

## **SATURATED FAT AND HEART DISEASE**

### **EXECUTIVE SUMMARY**

In order to continue the limits on saturated fat, health officials must show ample and consistent evidence that these fats damage health. The principal allegation against them has been that they cause heart disease, according to the diet-heart hypothesis which was first proposed in the 1950s.

Many large, government-funded RCTs (randomized, controlled clinical trials, which are considered the 'goldstandard' of science) were conducted all over the world in the 1960s and 70s in order to test the diet-heart hypothesis. Some 75,000 people were tested, in trials that on the whole followed subjects long enough to obtain "hard endpoints," which are considered more definitive than LDL-C, HDL-C, etc. However, the results of these trials did not support the hypothesis, and consequently, they were largely ignored or dismissed for decades—until scientists began rediscovering them in the late 2000s. The first comprehensive review of these trials was published in 2010 and since then, there have been nearly 20 such review papers, by separate teams of scientists all over the world. These papers are listed below.

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### **MAJOR REVIEW PAPERS**

#### **1. *Saturated Fats and Health: A Reassessment and Proposal for Food-based Recommendations: JACC State-of-the-Art Review***

This review, by a group of prominent scientists, mainly from the U.S., challenges the continued caps on saturated fats by the U.S. Dietary Guidelines.  
Astrup et al, JACC 2020

#### **Key Messages:**

"Taken together, the evidence from both cohort studies and randomized trials does not support the assertion that further restriction of dietary saturated fat will reduce clinical [cardiovascular] events."  
"Whole-fat dairy, unprocessed meat, eggs and dark chocolate are SFA[saturated-fatty acid]-rich foods with a complex matrix that are not associated with increased risk of CVD. The totality of available evidence does not support further limiting the intake of such foods."  
"...dietary effects on CVD risk may not be reliably reflected by changes in LDL-cholesterol levels..."  
"...the amount of circulating SFAs [saturated fatty acids] in blood is not related to saturated fat intake from the diet but instead tends to track more closely with dietary carbohydrate intake"  
"These historical facts demonstrate that saturated fats were an abundant, key part of the ancient human diet."  
"Taken together, these observations strongly support the conclusion that the healthfulness of fats is not a simple function of their content in SFA but a result of the various components in the food, often referred to as the "food matrix"

#### **Conclusions**

"The long-standing bias against foods rich in saturated fats should be replaced with a view towards recommending diets consisting of healthy foods. What steps could shift the bias? We suggest the following measures: 1) Enhance the public's understanding that many foods (e.g., whole-fat dairy) that play an important role in meeting dietary and nutritional recommendations may also be rich in saturated fats. 2) Make the public aware that low-carbohydrate diets high in saturated fat, which are popular for managing body weight, may also improve metabolic disease endpoints in some individuals, but emphasize that health effects of dietary carbohydrate – just like those of saturated fat – depend on the amount, type and quality of carbohydrate, food sources, degree of processing, etc. 3) Shift focus from the current paradigm that emphasizes the saturated fat content of foods as key for health, to one that centers on specific traditional foods, so that nutritionists, dietitians, and the public can easily identify healthful sources of saturated fats. 4) Encourage committees in charge of making macronutrient-based recommendations to translate those recommendations into appropriate, culturally sensitive dietary patterns tailored to different populations."

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

This recent review, by an international group of leading scientists, looked at a variety of aspects on the science of saturated fats and urged the World Health Organization to reconsider continued caps on these fats.  
Astrup et al, The BMJ (2019)

**Key Messages:**

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

**THE SCIENTIFIC EVIDENCE ON SATURATED FATS**

The most rigorous kind of data, which can demonstrate cause and effect, come from randomized, controlled clinical trials. Some 75,000 people have been tested in such trials, on the question: do saturated fats cause heart disease? Here is a list of these trials.

Reviews of these trials: There have now been more than a dozen systematic analyses of these trials, summarized in two “review of reviews,” or “umbrella review” papers (all cited below).

