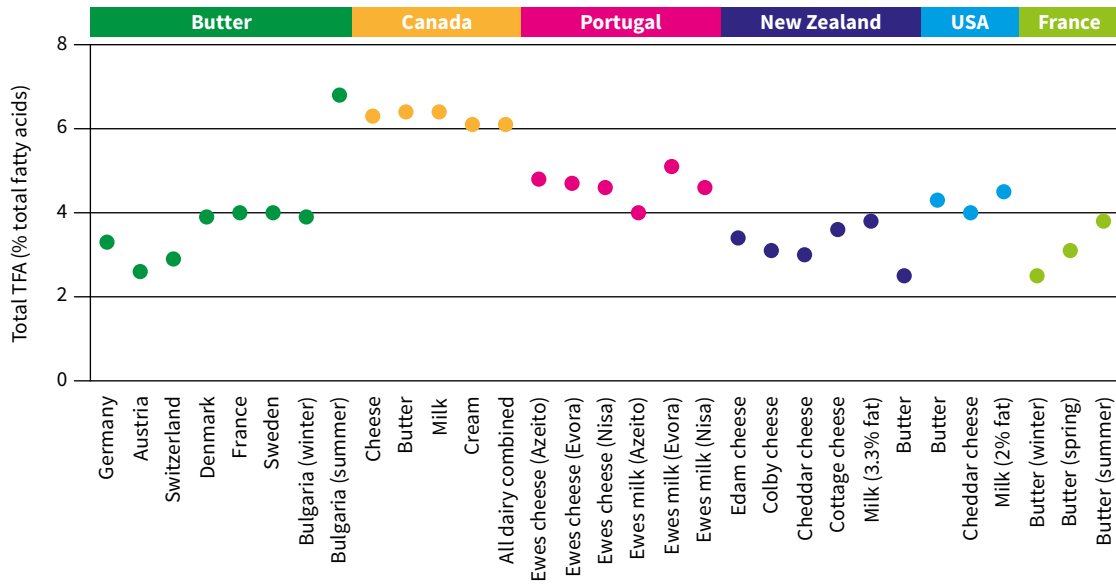


Fig. A8.2 SFA content (% of total fatty acids) of selected dairy products in different countries

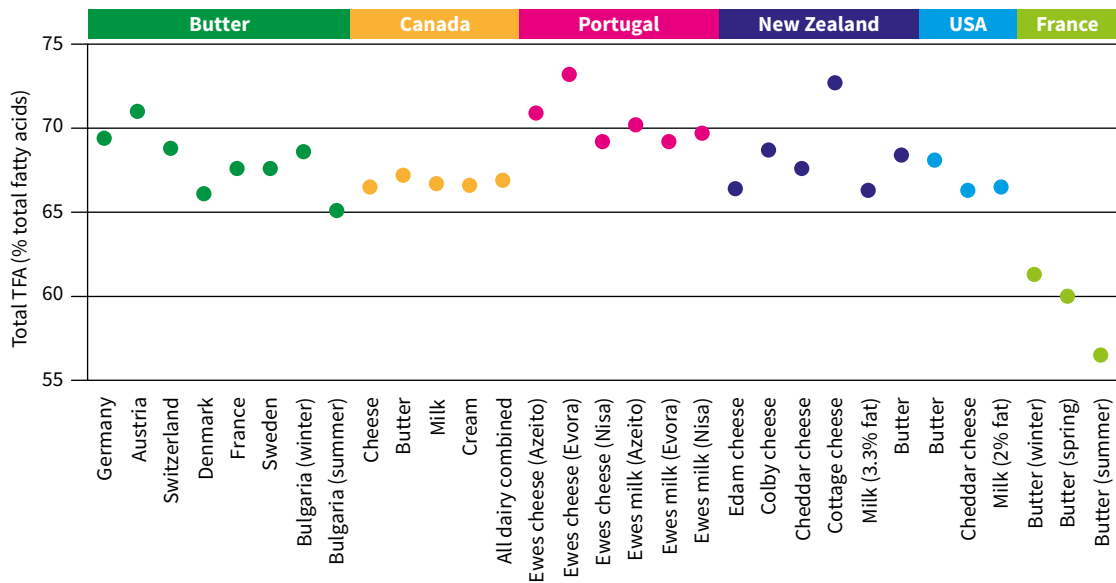
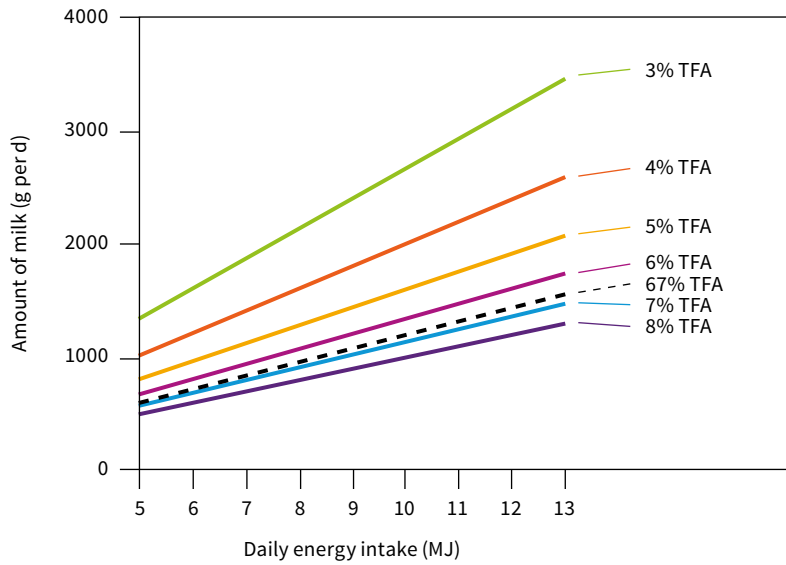
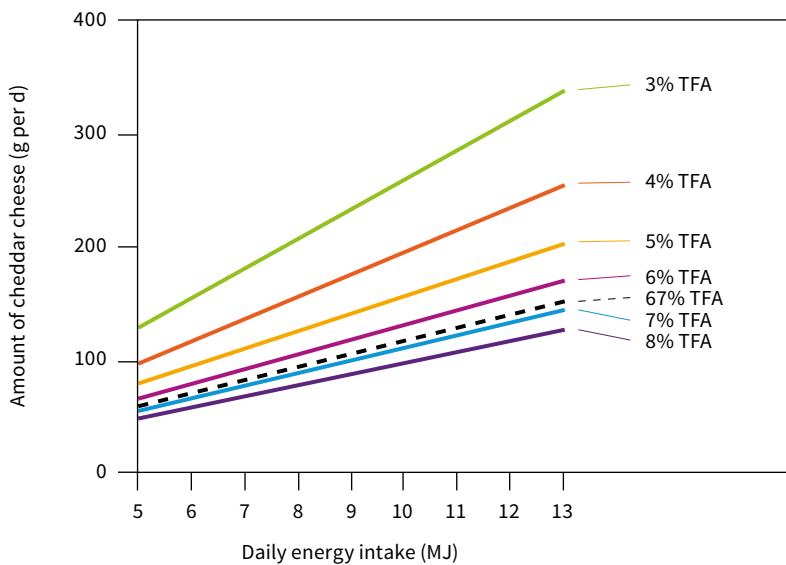


