DR. McDOUGALL'S
HEALTH & MEDICAL CENTER


## Ronald M. Krauss, MD—The Doctor Who Made Lard-eating Fashionable

Ronald M. Krauss, MD is a well-publicized author in both the lay press and medical journals. He is also a UCSF Adjuvant Professor, Endocrinologist, and the Director of Atherosclerosis Research at Children's Hospital Oakland Research Institute. Dr. Krauss' work has provided one of the most important foundations for popular discussions about how eating meat, dairy and eggs is not a health hazard for people. Even lard is back on the dinner table thanks in part to Dr. Krauss' publications.

Dr. Krauss has not turned nutrition wisdom about healthy eating head-over-heals alone. Robert Atkins, MD of the Atkins Diet fame, science-writer Gary Taubes, and best-selling authors William Davis, MD (Wheat Belly), and David Perlmutter, MD (Grain Brain) have made valuable contributions to this latest trend.

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## A Preliminary Evaluation of Chowdhury Meta-Analysis on the Association of Fatty Acids with Coronary Risk

I'm an active reader/researcher on nutrition, finance, climate change, and politics. The NY Times piece on the Chowdhury paper made me at first angry, and then very concerned. From previous research into these areas plus my work experience as an Intel engineer, I know how data can be cherry-picked and distorted. Thus, I felt compelled to do an objective evaluation of the saturated-fat claim in the Chowdhury paper, because it is this aspect that the mainstream media has latched on to. Could the net effect become as bad as Atkins in the 1990's, Gary Taubes in the previous decade, and the Paleo-diet proponents are doing in this decade? Too soon to tell.

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## Featured Recipes

- Chickpea Pot Pie Lasagna
- Stuffed Portobello Mushrooms
- Rustic Gnocchi
- Thick and Creamy Taco Soup

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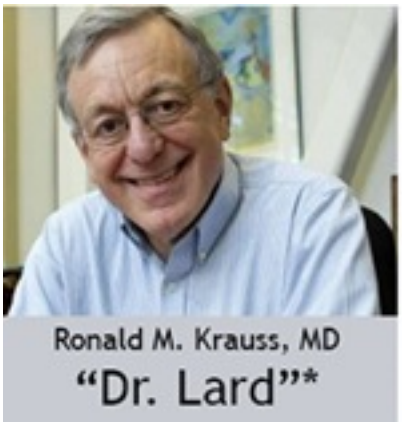
## Ronald M. Krauss, MD—The Doctor Who Made Lard-eating Fashionable





Ronald M. Krauss, MD is a well-publicized author in both the lay press and medical journals. He is a UCSF Adjuvant Professor, Endocrinologist, and the Director of Atherosclerosis Research at Children's Hospital Oakland Research Institute. Dr. Krauss' work has provided one of the most important foundations for popular discussions about how eating meat, dairy, and eggs are not health hazards for people. Even though it may not have been a direct intention of Dr. Krauss, lard is back on the dinner table thanks in part to his publications.

*If I (Dr. John McDougall) were publicly referred to as "Dr. Potato" or "Dr. Vegetable," I would consider this reference to be a compliment. I would not be offended. Such a descriptive title would mean that I have accurately communicated my beliefs about good nutrition. Thus, Dr. Krauss shall be known as "Dr. Lard."


BMJ

OBSERVATIONS

FROM THE HEART

Saturated fat is not the major issue

Let's bust the myth of its role in heart disease

Aseem Malhotra interventional cardiology specialist registrar, Croydon University Hospital, London

**World-changing Headlines followed this October 2013 British Medical Journal article**


Study Doubts Saturated Fat's Link to Heart Disease

Debate Continues On Healthful Foods

**World-changing headlines: March 2014 New York Times article**

(Saturated fat in everyday terms, in other words the foods on your plate, means beef, pork, lamb, chicken, cheese, milk, lard, and eggs.)

Dr. Krauss has not acted alone in turning nutrition wisdom on its head. Robert Atkins, MD of the Atkins Diet fame, Gary Taubes (science-writer) and best-selling authors William Davis, MD (Wheat Belly), and David Perlmutter, MD (Grain Brain) have made valuable contributions to this latest trend.

Articles like these that offer "nuggets of proof" that saturated fat-laden foods can be eaten guiltlessly have created a feeding frenzy within the meat, dairy, and egg industries. As a direct result, hundreds of millions of people worldwide—especially those who are looking to "hear good news about their bad habits"—will die of heart disease, diabetes, cancer, and obesity, and if left unchallenged, resulting increases in livestock production will accelerate global warming even faster than the current rate.

The lay press has gone wild with advice to eat more saturated fat. NPR stories question "fat as a villain," and famous food and cooking writers, like Mark Bittman, tell us, "Butter is Back." Even rotund physician Andrew Weil, MD recommends eating lard.

Dr. Krauss, however, has not always been in favor of eating animal flesh and fat. His research in 1986, before he started working for the beef and dairy industries, clearly explains that the high consumption of animal foods and low intake of plant foods promotes atherosclerosis (heart disease and strokes).

## Relationship of dietary fat, protein, cholesterol, and fiber intake to atherogenic lipoproteins in men[1–3]

*Paul T Williams, PhD, Ronald M Krauss, MD, Stacy Kindel-Joyce, RD, MS, Darlene M Dreon, RD, MS, MPH, Karen M Vranizan, MA, and Peter D Wood, DSc*

ABSTRACT Nutritional components (g/1000 kcal) obtained from 3-day diet records are compared to triglyceride, total cholesterol, low-density (LDL), intermediate-density (IDL), and very low-density (VLDL) lipoprotein concentrations of 77 free-living men. Polyunsaturated-fatty acid consumption correlated negatively with concentrations of triglycerides, total cholesterol, LDL- and VLDL-cholesterol, and total-lipoprotein mass of smaller-LDL particles ($S_f^0$ 0–7), IDL ($S_f^0$ 12–20), and VLDL ($S_f^0$ 20–400) in serum and plasma. Animal-protein consumption correlated positively and plant-protein consumption correlated negatively with triglycerides, smaller-LDL mass, VLDL-cholesterol, and VLDL-mass levels. Serum concentrations of smaller-LDL particles were also positively correlated with dietary-cholesterol intake and negatively correlated with crude-fiber consumption. Thus, diet-lipoprotein relationships observed cross-culturally and experimentally are further supported when detailed dietary measurements from 3-day diet records and lipoprotein measurements from repeated blood samplings are correlated in free-living men. *Am J Clin Nutr* 1986;44:788–97.

KEY WORDS Lipoproteins, cholesterol, population studies, diet, animal protein, plant protein

His opinions and writings changed after he started working for the National Cattleman's Beef Association and the National Dairy Council (as early as 1990).

His most famous publication was in March of 2010 in the American Journal of Clinical Nutrition (research funded by The National Dairy Council).

## Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease[1–5]

*Patty W Siri-Tarino, Qi Sun, Frank B Hu, and Ronald M Krauss*

**ABSTRACT**

**Background:** A reduction in dietary saturated fat has generally been thought to improve cardiovascular health.

**Objective:** The objective of this meta-analysis was to summarize the evidence related to the association of dietary saturated fat with risk of coronary heart disease (CHD), stroke, and cardiovascular disease (CVD; CHD inclusive of stroke) in prospective epidemiologic studies.

**Design:** Twenty-one studies identified by searching MEDLINE and EMBASE databases and secondary referencing qualified for inclusion in this study. A random-effects model was used to derive composite relative risk estimates for CHD, stroke, and CVD.

**Results:** During 5–23 y of follow-up of 347,747 subjects, 11,006 developed CHD or stroke. Intake of saturated fat was not associated with an increased risk of CHD, stroke, or CVD. The pooled relative risk estimates that compared extreme quantiles of saturated fat intake were 1.07 (95% CI: 0.96, 1.19; $P = 0.22$) for CHD, 0.81 (95% CI: 0.62, 1.05; $P = 0.11$) for stroke, and 1.00 (95% CI: 0.89, 1.11; $P = 0.95$) for CVD. Consideration of age, sex, and study quality did not change the results.

**Conclusions:** A meta-analysis of prospective epidemiologic studies showed that there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD. More data are needed to elucidate whether CVD risks are likely to be influenced by the specific nutrients used to replace saturated fat. *Am J Clin Nutr* 2010;91:535–46.

fat to saturated fat (P:S), a hypothesis supported by a recent pooling analysis conducted by Jakobsen et al (24).

The goal of this study was to conduct a meta-analysis of well-designed prospective epidemiologic studies to estimate the risk of CHD and stroke and a composite risk score for both CHD and stroke, or total cardiovascular disease (CVD), that was associated with increased dietary intakes of saturated fat. Large prospective cohort studies can provide statistical power to adjust for covariates, thereby enabling the evaluation of the effects of a specific nutrient on disease risk. However, such studies have caveats, including a reliance on nutritional assessment methods whose validity and reliability may vary (25), the assumption that diets remain similar over the long term (26) and variable adjustment for covariates by different investigators. Nonetheless, a summary evaluation of the epidemiologic evidence to date provides important information as to the basis for relating dietary saturated fat to CVD risk.

### SUBJECTS AND METHODS

#### Study selection

Two investigators (QS and PS-T) independently conducted a systematic literature search of the MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed/) and EMBASE (http://www.embase.com) databases through 17 September 2009 by using the following

This paper is the key research that is cited to argue that eating all that saturated fat and cholesterol, along with big doses of people-poisoning environmental chemicals and loads of infection-causing bacteria, parasites, and viruses is good for you and your family.

Unfortunately, the popular press is rarely inclined to publicize the criticism of this original publication by Dr. Krauss and associates. To be specific, I have never read in the New York Times or the Wall Street Journal any comment on the editorial in this same issue of the American Journal of Clinical Nutrition by Jeremiah Stamler, MD criticizing this flawed paper: the exact research that has received so much attention in the lay press.

See corresponding articles on pages 502 and 535.

