A joint meeting between the Nutrition Society and the Royal Society of Medicine was held at the Royal Society of Medicine,
London on 11–12 December 2012

Conference on 'Dietary strategies for the management of cardiovascular risk'

Reappraisal of SFA and cardiovascular risk

Thomas A. B. Sanders

Diabetes and Nutritional Sciences Division, School of Medicine, King's College London, Franklin-Wilkins Building,
150 Stamford Street, London SE1 9NH, UK

This review reappraises dietary advice to reduce and replace SFA for the prevention of CVD. In the 1970s, SFA accounted for about 18% UK food energy, by 2001 it had fallen to 13% and continues to be above the <11% target. Compared with carbohydrates, C_{12}–C_{16} SFA raise serum total cholesterol (TC), LDL-cholesterol (LDL-C) and HDL-cholesterol (HDL-C) without affecting the TC:HDL-C ratio; other SFA have neutral effects on the fasting lipid profile. Replacing 3% dietary SFA with MUFA or PUFA lowers LDL-C by 2% and TC:HDL-C ratio by 0·03. No other specific adverse effects of SFA compared with MUFA on risk CVD factors have been proven. Meta-analyses of prospective cohort studies report the relative risks (95% CI) of high *v.* low intakes of SFA to be 1·07 (0·96, 1·19) for CHD, 0·81 (0·62, 1·05) for stroke and 1·00 (0·89, 1·11) for CVD mortality and were not statistically significant. Exchanging 5% energy SFA for PUFA or carbohydrates found hazard ratios (95% CI) for CHD death to be 26% (−23, −3) and 4% (−18, 12; NS) lower, respectively. Meta-analysis of randomised controlled trials with clinical endpoints reports mean reductions (95% CI) of 14% (4, 23) in CHD incidence and 6% (−25, 4; NS) in mortality in trials, where SFA was lowered by decreasing and/or modifying dietary fat. In conclusion, SFA intakes are now close to guideline amounts and further reductions may only have a minor impact on CVD.

Saturated fatty acids: Lipid: CVD: Risk factors: Palmitic acid

A reduction in the intake of SFA has been a key dietary guideline in the prevention of CVD[1,2]. This advice has been based on the relationship between fat intake and serum total cholesterol (TC) concentrations and the evidence that elevated serum TC concentrations cause atherosclerosis, which is the underlying pathology causing CHD. A large body of experimental studies conducted in animals, including primates, shows that diets high in animal fats, usually with added cholesterol, causes hyperlipidaemia and result in atherosclerosis. However, primate studies find no differences between MUFA and SFA in their ability to promote atherosclerosis and low-fat diets are protective against atherosclerosis[3]. The International Atherosclerosis Project[4] noted that the prevalence of atherosclerosis varied markedly between different countries and was more prevalent in countries where fat intake was higher. Post-mortem assessment of service men killed in combat[5] or young trauma victims[6] showed that the extent of atherosclerosis in young people was positively related to serum LDL-cholesterol (LDL-C) and negatively related to HDL-cholesterol (HDL-C) cholesterol concentrations. Increasing age, male gender, smoking habit, elevated BMI and diabetes mellitus were positively associated with atherosclerosis development. However, it is research on inherited causes of raised LDL-C, particularly familial hypercholesterolaemia where the LDL receptor is defective[7], that established beyond doubt that elevated LDL-C causes atherosclerosis and the evidence that lowering LDL-C halts progression of atherosclerosis[8] and reduces the incidence of CHD.

LDL-C increases with age probably as a consequence of a decline in receptor mediator clearance of LDL-C and this decline in LDL receptor activity is further accelerated by a lack of oestrogen in postmenopausal women. Meta-analysis of prospective cohort studies[9], which are mainly in middle-aged and older men and women, show a strong relationship between BMI and LDL-C cholesterol (or its surrogate non-HDL-C). In men, non-HDL-C rises from 4·03 mmol/l in a linear manner to 4·83 mmol/l between BMI of 18·5 and 27 kg/m². In women, non-HDL-C rises from 3·94 to 4·56 mmol/l between BMI 20–22·5 and 30–32·5 kg/m². Increasing BMI probably acts to increase VLDL synthesis by recycling NEFA from adipose tissue to the liver where they are resynthesised into TAG and secreted as VLDL, which in turn are converted to LDL. Polymorphism in the apoE gene (carriage of the ε4 allele) also explains a significant proportion of the variance in LDL-C within the population even at a young age[10]. In UK adults, the median LDL-C is about 3·0 mmol/l but this rises substantially with age, especially in women following the menopause, independent of any change in SFA intake. Most cross-sectional studies fail to find any association between usual SFA intake and TC or LDL-C concentration because the size effect of SFA is small in relation to the total variance. However, cross-sectional studies of vegans, vegetarians and omnivores, who have low, medium and high intakes of SFA, respectively, show a clear dose response effect on TC and LDL-C with vegans having LDL-C values 1 mmol/l lower than omnivores even after adjustment of age and BMI[11,12].

Effects of different SFA on serum lipids and lipoproteins

In a meta-analysis of individual data from sixty-one prospective studies with 55 000 vascular deaths, Lewington et al.[13] found that a change in TC:HDL-C was twice as informative of risk as changes in TC, non-HDL-C or HDL-C, and it was estimated that a 1·33 change in the TC:HDL-C ratio increased risk of IHD mortality by one-third. There is some debate as to whether the TC:HDL-C is the best parameter to estimate risk posed by changes in fat intake or whether the focus should be on LDL-C, especially small dense LDL. Clinically the TC:HDL-C is useful in identifying individuals who may benefit from targeted intervention and certainly captures those with pure hypercholesterolaemia (i.e. elevated LDL-C but normal HDL-C and TAG concentrations) and those who have normal TC but very low HDL-C and raised TAG concentrations. These are distinct lipoprotein phenotypes with different causations: the former being due to decreased LDL receptor-mediated clearance of LDL and the latter being a consequence of overproduction of VLDL usually associated with central obesity. Many subjects with low HDL-C have a preponderance of small dense LDL particles, which are more atherogenic, and this may well be the reason why this atherogenic lipoprotein phenotype is associated with greater risk rather than the anti-atherogenic effects of HDL. As yet, there is no convincing evidence that lowering or increasing