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**REVIEWS OF DATA FROM RANDOMIZED CONTROLLED TRIALS:**

**“UMBRELLA REVIEW” PAPERS (REVIEW OF REVIEWS):**

**“Fat or fiction: the diet-heart hypothesis”(review of 17 systematic analysis of clinical-trial data)**

DuBroff et al, BMJ Evidence-Based Medicine (2019)

**Conclusion:** Diets that replace saturated fat with polyunsaturated fat do not convincingly reduce cardiovascular events or mortality...[We] must consider that the diet-heart hypothesis is invalid or requires modification.

**“Dietary Saturated Fat and Heart Disease: A Narrative Review” (review of 19 meta-analyses, including reviews of both clinical-trial data and observational studies)**

Heileson , Nutrition Reviews (2019)

**Conclusions:** Meta-analyses of observational studies found no association between SFA intake and heart disease, while meta-analyses of randomized controlled trials were inconsistent but tended to show a lack of an association.... The AHA [American Heart Association] stance regarding the strength of the evidence for the recommendation to limit SFAs for heart disease prevention may be overstated and in need of re-evaluation.

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**INDIVIDUAL META-ANALYSES AND SYSTEMATIC REVIEWS OF RANDOMIZED, CONTROLLED CLINICAL TRIALS (RCTS), which are the more rigorous evidence (presented in reverse chronological order):**

**1. “Reduction in saturated fat intake for cardiovascular disease” (2020)**

**Update on Cochrane review**

Hooper Lee, Martin N, Jimoh OF, Kirk C, Foster E, Abdelhamid AS

**Conclusion:** There are “no new conclusions” from this review compared to past Cochrane reviews. Saturated fats were found to have no effect on cardiovascular mortality or total mortality. Additionally, “There was little or no effect of reducing saturated fats on non-fatal myocardial infarction or CHD mortality, but effects on total (fatal or non-fatal) myocardial infarction, stroke and CHD events (fatal or non-fatal) were all unclear as the evidence was of very low quality. There was little or no effect on cancer mortality, cancer diagnoses, diabetes diagnosis, HDL cholesterol, serum triglycerides or blood pressure, and small reductions in weight, serum total cholesterol, LDL cholesterol and BMI. There was no evidence of harmful effects of reducing saturated fat intakes.”

**2. “Effects of Nutritional Supplements and Dietary Interventions on Cardiovascular Outcomes: An Umbrella Review and Evidence Map”**

Khan et al, Annals of Internal Medicine, 2019

**Conclusions (on fats):** “In our analysis, the Mediterranean diet, modified dietary fat, reduced dietary fat,

reduced saturated fat intake, omega-6 PUFA, or omega-3 ALA PUFA did not reduce the risk for mortality or cardiovascular outcomes.”

### **3. “Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association ”**

**(2017)**

Sacks et al, Circulation (the journal of the American Heart Association, original authors of the policy advocating for reduction in saturated fats, starting in 1961)

**Conclusions:** In summary, randomized controlled trials that lowered intake of dietary saturated fat and replaced it with polyunsaturated vegetable oil reduced CVD by  $\approx 30\%$ ...., Prospective observational studies in many populations showed that lower intake of saturated fat coupled with higher intake of polyunsaturated and monounsaturated fat is associated with lower rates of CVD and of other major causes of death and all-cause mortality.... Replacement of saturated with unsaturated fats lowers low-density lipoprotein cholesterol, a cause of atherosclerosis, linking biological evidence with incidence of CVD in populations and in clinical trials.... [W]e conclude strongly that lowering intake of saturated fat and replacing it with unsaturated fats, especially polyunsaturated fats, will lower the incidence of CVD.

[Note that this review did not look at the “hard outcome” data but arrived at its conclusions by looking exclusively at the results on LDL-cholesterol]

### **4. ‘The effect of replacing saturated fat with mostly n-6 polyunsaturated fat on coronary heart disease: a meta-analysis of randomized, controlled trials.’**

Hamley, Nutrition Journal (2017)

**Results:** When pooling results from only the adequately controlled trials there was no effect for major CHD events (RR = 1.06, CI = 0.86–1.31), total CHD events (RR = 1.02, CI = 0.84–1.23), CHD mortality (RR = 1.13, CI = 0.91–1.40) and total mortality (RR = 1.07, CI = 0.90–1.26). Whereas, the pooled results from all trials, including the inadequately controlled trials, suggested that replacing SFA with mostly n-6 PUFA would significantly reduce the risk of total CHD events (RR = 0.80, CI = 0.65–0.98, P = 0.03), but not major CHD events (RR = 0.87, CI = 0.70–1.07), CHD mortality (RR = 0.90, CI = 0.70–1.17) and total mortality (RR = 1.00, CI = 0.90–1.10).