# Diet-heart: a problematic revisit[1–3]

*Jeremiah Stamler*

The diet-heart revisit in this issue of the Journal (1, 2), concerning saturated fatty acids (SFAs) and coronary heart disease (CHD), is problematic in its thrust; it relates to numerous questions as follows, none of which are explicitly spelled out:

1) In univariate analyses of population-based observational data, are there direct relations of dietary SFAs to CHD?
2) In multivariate analyses controlled for possible confounders, are there independent direct relations of dietary SFAs to CHD?
3) Is the SFA-CHD relation similar for "hard" fatal CHD and "soft" total CHD?
4) Do limitations in quality of dietary data in epidemiologic studies on SFA-CHD influence results?
5) What are the findings from randomized controlled trials on SFA-CHD?
6) Is the SFA-CHD relation mainly attributable to adverse SFA influence on serum cholesterol (total cholesterol, LDL cholesterol)?
7) What about possible effects of dietary cholesterol?
8) With lower dietary SFA, which macronutrients are preferable to replace SFA?
9) Are dietary influences on serum lipoprotein particles clear or relevant? Do particle measurements enhance CHD risk assessment independent of serum lipids?
10) Do dietary SFAs or other macronutrients influence metabolic traits other than LDL cholesterol, particularly HDL choles-

(RRs) ranged from 1.22 to 2.77—ie, >1.07, which was the estimated CHD RR in the meta-analysis (2). Do these larger RRs reflect freedom from confounding and overadjustment? Analyses are needed to clarify this; the 2 current articles (1, 2) give no such data.

The meta-analysis (2) states briefly that the Ni-Hon-San Study and the Seven Countries Study found significant cross-population relations between SFA and CHD, as have multiple ecological analyses (3). The authors ignore these findings in their assessments and conclusions.

Regarding item 2, in multivariate analyses the question is: Does SFA relate to CHD independently of multiple covariates (including dietary and serum lipids)? The 2 articles (1, 2) never make this clear. Thus, the Abstract in the meta-analysis simply states, "Intake of saturated fat was not associated with an increased risk of CHD" (2). A precise characterization is as follows: There was a statistically nonsignificant relation of SFA to CHD (RR: 1.07) independent of other dietary lipids, serum lipids, and other covariates.

As to item 3, the meta-analysis did not compare SFA–fatal CHD and SFA–total CHD outcomes (total CHD is undefined). This merits exploration. My calculations, from data for 16 CHD studies (meta-analysis tables), with RRs weighted by person-years of exposure, yielded contrasting CHD risks: for "hard" fatal CHD (11 studies), the RR was 1.32; for "soft" total

Nor have I seen any writer or reporter from any newspaper, TV, radio, or website do an in-depth investigative reporting on the criticisms found in not one, but several, letters to the editor that followed in the same journal, American Journal of Clinical Nutrition.

An outside observer might think that the press was in cahoots with meat, dairy, and egg industries—but who would ever believe such nonsense? Likely, they are just too busy with stories about movies stars' divorces, etc. to trouble themselves with these multibillion-dollar medical and food problems.

I am not surprised that you are confused when there is so much money available to publicize the meat, dairy, and egg industries' viewpoints: One that also condemns you and your family to poor health and possibility of financial ruin. Maybe a little name -calling and a few facts will challenge the "lard experts" to share a public platform with me. But this is unlikely since ignoring the truth has worked so well and so far.

On a personal note: I am getting so tired from punching them that my arms are weak.

## A Preliminary Evaluation of Chowdhury Meta-Analysis on the Association of Fatty Acids with Coronary Risk

Fred Pollack
March 31, 2014

I'm an active reader/researcher on nutrition, finance, climate change, and politics. The NY Times piece on the Chowdhury paper made me at first angry, and then very concerned. From previous research into these areas plus my work experience as an Intel engineer, I know how data can be cherry-picked and distorted. Thus, I felt compelled to do an objective evaluation of the saturated-fat claim in the Chowdhury paper, because it is this aspect that the mainstream media has latched on to. Could the net effect become as bad as Atkins in the 1990's, Gary Taubes in the previous decade, and the Paleo-diet proponents are doing in this decade? Too soon to tell.

About Fred

I live with my wife, Iris, in Miami Beach. We are both 65. I worked at Intel for 23 years, and retired in early 2001. For most of my last 8 years at Intel, I directed the planning for Intel's future microprocessors. In January 1993, I was named an Intel Fellow.

My wife and I have been eating a low-fat whole-food plant-based diet since February 2009.

Email: fjpollack@gmail.com

Am I biased? Sure. I'm biased by all the research that I have read, and by my own experiences. But as a trained scientist and engineer, I know how to do an objective evaluation, and that is all that I can promise. In finance, they say "follow the money." In this case, I will follow the data to see where it takes me.

### Preamble

The Chowdhury et al article [1] was published online at the Annals of Internal Medicine http://annals.org/article.aspx?articleID=1846638]. on March 18, 2014. It is behind a paywall, and can be purchased for $20, as I did. If you decide to do this, be sure to also download the two supplements. Also, click on the "Comments" tab to see some of the negative comments by Chowdhury's peers, e.g. by Dr. Walter Willet, Chairman of Nutrition of the Harvard school of Public Health. Dr. Willet, in an online Science Magazine article, http://news.sciencemag.org/health/2014/03/scientists-fix-errors-controversial-paper-about-saturated-fats, was quoted to say, "They have done a huge amount of damage . . . I think a retraction with similar press promotion should be considered."

My analysis is written for the reader who wants to understand the details behind this study, and related research. This is Part 1 - Part 2 will be in the next newsletter.

**Introduction**

The meta-analysis of dietary fatty acids and risk of coronary heart disease by Chowdhury et al. [1] concludes that ***"Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsatuated fatty acids and low consumption of total saturated fats."*** This paper will examine this claim w.r.t. the intake of Saturated Fat Acids (SFAs) and its relationship to coronary disease. To make the claim, the Chowdhury analysis cites 20 observational studies. The next version of this paper will include a detailed review of each of these. To date, I've read and analyzed about 9 of these studies. Thus, my general observations/ conclusions are preliminary.

In this paper, I'll present my detailed analysis of 2 of the 20 studies - one that shows the most benefit to higher intakes of SFA (MALMO) and one that shows the most harm (Oxford Vegetarian). And, I'll also present some data from a 3rd study - the Nurses Health Study (NHS), but time does not permit a full analysis in this version.

What is the dietary guideline for SFA intake? The USDA guideline is ≤10% of daily calories. This is the same as several other countries' guideline. The American Heart Association recommends <7% of calories. And, the DASH (Dietary Approaches to Stop Hypertension) has the nutrient goal of 6% of calories from SFA.

As noted in the FAO/Who Report [3], "The relationship between dietary fats and CVD, especially coronary heart disease, has been extensively investigated, with strong and consistent associations emerging from a wide body of evidence accrued from animal experiments, as well as observational studies, clinical trials and metabolic studies conducted in diverse human populations." And, from the Scientific Conference on Dietary Fatty Acids and Cordiovascular Health Summary [4]: "Based on a large body of evidence, it is apparent that the optimal diet for reducing risk of chronic diseases is one in which saturated fatty acids are reduced and trans fatty acids from manufactured fats are virtually eliminated. Because of the growing health benefits recognized for unsaturated fatty acids, it is likely that a mixture of these fatty acids in the diet will confer the greatest health benefits within the context of a total fat intake that is considered moderate." And, this study notes, "Current dietary guidance in general recommends a diet that contains ≤30% of energy as fat, ≤10% of energy as saturated fatty acids, up to 10% of energy as PUFAs[1], and <300 mg of cholesterol per day."

Thus, for Chowdhury et al to challenge the SFA guidelines based on the vast body of existing research is an *extraordinary* claim.

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[1] PUFA - Polyunsaturated Fatty Acids. MUFA - Monounsaturated Fatty Acids.

***"Extraordinary claims require extraordinary evidence"***[2]

Meta-analyses are viewed as the "gold-standard", because they combine the results of a collection of different studies performed by different researchers. Thus, if a few turn out to be bad (e.g. poorly constructed, researcher bias, incorrect analysis), the expectation is that they will be overwhelmed in the meta-analysis by all the good or valid studies. But what if: the reverse occurs, i.e. the majority of studies are not good; and/or, the chosen studies do not test the proposed hypothesis. In these cases, the meta-analysis is not made of "gold" - it's just "paper".

*"Things are seldom what they seem, Skim milk masquerades as cream"*[3]

The only way to tell if we are dealing with Skim milk or Cream is to dig into Chowdhury et al's referenced studies. As scientists, we need to be both "open to challenging the common wisdom," but skeptical.

Based on my initial analysis, Chowdhury has not chosen "good" studies to back up his claim, and few are applicable to Chowdhury's claim w.r.t. dietary guidelines for Saturated Fat intake. The next section of this paper will discuss several shortcomings in the referenced studies. After that, I'll present my analysis of the MALMO and Oxford Vegetarian studies.

But first, I want to point you to a comparable meta-analysis, and its analysis. In 2010, Siri-Tarino et al published the paper "Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease," in the American Journal of Clinical Nutrition[2]. As the Chowdhury paper says about the Siri-Tarino paper, ". . .prospective observational studies have questioned whether there really are associations between saturated fat consumption and cardiovascular disease." Most of the 20 studies of the Chowdhury meta-analysis are also used in the Siri-Tarino meta-analysis. Plant Positive has reviewed some of the studies referenced in the Siri-Tarino paper, and his analysis is online at http://www.plantpositive.com/siri-tarinos-meta-analysis-par/.

## Preliminary Analysis

First, look at Supplement Figure 2 from the Chowdhury paper summarizing the SFA impact on Coronary outcomes:

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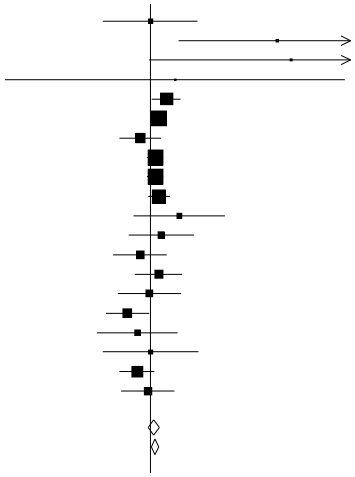
[2] Made popular by Carl Sagan on *Cosmos*.