HDL-C modifies risk of cardiovascular events. Furthermore, recent Mendelian randomisation studies that have compared genotypes that cause 0·13 mmol/l higher HDL-C concentrations have not been able to demonstrate correspondingly a lower risk of CVD. In contrast, increased LDL-C concentrations attributed to genetic effects are strongly associated with increased CVD risk[14]. Meta-analyses[15,16] indicate that a 1 mmol/l reduction in LDL-C is accompanied by a 10 % reduction in total mortality and 20 % reduction in major CVD events. Moreover, there is a clear dose–response relationship between the degree of LDL-C reduction and risk independent of any drop in HDL-C. However, a greater reduction in risk may result from lower lifetime LDL-C especially as atherosclerosis is a disorder developing over many decades.

Keys et al.[17] conducted a series of studies in healthy volunteers comparing the effects of different mixtures of fatty acids on TC at about 40 % dietary energy from fat. They found that C_{12}–C_{16} SFA raised serum TC, PUFA had a weaker but opposite lowering effect and that MUFA and stearic acid (18 : 0) were neutral. Dietary cholesterol had a modest cholesterol raising effect particular over the first 400 mg of intake. Keys et al. developed a series of equations to predict changes in serum cholesterol the most commonly cited version is described as under[18]:

$$\Delta\text{serum cholesterol} = 2{\cdot}3(\Delta S) - \Delta P + 1{\cdot}5(\sqrt{\Delta C})$$

where Δserum cholesterol is presented as mg/dl, ΔS is the difference in % energy from SFA excluding stearic acid, ΔP is the difference in % energy from PUFA and ΔC is the difference in cholesterol content in mg/1000 kcal (to convert to mmol/l divide by 38·5). Similar predictions were made by equations developed by Hegsted et al.[19] using a different set of experiments. These early studies, however, did not measure LDL-C and HDL-C. Mensink & Katan[20] conducted a meta-analysis of twenty-seven dietary trials, which forms the basis of the later review of sixty studies[21], where they estimated effects of individual fatty acids on TC:HDL-C ratios and also compared the effects with exchange with carbohydrates. Palmitic (16 : 0), myristic (14 : 0) and lauric (12 : 0) acids with increasing magnitude raised LDL-C but stearic acid (18 : 0) had no effect on LDL-C (Fig. 1). Trans fatty acids raised LDL-C but oleic and polyunsaturated had an LDL-C cholesterol-lowering effect compared with carbohydrate. Replacing fat with carbohydrates increased fasting TAG concentration and lowered HDL-C with the exception of trans fatty acids and stearic acid (Fig. 2). Comparable changes were noted in apoB and apoA1 concentrations to those of LDL-C and HDL-C, respectively. The net effect of replacing dietary SFA with carbohydrate on the TC:HDL-C ratio was null but replacing SFA with MUFA and PUFA is to lower the TC:HDL ratio and the apoB:A1 ratio. Replacing trans fatty acids with SFA, MUFA or PUFA lowers the TC:HDL-C ratio (Fig. 3). It is to be noted that the differences between myristic, palmitic and stearic acid on TC:HDL-C are not significantly different from each other or from
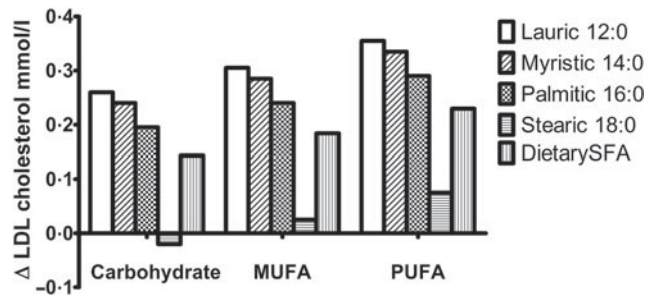
Fig. 1. Changes in LDL-C concentration that result from swapping 5% energy as carbohydrate or MUFA or PUFA with different SFA or a mixture of dietary SFA, representing the proportions in the UK diet. Adapted from reference[21].
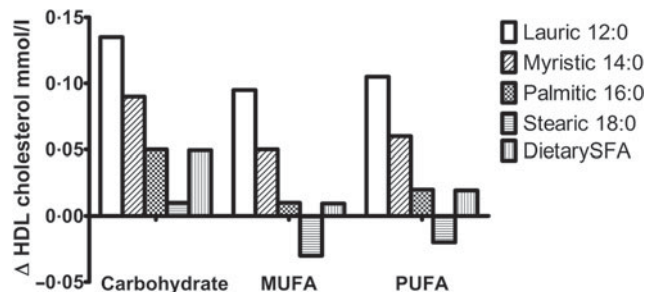

Fig. 2. Changes in HDL-C concentrations that result from swapping 5% energy as carbohydrate or MUFA or PUFA with different SFA or a mixture of dietary SFA, representing the proportions in the UK diet. Adapted from reference[21].

Fig. 3. Effects (mean values with 95% CI) on the ratio TC:HDL-C resulting from the exchange of 5% energy as carbohydrate with equivalent amounts of food energy provided by different saturated, *trans*, MUFA and PUFA. Adapted from reference[21].

carbohydrate. In the case of lauric acid (12:0), the net effect was to decrease the TC:HDL-C ratio to a similar extent to PUFA or MUFA. On the basis of lauric acid lowering the TC:HDL-C ratio, it has been suggested that coconut oil is good for cardiovascular health. The wisdom of this advice is questionable because several studies[22–24] show coconut oil, which is rich in caproic (8:0) and caprylic (10:0) acid as well as lauric (12:0) and myristic (12:0) acids, raises LDL-C and the TC:HDL-C ratio compared with olive oil or palm olein where the SFA are provided mainly by palmitic acid. Furthermore, coconut oil is relatively atherogenic in animal models especially when fed with dietary cholesterol[25]. In contrast, palm oil, which is rich in palmitic acid, does not have different effects on LDL-C from high oleic acid safflower oil in primates in the absence of dietary cholesterol[26]. Very little research has been conducted on caproic and caprylic acids but the available evidence[21] does not indicate adverse effect on fasting plasma lipids. The atherogenicity of coconut oil may in part be due to its very low linoleic acid and oleic acid content compared with palm oil, which contains about 10 and 40% of these fatty acids, respectively.