**Conclusion:** “Available evidence from adequately controlled randomised controlled trials suggest replacing SFA with mostly n-6 PUFA is unlikely to reduce CHD events, CHD mortality or total mortality. The suggestion of benefits reported in earlier meta-analyses is due to the inclusion of inadequately controlled trials. These findings have implications for current dietary recommendations.”

### **5. “Evidence from prospective cohort studies does not support current dietary fat guidelines: a systematic review and meta-analysis”**

Harcombe et al, British Journal of Sports Medicine (2016)

**Results:** Across 7 studies, involving 89 801 participants (94% male), there were 2024 deaths from CHD during the mean follow-up of  $11.9 \pm 5.6$  years. The death rate from CHD was 2.25%. Eight data sets were suitable for inclusion in meta-analysis; all excluded participants with previous heart disease. Risk ratios (RRs) from metaanalysis were not statistically significant for CHD deaths and total or saturated fat consumption. The RR from meta-analysis for total fat intake and CHD deaths was 1.04 (95% CI 0.98 to 1.10). The RR from meta-analysis for saturated fat intake and CHD deaths was 1.08 (95% CI 0.94 to 1.25).

**Conclusions:** Epidemiological evidence to date found no significant difference in CHD mortality and total fat or saturated fat intake and thus does not support the present dietary fat guidelines. The evidence per se lacks generalisability for population-wide guidelines.

### **6. “Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary**

**Experiment (1968-73)”**

Ramsden, The BMJ (2016)

**Details:** This paper contains, as a separate piece of research, a systematic review and meta-analysis of clinical

trials in which saturated fats were replaced by “oils rich in linoleic acid (such as corn oil, sunflower oil, safflower oil, cottonseed oil, or soybean oil).” (5 trials, 10,808 participants)

Results: “There was no evidence of benefit on mortality from coronary heart disease (hazard ratio 1.13, 95% confidence interval 0.83 to 1.54).”

**Conclusion:** “Although limited, available evidence from randomized controlled trials provides no indication of benefit on coronary heart disease or all cause mortality from replacing saturated fat with linoleic acid rich vegetable oils.”

#### **7. “Reduction in saturated fat intake for cardiovascular disease,” (systematic review and meta-analysis of randomized, controlled clinical trials)**

Hooper et al, Cochrane Database Systematic Review, 2015

**Details:** This is a systematic review and meta-analysis of randomized controlled trials, performed by the Cochrane collaboration – an independent organization of scientists. The trials reviewed include more than 59,000 participants.

**Findings:** The study found no statistically significant effects of reducing saturated fat on the following outcomes: all-cause mortality, cardiovascular mortality, fatal MIs (myocardial infarctions), non-fatal MIs, stroke, coronary heart disease mortality, coronary heart disease events. The one significant finding was an effect for saturated fats on cardiovascular events. However this finding lost significance when subjected to a sensitivity analysis (Table 8, page 137).

**Conclusion:** People who reduced their saturated fat intake were just as likely to die, or get heart attacks or strokes, compared to those who ate more saturated fat.

#### **7. “Dietary fatty acids in the secondary prevention of coronary heart disease: a systematic review, meta-analysis and meta-regression,” (on clinical trials)**

Schwingshackl and Hoffman, BMJ Open (2014)

**Details:** This paper compares low-fat trials to high-fat trials and only includes those with detailed reporting on cholesterol risk factors. **A total of 32 trials on nearly 9,000 participants analyzed.**

**Conclusion:** (looking only at subjects with existing CVD) The present systematic review provides no evidence (moderate quality evidence) for the beneficial effects of reduced/modified fat diets in the secondary prevention of coronary heart disease. Recommending higher intakes of polyunsaturated fatty acids in replacement of saturated fatty acids was not associated with risk reduction.