[3] From *HMS Pinafore.* Gilbert & Sullivan. Obviously, not vegans.

| Study | Participant | Event | Adjustment | RR (95% CI) |
|---|---|---|---|---|
| **SFA** | | | | |
| EUROASPIRE | 400 | 34 | ++ | 1.00 (0.68, 1.46) |
| Oxford Vegetarian | 10802 | 45 | + | 2.77 (1.25, 6.13) |
| EPIC-Greece | 1013 | 46 | + | 3.10 (0.99, 9.63) |
| BLSA | 501 | 71 | + | 1.22 (0.31, 4.77) |
| LRC | 4546 | 92 | + | 1.14 (1.01, 1.27) |
| IBDH | 1001 | 110 | ++ | 1.07 (1.00, 1.14) |
| Caerphilly | 2423 | 137 | + | 0.92 (0.78, 1.09) |
| HLS | 2676 | 155 | + | 1.04 (0.97, 1.11) |
| FRAM | 813 | 208 | + | 1.04 (0.97, 1.11) |
| WES | 1900 | 215 | ++ | 1.07 (0.98, 1.17) |
| Glostrup Multi-centre | 3686 | 326 | + | 1.26 (0.87, 1.82) |
| SHS | 2938 | 403 | ++ | 1.09 (0.84, 1.42) |
| JACC | 58453 | 420 | + | 0.92 (0.74, 1.14) |
| HPFS | 43757 | 734 | + | 1.07 (0.88, 1.29) |
| KIHD* | 2641 | 737 | + | 0.99 (0.77, 1.28) |
| MALMO | 20440 | 1010 | + | 0.83 (0.70, 0.99) |
| IIHD | 10059 | 1070 | ++ | 0.90 (0.65, 1.24) |
| HHS | 8006 | 1177 | ++ | 1.00 (0.68, 1.47) |
| ATBC | 21930 | 1399 | + | 0.90 (0.78, 1.03) |
| NHS | 78778 | 1766 | + | 0.98 (0.79, 1.21) |
| *Overall, random effects (I-squared = 35.5%, p = 0.059)* | | | | *1.03 (0.98, 1.07)* |
| *Overall, fixed-effect* | | | | *1.04 (1.01, 1.07)* |



* Estimates were available through correspondence with the study authors. § ++, studies adjusted for conventional risk factors (including lipids); +, adjusted for non-lipid conventional risk factors e.g. age, sex, BMI, smoking and history of diabetes. EUROASPIRE, European Action on Pre-existing CVD and Primary Prevention through intervention to reduce events; EPIC-Greece, European Prospective Investigation of Cancer Greece; BLSA, Baltimore Longitudinal Study of Aging; LRC, Lipid Research Clinics; IBDH, Ireland-Boston Diet Heart Study; HLS, Health and Lifestyle Survey; FRAM, Framingham Heart Study; WES, Western Electric Study; SHS, Strong Heart Study; HPFS, Health Professionals' Follow up Study; KIHD, Kuopio Ischaemic Heart Disease Risk Factor Study; JACC, Japan Collaborative Cohort Study; MALMO, Malmo Diet and Cancer Study; IIHD, Israeli Ischaemic Heart Disease Study; HHS, Honolulu Heart Study; ATBC, Alpha-Tocopherol Beta Carotene Study; NHS, Nurses' Health Study.

Note that only 2 studies reached statistical significance, i.e. the full range of the confidence interval (CI) was either fully below or above 1.0: MALMO (higher SFA intake is helpful) and Oxford Vegetarian (higher SFA intake is harmful), thus, completely opposite conclusions. We will cover both in detail after the next section.

## Grading of Studies

With each of the 20 studies, I am going to apply a subjective qualitative grading based on 8 parameters. These are not meant to replace the ones that the Chowdhury paper employed, but rather to supplement them. In this section, I will explain each parameter, and also provide a summary assessment based on the 9 studies that I have read/ analyzed so far.

1) *Over-adjustment with Lipids*. In the above figure, 6 studies are marked (++) to indicate that in addition to adjusting for conventional risk factors, lipids (i.e. cholesterol levels) were also included in the adjustment. From the main Chowdhury paper, "Studies that reported RRs with differing degrees of adjustment for other risk factors used the most adjusted estimate that did not include adjustment for blood lipids or circulating fatty acids (because *circulating lipids may act as potential mediators for the associations between fatty acids and coronary disease*)." But apparently 6 of the studies only published adjustments that included "blood lipids". This results in an over-adjustment, since SFA intake causes an increase in LDL and Total Cholesterol. This alone suggests that these 6 studies (i.e. 30% of the studies) should not have been included in the meta-analysis.
2) *Sufficient Test of SFA Guidelines*. Most of the studies that I've reviewed to date, divide the study population into either fifths (quintiles), fourths (quartiles), or thirds

(tertiles). Now suppose a study divides the population into quintiles (of equal sizes). Ideally to test the validity of the ≤10% of energy from SFA intake, it would be appropriate for 2 of the quintiles to have mean SFA intakes ≤10%. Or, if divided into quartiles or tertiles, then 1. Until I review all 20 studies, I won't know how many this screen would eliminate. My current estimate is that it will probably eliminate about 15 or more of them. But Chowdhury et al make it more interesting. Whenever a study uses quartiles or quintiles, they readjust the data using statistical means, to transform the analysis into tertiles. So how many of the studies would this filter out of the 20, because not even 1 tertile would have a mean of ≤10% from SFA? Probably about 17. And, here is what the MALMO authors said about this issue w.r.t their study, "Further, one should note that *only 1.2 percent of the present study population actually followed national Swedish recommendations (less than 10 energy percent) on saturated fat intake.* ***Strictly speaking, <u>the SFA- CVD hypothesis is thus not fully testable in this population.</u>"***

3) *Homogeneity.* The question to examine is whether a study population is from a single area and eats approximately the same diet. For example, consider the population for the Caerphilly study - ~2,400 men, ages 45-59, from small a town in of South Wales, England (Caerphilly and 5 adjacent towns - total population, 41,000) in the early 1980's. In the next section, the MALMO study is discussed. Malmo is the 3rd largest city in Sweden, probably also homogenous (e.g. relatively few citizens from countries with a different diet pattern; in fact, any candidates that were not sufficiently fluent in Swedish were excluded; and, any candidates that indicated that they had changed their diet in the past, were also excluded). As one measure consider the mean SFA intake (% of energy) for each quintile of the Malmo study population: men (13.0, 15.2, 16.8, 18.9, 22.7), women (12.9, 15.1, 16.7, 18.6, 22.1). An increase of 2 pats of butter (5.2g of SFA, ~1.8% of energy for men and ~2.2% for women) is enough to move a person 1 quintile. Also, note the ratio in SFA intake from the 5th quintile to the 1st one is ~1.7, but with the tertile transformation, this probably drops to ~1.5.
4) *Food/Lifestyle Questionnaire.* This involves a Food Frequency Questionaire (FFQ), as well as a Lifestyle one about health status, medications, exercise, smoking habits, etc. In almost all the studies, FFQ/Lifeststyle data is only obtained at the beginning of the study, and there is no knowledge of any changes from then on. Some studies are very diligent in their process to get the FFQ/Lifestyle right, e.g. using a diet-history method, and a diet interview. MALMO seemed to be quite good at this, from what they describe. Nevertheless, over the period of time that many of these studies last (5 to 20+ years), the socioeconomic changes (e.g. growth of eating out, more fast food restaurants, more emphasis on not smoking, people retiring, new medication prescriptions e.g. for cholesterol and blood pressure, etc), how valid is a study that lasts 10+ years with no new information on diet and lifestyle of the population?
5) *Missing Data in the Study.* Many of the studies did not include TFA (trans-fatty acid intake), and this is mentioned in the papers as a shortcoming of the respective studies. Many of the studies do not do a blood test to look at cholesterol and blood glucose at the beginning of the study. Such tests might be a check on the FFQ/ Lifestyle information.
6) *Missing Data in the Paper*, but in the study itself. There are almost an infinite number of ways to slice and dice the info of a study's population, but only a small amount can

reasonably be published in an article. Thus, the data necessary to try to figure out what is going on with a particular variable, e.g. SFA, is often not in the article.

7) *Confounders*, potentially leading to Overadjustment. This is an area that is way outside of my expertise. When I do see the raw data the way that I would like to see it presented, in many of the studies there are correlations, for example, in the highest quintile of SFA intake it usually contains people that also have a higher intake of dietary cholesterol, a lower intake of fiber, lower physical activity, and a higher smoking level when compared to the people in lowest quintile of SFA intake. The 2012 Malmo paper summarizes this problem best, "Like many other studies, our study suffers from relatively high correlations between some nutrients." When you combine this with the homogeneity and the 1-time FFQ/Lifestyle problems, it is challenging to have confidence in the fully adjusted numbers. And, sometimes when you just look at the adjusted numbers (vs less adjusted ones), it looks more like "noise."
8) *Food vs. Nutrients.* The problem is best summarized by a comment in the 2012 MALMO paper, "*This illustrates one of the major problems with studies of nutrient intake: the nutrient variables are also, perhaps even primarily, markers of the foods they derive from.* ***Foods contain many nutrients and other bioactive substances that interact in complex ways and may therefore differ in their health effects in ways not captured by differences in the content of single nutrients.***" T. Colin Campbell (author of the China Study) wrote a whole book about this, "Whole: Rethinking the Science of Nutrition." To quote from there, "Every apple contains thousands of antioxidants whose names, beyond a few like vitamin C, are unfamiliar to us, and each of these powerful chemicals has the potential to play an important role in supporting our health. They impact thousands upon thousands of metabolic reactions inside the human body. But calculating the specific influence of each of these chemicals isn't nearly sufficient to explain the effect of the apple as a whole. Because almost every chemical can affect every other chemical, there is an almost infinite number of possible biological consequences."