Palm oil is now the major vegetable oil produced globally, mainly in Indonesia and Malaysia. Production has increased dramatically over the past two decades in Indonesia and Malaysia; it has largely replaced coconut oil and peanut oil as the main culinary oil. Several studies have compared the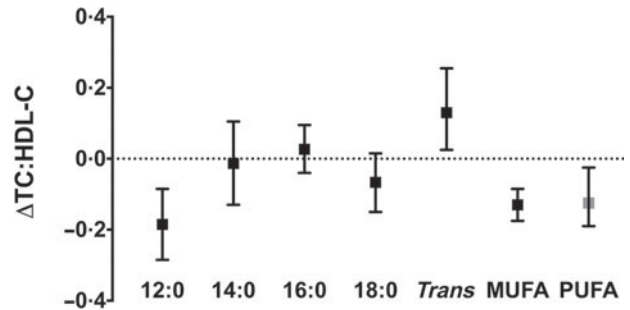 effect of palm olein (a fraction of palm oil containing about 45% palmitic acid, 42% oleic and 10–12% linoleic acid) with refined olive oil on blood lipids. Typically this exchange results in 4·5–6·6% energy palmitic acid being replaced by oleic acid. Both fats palm olein and olive oil have similar proportions of linoleic acid and stearic acid and only traces of lauric and myristic acid and do not contain cholesterol and so are ideal for comparing the effects of oleic *v*. palmitic acid. Two crossover studies found no differences between diets in TC and LDL-C[27,28] in men, the study by Voon *et al*.[24] showed a non-significant trend for TC and LDL-C to be slightly higher with values intermediate between olive oil and coconut oil, a crossover study of 43 Danish men found TC and LDL-C to be 0·15 mmol higher on palm olein compared with olive oil but no difference in TC:HDL-C ratio[29]. Average total fat intakes are in the range of 25–30% energy in South East Asian diet and providing total fat intakes remain at this level, the use of palm oil as the main culinary fat is unlikely to have any adverse impact on CVD.

Some recent studies have evaluated the effects of diets with a reduced SFA content in participants with the metabolic syndrome. The RISCK study[30] compared the effects SFA reduction by replacing it with either MUFA or carbohydrate in 548 participants with features of the metabolic syndrome with the diets taken for 24 weeks after a run-in period of 4 weeks on a SFA-rich diet. The participants were overweight/obese and had elevated waist circumference (waist >80 cm for women and >94 cm for men) and were moderately insulin resistant but not diabetic. The intake of SFA was about 7% lower on the low SFA diets compared with the high SFA control diet and lowered the LDL-C by 8%, but the low SFA/high MUFA diets lowered the TC:HDL-C ratio compared with the low fat/high carbohydrate diet by 0·16 (Fig. 4). There was no evidence to show that decreasing SFA intake lowered the proportion of small dense LDL. LIPGENE[31], which was a large pan-European study in 417 participants with metabolic syndrome was unable to detect any difference in serum lipids or lipoprotein concentrations between participants fed SFA-rich, low SFA/high carbohydrate and MUFA-rich diets taken for 12-week periods. We have recently completed a randomised controlled trial (CRESSIDA study; Reidlinger D, Darzi J, Hall W, Berry S, Seed P,
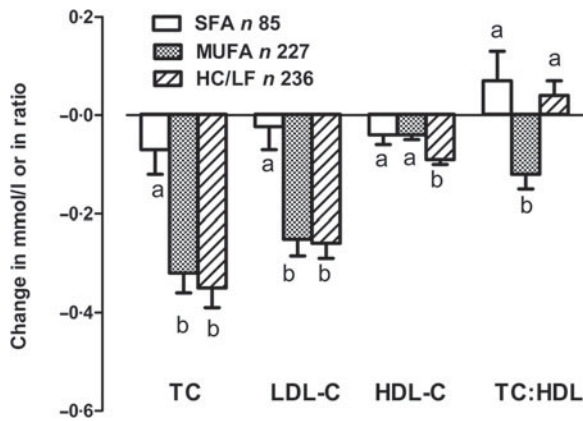
Fig. 4. Changes at 24 weeks in serum lipids with a 7–8% reduction in SFA and replacement by MUFA or carbohydrates (HC/LF) in participants with features of the metabolic syndrome. Mean changes with SED. Values not sharing similar superscripts are significantly different from each other $P < 0.05$. Adapted from reference[30].

Chowienczyk P, Sanders TA, unpublished results) comparing a traditional British diet with a cardioprotective diet similar to that advocated by the Department of Health[2] in 163 men and women aged 45–70 years using a parallel design with the respective diets being taken for 3 months. SFA was 7% energy lower and PUFA intake was about 2% greater on the cardioprotective diet compared with control diet. LDL-C fell by 0·3 mmol/l (10%) and TC:HDL-C increased by 0·04 comparable with our findings in the RISCK study. It would appear that decreasing SFA intake by 7% energy lowers LDL-C by 8–10%, which would be predicted decrease risk of CVD events by 5–6% and fatal CVD by 2–3%. There is little evidence to indicate greater reductions in LDL-C can be obtained in patients with hypercholesterolaemia by lowering SFA intake and LDL-C is now more effectively controlled by statins. However, dietary fat modification does lower LDL-C in addition to statin treatment[32].

