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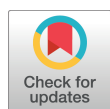
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ANALYSIS

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WHO draft guidelines on dietary saturated and trans fatty acids: time for a new approach?

The 2018 WHO draft guidance on fatty acids fails to consider the importance of the food matrix, argue **Arne Astrup and colleagues**

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Key messages

The 2018 WHO draft guidelines on dietary saturated fatty acids and trans fatty acids recommend reducing total intake of saturated fat and replacing it with polyunsaturated and monounsaturated fatty acids

The recommendations fail to take into account considerable evidence that the health effects of saturated fat varies depending on the specific fatty acid and on the specific food source

Maintaining general advice to reduce total saturated fatty acids will work against the intentions of the guidelines and weaken their effect on chronic disease incidence and mortality

A food based translation of the recommendations for saturated fat intake would avoid unnecessary reduction or exclusion of foods that are key sources of important nutrients

Non-communicable diseases are the world's leading cause of death, responsible for 72% of the 54.7 million deaths in 2016.[1] Cardiovascular diseases are responsible for approximately 45% of all deaths from non-communicable diseases, with modifiable risk factors such as diet, physical activity, smoking, and alcohol intake being major causes of disease.

Among dietary factors, the World Health Organization considers saturated fatty acids and trans fatty acids to be important. Consensus exists on the health benefits of eliminating industrially produced trans fatty acids—that it will reduce incidence of cardiovascular disease and mortality.[2] Foods containing more than 2% total fat as trans fat were banned in Denmark in 2004, and similar legislation is soon to be implemented throughout the European Union. In the United States the Food and Drug Administration no longer considers industrial trans fats to be "generally regarded as safe."

Many governments consider WHO dietary guidelines to be state of the art scientific evidence, translating them into regional and national dietary recommendations. These guidelines have potential health implications for billions of people, so the consistency of the science behind such recommendations and the validity of the conclusions are crucial. Here, we look at the evidence linking saturated fat intake and cardiovascular risk and find that the WHO draft guidelines have excluded some important aspects and studies.

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WHO draft guidelines

WHO draft guidelines on dietary saturated and trans fatty acids for adults and children were published for consultation in May 2018. They recommend reducing intake of total saturated fatty acids to less than 10% of total energy consumption and replacing with polyunsaturated fat and monounsaturated fat to reduce incidence of cardiovascular disease and related mortality.[2] But this fails to take into account considerable evidence that the health effects vary for different saturated fatty acids and that the composition of the food in which they are found is crucially important (box 1).[4-6] Food composition has a substantial effect on lipid digestion, absorption kinetics, and postprandial lipaemia,[3] which is an independent risk factor for cardiovascular disease.[7]

Box 1: Saturated fat in food products[3]

Saturated fatty acids are found in a wide diversity of foods that vary in composition and structure, resulting in different physiological effects. Stearic acid in dark chocolate, palmitic acid in meat, and heptadecanoic acid in dairy products have completely different physiological effects. Moreover, the food matrix in which the fatty acids exist has major importance for these effects.

Dairy products, for example, have very different compositions and milk fat structures. Full fat milk is a natural emulsion of fat globules enclosed in milk fat globule membrane, but when homogenised the fat droplets become much smaller and covered with proteins. Butter is a water in oil emulsion. Yoghurt is a fermented food containing live cultures, in which milk fat globules are dispersed in a gelled milk protein matrix. Cheese is one of the most complex dairy matrices. It is a fermented food containing live cultures, where fat is present in milk fat globules and sometimes as "free fat inclusions," in a solid matrix rich in milk proteins, calcium, and milk fat globule membrane. Ice cream contains a combination of crystallised fat globules around air bubbles and ice crystals in a liquid syrup phase.

Foods from other animal sources that contain saturated fatty acids also have a wide range of compositions and structures. Animal fats, such as lard and tallow, are 100% lipids. In unprocessed meat, lipids are mostly in adipocytes and intracellular lipid droplets of muscle. Processed meats can contain fat inclusions in a gelled protein matrix, free fat domains, and remnant adipocytes, depending on the type of processing. Egg yolk contains lipids structured as lipoproteins of both low and high density.

In processed foods such as pastries and biscuits (cookies) the fat inclusions (composed of palm oil, butter, or other fats) are embedded in a solid, carbohydrate matrix, often rich in sugar. Chocolate is composed of particles (sugar) and fermentation products from cocoa beans embedded in solid fat. Vegetable oils that are rich in saturated fatty acids, such as palm oil and coconut oil, are 100% lipids.

The saturated fatty acids in these different foods are also present as different types of lipid molecules—notably triglycerides and phospholipids. In these molecules, saturated fatty acids can be esterified at different positions depending on the source of fat.

How robust is the evidence linking saturated fat to cardiovascular disease?