## Studies

In this section, I'm going to describe only 2 of the 20 studies of the Chowdhury meta-analysis w.r.t. the effect of SFA intake on Coronary Events. The studies that I am going to cover are the only 2 that reached statistical significance according to the statistics presented in the supplementary section of the Chowdhury paper. The Figure presented in the Preliminary Analysis section shows this. Another good reason for choosing these 2 studies is that they reach completely opposite conclusions - according to Chowdhury paper, the MALMO study shows that a *high SFA intake results in less coronary events*, and the Oxford Vegetarian study shows the opposite. Note that despite its name, the Oxford Vegetarian study includes *both meat eaters and Vegetarians*. It is also worth noting that both of these studies were also included in the Siri-Tarino meta-analysis.

**MALMO Study**

The Chowdhury paper references two MALMO studies [5, 6] - one from 2012 and the other from 2007. The 2012 paper is the better one, but the 2007 paper has some data that is not in the 2012 paper, and thus is also useful. The Siri-Tarino paper (published in 2010) also uses MALMO in its meta-analysis, but only references the 2007 paper.

Note that Chowdhury and Siri-Tario score the MALMO study differently:

| | RR (95% CI) |
|---|---|
| Chowdhury | 0.83 (0.70 - 0.99) |
| Siri-Tarino | 0.95 (0.74 - 1.21) |

The Study Population. As noted in the 2012 abstract: "data from 8,139 male and 12,535 female participants (aged 44–73 y) of the Swedish population-based Malmo¨ Diet and Cancer cohort. The participants were without history of CVD and diabetes mellitus, and had reported stable dietary habits in the study questionnaire. Diet was assessed by a validated modified diet history method, combining a 7-d registration of cooked meals and cold beverages, a 168-item food questionnaire (covering other foods and meal patterns), and a 1-hour diet interview. Sociodemographic and lifestyle data were collected by questionnaire. iCVD cases, which included coronary events (myocardial infarctions or deaths from chronic ischemic heart disease) and ischemic strokes, were ascertained via national and local registries."

Recruitment was between 1991-1996, and mean follow-up was 13.5 years in the 2012 paper and 8.4 years in the 2007 one.

And from the 2012 conclusion: "In this well-defined population, a high fiber intake was associated with lower risk of iCVD, but ***there were no robust associations between other macronutrients and iCVD risk."*** This included associations for total Fat and SFA. Thus, I can't explain why the Chowdhury statistical analysis finds that there is an association of a high-SFA diet with lower iCVD risk.

From the 2007 conclusion: "In relation to risks of cardiovascular events, our results do not suggest any benefit from a limited total or saturated fat intake, nor from relatively high intake of unsaturated fat."

The 2007 article focused on Fat (including SFA) and used quartiles. The 2012 article focused on these as well plus many others (e.g. Fiber, Carbs, Protein, etc). Both articles look at the Fat issue in slightly different ways. So it is worth covering both - first, the 2007 paper.

The 2007 results section (from abstract) state: "No trend towards higher cardiovascular event risk for women or men with higher total or saturated fat intakes, was observed. Total fat: HR (95% CI) for fourth quartile was 0.98 (0.77–1.25) for women, 1.02 (0.84–1.23) for men; saturated fat: 0.98 (0.71–1.33) for women and 1.05 (0.83–1.34) for men. Inverse associations between unsaturated fat intake and cardiovascular event risk were

not observed." Note that these numbers are different from both Siri-Tarino and Chowdhury numbers.

In Malmo, iCVD is both coronary events (CE) and ischemic strokes. Haemorrhagic strokes were excluded because the causes for them are believed to be different than ischemic strokes (which are believed to have similar causes as CEs).

Table 1 of the 2007 article (produced below) provides one way to view the Study population:

**Table 1 Baseline characteristics and diet composition within quartiles of total fat intake for women (left) and men (right)**

| | 1st | 2nd | 3rd | 4th | 1st | 2nd | 3rd | 4th |
|---|---|---|---|---|---|---|---|---|
| *N* (*n*) | 4193 (153) | 4222 (140) | 4224 (139) | 4228 (151) | 2565 (225) | 2611 (239) | 2674 (247) | 2677 (262) |
| Age (years) | 57.8 | 57.7 | 57.2 | 56.9 | 59.1 | 59.3 | 59.0 | 58.9 |
| % current smoker | 20.8 | 24.4 | 29.4 | 37.4 | 21.5 | 24.9 | 28.1 | 40.4 |
| BMI (kg/m$^2$) | 25.7 | 25.6 | 25.4 | 24.9 | 26.3 | 26.3 | 26.2 | 26.1 |
| SBP (mmHg) | 140 | 139 | 139 | 139 | 144 | 144 | 144 | 144 |
| Alcohol intake (g/day) | 5.9 | 7.3 | 8.2 | 9.3 | 12.8 | 14.2 | 16.7 | 18.7 |
| Physical activity score | 8425 | 8083 | 7674 | 7539 | 9035 | 8509 | 8163 | 7809 |
| Energy intake (kcal/day) | 1834 | 1965 | 2041 | 2164 | 2425 | 2556 | 2668 | 2808 |
| % energy from fat | 30.8 | 36.5 | 40.3 | 46.1 | 31.8 | 37.8 | 41.7 | 47.7 |
| % from saturated fats | 12.7 | 15.5 | 17.5 | 20.9 | 12.8 | 15.7 | 17.7 | 21.3 |
| % from monounsaturated fats | 10.8 | 12.7 | 14.0 | 15.7 | 11.2 | 13.4 | 14.8 | 16.6 |
| % from polyunsaturated fats | 5.1 | 5.8 | 6.3 | 6.8 | 5.5 | 6.2 | 6.7 | 7.1 |
| % energy from carbohydrates | 52.2 | 47.0 | 43.8 | 38.7 | 51.7 | 46.2 | 42.9 | 37.6 |
| % energy from protein | 16.6 | 16.3 | 15.8 | 15.2 | 16.1 | 15.8 | 15.3 | 14.8 |
| Fibre intake[a] (g/day) | 22.6 | 19.9 | 18.0 | 15.4 | 26.3 | 22.7 | 20.4 | 17.3 |
| Fruit and vegetable intake[a] (g/day) | 488 | 420 | 369 | 304 | 429 | 364 | 323 | 272 |

Numbers are presented as percentages. [a]Age and energy-adjusted means. BMI, body mass index; (*n*), number of events; *N*, number of individuals within each quartile; SBP, systolic blood pressure.

Please note the following correlations with %Energy intake from Fat, which defines each quartile:

1) For both men and women, positive correlations with: %current-smoker, alcohol-intake, energy-intake, and % Energy from all total fat components (i.e. SFA, MUFA, PUFA)
2) For both men and women, inverse correlations with: physical-activity, % energy from carbs, % energy from protein, Fibre intake, and Fruit-and-vegetable intake.
3) For both men and women the values that remain about the same across all 4 quartiles: Age, BMI, and SBP.

In case you are wondering about trans-fats, the paper says, "*The fact that trans-fatty acids were not recorded as a separate variable could have confounded the results considerably.* Also, the range of unsaturated fat intake was relatively modest, diminishing the possibilities of revealing statistically significant differences between the quartiles. Further more, diet was only assessed at one point in time, decreasing the reliability of the dietary assessment."

Observations:

1) None of the quartiles indicate a healthy population with a healthy diet and lifestyle.
2) As I mentioned in the previous section, a homogenous population like this one leads to small differences. The unsaturated fat difference is modest. And, even with SFA, an increase of ~1tbsp butter (7g SFA, 100kcal) or about 2 to 3 inch cubes of cheese is enough to move an individual 1 quartile.

3) Based solely on the above "raw" (i.e. unadjusted numbers), the identified trends (Fat, SFA, Smoking, Fibre-intake, Fruit-Vegetable intake, physical activity) imply that we should see a correlation with number of events, in particular, far more events in the 4th quartile than the 1st one. Yet for women, quartiles 1 and 4 are effectively the same, 2 and 3 are about the same, and both 1 and 4 are more than 2 and 3. For men, we do see the expected trend, but it is not substantial and could conceivably be due to "smoking".

Turning to the adjusted results, table 2 from the 2007 paper, below. Note w.r.t. quartiles, this is different from Table 1. In Table 2, each category of fat defines the quartile. When you look at the mean fat intake for each quartile in table 2, it is different from table 1, except for total fat. Thus, one cannot look at the characteristics in table 1 and apply them to SFA quartiles in table 2. However, since there is a close correlation with this population of %SFA of energy intake with that of %Total fat, it should be close.

The only quartile that reached statistical significance (P<0.05) w.r.t. %SFA intake was women in quartile 3 with the "Crude" adjustment, RR 0.74 (0.56-0.97). "Crude" is never defined in the article, but based on context, I think it is principally Age. "Adjusted" though is defined as "Adjusted for age, smoking habits, alcohol consumption, socio-economic status, marital status, physical activity, body mass index, fibre intake, and blood pressure."

As the 2007 paper says: "Even though 1556 endpoints were registered, *the difference in HR between the first and the fourth quartiles would have needed to be 30–40% to be significantly detectable. Such differences were not observed for any of the types of fat analysed in our study.* It should be noted that traditional cardiovascular risk factors such as current smoking [HR 2.49 (2.03–3.05) for women; 2.16 (1.81–2.57) for men] and systolic blood pressure [10 mmHg increase – HR 1.24 (1.18–1.29) for women; 1.20 (1.16–1.23) for men] were highly significant (P<0.0001) in our multivariate analysis. This emphasizes that even though a weak relationship exists in our study between fat intake and CVE, the association between dietary fats and CVE risk would thus, not be in the order of the association with smoking and blood pressure."

So, the above implies that we cannot deduce an HR for SFA w.r.t. coronary events or cardiovascular events (i.e. coronary events + ischemic stroke).

Now on to the 2012 article, which is the far better one.