#### **9. “Association of Dietary, Circulating, and Supplement Fatty Acids with Coronary Risk: A Systematic Review and Meta-analysis” (on observational data on all fatty acids and RCTs on supplementation with polyunsaturated fats, o3s or o6s)**

Chowdhury, et al, Annals of Internal Medicine (2014)

**Details:** RCT data reviewed is on 105,085 participants; observational data is on roughly 550,000 participants. The RCT analysis combined trials that increased either omega 3s or omega 6s.

**Conclusion:** “Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats.”

#### **10. “Reduced or Modified Dietary Fat For Preventing Cardiovascular Disease” (Systematic Review and Metaanalysis) (Analysis of clinical trials)**

Hooper L, Cochrane Database Syst Review (2012), An independent organization of scientists who specialize in systematic reviews. This review is an update on one conducted in 2011.

**Conclusions:** There were no clear effects of dietary fat changes on total mortality, cardiovascular mortality, stroke, total MIs or non-fatal MIs. Reducing saturated fat by reducing and/or modifying dietary fat reduced the risk of cardiovascular events by 14%,” This finding was for men only and disappeared upon the authors “Removing studies with systematic differences in care between intervention and control groups, or other dietary differences.”

#### **11. “Effects on Coronary Heart Disease of Increasing Polyunsaturated Fat in Place of Saturated Fat: A Systematic Review and Meta-analysis of Randomized Controlled Trials”**

Mozaffarian et al, PLOS Medicine (2010)

**Conclusions:** “These findings provide evidence that consuming PUFA in place of SFA reduces CHD events in RCTs. This suggests that rather than trying to lower PUFA consumption, a shift toward greater population PUFA consumption in place of SFA would significantly reduce rates of CHD”

## **12. “Dietary Fat and Coronary Heart Disease: Summary of Evidence From Prospective Cohort and Randomised Controlled Trials” (review of observational data and clinical trials)**

Skeaff, Annals of Nutrition and Metabolism (2009)

**Conclusions:** “Intake of SFA was not significantly associated with CHD mortality, with a RR of 1.14 (95% CI 0.82–1.60,  $p = 0.431$ ) for those in the highest compared with the lowest category of SFA intake (fig. 6). Similarly SFA intake was not significantly associated CHD events (RR 0.93, 95% CI 0.83–1.05,  $p = 0.269$  for high vs. low categories). Moreover, there was no significant association with CHD death (RR 1.11, 95% CI 0.75–1.65,  $p = 0.593$ ) per 5% TE increment in SFA intake.”

## **NON-SYSTEMATIC REVIEWS ON CLINICAL TRIALS**

### **“Saturated Fat, Carbohydrate, and Cardiovascular Disease” (Review of clinical trials)**

Siri-Tarino et al, American Journal of Clinical Nutrition (2010)

**Conclusions:** “Although substitution of dietary polyunsaturated fat for saturated fat has been shown to lower CVD risk, there are few epidemiologic or clinical trial data to support a benefit of replacing saturated fat with carbohydrate.”

## **REVIEWS OF OBSERVATIONAL STUDIES:**

Meta-analyses and systematic reviews (in reverse chronological order):

### **1. “Dietary total fat, fatty acids intake, and risk of cardiovascular disease: a dose-response meta-analysis of cohort studies”**

Zhu et al, Lipids in Health and Disease (2019)

**Conclusion:** “This current meta-analysis of cohort studies suggested that total fat, SFA, MUFA, and PUFA intake were not associated with the risk of cardiovascular disease. However, we found that higher TFA intake is associated with greater risk of CVDs in a dose-response fashion. Furthermore, the subgroup analysis found a cardio-protective effect of PUFA in studies followed up for more than 10 years. Dietary guidelines taking these findings into consideration might be more credible.”

### **2. “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.” (on observational data)**

de Souza et al, The BMJ (Clinical Research ed.) (2015)

**Conclusion:** “Saturated fats are not associated with all cause mortality, CVD, CHD, ischemic stroke, or type 2 diabetes, but the evidence is heterogeneous with methodological limitations.”