Effects of SFA on other surrogate risk markers of CVD

It is now recognised that the rupture of an unstable atherosclerotic plaque causing a thrombosis that results in arterial occlusion usually precipitates clinical CVD events. Atherosclerosis is regarded as a chronic inflammatory process. Inflammation can make plaques more susceptible to rupture as well as making blood more likely to clot. Thrombosis is much more amenable to change in the short-term than the effects of LDL-C on atherosclerosis. It is currently believed that much of the recent reduction in CHD mortality[33] is probably due to modification of factors that reduce risk of thrombosis, such as smoking cessation, better management of blood pressure, use of aspirin, prophylactic anti-coagulant therapy and the use of fibrinolytic agents post myocardial infarction. High intakes of dietary fat may have an influence on the processes that lead to thrombosis and may also influence insulin resistance.

Vascular function

Impaired endothelial function is associated with the development of CVD and Keogh et al[34] in Australia provided evidence to suggest that SFA may cause endothelial dysfunction. This conclusion was based on data from a 3-week crossover design trial in middle-aged moderately overweight subjects measuring flow-mediated dilation (FMD) with different diets. The dietary intervention involved exchanging either 20 g high-PUFA margarine and 35 g walnuts (PUFA) or 20 g high-MUFA margarine and 45 g almonds (MUFA) or 50 g butter (SFA) or 70 g sultanas and 50 g jam (high carbohydrate) in the diet of the participants for 3-week periods. The mean FMD was 5·41 (SD 2·45)% on the SFA diet v. 10·80 (SD 3·69)% on the other diets and there were no differences between a high carbohydrate diet and the other MUFA or PUFA diets. However, interpretation of the results of that study are confounded by the use of high intakes of walnuts and almonds and sultanas, which contain polyphenolic compounds that have antioxidant and other pharmacological properties and can influence endothelial function[35]. In this context, it is relevant to consider the beneficial effects on FMD that have been reported in subjects given virgin olive oil[36,37], which are now being attributed to it polyphenol content rather than it high MUFA content. The 24-week RISCK trial found no differences in FMD or arterial stiffness from replacing SFA with carbohydrate or MUFA[38]; differences between treatments were <0·5% FMD units. The 12-week CRESSIDA study, which compared current UK dietary guidelines with a traditional UK diet also found no effect of SFA reduction on FMD (Sanders TAB, Reidlinger D, Darzi J, Hall WL, Chowienczyk PJ, unpublished results). Meals high in fat cause acute impairment of endothelial function compared with low fat, high carbohydrate meals[39,40] that appears to be related to the extent to which plasma TAG is elevated in the postprandial period which appears greater following MUFA than after SFA. Therefore, the current evidence indicates that SFA do not have specific adverse effects on FMD.

Thrombosis and inflammation

Mildly elevated levels of C-reactive protein and increased fibrinogen concentrations are associated with inflammation and blood coagulation and increased risk of CVD[41]. There is a clear relationship between body fat content and elevated C-reactive protein and fibrinogen but no specific effect of dietary SFA v. MUFA on these inflammatory markers[30]. Early animal research suggested that some saturated fats, particularly stearic acid, were thrombogenic. However, prospective cohort studies have found factor VII coagulant (FVIIc) activity to be associated with increased risk of fatal CHD. Cross-sectional dietary analysis showed FVIIc to be associated with total fat intake and elevated plasma TAG concentrations. FVIIc was then observed to vary from

day to day in line with fat intake and it was shown that meals high in fat typically containing 50 g or more raised FVIIc by increasing the concentration the fraction present in the activated form FVIIa. These elevations persist for up to 24 h. Meals high in long-chain fatty acid compared with low-fat meals result in postprandial lipaemia and this can lead to activation of factor VII[42,43]. In this respect meals rich in oleic acid results in greater elevations of plasma TAG and, high levels of FVIIa compared with SFA[42,44,45]. However, the effects of SFA on postprandial lipaemia and factor VII are dependent on fatty acid chain length and physical properties. Medium and short chain saturated fatty acid do not result in postprandial lipaemia and activation of FVIIa[43,46,47]. This in part may explain why butterfat results in slightly less lipaemia than high oleic fats such as olive oil. High melting point fats, which are found in some natural fats such as shea butter[44] and interesterified fats[45,48,49], also result in decreased postprandial lipaemia and decreased factor VII activation. However, the effects fat on FVII are transient and reflect recent fat intake[50] and the differences between SFA and MUFA only seem relevant over a period of 24 h following the consumption of high-fat meals. SFA do not appear to have specific effects on indices of fibrinolysis[30,51]. The RISCK study[30] was unable to demonstrate any long-term effects of lower SFA intake on plasminogen activator inhibitor type 1 or FVIIc activities. However, it is to be noted that participants were asked to refrain from foods high in fat on the day prior to the measurements. With respect to thrombotic risk factors and postprandial lipaemia, it seems the replacement of fat with carbohydrate has favourable effects[52].

Insulin resistance

Insulin resistance is associated with the metabolic syndrome is believed to be a strong predictor of risk of CVD. A review by Reserus, Willett & Hu[53] suggested that SFA may have adverse effects on insulin release and glucose homoeostasis. However, this conclusion was based on a number of small trials; the only one major study that had addressed this question was the KANWU study[54]. This reported an improvement in insulin sensitivity when SFA, mainly derived from animal fats and lard, were replaced by MUFA in the diet but the difference between treatments was of borderline significance. The RISCK study[30] found no evidence for adverse effects of SFA on insulin sensitivity nor did the LIPGENE[31] study or the study by Bos et al.[55] The current evidence suggests that there is probably no difference between SFA and MUFA on insulin resistance in human subjects.