Unlike the 2007 article, the 2012 one gives us quintiles AND we can look at 13 different nutrient quintiles (Carbs, Monosaccharides, Disaccharides, Starch, Fiber, Fat, SFA, MUFA, PUFA, n-3 FA, Long-chain n-3 FA, n-6 FA, Protein). Each distribution is in terms of non-alcohol energy percentages.

**Table 2.** Distribution of non-alcohol energy percentages from selected nutrients in participants of the Malmö Diet and Cancer cohort with stable dietary habits (medians).

| | Sex | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Men (n = 8,139) | | | | | Women (n = 12,535) | | | | |
| | Quintiles | | | | | Quintiles | | | | |
| | 1 | 2 | 3 | 4 | 5 | 1 | 2 | 3 | 4 | 5 |
| Carbohydrate | 36.6 | 41.2 | 44.2 | 47.2 | 51.7 | 37.8 | 42.1 | 45.0 | 47.9 | 52.2 |
| Monosaccharides | 3.6 | 4.9 | 6.0 | 7.3 | 9.5 | 4.5 | 6.2 | 7.4 | 8.9 | 11.2 |
| Disaccharides | 7.4 | 10.0 | 11.9 | 14.1 | 17.5 | 8.8 | 11.2 | 12.9 | 14.9 | 18.2 |
| Starch | 20.0 | 23.1 | 25.3 | 27.7 | 31.3 | 19.1 | 21.9 | 23.8 | 25.9 | 29.1 |
| Fiber[a] | 5.8 | 7.1 | 8.2 | 9.3 | 11.4 | 6.5 | 8.1 | 9.3 | 10.6 | 12.9 |
| Fat, total | 33.0 | 37.4 | 40.3 | 43.5 | 48.1 | 32.0 | 36.2 | 39.1 | 42.1 | 46.5 |
| Saturated fat | 13.0 | 15.2 | 16.8 | 18.9 | 22.7 | 12.9 | 15.1 | 16.7 | 18.6 | 22.1 |
| Monounsaturated fat | 11.4 | 13.1 | 14.2 | 15.3 | 17.0 | 11.0 | 12.5 | 13.6 | 14.6 | 16.1 |
| Polyunsaturated fat | 4.5 | 5.5 | 6.2 | 7.1 | 8.5 | 4.3 | 5.1 | 5.8 | 6.6 | 8.0 |
| n-3 fatty acids | 0.70 | 0.86 | 0.99 | 1.14 | 1.40 | 0.67 | 0.82 | 0.94 | 1.08 | 1.34 |
| Long-chain n-3 fatty acids | 0.08 | 0.13 | 0.19 | 0.30 | 0.53 | 0.07 | 0.12 | 0.18 | 0.27 | 0.49 |
| n-6 fatty acids | 3.5 | 4.3 | 5.0 | 5.8 | 7.1 | 3.3 | 4.0 | 4.7 | 5.4 | 6.7 |
| Protein | 12.5 | 14.0 | 15.2 | 16.4 | 18.4 | 12.9 | 14.5 | 15.7 | 16.9 | 18.9 |

[a]Expressed as grams per 1000 kcal reported energy intake.
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Next are the tables for Risk of iCVD looking at each macronutrient. Tables 3 and 4 below are for women and reproduced from the paper. Following that is Table S5 for men and reproduced from the supplementary info available online.

First lets look at SFA, for men and women? With both Basic and Full adjustment, quintile 5 vs quintile 1 did not reach statistical significance. Nevertheless, it is interesting to look at quintile 5 numbers for both men and women. With the Basic adjustment, increased SFA is harmful. With the Full adjustment it is helpful. Given the correlations with SFA (in particular, fiber, smoking, physical activity), perhaps there is over-adjustment. Again, with Basic or Full adjustments, statistical significance was not reached for men or women.

Now consider other macronutrients intake. The story is almost the same for both men and women. With just the Basic adjustment, statistical significance was reached for monosaccharides, starch, fiber, and MUFA. More was helpful for the first 3 of these and more was harmful for MUFA. But after Full adjustment, the only one that retained statistical significance was fiber, but just for women (although it was close for men). But note that fiber was in the full adjustment. Since whole fruits contain monosaccharides (glucose and fructose) and fiber, the Full adjustment for monosaccharides could be an over-adjustment. Similarly, since root vegetables, whole grains, and legumes contain both starch and fiber, the Full adjustment for starch could be an over-adjustment, as well.

Tables 3 and 4 combined from the 2012 article: Risk of total ischemic cardiovascular disease in 12,535 *women* (687 cases)[a] by intake of macronutrient intake (multivariate hazard ratios with 95% confidence intervals per quintile of energy-adjusted intake).

| *Women (n = 12,535)* | | *1 (n = 2,507)* | *2 (n = 2,507)* | *3 (n = 2,507)* | *4 (n = 2,507)* | *5 (n = 2,507)* | *P for trend* |
|---|---|---|---|---|---|---|---|
| **Carbohydrates** | c/py[b] | 138/29,599 | 135/29,633 | 137/30,078 | 124/30,021 | 153/30,241 | |
| | Basic[c] | 1.00 | 0.91 (0.72–1.16) | 0.88 (0.69–1.11) | 0.75 (0.58–0.95) | 0.90 (0.71–1.13) | 0.14 |
| | **Full[d]** | **1.00** | **1.02 (0.80–1.31)** | **1.08 (0.84–1.38)** | **0.89 (0.69–1.16)** | **1.18 (0.91–1.54)** | **0.48** |
| **Monosaccharides** | c/py | 142/29,225 | 131/29,791 | 140/30,044 | 124/30,090 | 150/30,421 | |
| | Basic | 1.00 | 0.78 (0.61–0.99) | 0.75 (0.59–0.95) | 0.64 (0.50–0.81) | 0.72 (0.58–0.91) | 0.003 |
| | **Full** | **1.00** | **0.96 (0.75–1.22)** | **1.00 (0.78–1.28)** | **0.89 (0.68–1.16)** | **1.10 (0.84–1.43)** | **0.67** |
| **Disaccharides** | c/py | 129/29,908 | 124/29,982 | 126/30,195 | 136/29,940 | 172/29,546 | |
| | Basic | 1.00 | 0.85 (0.66–1.09) | 0.76 (0.59–0.97) | 0.81 (0.64–1.04) | 1.06 (0.84–1.34) | 0.55 |
| | **Full** | **1.00** | **0.87 (0.68–1.12)** | **0.79 (0.62–1.02)** | **0.80 (0.62–1.03)** | **0.94 (0.74–1.19)** | **0.57** |
| **Starch** | c/py | 181/29,551 | 146/29,818 | 116/29,931 | 128/29,782 | 116/30,491 | |
| | Basic | 1.00 | 0.79 (0.64–0.99) | 0.65 (0.52–0.82) | 0.74 (0.59–0.94) | 0.68 (0.54–0.87) | 0.001 |
| | **Full** | **1.00** | **0.89 (0.71–1.11)** | **0.77 (0.61–0.99)** | **0.89 (0.69–1.13)** | **0.88 (0.68–1.15)** | **0.34** |
| **Fiber** | c/py | 173/28,876 | 131/29,510 | 133/29,990 | 125/30,265 | 125/30,930 | |
| | Basic | 1.00 | 0.67 (0.53–0.84) | 0.63 (0.50–0.79) | 0.56 (0.44–0.71) | 0.54 (0.42–0.68) | <0.001 |
| | **Full** | **1.00** | **0.77 (0.61–0.97)** | **0.80 (0.64–1.02)** | **0.71 (0.56–0.91)** | **0.76 (0.59–0.97)** | **0.022** |
| **Protein** | c/py | 168/29,838 | 127/30,261 | 124/30,002 | 128/29,766 | 140/29,705 | |
| | Basic | 1.00 | 0.76 (0.60–0.95) | 0.79 (0.62–0.99) | 0.83 (0.66–1.05) | 0.92 (0.72–1.17) | 0.66 |
| | **Full** | **1.00** | **0.81 (0.64–1.03)** | **0.85 (0.67–1.08)** | **0.88 (0.69–1.12)** | **0.97 (0.76–1.24)** | **0.96** |
| **Fat, total** | c/py[b] | 144/30,265 | 128/29,925 | 139/29,851 | 134/29,985 | 142/29,546 | |
| | Basic[c] | 1.00 | 0.91 (0.72–1.16) | 1.06 (0.84–1.35) | 1.07 (0.84–1.35) | 1.15 (0.91–1.46) | 0.12 |
| | **Full[d]** | **1.00** | **0.86 (0.67–1.09)** | **0.95 (0.75–1.22)** | **0.89 (0.69–1.15)** | **0.86 (0.66–1.13)** | **0.44** |
| **Saturated fat** | c/py | 145/30,428 | 135/29,989 | 133/29,976 | 131/29,697 | 143/29,483 | |
| | Basic | 1.00 | 0.96 (0.76–1.22) | 0.98 (0.77–1.24) | 1.00 (0.79–1.27) | 1.11 (0.88–1.41) | 0.38 |
| | **Full** | **1.00** | **0.94 (0.74–1.19)** | **0.89 (0.69–1.14)** | **0.84 (0.64–1.08)** | **0.87 (0.66–1.14)** | **0.22** |
| **Monouns. fat** | c/py | 138/30,141 | 130/30,084 | 126/29,822 | 135/29,797 | 158/29,727 | |
| | Basic | 1.00 | 0.97 (0.76–1.24) | 0.95 (0.75–1.22) | 1.09 (0.86–1.39) | 1.28 (1.02–1.62) | 0.019 |
| | **Full** | **1.00** | **0.90 (0.71–1.15)** | **0.86 (0.67–1.11)** | **0.94 (0.73–1.22)** | **0.98 (0.76–1.27)** | **0.94** |
| **Polyuns. fat** | c/py | 145/29,559 | 135/29,696 | 134/29,933 | 142/30,259 | 131/30,125 | |
| | Basic | 1.00 | 0.93 (0.73–1.17) | 0.98 (0.78–1.24) | 1.08 (0.85–1.36) | 1.06 (0.84–1.34) | 0.34 |
| | **Full** | **1.00** | **0.90 (0.71–1.14)** | **0.94 (0.74–1.20)** | **1.04 (0.82–1.32)** | **0.94 (0.74–1.20)** | **0.91** |
| **n-3 fatty acids** | c/py | 121/29,935 | 121/30,024 | 130/30,030 | 150/29,833 | 165/29,749 | |
| | Basic | 1.00 | 0.92 (0.71–1.18) | 0.96 (0.75–1.23) | 1.07 (0.84–1.36) | 1.09 (0.86–1.38) | 0.22 |
| | **Full** | **1.00** | **0.91 (0.71–1.18)** | **0.92 (0.71–1.18)** | **1.02 (0.80–1.30)** | **1.03 (0.81–1.38)** | **0.50** |
| **Long-chain n-3** | c/py | 109/29,809 | 117/29,815 | 133/30,046 | 154/29,937 | 174/29,965 | |
| | Basic | 1.00 | 0.86 (0.66–1.11) | 0.87 (0.68–1.13) | 0.98 (0.77–1.26) | 0.99 (0.78–1.27) | 0.51 |
| | **Full** | **1.00** | **0.88 (0.68–1.15)** | **0.94 (0.72–1.21)** | **1.02 (0.80–1.32)** | **1.07 (0.83–1.37)** | **0.25** |
| **n-6 fatty acids** | c/py | 145/29,437 | 154/29,642 | 130/29,982 | 131/30,206 | 127/30,306 | |
| | Basic | 1.00 | 1.14 (0.91–1.43) | 0.98 (0.77–1.24) | 1.08 (0.85–1.37) | 1.11 (0.87–1.42) | 0.59 |
| | **Full** | **1.00** | **1.07 (0.85–1.35)** | **0.96 (0.76–1.22)** | **1.04 (0.81–1.32)** | **0.98 (0.76–1.25)** | **0.75** |

