Convincing evidence supports reducing saturated fat to decrease cardiovascular disease risk

Penny M Kris-Etherton,[1] Kristina Petersen,[1] Linda Van Horn[2]

[1]Department of Nutritional Sciences, The Pennsylvania State University, University Park, Pennsylvania, USA
[2]Feinberg School of Medicine, Northwestern University Medical School, Chicago, Illinois, USA

Correspondence to
Dr Penny M Kris-Etherton;
pmk3@psu.edu

INTRODUCTION

Treatment guidelines and population-based recommendations evolve from research vetted by the scientific community. Healthcare providers require practice guidelines resulting from rigorous review of the totality of evidence. Open discussion/debate among experts is fundamental and encouraged, but blatant disregard for scientific process can lead to confusion and public distrust. A recent example is the controversy among scientists, healthcare professionals and the public about dietary saturated fat (SFA) recommendations to lower risk of cardiovascular disease (CVD).

Dietary recommendations for SFA from authoritative organisations

More than 60 years ago (in 1957), the American Heart Association (AHA) proposed that modifying dietary fat could reduce the incidence of coronary heart disease (CHD). This was based on research, including controlled feeding studies, and endpoint measures of blood lipids and blood pressure.[1] In 1980, the first Dietary Guidelines for Americans recommended 'avoiding too much SFA'.[2] For decades, research has substantiated this consistent dietary recommendation from authoritative organisations to decrease SFA to reduce CVD risk.[3–6] Current dietary guidelines for SFA and evidence ratings are summarised in table 1. While the strong evidence to reduce SFA specifically targets decreasing low-density lipoprotein (LDL)-cholesterol, it is very much germane to CVD risk reduction.

Challenging practice guidelines and population-based recommendations: the SFA SAGA

In 2010, a meta-analysis of 21 prospective epidemiological studies totalling 347 747 subjects reported that higher intake of SFA was not associated with an increased risk of CHD, stroke or CVD.[7] Aspects of this methodology were widely criticised,[8–10] most notably the failure to account for the proportional differences in dietary macronutrient composition with varying SFA intake.[8 10] Using similar meta-analytic methods, and again without considering the macronutrient composition of diets differing in SFA, Chowdhury *et al* and also de Souza *et al* further concluded that SFA was not associated with CHD or CVD or CHD mortality.[11 12] Additional analyses of prospective cohort studies and randomised controlled trials that carefully evaluated both the dietary nutrient profile and SFA intake have consistently demonstrated a lower risk of CHD when polyunsaturated fatty acids (PUFAs) are consumed instead of SFA.[13 14] More recently,[15] findings from the Nurses' Health Study (NHS) (1980–2010) and Health Professionals Follow-up Study (1986–2010) suggested that lowering energy from SFA by 5% and proportionally increasing PUFA, monounsaturated fatty acids (MUFAs) or carbohydrates from whole grains was associated with a 25%, 15% and 9% lower risk of CHD, respectively (PUFAs: HR: 0.75, 95% CI 0.67 to 0.84; p<0.0001; MUFAs: HR: 0.85, 95% CI 0.74 to 0.97; p=0.02; carbohydrates from whole grains: HR: 0.91, 95% CI 0.85 to 0.98; p=0.01).[15] Similarly, lower intake of predominant long-chain SFA in favour of other macronutrients and plant proteins reduced risk of CHD in the NHS and the Health Professionals Follow-up Study.[16] Consumption of 1% of energy from plant proteins instead of C12:0–C18:0 SFA decreased CHD risk (HR: 0.93, 95% CI 0.89 to 0.97; p=0.001).

The clinical trial evidence has focused on evaluating replacement of SFA with PUFA. Based on three recent meta-analyses of clinical studies,[17–19] the debate continues. The first two papers concluded that the evidence does not support current recommendations to replace SFA with PUFA since there was no effect on CHD mortality and total/all-cause mortality.[17 18] Hamley[18] also reported no effect on major CHD events and total CHD

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Table 1 Authoritative recommendations for saturated fat and evidence ratings

Recommendation			Evidence rating	
2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk	**NHLBI grade**	**NHLBI evidence statements**	**ACC/AHA COR**	**ACC/AHA COR**
Aim for a dietary pattern that achieves 5%–6% of calories from SFA	A (strong)*	Evidence statement 11 – strength of evidence: high†	I‡	A§
Reduce per cent of calories from SFA	A (strong)*	Evidence statement 11 – strength of evidence: high†	I‡	A§
2015 National Lipid Association recommendations for patient-centred management of dyslipidaemia: part 2	**Grade**		**Strength of recommendation**	
Dietary SFA may be partially replaced with unsaturated fats (MUFA and PUFA), as well as proteins, to reach a goal of <7% of energy from SFA.	A*		Moderate¶	
Scientific report of the 2015 Dietary Guidelines Advisory Committee	**DGAC grade**			
Strong and consistent evidence from RCTs and statistical modelling in prospective cohort studies shows that replacing SFA with PUFA reduces the risk of CVD events and coronary mortality.	Strong**			
2016 ESC/EAS guidelines for the management of dyslipidaemias	**Magnitude of the effect**		**Level of evidence**	
For SFA, consumption should be <10% of the total caloric intake and should be further reduced (<7% of energy) in the presence of hypercholesterolaemia.	+++††		A‡‡	

Strength of recommendation – strong: there is high certainty, based on evidence, that the net benefit is substantial.