Evidence using clinical endpoints from prospective cohort studies

A re-evaluation of the role of SFA in the causation of CVD is long overdue[56]. In part this is because making dietary recommendations based on changes in surrogate risk markers for disease do not necessarily translate into disease risk reduction, especially when dietary components affect risk factors in different directions. Secondly, the approach to formulating dietary guidelines has become more systematic relying on meta-analysis of randomised controlled trials and prospective cohort studies rather than on eminence-based reviews. The Seven Countries Study was an observational study that compared the incidence of CHD between USA, Northern Europe (Holland and Finland), Southern Europe (former Yugoslavia, Italy and Greece) and Japan. It reported low rates of CHD in Southern Europe and Japan and high rates in Northern Europe/ USA. Dietary intake estimates for centre were based on chemical analysis of representative diets rather than individual intakes. SFA intake was from <5% energy in Japan, about 10% in the Mediterranean countries to about 20% in Northern Europe/USA. It was suggested that two-thirds of the difference in median cholesterol concentrations between countries (4·2–6·5 mmol/l) could be explained by differences in SFA and cholesterol intake. However, the relationship only held for regional estimates of SFA intake but not for individual dietary intake data (Kromhout D, personal communication). However, follow-up studies confirmed the lower incidence of CHD in Southern Europe and Japan and the relationship with TC both between cohort and within-cohorts[57]. The current view is that a Mediterranean dietary pattern is related to a lower risk of CHD[58].

Siri-Terano[59] conducted a meta-analysis of prospective studies that have measured SFA intake and have related it to risk of CHD mortality. They report that the relative risks (95% CI) of high v. low intakes of SFA were 1·07 (0·96, 1·19) for CHD, 0·81 (0·62, 1·05) for stroke and 1·00 (0·89, 1·11) for CVD mortality and were not statistically significant. This review, although meticulously conducted, has been controversial and criticised for adjusting for serum cholesterol in the analysis. However, even without adjustment for serum cholesterol there are no significant trends to indicate any increase in risk and the size effects are small. Furthermore, as discussed earlier variations in dietary SFA intakes only explain a very small part of the variance in serum cholesterol in the population. In contrast, estimates of dietary intake of *trans* fatty acids have been found to be more strongly associated with CHD mortality[60] and risk estimates suggest that replacing 2% energy *trans* fatty acids with SFA would lower risk of CHD by 17%. Jakobsen et al.[61] pooled data from eleven cohort studies and modelled the impact of replacing 5% energy SFA with either carbohydrates, MUFA or PUFA (Fig. 5). A caveat regarding this type of analysis is that is influenced by the overall dietary pattern not just the nutrients of interest. The hazards ratio for replacing SFA with carbohydrate was 7% significantly higher for CHD incidence but 4% lower for CHD mortality. Further analysis[62] suggested that the hazards ratio for myocardial infarction incidence was 12% (95% CI −28, 7) lower for low glycaemic index carbohydrates and 33% (8, 64) higher for high glycaemic index carbohydrates. Replacement with MUFA increased the hazards ratio for CHD incidence and mortality by 19 and 1%, respectively, whereas statistically
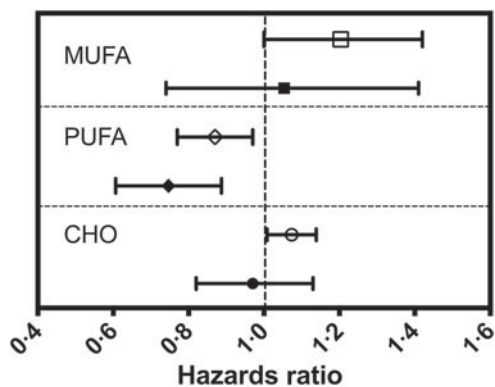
Fig. 5. Hazards ratios with 95% CI for CHD incidence (open symbols) and mortality (closed symbols) estimated from exchanging 5% energy SFA with MUFA or PUFA or carbohydrate CHO from pooled analysis of eleven cohort studies. Adapted from reference[61].

significant reductions in hazards ratio for CHD incidence and mortality of 13 and 26% were reported when SFA were replaced by PUFA.

Randomised controlled trials with clinical endpoints

Several randomised controlled trials were conducted mainly in the 1960–1970s to evaluate the effect of decreasing SFA intake and replacing it with carbohydrate or PUFA on CHD incidence and mortality; by current standards they were all statistically underpowered. The Women's Health Initiative Randomized Dietary Modification Trial[63] is a large well-powered study, which was set up to evaluate whether a reduction in dietary fat intake would reduce breast cancer in women, also evaluated the impact of fat reduction on CHD risk. Although on an intention to treat analysis showed no effect, a *post hoc* analysis found women who had sustained weight loss did show benefit in terms of decreased CHD incidence. Hooper *et al.* in a Cochrane review[64] of dietary interventions concluded that modification of fat intake results in a significant 14% (95% CI 4, 23) reduction in CHD incidence and a non-significant 7% reduction in cardiovascular mortality especially when TC was lowered. However, there was a suggestion from the non-significant 23% reduction in risk for an even better outcome when fat was both reduced and modified.

Recent dietary guidelines and current intakes

WHO/FAO[1] reviewed the evidence and on the basis of the data from the prospective cohort studies concluded that there was convincing evidence that replacing SFA with PUFA decreased risk of CHD but indicated that there was probable evidence that replacing SFA with refined carbohydrate has no benefit on CHD and may even increase risk. The WHO/FAO group could come to no agreement on the upper level of intake of total fat because of the lack of evidence. The Institute of Medicine review for the Dietary Guidelines for Americans[65] came to similar conclusions. Both of these reports recommended that no more than 10% energy be derived from SFA. The French dietary guidelines[66] interestingly have focused on cholesterol raising SFA and have excluded stearic acid and short and medium chain fatty acids from recommendations with the upper limit being 14·5% energy from SFA. In this context, it is worth mentioning in passing that the French consume more cheese and butter compared with other countries in the European Union, yet boast lower rates of CHD (the French Paradox) than many other European countries[67].

Current intakes and conclusions

Intakes of SFA have fallen markedly in many countries including the UK over a period of 30–40 years and current UK intakes are in the range of 12–13%. The UK Dietary National Dietary and Nutritional Survey[68] shows that SFA intake fell from about 17% energy in 1986/1987 to about 13% in 2001 where it has remained since. This fall in SFA intake was accompanied by a modest reduction in total fat intake from 42% to about 35% energy and about a 50% increase in the intake of PUFA. These changes were probably mainly caused by changes in the food supply chain rather than individuals making healthier choices: vegetable oils replaced animal fats, the skimmed milks became widely available but the butter fat disappeared back into the food chain; the lower cost of poultry and pork compared with beef and lamb encouraged a change to these leaner meats; yellow fat spread (butter, margarine) consumption also fell along with a reduction in bread intake. Serum cholesterol fell from a mean of 5·7 mmol/l in 1986 to 5·1 mmol/l in 2000/2001 but remained at level since[69]. For reasons that remain uncertain CHD incidence and mortality has fallen markedly in the UK by about 50% in the last decade across all regions[33].