[a]12,402 women and 676 cases in the full model due to missing values.
[b]Cases/person years.
[c]Basic model: Adjusted for age, method version, total energy intake (continuous), and season.
[d]Full model: Adjusted for age, method version, total energy intake (continuous), season, BMI class, smoking category, education, alcohol category, systolic blood pressure, antihypertensive treatment, antihyperlipidemic treatment, leisure time physical activity (quartiles) and quintiles of energy-adjusted dietary fiber.
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Table S5: Risk of total ischemic cardiovascular disease in 8,139 *men* (1089 cases) by macronutrient intake (multivariate hazard ratios with 95% confidence intervals per quintile of energy-adjusted intake).

| | | *1 (n=1,627)* | *2 (n=1,628)* | *3 (n=1,628)* | *4 (n=1,628)* | *5 (n=1,628)* | *P for trend* |
|---|---|---|---|---|---|---|---|
| **Carbohydrates** | c / py[13] | 214 / 18,706 | 225 / 18,688 | 222 / 18,945 | 212 / 18,940 | 216 / 18,922 | |
| | Basic[14] | 1.00 | 0.98 (0.82-1.19) | 0.96 (0.80-1.16) | 0.86 (0.71-1.04) | 0.90 (0.74-1.09) | 0.12 |
| | **Full[15]** | **1.00** | **1.09 (0.90-1.32)** | **1.12 (0.92-1.36)** | **1.04 (0.85-1.28)** | **1.09 (0.88-1.35)** | **0.63** |
| **Monosaccharides** | c / py | 229 / 18,408 | 233 / 18,830 | 211 / 19,053 | 217 / 18,963 | 199 / 18,947 | |
| | Basic | 1.00 | 0.91 (0.76-1.10) | 0.74 (0.62-0.90) | 0.74 (0.62-0.90) | 0.69 (0.57-0.84) | <0.001 |
| | **Full** | **1.00** | **1.03 (0.85-1.24)** | **0.91 (0.74-1.11)** | **0.95 (0.77-1.16)** | **0.91 (0.73-1.14)** | **0.31** |
| **Disaccharides** | c / py | 195 / 19,205 | 208 / 19,043 | 211 / 19,037 | 236 / 18,646 | 239 / 18,270 | |
| | Basic | 1.00 | 1.02 (0.84-1.24) | 1.00 (0.82-1.22) | 1.10 (0.91-1.34) | 1.13 (0.93-1.37) | 0.13 |
| | **Full** | **1.00** | **1.07 (0.88-1.31)** | **1.04 (0.85-1.27)** | **1.11 (0.91-1.35)** | **1.04 (0.85-1.27)** | **0.66** |
| **Starch** | c / py | 245 / 18,312 | 216 / 18,657 | 225 / 18,900 | 193 / 19,086 | 210 / 19,246 | |
| | Basic | 1.00 | 0.86 (0.72-1.03) | 0.90 (0.75-1.08) | 0.77 (0.64-0.93) | 0.88 (0.73-1.06) | 0.083 |
| | **Full** | **1.00** | **0.94 (0.78-1.14)** | **0.99 (0.82-1.21)** | **0.94 (0.76-1.16)** | **1.10 (0.88-1.37)** | **0.50** |
| **Fiber** | c / py | 246 / 18,095 | 219 / 18,714 | 213 / 18,916 | 220 / 18,972 | 191 / 19,504 | |
| | Basic | 1.00 | 0.84 (0.70-1.01) | 0.78 (0.65-0.94) | 0.79 (0.66-0.95) | 0.65 (0.54-0.79) | <0.001 |
| | **Full** | **1.00** | **0.93 (0.78-1.12)** | **0.93 (0.77-1.12)** | **1.00 (0.82-1.20)** | **0.85 (0.70-1.04)** | **0.30** |
| **Fat, total** | c / py | 211 / 19,060 | 218 / 18,736 | 203 / 19,002 | 226 / 18,813 | 231 / 18,589 | |
| | Basic | 1.00 | 1.04 (0.86-1.25) | 0.97 (0.80-1.18) | 1.10 (0.91-1.34) | 1.18 (0.98-1.43) | 0.071 |
| | **Full** | **1.00** | **0.99 (0.82-1.20)** | **0.92 (0.75-1.13)** | **1.01 (0.82-1.24)** | **0.95 (0.77-1.18)** | **0.77** |
| **Saturated fat** | c / py | 217 / 19,010 | 221 / 19,027 | 209 / 19,065 | 212 / 18,743 | 230 / 18,355 | |
| | Basic | 1.00 | 0.99 (0.82-1.20) | 0.97 (0.80-1.17) | 1.01 0.83-1.22) | 1.08 (0.89-1.30) | 0.4 |
| | **Full** | **1.00** | **0.94 (0.78-1.14)** | **0.94 (0.77-1.15)** | **0.91 (0.74-1.12)** | **0.89 (0.72-1.11)** | **0.32** |
| **Monouns. fat** | c / py | 201 / 18,996 | 216 / 18,759 | 218 / 18,947 | 234 / 18,818 | 220 / 18,681 | |
| | Basic | 1.00 | 1.04 (0.86-1.26) | 1.07 (0.88-1.30) | 1.15 (0.96-1.40) | 1.16 (0.96-1.40) | 0.064 |
| | **Full** | **1.00** | **0.97 (0.80-1.18)** | **1.00 (0.82-1.23)** | **1.02 (0.84-1.25)** | **0.92 (0.74-1.14)** | **0.64** |
| **Polyuns. fat** | c / py | 226 / 18,331 | 218 / 18,752 | 220 / 18,959 | 194 / 19,165 | 231 / 18,993 | |
| | Basic | 1.00 | 0.97 (0.80-1.16) | 1.00 (0.83-1.21) | 0.87 (0.72-1.06) | 1.08 (0.90-1.29) | 0.81 |
| | **Full** | **1.00** | **0.95 (0.79-1.14)** | **0.97 (0.80-1.17)** | **0.85 (0.70-1.03)** | **1.05 (0.87-1.27)** | **0.98** |
| **n-3 fatty acids** | c / py | 200 / 19,053 | 199 / 18,914 | 232 / 18,809 | 221 / 18,869 | 237 / 18,556 | |
| | Basic | 1.00 | 1.01 (0.83-1.22) | 1.11 (0.92-1.35) | 1.05 (0.86-1.27) | 1.05 (0.87-1.27) | 0.52 |
| | **Full** | **1.00** | **1.00 (0.82-1.21)** | **1.10 (0.91-1.33)** | **0.97 (0.80-1.18)** | **1.02 (0.84-1.24)** | **0.92** |
| **Long-chain n-3** | c / py | 175 / 19,250 | 230 / 18,647 | 240 / 18,730 | 222 / 18,856 | 222 / 18,717 | |
| | Basic | 1.00 | 1.22 (1.00-1.49) | 1.24 (1.02-1.50) | 1.10 (0.90-1.34) | 1.03 (0.84-1.26) | 0.66 |
| | **Full** | **1.00** | **1.24 (1.02-1.51)** | **1.22 (1.00-1.48)** | **1.09 (0.89-1.33)** | **1.03 (0.84-1.26)** | **0.59** |
| **n-6 fatty acids** | c / py | 228 / 18,274 | 223 / 18,514 | 208 / 19,031 | 201 / 19,230 | 229 / 19,151 | |
| | Basic | 1.00 | 1.02 (0.85-1.23) | 0.95 (0.79-1.15) | 0.93 (0.77-1.13) | 1.10 (0.91-1.32) | 0.65 |
| | **Full** | **1.00** | **1.02 (0.85-1.23)** | **0.95 (0.78-1.15)** | **0.94 (0.78-1.14)** | **1.10 (0.91-1.32)** | **0.62** |
| **Protein** | c / py | 243 / 18,516 | 222 / 18,823 | 234 / 18,773 | 195 / 19,072 | 195 / 19,017 | |
| | Basic | 1.00 | 0.91 (0.76-1.09) | 1.00 (0.83-1.20) | 0.84 (0.70-1.02) | 0.90 (0.74-1.09) | 0.19 |
| | **Full** | **1.00** | **0.92 (0.77-1.11)** | **1.07 (0.89-1.28)** | **0.88 (0.72-1.07)** | **0.90 (0.73-1.10)** | **0.28** |