Evidence from randomised controlled trials with clinical endpoints

Several recently published meta-analyses of observational studies and randomised controlled trials (RCTs) have found that total saturated fat is not associated with non-communicable diseases including coronary heart disease, cardiovascular disease, and all cause mortality.[8-10] By contrast, a Cochrane analysis that included data from only 15 RCTs found an association between reduced intake of saturated fat and a decrease in the composite endpoint of cardiovascular events (relative risk 0.83, 95% confidence interval 0.72 to 0.96). But it also found no significant association between reducing saturated fatty acids and total mortality (0.97, 0.90 to 1.05), cardiovascular disease mortality (0.95, 0.80 to 1.12), fatal and non-fatal myocardial infarction (0.90, 0.80 to 1.01), non-fatal myocardial infarction (0.95, 0.80 to 1.13), stroke (1.00, 0.89 to 1.12), coronary heart disease events (0.87, 0.74 to 1.03), and coronary heart disease mortality (0.98, 0.84 to 1.15).[11]

Evidence from randomised controlled trials with surrogate endpoints

The WHO draft guidance relies heavily on a meta-analysis of 84 RCTs that tested the effect of modifying saturated fat intake on serum lipid and lipoprotein concentrations, including low density lipoprotein (LDL) cholesterol, and the ratio of total cholesterol to high density lipoprotein cholesterol.[12] This approach—which focuses on total saturated fatty acids, ignores food sources, and uses surrogate endpoints—is problematic for several reasons.

First, not all saturated fatty acids are equal; the magnitudes and even directions of the effects on both surrogate and long term endpoints vary depending on fatty acid. Using the ratio of total cholesterol to high density lipoprotein cholesterol as a biomarker of cardiovascular disease risk, for example, is a problem because the ratios are different for lauric acid (12:0) myristic acid (14:0), palmitic acid (16:0), and stearic acid (18:0).[13] Moreover, high plasma concentrations of the heptadecanoic acid (17:0) are associated with a reduced risk of coronary heart disease.[14] Thus, saturated fatty acids cannot be viewed as one homogeneous group with regard to effects of diet on disease risk.

Second, it is unclear whether the observed changes in serum lipoproteins translate into a reduction in cardiovascular endpoints and mortality regardless of food source.[4] Most trials included in the meta-analysis did not investigate whole food sources of saturated fat. Instead, some studies compared the effect of diets supplemented with fats rich in saturated fatty acids, monounsaturated fat, or polyunsaturated fat (such as cocoa butter, olive oil, soybean oil, and dairy butter) and others used fats not commonly found in diets (such as synthetic fats high in myristic acid).[12] The food matrix in which the fatty acids exist (box 1) might be more important for the effect on cardiovascular disease risk than the saturated fat content (see supplementary file online).

Third, the meta-analysis mainly used LDL cholesterol concentration as a marker for cardiovascular disease risk, which could lead to erroneous conclusions. The atherogenicity of LDL particles is determined by, among other things, size. Small and medium LDL particles show the strongest association with risk of cardiovascular disease, whereas large particles show no association.[15] The rise in serum LDL cholesterol concentration from total saturated fat consumption has been linked to a parallel increase in particle size, so it might not translate into an increased risk of cardiovascular disease.[16]

The PURE study, which included over 100 000 people, shows why a broader view of biomarkers of cardiovascular disease is needed to inform guidelines. It found that diets high in saturated fatty acids were associated not only with higher serum concentrations of LDL cholesterol, but also with higher concentrations of HDL cholesterol, lower concentrations of triglycerides, and a lower apolipoprotein B:apolipoprotein A ratio.[17] The study also found that diets high in saturated fat were not associated with cardiovascular disease events, except for a lower risk of stroke.[18] The relevance of this observation is confirmed by at least three randomised trials comparing diets with different fats on clinical endpoints.[10 19 20]

Mediterranean-style diets were associated with a significant reduction in major cardiovascular disease events without any reduction in LDL cholesterol in the Lyon Diet Heart Study[19] and in updated analyses of the PREDIMED trial,[20] which both showed that LDL cholesterol concentration is not a valid biomarker for alterations in cardiovascular disease risk caused by dietary changes.