In terms of meeting government targets for SFA intake (<11% energy), there is little scope for further increasing the intake of PUFA, which is close to the 6% target. From a practical point of view palmitic and stearic acid are the major SFA in diet and palmitic acid normally accounts for about two-thirds of the SFA intake in Western diets. This would suggest that reducing SFA intake by 3% might lower LDL-C slightly (0·12 mmol/l) when exchanged for MUFA but it remains uncertain whether replacing SFA with MUFA will translate into reduced CVD risk. However, there are likely to be health benefits from restricting fat intake in terms of weight loss[70], providing the energy is not replaced by carbohydrate or alcohol. Lowering SFA intake to <11% energy is relatively easy to achieve by modifying the types of oils in the diet, using reduced fat dairy products and restricting the intake of fat from meat and would be predicted to lower LDL-C by 2%. Achieving an intake well below 7% requires a more substantial shift in the overall dietary pattern to something closer to a vegan diet, which introduces a different set of nutritional issues such as low vitamin B_{12} intake, low calcium intake, etc.

Perhaps the more important issue is the overall balance of the diet in relation to cardiovascular risk. It would be unwise to discourage the oily fish (salmon, mackerel, herring) and nuts because of their relatively high SFA content, especially as both oily fish consumption and nuts are associated with decreased risk of CVD[65]. In the UK diet, the major sources of total fat and SFA are meat, dairy and cereals products (mainly pies, cakes and biscuits). The consumption of fatty meat products such as pies, sausages and burgers has been linked to increased CHD risk[71] whereas milk, yoghurt and cheese, but not butter, are associated with a lower risk of CHD[65,72]. In this context, it is relevant to note that two large prospective cohort studies have found the proportion of C_{15}, which is associated with dairy fat consumption, to be associated with a lower risk of CHD[73,74]. Fat can easily be removed from meat and this has the other advantage of reducing energy intake. The other foods making a major contribution to SFA intake, as well as energy, are cakes, biscuits and chocolate confectionary. Reformulation of these products is difficult without changing their taste and organoleptic characteristics. Consequently, it remains sensible to advise only occasional consumption of these foods and this is consistent current healthy eating advice.

In conclusion, the dietary target of <11% energy for SFA intake can be readily achieved but achieving lower intakes is more challenging and would require a major change in dietary patterns.

Conflict of interest statement

None.

References

1. WHO/FAO (2010) Fats and Fatty Acids in Human Nutrition. Report of an Expert Consultation. Rome, Italy: Food and Agricultural Organisation; available at http://www.fao.org (accessed 01 August 2012).
2. Department of Health (1994) Nutritional Aspects of Cardiovascular Disease. Report on Health and Social Subjects No 46. London: HMSO.
3. Degirolamo C & Rudel LL (2010) Dietary monounsaturated fatty acids appear not to provide cardioprotection. *Curr Atheroscler Rep* **12**, 391–396.
4. McGill HC Jr & Strong JP (1968) The geographic pathology of atherosclerosis. *Ann N Y Acad Sci* **149**, 923–927.
5. Webber BJ, Seguin PG, Burnett DG et al. (2012) Prevalence of and risk factors for autopsy-determined atherosclerosis among US service members, 2001–2011. *JAMA* **308**, 2577–2583.
6. McGill HC Jr, McMahan CA & Gidding SS (2008) Preventing heart disease in the 21st century: implications of the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study. *Circulation* **117**, 1216–1227.
7. Humphries SE, Whittall RA, Hubbart CS et al. (2006) Genetic causes of familial hypercholesterolaemia in patients in the UK: relation to plasma lipid levels and coronary heart disease risk. *J Med Genet* **43**, 943–949.
8. Thompson GR (2009) History of the cholesterol controversy in Britain. *QJM* **102**, 81–86.
9. Whitlock G, Lewington S, Sherliker P et al. (2009) Body mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* **373**, 1083–1096.
10. Smart MC, Dedoussis G, Louizou E et al. (2010) APOE, CETP and LPL genes show strong association with lipid levels in Greek children. *Nutr Metab Cardiovasc Dis* **20**, 26–33.
11. Crowe FL, Appleby PN, Travis RC et al. (2013) Risk of hospitalization or death from ischemic heart disease among British vegetarians and nonvegetarians: results from the EPIC-Oxford cohort study. *Am J Clin Nutr* **97**, 597–603.
12. Sanders TA, Ellis FR & Dickerson JW (1978) Studies of vegans: the fatty acid composition of plasma choline phosphoglycerides, erythrocytes, adipose tissue, and breast milk, and some indicators of susceptibility to ischemic heart disease in vegans and omnivore controls. *Am J Clin Nutr* **31**, 805–813.
13. Lewington S (2007) 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* **370**, 1829–1839.
14. Voight BF, Peloso GM, Orho-Melander M et al. (2012) Plasma HDL cholesterol and risk of myocardial infarction: a Mendelian randomisation study. *Lancet* **380**, 572–580.
15. Law MR, Wald NJ & Rudnicka AR (2003) Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. *BMJ* **326**, 1423.
16. Baigent C, Blackwell L, Emberson J et al. (2010) Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. *Lancet* **376**, 1670–1681.
17. Keys A, Anderson JT & Grande F (1957) Prediction of serum-cholesterol responses of man to changes in fats in the diet. *Lancet* **273**, 959–966.
18. Keys A, Anderson JT & Grande F (1965) Serum cholesterol response to changes in the diet. IV. Particular saturated fatty acids in the diet. *Metabolism* **14**, 776–776.
19. Hegsted DM, McGandy RB, Myers ML et al. (1965) Quantitative effects of dietary fat on serum cholesterol in man. *Am J Clin Nutr* **17**, 281–295.
20. Mensink RP & Katan MB (1992) Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. *Arterioscler Thromb* **12**, 911–919.
21. Mensink RP, Zock PL, Kester AD et al. (2003) 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* **77**, 1146–1155.