### **3. “Evidence from prospective cohort studies does not support current dietary fat guidelines: a systematic review and meta-analysis”**

Harcombe et al, British Journal of Sports Medicine (2016)

**Results:** Across 7 studies, involving 89 801 participants (94% male), there were 2024 deaths from CHD during the mean follow-up of 11.9±5.6 years. The death rate from CHD was 2.25%. Eight data sets were suitable for inclusion in meta-analysis; all excluded participants with previous heart disease. Risk ratios (RRs) from metaanalysis were not statistically significant for CHD deaths and total or saturated fat consumption. The RR from meta-analysis for total fat intake and CHD deaths was 1.04 (95% CI 0.98 to 1.10). The RR from meta-analysis for saturated fat intake and CHD deaths was 1.08 (95% CI 0.94 to 1.25).

**Conclusions:** Epidemiological evidence to date found no significant difference in CHD mortality and total fat or

saturated fat intake and thus does not support the present dietary fat guidelines. The evidence per se lacks generalisability for population-wide guidelines.

#### **4.A Systematic Review of the Evidence Supporting a Causal Link Between Dietary Factors and Coronary Heart Disease” (review of observational data and clinical trials)**

Mente , et al, Archives of Internal Medicine (2009)

**Conclusions:** “The evidence supports a valid association of a limited number of dietary factors and dietary patterns with CHD.... Insufficient evidence (< or =2 criteria) of association is present for intake of supplementary vitamin E and ascorbic acid (vitamin C); saturated and polyunsaturated fatty acids;...”

#### **5.”Dietary Fat and Coronary Heart Disease: Summary of Evidence From Prospective Cohort and Randomised Controlled Trials” (review of observational data and clinical trials)**

Skeaff et al, Annals of Nutrition and Metabolism (2009)

**Conclusions:** “Intake of SFA was not significantly associated with CHD mortality, with a RR of 1.14 (95% CI 0.82–1.60,  $p = 0.431$ ) for those in the highest compared with the lowest category of SFA intake (fig. 6). Similarly SFA intake was not significantly associated CHD events (RR 0.93, 95% CI 0.83–1.05,  $p = 0.269$  for high vs. low categories). Moreover, there was no significant association with CHD death (RR 1.11, 95% CI 0.75–1.65,  $p = 0.593$ ) per 5% TE increment in SFA intake.”

#### **NON-SYSTEMATIC REVIEWS OF OBSERVATIONAL STUDIES:**

##### **“Saturated Fats Versus Polyunsaturated Fats Versus Carbohydrates for Cardiovascular Disease Prevention and Treatment”**

Patty et al, Annual Review of Nutrition (2015)

**Conclusions:** “Replacement of SFAs with polyunsaturated fatty acids has been associated with reduced CVD risk, although there is heterogeneity in both fatty acid categories. In contrast, replacement of SFAs with carbohydrates, particularly sugar, has been associated with no improvement or even a worsening of CVD risk... Replacement of SFAs with CHOs [carbohydrates] has not been associated with benefit and may be associated with increased CVD risk....The effects of various SFA replacement scenarios on CVD risk factors other than lipids and lipoproteins are ambiguous...”

#### **LARGEST-EVER SINGLE OBSERVATIONAL STUDY:**

The PURE Study: largest-ever epidemiological study, contradicts diet-heart hypothesis

##### **“Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study”**

Dehghan et al, The Lancet (2017)

**Interpretation of findings:** “High carbohydrate intake was associated with higher risk of total mortality, whereas total fat and individual types of fat were related to lower total mortality. Total fat and types of fat were not associated with cardiovascular disease, myocardial infarction, or cardiovascular disease mortality, whereas saturated fat had an inverse association with stroke. Global dietary guidelines should be reconsidered in light of these findings.”

#### **LONGEST-EVER SINGLE OBSERVATIONAL STUDY:**

The Boyd Orr Cohort study: longest-ever epidemiological study, contradicts the diet-heart hypothesis

##### **“Diet in childhood and adult cardiovascular and all cause mortality: the Boyd Orr cohort”**

Ness et al, Heart (2005)

**Methods:** 4028 people (from 1234 families) took part in Boyd Orr’s survey of family diet and health in Britain between 1937 and 1939 and were followed up through the National Health Service central register to 2000.

**Conclusions:** No significant associations for childhood saturated fat intake and cardiovascular mortality or any cause of death. For all-cause mortality the rate ratio between the highest and lowest quartiles of saturated fat intake was 0.91 (95% CI 0.70 to 1.17,  $p$  for trend 0.2) after adjustment for age, sex, and energy intake.