Reanalysis of the Minnesota Coronary Experiment (a double blind randomised controlled trial that tested whether replacing saturated fat with polyunsaturated fat reduced coronary heart disease and death) also supports the claim that serum cholesterol is not a valid surrogate biomarker for cardiovascular disease risk when making dietary changes.[10] Despite the finding that the polyunsaturated fat diet produced a 13% greater reduction in serum cholesterol than the saturated fat diet, there was no reduction in cardiovascular disease endpoints.[10]

The reanalysis found a 22% higher mortality for each 0.78 mmol/L reduction in serum cholesterol caused by the polyunsaturated diet.[10] A meta-analysis found that cholesterol lowering using polyunsaturated fat diets did not show any evidence of benefit on mortality from coronary heart disease (1.13, 0.83 to 1.54) or all cause mortality (1.07, 0.90 to 1.27).[10]

Evidence from observational studies and food based analyses of cardiovascular disease risks

The WHO draft guidelines exclude substantial evidence derived from observational studies and meta-analyses of prospective cohort studies. The guideline argues that the quality of evidence for relevant outcomes from such studies is lower than from analyses of RCTs and that it was not possible to assess the potential differential effects of replacing saturated fatty acids with different nutrients. But observational studies are valuable for assessing the association between saturated fat and long term endpoints, such as cardiovascular disease.[8 9 21]

Observational studies are also useful for examining the foods consumed in people's diets rather than examining individual nutrients. Longstanding evidence indicates that the food matrix is more important than its fatty acid content for predicting the effect of a food on risk of coronary heart disease. This was the conclusion of an expert consensus panel, that some of us took part in, nearly 10 years ago.[21] Ample food based studies have examined whether foods with high saturated fat content, which are likely to be consumer targets for the WHO recommendation, contribute to cardiovascular disease events and mortality (table 1). A recommendation to reduce intake of total saturated fat without considering specific fatty acids and food sources is not evidence based; will distract from other more effective food based recommendations; and might cause a reduction in the intake of nutrient dense foods that decrease the risk of cardiovascular disease, type 2 diabetes, other serious non-communicable diseases, malnutrition, and deficiency diseases and could further increase vulnerability to nutrient deficiencies in groups already at risk.

Discussion

To understand why the current misconceptions about saturated fat are so solidly anchored in major public health bodies, including WHO, we must consider the historical evolution of guidelines.

Up until the 1950s nutrition science focused on single nutrients, and major public health policies focused on deficiencies in micronutrients, leading to fortification of selected staple foods; for example, iodine in salt and vitamin B$_3$ and iron in wheat flour and bread.[4] Nutrition science then changed focus to policies for preventing chronic diseases such as cardiovascular disease in affluent countries, and the single nutrient approach was maintained. This was based mainly on cross country comparisons between saturated fat intake and cardiovascular disease mortality. The simple two step deductive reasoning that "dietary fat, and saturated fat in particular, increases serum

cholesterol" and "serum cholesterol is a risk factor for coronary heart disease" led to the conclusion that all dietary fat, and saturated fat in particular, should be reduced to prevent cardiovascular disease.[4] The US dietary guidelines published in 1980, and international guidelines ever since, have focused on reducing intake of saturated fat.

Guidelines have an immense effect on dietary advice for individuals and the production of ready to eat meals and meals served in restaurants. Historically, the focus on reducing saturated fat led to the proliferation of industrially produced food products low in fat, saturated fat, and cholesterol and to the dissemination of products based on technologies to replace saturated fat. One example is the production of margarine and spreads based on partial hydrogenation of vegetable oils, which increased the content of trans fatty acids from zero to up to 40% of total fat.[34]

The widespread consumption of trans fat is considered to have been responsible for 6% to 19% of all coronary heart disease events in the US in 2006[35] and to have caused about 2700 deaths annually and loss of 570 000 life years in the UK every year.[36] Denmark banned trans fats in 2004, and analyses have attributed the subsequent larger decline in coronary heart disease mortality in Denmark than in other EU countries to the elimination of trans fat from foods.[37]

Scientific and policy missteps may have led to many unnecessary deaths globally, and lessons should be learned. We think that recommendations to reduce intake of total saturated fat without considering specific fatty acids and food sources are not based on evidence and will distract from other, more effective, food based recommendations. Recommendations to reduce saturated fat might cause a reduction in the intake of nutrient dense foods that are important for preventing disease and improving health. We're concerned that, based on several decades of experience, a focus on total saturated fat might have the unintended consequence of misleading governments, consumers, and industry towards promoting foods low in saturated fat but rich in refined starch and sugar.

The WHO guidelines on saturated fat should consider different types of fatty acids and, more importantly, the diversity of foods containing saturated fatty acids that might be harmful, neutral, or even beneficial in relation to major health outcomes. We strongly recommend a more food based translation of how to achieve a healthy diet and reconsideration of the draft guidelines on reduction in total saturated fatty acids.