22. Ng TKW, Hassan K, Lim JB et al. (1991) Nonhypercholesterolemic effects of a palm-oil diet in Malaysian volunteers. *Am J Clin Nutr* **53**, 1015S–1020S.

23. Sundram K, Hayes KC & Siru OH (1994) Dietary palmitic acid results in lower serum cholesterol than does a lauricmyristic acid combination in normolipemic humans. *Am J Clin Nutr* **59**, 841–846.

24. Voon PT, Ng TKW, Lee VKM et al. (2011) Diets high in palmitic acid (16:0), lauric and myristic acids (12:0+14:0), or oleic acid (18:1) do not alter postprandial or fasting plasma homocysteine and inflammatory markers in healthy Malaysian adults. *Am J Clin Nutr* **94**, 1451–1457.

25. Fless GM, Fischer-Dzoga K, Juhn DJ et al. (1982) Structural and functional changes of rhesus serum low density lipoproteins during cycles of diet-induced hypercholesterolemia. *Arteriosclerosis* **2**, 475–486.

26. Khosla P & Hayes KC (1992) Comparison between the effects of dietary saturated (16:0), monounsaturated (18:1), and polyunsaturated (18:2) fatty acids on plasma lipoprotein metabolism in cebus and rhesus monkeys fed cholesterol-free diets. *Am J Clin Nutr* **55**, 51–62.

27. Ng TK, Hayes KC, DeWitt GF et al. (1992) Dietary palmitic and oleic acids exert similar effects on serum cholesterol and lipoprotein profiles in normocholesterolemic men and women. *J Am Coll Nutr* **11**, 383–390.

28. Choudhury N, Tan L & Truswell AS (1995) Comparison of palmolein and olive oil: effects on plasma lipids and vitamin E in young adults. *Am J Clin Nutr* **61**, 1043–1051.

29. Tholstrup T, Hjerpsted J & Raff M (2011) Palm olein increases plasma cholesterol moderately compared with olive oil in healthy individuals. *Am J Clin Nutr* **94**, 1426–1432.

30. Jebb SA, Lovegrove JA, Griffin BA et al. (2010) Effect of changing the amount and type of fat and carbohydrate on insulin sensitivity and cardiovascular risk: the RISCK (Reading, Imperial, Surrey, Cambridge, and Kings) trial. *Am J Clin Nutr* **92**, 748–758.

31. Tierney AC, McMonagle J, Shaw DI et al. (2011) Effects of dietary fat modification on insulin sensitivity and on other risk factors of the metabolic syndrome-LIPGENE: a European randomized dietary intervention study. *Int J Obes (2005)* **35**, 800–809.

32. Hunninghake DB, Stein EA, Dujovne CA et al. (1993) The efficacy of intensive dietary therapy alone or combined with lovastatin in outpatients with hypercholesterolemia. *N Eng J Med* **328**, 1213–1219.

33. Smolina K, Wright FL, Rayner M et al. (2012) Determinants of the decline in mortality from acute myocardial infarction in England between 2002 and 2010: linked national database study. *BMJ* **344**, d8059.

34. Keogh JB, Grieger JA, Noakes M et al. (2005) Flow-mediated dilatation is impaired by a high-saturated fat diet but not by a high-carbohydrate diet. *Arterioscler Thromb Vasc Biol* **25**, 1274–1279.

35. Andriantsitohaina R, Auger C, Chataigneau T et al. (2012) Molecular mechanisms of the cardiovascular protective effects of polyphenols. *Br J Nutr* **108**, 1532–1549.

36. Fuentes F, Lopez-Miranda J, Sanchez E et al. (2001) Mediterranean and low-fat diets improve endothelial function in hypercholesterolemic men. *Ann Int Med* **134**, 1115–1119.

37. Jimenez-Morales AI, Ruano J, Delgado-Lista J et al. (2011) NOS3 Glu298Asp polymorphism interacts with virgin olive oil phenols to determine the postprandial endothelial function in patients with the metabolic syndrome. *J Clin Endocrinol Metab* **96**, E1694–E1702.

38. Sanders TA, Lewis FJ, Goff LM et al. (2013) SFAs do not impair endothelial function and arterial stiffness. *Am J Clin Nutr* **98**, 677–683.

39. Ong PJ, Dean TS, Hayward CS et al. (1999) Effect of fat and carbohydrate consumption on endothelial function. *Lancet* **354**, 2134.

40. Berry SE, Tucker S, Banerji R et al. (2008) Impaired postprandial endothelial function depends on the type of fat consumed by healthy men. *J Nutr* **138**, 1910–1914.

41. Kaptoge S, Di Angelantonio E, Pennells L et al. (2012) C-reactive protein, fibrinogen, and cardiovascular disease prediction. *N Eng J Med* **367**, 1310–1320.

42. Sanders TA, de Grassi T, Miller GJ et al. (1999) Dietary oleic and palmitic acids and postprandial factor VII in middle-aged men heterozygous and homozygous for factor VII R353Q polymorphism. *Am J Clin Nutr* **69**, 220–225.

43. Sanders TA, de Grassi T, Miller GJ et al. (2000) Influence of fatty acid chain length and cis/trans isomerization on postprandial lipemia and factor VII in healthy subjects (postprandial lipids and factor VII). *Atherosclerosis* **149**, 413–420.

44. Berry SE, Miller GJ & Sanders TA (2007) The solid fat content of stearic acid-rich fats determines their postprandial effects. *Am J Clin Nutr* **85**, 1486–1494.

45. Berry SE, Woodward R, Yeoh C et al. (2007) Effect of interesterification of palmitic acid-rich triacylglycerol on postprandial lipid and factor VII response. *Lipids* **42**, 315–323.