The MALMO paper also separated out the components of iCVD into Coronary Events (CE) and ischemic stroke. It is not clear to me whether or not the Chowdhury paper includes or excludes ischemic stroke in their analysis. So with that in mind, here are the most relevant excerpts, from the MALMO 2012 supplement for both Men (S1) and Women (S2) looking at just coronary events (i.e. iCVD - ischemic strokes):

**Table S1 Risk of coronary event in 8,139 men (688 cases) by macronutrient intake (multivariate hazard ratios with 95% confidence intervals per quintile of energy-adjusted intake).**

Excerpts

| | | *1 (n=1,627)* | *2 (n=1,628)* | *3 (n=1,628)* | *4 (n=1,628)* | *5 (n=1,628)* | *P for trend* |
|---|---|---|---|---|---|---|---|
| **Fiber** | c / py | 150 / 18,095 | 137 / 18,714 | 133 / 18,916 | 142 / 18,972 | 126 / 19,504 | |
| | Basic | 1.00 | 0.87 (0.69-1.10) | 0.82 (0.64-1.03) | 0.86 (0.68-1.08) | 0.72 (0.57-0.92) | 0.018 |
| | **Full** | **1.00** | **0.97 (0.77-1.23)** | **0.98 (0.77-1.24)** | **1.09 (0.86-1.38)** | **0.97 (0.75-1.25)** | **0.85** |
| **Fat, total** | c / py | 139 / 19,060 | 147 / 18,736 | 119 / 19,002 | 131 / 18,813 | 152 / 18,589 | |
| | Basic | 1.00 | 1.06 (0.84-1.33) | 0.86 (0.67-1.09) | 0.96 (0.75-1.22) | 1.15 (0.91-1.45) | 0.51 |
| | **Full** | **1.00** | **1.02 (0.80-1.29)** | **0.83 (0.65-1.08)** | **0.91 (0.70-1.18)** | **0.97 (0.74-1.27)** | **0.58** |
| **Saturated fat** | c / py | 139 / 19,010 | 155 / 19,027 | 128 / 19,065 | 126 / 18,743 | 140 / 18,355 | |
| | Basic | 1.00 | 1.09 (0.86-1.37) | 0.92 (0.72-1.17) | 0.92 (0.72-1.17) | 1.00 (0.79-1.28) | 0.56 |
| | **Full** | **1.00** | **1.04 (0.82-1.31)** | **0.92 (0.71-1.18)** | **0.86 (0.66-1.11)** | **0.86 (0.66-1.13)** | **0.12** |

[1] Cases / person years.
[2] Basic model: Adjusted for age, method version, total energy intake (continuous), and season.
[3] Full model: Adjusted for age, method version, total energy intake (continuous), season, BMI class, smoking category, education, alcohol category, systolic blood pressure, antihypertensive treatment, antihyperlipidemic treatment, leisure time physical activity (quartiles) and quintiles of energy-adjusted dietary fiber. There are only 8,038 men and 680 cases in the full model due to missing values.

**Table S2 Risk of coronary event in 12,535 women (333 cases) by macronutrient intake (multivariate hazard ratios with 95% confidence intervals per quintile of energy-adjusted intake).**

Excerpts:

| | | *1 (n=2,507)* | *2 (n=2,507)* | *3 (n=2,507)* | *4 (n=2,507)* | *5 (n=2,507)* | *P for trend* |
|---|---|---|---|---|---|---|---|
| **Fiber** | c / py | 87 / 28,876 | 71 / 29,510 | 59 / 29,990 | 55 / 30,265 | 61 / 30,930 | |
| | Basic | 1.00 | 0.73 (0.53-1.00) | 0.56 (0.40-0.79) | 0.50 (0.36-0.71) | 0.54 (0.38-0.75) | <0.001 |
| | **Full** | **1.00** | **0.84 (0.62-1.17)** | **0.73 (0.52-1.03)** | **0.65 (0.46-0.93)** | **0.78 (0.55-1.11)** | **0.067** |
| **Fat, total** | c / py | 71 / 30,265 | 62 / 29,925 | 65 / 29,851 | 60 / 29,985 | 75 / 29,546 | |
| | Basic | 1.00 | 0.89 (0.63-1.25) | 0.99 (0.70-1.39) | 0.94 (0.66-1.33) | 1.19 (0.85-1.66) | 0.29 |
| | **Full** | **1.00** | **0.81 (0.57-1.14)** | **0.88 (0.62-1.24)** | **0.77 (0.53-1.12)** | **0.87 (0.60-1.28)** | **0.52** |
| **Saturated fat** | c / py | 82 / 30,428 | 58 / 29,989 | 63 / 29,976 | 59 / 29,697 | 71 / 29,483 | |
| | Basic | 1.00 | 0.72 (0.52-1.02) | 0.80 (0.57-1.12) | 0.77 (0.55-1.09) | 0.93 (0.67-1.30) | 0.77 |
| | **Full** | **1.00** | **0.68 (0.48-0.95)** | **0.68 (0.48-0.96)** | **0.60 (0.41-0.86)** | **0.67 (0.46-0.97)** | **0.037** |

After Full adjustment, only a high SFA intake was protective, but in just women. But now look at that entire line. Quintiles 2 through 5 all show about the same benefit (all versus quintile 1), and all are statistically significant. What does this imply? If a woman in quintile 1 is eating the mean SFA intake of 12.9% of her calories from SFA, she can significantly reduce her chances of a coronary event (e.g. a heart attack) by adding 2 pats of butter to her diet.

With Basic adjustments of the CE data, statistical significance is reached only for fiber for both men and women. And, it does not reach significance with the Full adjustment. But, look in quintile 4 for women, Full adjustment, fiber did reach statistical significance. This would seem to imply that a woman in quintile 5 for fiber, may want to lower her fiber intake.

The authors go on to note, "Among women, there was a protective association between fiber and CE after exclusion of low and high energy reporters. *There was also a protective association between saturated fat intake and CE among women; t**his association, however, was dependent on fiber being present in the statistical model**. Indeed, we discovered statistical interactions between intake of fiber and saturated fat, which also were different between men and women.*"

Now lets turn to more of the comments by the authors in the discussion. Some of their comments refer to analysis/adjustments that were not shown in tables or graphs in the article or supplement. Emphasis is mine, below.

1) "…the lower risk of iCVD associated with a high fiber intake among women was clearly the most consistent and robust in multivariate analyses."

2) "*This illustrates one of the major problems with studies of nutrient intake: the nutrient variables are also, perhaps even primarily, markers of the foods they derive from.*[4] *Foods contain many nutrients and other bioactive substances that interact in complex ways and may therefore differ in their health effects in ways not captured by differences in the content of single nutrients.*"

3) "Like many other studies, our study suffers from relatively high correlations between some nutrients."

4) "Further, one should note that *only 1.2 percent of the present study population actually followed national Swedish recommendations (less than 10 energy percent) on saturated fat intake. **Strictly speaking, the SFA- CVD hypothesis is thus not fully testable in this population.*** On the other hand, fiber intake in Sweden is generally low, compared to other European countries. It is therefore noteworthy that the apparent effects of higher fiber intake are rather strong in the present study."

5) "The fiber-SFA interactions are not easily explained. *We do not know of any experimental evidence giving any clues to potential biological mechanisms that would be involved to produce a protective effect of SFA*, . . . *Further, there was no protective effect of SFA on iCVD risk neither in men, nor in women, when inadequate energy reporters were excluded and fiber was not included in the multivariate model (p for trend = 0.80 in both genders).*"

6) "In addition, the Spearman correlation coefficient between the saturated fat and fiber quintiles was -0.49 in both men and women. Further, ***the fiber-SFA interaction made SFA appear protective against CE in women.***"

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[4] Here is the article they reference (note the title): Jacobs DR, Jr., Tapsell LC (2007) Food, not nutrients, is the fundamental unit in nutrition. Nutr Rev 65: 439–450.

7) "The strengths of this study include the high-quality dietary data, the size of the population-based cohort, the 99.3% complete follow-up, the high-quality case ascertainment and the inclusion of persons with stable dietary habits only, the latter being an advantage few comparable studies have. The importance of good quality confounder data may be appreciated by considering the differences between the results of the basic and the more fully adjusted models. *It may be noted that BMI, smoking, education, alcohol habits, blood pressure and hyperlipidemia were all significantly associated with iCVD risk (data not shown).* ***Weaknesses (in addition to those already mentioned) include the facts that we only had one dietary measurement and no available biomarkers of intake.***"

**MALMO Grading**

1) *Overadjustment with Lipids*. **Not applicable**.
2) *Sufficient Test of SFA Guidelines*. **F**. The lowest quintile of SFA was 13%. And, the authors note that only 1.2% of the population met the Swedish guideline for SFA intake, 10% or less.
3) *Homogeneity.* **F**.
4) *Food/Lifestyle Questionnaire*. **C**. An **A/B** for diligence for the initial process and data gathering. But no follow-up over the mean 13.5 year follow-up. Looking at some online data for Sweden, overall butter consumption fell in the 1990's. I suspect smoking also declined. And, based on the profile of the population at the beginning of the study, it seems likely that many more were put on statins and blood pressure meds during the study period.
5) *Missing Data in the Study.* **C**. As one example, the authors note that trans-fat data was not collected. Another is that they did not do any blood work, e.g. cholesterol and glucose.
6) *Missing Data in the Paper*. **B**. The paper did not present the characteristics by SFA quintile. On the positive side, the 2007 paper did have some of this by Total Fat, and it seems likely that an SFA breakdown would be close.
7) *Confounders*. **D**. This problem was mentioned in the 2012 paper, and noted predominantly in the interaction with fiber and SFA.
8) *Food vs. Nutrients*. **D**. I suspect that this is going to be a problem in almost all the studies. The only reason that I grade this a D and not an F, is that the authors point this out as a problem with their study, and all such comparable macronutrient studies.

The grades for both (2) and (3) alone make the study an inappropriate one for testing the validity of the existing SFA guidelines.