foods research centre. Her research interests include sensory evaluation, food consumption patterns, food structures, and their effect on human health. MLG is an expert in fatty acid nutrition; anti-inflammatory, anti-aggregatory and antioxidant effects of bioactive nutrients, dietary supplement, and functional foods. IG is a registered nutritional scientist with research based expertise in the association between dairy products and risk of cardiovascular diseases and type 2 diabetes and was a member of the group that first identified a beneficial association between dairy consumption and central arterial stiffness in a longitudinal study. FJK is emeritus professor in Nutrition and Health at Wageningen University, the Netherlands. He has been working on diet and health in Western, Asian, and African populations, looking at both undernutrition and overnutrition. He was dean of science at Wageningen University for several years. RMK is a fellow of the American Society of Nutrition and the American Heart Association (AHA), where he twice led publication of Dietary Guidelines for Healthy Americans. He was also the founding chair of the AHA council on nutrition, physical activity, and metabolism, and is a national spokesperson for the AHA. In addition, he has served on the committee on dietary recommended intakes for macronutrients and the committee on biomarkers of chronic disease of the US National Academy of Medicine (NAM), and was a reviewer for the NAM report on optimising the process for establishing the dietary guidelines for Americans. BL is chair of nutrition at Laval University in Québec City, Canada. He conducts translational research aimed at better understanding the effects of diet on cardiometabolic health from physiological, clinical, and public health perspectives. J-ML is an endocrinologist and a nutritionist. He is medical doctor in the internal medicine department of the University Hospital in Lille, France, and head of the nutrition department of Institut Pasteur de Lille, France. He is also expert for the French Agency for Food Safety and for the Haute Autorité de Santé, France. PL is an expert in saturated fatty acid function and metabolism and chaired the French panel for lipid guidelines in the Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail. MM is an expert on the ability of dietary interventions (including supplements, foods, and whole dietary patterns) to modify nutritional status and risk of chronic disease, particularly diabetes and cardiovascular disease. RM is an expert in elucidating health effects of dietary habits, quantifying global consumption patterns, and evaluating the comparative effectiveness of nutrition sensitive interventions. M-CM is an expert in the effects of the supramolecular structures of dietary lipids in foods on postprandial metabolism and metabolic inflammation in the frame of dietary prevention of obesity, cardiovascular diseases, and type 2 diabetes. She has expertise in the structure-function relation of milk fat globules and proposed the concept of "fast versus slow lipid" structures. She is leader of the postprandial lipids and lipoproteins: regulations and functional impacts team in the CarMeN laboratory in Lyons, France. DM is a cardiologist and public health expert whose research aims to produce robust, high quality evidence on dietary priorities for cardiometabolic health, corresponding disease specific burdens, and effective policies to reduce these burdens, with research investigations spanning epidemiological studies, evidence syntheses, clinical trials, national and global demography, and policy analyses and implementation. SSS-M is a leading expert in clinical epidemiology and nutritional science, in the field of type 1 and 2 diabetes and cardiovascular diseases. Several original cohort analyses, systematic reviews, and meta-analyses on dairy products were led by her for which she obtained an international award.

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Table

Table 1| Nutrient dense foods that also contain substantial amounts of saturated fat

Food	Nutrients	Evidence linking food to cardiovascular disease and diabetes
Eggs	13 essential vitamins and minerals (eg, vitamin D, riboflavin, iodine), high quality protein, α-linolenic acid (n-3), lutein, zeaxanthin, and choline	No association with coronary heart disease, reduced risk of stroke. RCT data show that two eggs a day has beneficial effects on cardiovascular disease biomarkers,[22 23] and improved glycaemic control in type 2 diabetes[24]
Dark chocolate	Stearic acid is the major saturated fat. Also rich in fibre, iron, magnesium, potassium, phosphorus, zinc, and selenium. Contains polyphenols, flavanols, and catechins. Contains added sugar	The WHO draft guidelines state that stearic acid has no harmful effect on "any outcome assessed." Meta-analyses of observational evidence find dark chocolate consumption to be associated with a substantial reduction in risk of cardiovascular disease.[25 26] RCTs find beneficial effects on cardiovascular disease biomarkers (HDL and LDL cholesterol, blood pressure, etc)[27]
Cheese	Full fat cheese is high in medium and long chain saturated fatty acids (C13:0, C20:0, C18:2t10c12, and C20:2n-6), a wide diversity of typical bioactive fatty acids (conjugated linoleic acid, phytanic acid, trans palmitoleic acid), protein, calcium, magnesium, and lactic acid bacteria (that produce short chain fatty acids), and has a complex matrix structure	Meta-analyses of food based observational studies find that cheese intake is associated with slightly reduced risk of cardiovascular disease.[28 29] Mechanistic studies and RCTs show that cheese intake has favourable effects on biomarkers of cardiovascular disease (blood lipids and blood pressure) and that these effects cannot be predicted based on content of total saturated fat and sodium[30 31]
Meat	Meat is a major source of high quality protein, bioavailable iron, minerals, and vitamins, but is also a source of saturated fat	Meta-analyses of observational studies find that intake of processed meat, but not red meat, is associated with a higher risk of coronary heart disease, which indicates that processing or factors other than the saturated fat content are responsible for any link to cardiovascular disease.[32] A meta-analysis found no difference in cardiovascular disease risk factors between groups with more and less than 0.5 daily servings of meat[33]