46. Oakley FR, Sanders TA & Miller GJ (1998) Postprandial effects of an oleic acid-rich oil compared with butter on clotting factor VII and fibrinolysis in healthy men. *Am J Clin Nutr* **68**, 1202–1207.

47. Sanders TA, Oakley FR, Cooper JA et al. (2001) Influence of a stearic acid-rich structured triacylglycerol on postprandial lipemia, factor VII concentrations, and fibrinolytic activity in healthy subjects. *Am J Clin Nutr* **73**, 715–721.

48. Sanders TA, Berry SE & Miller GJ (2003) Influence of triacylglycerol structure on the postprandial response of factor VII to stearic acid-rich fats. *Am J Clin Nutr* **77**, 777–782.

49. Sanders TA, Filippou A, Berry SE et al. (2011) Palmitic acid in the sn-2 position of triacylglycerols acutely influences postprandial lipid metabolism. *Am J Clin Nutr* **94**, 1433–1441.

50. Sanders TA, Lewis F, Slaughter S et al. (2006) Effect of varying the ratio of n-6 to n-3 fatty acids by increasing the dietary intake of alpha-linolenic acid, eicosapentaenoic and docosahexaenoic acid, or both on fibrinogen and clotting factors VII and XII in persons aged 45–70 y: the OPTILIP study. *Am J Clin Nutr* **84**, 513–522.

51. Sanders TA, de Grassi T, Acharya J et al. (2004) Postprandial variations in fibrinolytic activity in middle-aged men are modulated by plasminogen activator inhibitor I 4G-675/5G genotype but not by the fat content of a meal. *Am J Clin Nutr* **79**, 577–581.

52. Miller GJ (2005) Dietary fatty acids and the haemostatic system. *Atherosclerosis* **179**, 213–227.

53. Riserus U, Willett WC & Hu FB (2009) Dietary fats and prevention of type 2 diabetes. *Prog Lipid Res* **48**, 44–51.

54. Vessby B, Uusitupa M, Hermansen K et al. (2001) Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU Study. *Diabetologia* **44**, 312–319.

55. Bos MB, de Vries JH, Feskens EJ et al. (2010) Effect of a high monounsaturated fatty acids diet and a Mediterranean

diet on serum lipids and insulin sensitivity in adults with mild abdominal obesity. *Nutr Metab Cardiovasc Dis* **20**, 591–598.

56. Astrup A, Dyerberg J, Elwood P *et al.* (2011) The role of reducing intakes of saturated fat in the prevention of cardiovascular disease: where does the evidence stand in 2010? *Am J Clin Nutr* **93**, 684–688.

57. Verschuren WM, Jacobs DR, Bloemberg BP *et al.* (1995) Serum total cholesterol and long-term coronary heart disease mortality in different cultures. Twenty-five-year follow-up of the seven countries study. *JAMA* **274**, 131–136.

58. Huijbregts P, Feskens E, Rasanen L *et al.* (1997) Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and The Netherlands: longitudinal cohort study. *BMJ* **315**, 13–17.

59. Siri-Tarino PW, Sun Q, Hu FB *et al.* (2010) Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *Am J Clin Nutr* **91**, 535–546.

60. Mozaffarian D & Clarke R (2009) 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* **63**, Suppl. 2, S22–S33.

61. Jakobsen MU, O'Reilly EJ, Heitmann BL *et al.* (2009) Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. *Am J Clin Nutr* **89**, 1425–1432.

62. Jakobsen MU, Dethlefsen C, Joensen AM *et al.* (2010) Intake of carbohydrates compared with intake of saturated fatty acids and risk of myocardial infarction: importance of the glycemic index. *Am J Clin Nutr* **91**, 1764–1768.

63. Howard BV, Van Horn L, Hsia J *et al.* (2006) Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA* **295**, 655–666.

64. Hooper L, Summerbell CD, Thompson R *et al.* (2012) Reduced or modified dietary fat for preventing cardiovascular disease. *Cochrane Database Syst Rev* **5**, CD002137.

65. Mozaffarian D, Appel LJ & Van Horn L (2011) Components of a cardioprotective diet: new insights. *Circulation* **123**, 2870–2891.

66. Legrand P, Morise A & Kalonji E (2011) Update of French nutritional recommendations for fatty acids. *World Rev Nutr Diet* **102**, 137–143.

67. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P *et al.* (1994) Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation* **90**, 583–612.

68. Hoare LHJ, Bates C, Prentice A *et al.* (2004) *The National Diet & Nutrition Survey: Adults Aged 19 to 64 Years.* London: The Stationary Office.

69. Bates BLL, Prentice A, Bates C *et al.* (2012) *National Diet and Nutrition Survey. Headline results from Years 1, 2 and 3 (combined) of the Rolling Programme (2008/2009–2010/11)*; available at http://webarchive.nationalarchives.gov.uk. (accessed 30 July 2013).

70. Hooper L, Abdelhamid A, Moore HJ *et al.* (2012) Effect of reducing total fat intake on body weight: systematic review and meta-analysis of randomised controlled trials and cohort studies. *BMJ* **345**, e7666.

71. Rohrmann S, Overvad K, Bueno-de-Mesquita HB *et al.* (2013) Meat consumption and mortality–results from the European Prospective Investigation into Cancer and Nutrition. *BMC Med* **11**, 63.

72. Patterson E, Larsson SC, Wolk A *et al.* (2013) Association between dairy food consumption and risk of myocardial infarction in women differs by type of dairy food. *J Nutr* **143**, 74–79.

73. Khaw KT, Friesen MD, Riboli E *et al.* (2012) Plasma phospholipid fatty acid concentration and incident coronary heart disease in men and women: the EPIC-Norfolk prospective study. *PLoS Med* **9**, e1001255.

74. de Oliveira Otto MC, Nettleton JA, Lemaitre RN *et al.* (2013) Biomarkers of dairy fatty acids and risk of cardiovascular disease in the multi-ethnic study of atherosclerosis. *J Am Heart Assoc* **2**, e000092.