Fig. A8.3 Amount of milk (3.3% fat) that provides 1% of total daily energy intake from TFA



Note: Each coloured line represents milk with a given TFA content (% of total fatty acids) of milk fat. The black dotted line represents the amount of milk (3.3% fat) that provides 10% of daily energy from SFA.

Fig. A8.4 Amount of cheddar cheese (34% fat) that provides 1% of total daily energy intake from TFA



Note: Each coloured line represents cheese with a given TFA content (% of total fatty acids) of cheese fat. The black dotted line represents the amount of cheddar cheese (34% fat) that provides 10% of daily energy from SFA.

Annex 8 references

1. Marekov I, Panayotova S, Tarandjiiska R. Fatty acid composition and seasonal variation of *trans* fatty acid content in Bulgarian butter fats by silver ion TLC and GC. *J Liq Chromatog Relat Technol.* 2009;32(9):1183–95.
2. Mendis S, Cruz-Hernandez C, Ratnayake WMN. Fatty acid profile of Canadian dairy products with special attention to the *trans*-octadecenoic acid and conjugated linoleic acid isomers. *J AOAC Int.* 2008;91(4):811–19.
3. Partidário AM, Ribeiro JCS, Prates JAM. Fatty acid composition and nutritional value of fat in three PDO ewes' milk Portuguese cheeses. *Dairy Sci Technol.* 2008;88(6):683–94.
4. New Zealand food composition database [website]. Auckland: New Zealand Institute for Plant & Food Research, New Zealand Ministry of Health; 2014 (<http://www.foodcomposition.co.nz>, accessed 1 January 2023).
5. USDA national nutrient database for standard reference, release 27 (revised), version current: May 2015 [website]. United States Department of Agriculture (<http://www.ars.usda.gov/ba/bhnrc/ndl>, accessed 1 January 2023).
6. Ledoux M, Chardigny J-M, Darbois M, Soustre Y, Sébédio J-L, Laloux L. Fatty acid composition of French butters, with special emphasis on conjugated linoleic acid (CLA) isomers. *J Food Compost Anal.* 2005;18(5):409–25.

For more information, please contact:

Department of Nutrition and Food Safety
World Health Organization
Avenue Appia 20
1211 Geneva 27
Switzerland

Email: nutrition@who.int
<https://www.who.int/teams/nutrition-and-food-safety>