Evidence Statement 11: when food was supplied to adults in a dietary pattern that achieved a macronutrient composition of 5%–6% saturated fat, 26%–27% total fat, 15%–18% protein and 55%–59% carbohydrate compared with the control diet (14%–15% saturated fat, 34%–38% total fat, 13%–15% protein and 48%–51% carbohydrate), LDL-C was lowered 11–13 mg/dL in two studies and 11% in another study. Strength of evidence: high.

Classification of recommendation (COR): class I: benefit >>> risk; procedure/treatment should be performed/administered.

Level of evidence: level A: multiple populations evaluated; data derived from multiple randomised clinical trials or meta-analyses.

RCTs with minor limitations affecting confidence in, or applicability of, the results. Well-designed, well-executed non-randomised controlled studies and well-designed, well-executed observational studies. Well-conducted meta-analyses of such studies. Moderately certain about the estimate of effect; further research may have an impact on our confidence in the estimate of effect and may change the estimate.

+++ – Marked effects.

Level of evidence – A: data derived from multiple randomised clinical trials or meta-analyses.

ACC, American College of Cardiology; AHA, American Heart Association; COR, Classification of recommendation; CVD, cardiovascular disease; DGAC, Dietary Guidelines Advisory Committee; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; LDL-C, low-density lipoprotein-cholesterol; MUFA, monounsaturated fatty acid; NHLBI, National Heart, Lung, and Blood Institute; PUFA, polyunsaturated fatty acid; RCT, randomised controlled trial; SFA, Saturated fatty acid.

events. In contrast, the recent AHA Presidential Advisory on dietary fats and CVD[19] concluded that 'lowering intake of SFA and replacing it with unsaturated fats, especially PUFAs, will lower the incidence of CVD'. This conclusion was based on both epidemiological evidence as well as a meta-analysis of four well-controlled clinical trials, the latter of which demonstrated a 29% reduction in CHD events when SFA was replaced with PUFA. This disagreement reflects the studies included in the meta-analyses. Harcombe et al[17] and Hamley[18] included studies that were excluded by Sacks et al[19] due to methodological concerns (discussed in the AHA Presidential Advisory). Since this debate still continues, it is important to recognise the robust literature that demonstrates that lowering SFA reduces LDL-cholesterol (table 2), an established causal factor in the development of atherosclerosis.[20]

The need for rigorous dietary research: learning from the SFA debate

Dietary patterns are comprised of foods and nutrients, and this inter-relationship must be acknowledged in dietary research.[21] A reductionist approach has plagued SFA research and demonstrates the hazards of isolating a single nutrient and failing to account for the overall nutrient composition. This leads to confusion and unintended deleterious consequences (eg, a reduction in fat intake and an increase in refined carbohydrates) and impedes accurate translation of nutrition research.

Table 2*† Predicted effects of macronutrient replacement of dietary saturated fatty acids with PUFA, MUFA and carbohydrate on lipoprotein lipids based on results from controlled feeding trials* Predicted effects* on lipoprotein lipids of replacing 5% of energy from saturated fatty acids with the 5% of energy from the specified dietary component, mg/dL.

Dietary component	LDL-C	TG	HDL-C
PUFA	−9.0	−2.0	−1.0
MUFA	−6.5	+1.0	−6.0
CHO†	−6.0	+9.5	−2.0

Results are summarised from controlled feeding trials of subjects with average to mildly dyslipidaemic baseline levels of lipoprotein lipids. Effects may be more pronounced in those with higher baseline values. Taken from ref 4.

A meta-analysis of randomised controlled trials showed greater improvements in LDL-C with whole grains versus refined grains.[23] Compared with refined grains, whole grains reduced LDL-C by 3.48 mg/dL (95% CI 5.8 to 1.16; p<0.01). TG and HDL-C did not significantly improve in response to whole grains versus refined grains (TG mean difference −3.5 mg/dL, 95% CI −7.1 to 0.9, p=0.10; HDL-C mean difference −0.4, 95% CI −1.2 to 0.8, p=0.59).

CHO, Carbohydrate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein-cholesterol; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; TG, Triglycerides.

Future epidemiological research requires a more holistic approach to account for macronutrient substitutions. This translational approach favors support of healthy eating patterns and reduces unforeseen adverse effects more common when single nutrient recommendations are issued. Clinical research likewise benefits from dietary interventions that address the total dietary pattern including the influence of replacement foods and nutrients on the outcomes assessed.

Summary and perspective

Although there is no biological requirement for SFA, a healthy diet will provide some SFA by virtue of meeting food-based dietary guidelines. A diet that limits SFA to <7% of calories accommodates a modest intake while achieving the recognised benefits of unsaturated fatty acids.

► Observational studies show cardiovascular benefits associated with lowering SFA and proportionally increasing PUFA, MUFA, whole grains and plant proteins.

► Epidemiological research that ignores nutrient differences in diets across the spectrum of SFA intake demonstrates no association of SFA with CVD risk. SFA intake is typically lowered and proportional increases in refined carbohydrates occur. Thus, the appropriate conclusion is that SFA and refined carbohydrates are equally deleterious on CVD risk. The controversy about the clinical trial evidence stems from studies with methodological problems and inclusion of these studies in meta-analyses.

► Recommendations to decrease SFA for CVD risk reduction are supported by robust evidence of a CVD benefit. The consensus of many scientists is to focus on a replacement message[22 23] that SFA be replaced with PUFA, MUFA, whole grains and plant proteins. This can be achieved with many healthy dietary patterns.

► Nutrition research must consider dietary patterns and the complex inter-relationship between dietary components to ensure translation into meaningful and health-promoting dietary recommendations.

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