## The Oxford Vegetarian Study

Both the Chowdhury and Siri-Tarino reference the same paper [8]. They graded them identically:

RR (95% CI)
2.77 (1.25 - 6.13)

Thus, this study found a major coronary risk to a high SFA diet.

Although participants were drawn from an overall homogeneous population, namely England and Wales, the way they recruited assured a heterogenous composition. As the authors note, “The study differs from previous prospective studies of diet and IHD in that the volunteers were individuals whose self selected diet resembled, in nutrient content, current dietary recommendations rather than the relatively high saturated fat diet typical of most affluent societies.”

Participant Selection: “Vegetarian participants were recruited through the Vegetarian Society of the United Kingdom and news media. The non-vegetarian controls were their friends and relatives. A semiquantitative food frequency questionnaire was completed and information gathered concerning smoking and exercise habits, social class, weight, and height at the time of recruitment to the study (September 1980 to January 1984, median year of recruitment 1981).” “Subjects under 16 years and those with diagnosed cancer (excluding non-melanoma skin cancer) at entry were excluded from the analyses as were those who failed to provide full information concerning smoking habits, height, weight, and employment category.” Some of the characteristics of the group are in table 1, below:

*Table 1 Number (percentage) of men and women with various lifestyle related characteristics and with pre-existing disease at the time of entry to the study*

| | *Men* | *Women* |
|---|---|---|
| Number of subjects | 4102 | 6700 |
| Median age at entry (years) | 34 | 33 |
| *Diet group* | | |
| Meat eater | 2147 (52.3) | 2751 (41.1) |
| Semi-vegetarian | 387 (9.4) | 962 (14.4) |
| Vegetarian/vegan | 1568 (38.2) | 2987 (44.6) |
| *Smoking habits* | | |
| Never smoked | 1787 (43.6) | 4021 (60.0) |
| Ex-smoker | 1302 (31.7) | 1588 (23.7) |
| Current smoker | | |
| < 10 cigarettes/day | 531 (12.9) | 487 (7.3) |
| ⩾ 10 cigarettes/day | 482 (11.8) | 604 (9.0) |
| *Body mass index (kg/m²)* | | |
| < 20 | 592 (14.4) | 1777 (26.5) |
| 20– | 1560 (38.0) | 2804 (41.9) |
| 22.5– | 1259 (30.7) | 1425 (21.3) |
| ⩾ 25 | 691 (16.8) | 694 (10.4) |
| *Social class* | | |
| I–II | 2190 (53.4) | 3040 (45.4) |
| III–V | 1088 (26.5) | 2017 (30.1) |
| Others | 824 (20.1) | 1643 (24.5) |
| *Pre-existing disease** | | |
| No | 3832 (93.4) | 6148 (91.8) |
| Yes | 270 (6.6) | 552 (8.2) |

* Angina, heart disease, hypertension, diabetes or stroke.

"Vegetarianism was defined as never eating fish or meat or foods derived from animal products other than dairy foods and eggs. Individuals who ate meat occasionally but less than once a week or who ate fish but not meat were described as semi-vegetarians."

The distribution of intakes was in tertiles (thirds). The lowest intake was regarded as the reference group. Table 2 below looks at the tertiles for the intake of fiber, animal fat, animal saturated fat, and cholesterol:

*Table 2 Tertiles of the distribution of intake of total fat, saturated fat, and dietary cholesterol from animal foods*

| | *Men* | | *Women* | |
|---|---|---|---|---|
| | *Tertiles* | *Median intake for each tertile* | *Tertiles* | *Median intake for each tertile* |
| Total animal fat | 43.6 and<br>61.9 g/day | 25.5<br>52.4<br>74.8 | 37.0 and<br>55.1 g/day | 23.6<br>45.2<br>67.0 |
| Saturated animal fat | 23.9 and<br>34.0 g/day | 14.6<br>27.4<br>41.0 | 20.6 and<br>31.0 g/day | 13.7<br>26.3<br>38.1 |
| Dietary cholesterol | 214.0 and<br>345.1 mg/day | 155.6<br>277.1<br>431.4 | 195.8 and<br>291.1 mg/day | 137.7<br>244.6<br>378.1 |
| Dietary fibre | 22.4 and<br>32.5 g/day | 17.9<br>27.3<br>39.6 | 20.9 and<br>29.1 g/day | 16.5<br>24.7<br>35.0 |

Animal foods include meat, eggs, milk, and cheese. Plant foods, especially oils, nuts and seeds, contain significant amounts of fats, including some saturated fat (but a very low percentage compared to animal foods). And, this paper does not provide this data.

To describe the mortality of the study group as a whole, they calculated standardized mortality ratios (SMRs) for men and women for all major causes of death using national mortality data for England and Wales. "A total of 525 deaths were observed in more than 143,000 person-years at risk; overall mean duration of follow up 13.3 years. SMRs for all cause mortality in the entire cohort were 0.48 (95% CI 0.42 to 0.54) for men, and 0.57 (0.50 to 0.64) for women. SMRs for IHD were 0.44 (0.35 to 0.56) for men, and 0.46 (0.35 to 0.61) for women, and for all malignant neoplasms 0.56 (0.44 to 0.69) and 0.75 (0.63 to 0.89) for men and women, respectively." Thus, as the title of the paper implies, the recruited population were made up of health-conscious individuals. From the paper, "These findings relate to people who are mainly non-smokers, of high social class, and relatively lean. It is not surprising that all cause mortality is about half that expected for the population of England and Wales."

Table 4 presents the adjusted Death Rate ratio for subjects with *no pre-existing disease* for selected dietary factors. Just 5 factors reached statistical significance for Ischemic Heart Disease: total animal fat, saturated animal fat, dietary cholesterol, eggs, and cheese. The figures for saturated animal fat were exactly the ones reported in both Chowdhury and Siri-Tarino meta-analyses. Interestingly, dietary fiber did not reach statistical significance (but it did come close.)

*Table 4 Death rate ratio (95% confidence interval) for selected dietary factors, each adjusted for age, sex, smoking and social class for subjects with no evidence of pre-existing disease at the time of recruitment*

| | *Ischaemic heart disease* | | | *All causes of death* | | |
|---|---|---|---|---|---|---|
| | *No of deaths (64)* | *Death rate ratio* | *Trend* | *No of deaths (392)* | *Death rate ratio* | *Trend* |
| *Diet group* | | | | | | |
| Meat eater | 32 | 100 | | 170 | 100 | |
| Semi-vegetarian | 7 | 108 (47–248) | NS | 45 | 102 (73–143) | NS |
| Vegetarian/vegan | 25 | 83 (48–143) | | 177 | 102 (82–127) | |
| *Meat* | | | | | | |
| None eaten | 29 | 100 | | 209 | 100 | |
| Less than daily | 18 | 153 (84–279) | NS | 83 | 102 (79–133) | NS |
| Daily | 17 | 118 (64–218) | | 94 | 101 (79–130) | |
| *Eggs (per week)* | | | | | | |
| < 1 | 8 | 100 | | 89 | 100 | |
| 1–5 | 33 | 128 (59–279) | p < 0.01 | 203 | 74 (58–96)* | NS |
| 6+ | 23 | 268 (119–602)* | | 89 | 92 (68–123) | |
| *Milk (pints per day)* | | | | | | |
| Less than half | 18 | 100 | | 138 | 100 | |
| Half | 21 | 76 (40–143) | NS | 139 | 70 (55–88)** | NS |
| More than half | 24 | 150 (81–278) | | 106 | 87 (68–113) | |
| *Cheese (excluding cottage)* | | | | | | |
| < once per week | 5 | 100 | | 55 | 100 | |
| 1–4 times per week | 16 | 123 (45–335) | p < 0.01 | 120 | 86 (62–118) | NS |
| ⩾ 5 times per week | 43 | 247 (97–626) | | 208 | 102 (76–137) | |
| *Total animal fat* | | | | | | |
| 1st tertile | 9 | 100 | | 116 | 100 | |
| 2nd tertile | 15 | 179 (78–409) | p < 0.01 | 95 | 85 (65–112) | NS |
| 3rd tertile | 21 | 329 (150–721)** | | 99 | 105 (80–138) | |
| *Saturated animal fat* | | | | | | |
| 1st tertile | 9 | 100 | | 111 | 100 | |
| 2nd tertile | 17 | 211 (94–474) | p < 0.01 | 100 | 95 (73–125) | NS |
| 3rd tertile | 19 | 277 (125–613)* | | 99 | 106 (80–139) | |
| *Dietary cholesterol* | | | | | | |
| 1st tertile | 8 | 100 | | 116 | 100 | |
| 2nd tertile | 15 | 181 (77–429) | p < 0.001 | 90 | 74 (56–97)* | NS |
| 3rd tertile | 22 | 353 (157–796)** | | 104 | 102 (78–134) | |
| *Fish* | | | | | | |
| Never eaten | 26 | 100 | | 184 | 100 | |
| < once per week | 13 | 121 (62–238) | NS | 82 | 97 (74–126) | NS |
| ⩾ once per week | 25 | 123 (70–217) | | 123 | 96 (76–121) | |
| *Green vegetables* | | | | | | |
| < once per week | 4 | 100 | | 39 | 100 | |
| 1–4 times per week | 29 | 119 (42–340) | NS | 171 | 74 (52–105) | NS |
| ⩾ 5 times per week | 30 | 134 (47–384) | | 176 | 89 (63–126) | |
| *Carrots* | | | | | | |
| < once per week | 14 | 100 | | 60 | 100 | |
| 1–4 times per week | 29 | 57 (30–108) | NS | 226 | 107 (80–142) | NS |
| ⩾ 5 times per week | 18 | 76 (37–157) | | 96 | 99 (72–138) | |
| *Fresh or dried fruit* | | | | | | |
| < 5 times per week | 17 | 100 | | 106 | 100 | |
| 5–9 times per week | 29 | 107 (58–196) | NS | 151 | 89 (69–114) | NS |
| ⩾ 10 times per week | 17 | 89 (44–180) | | 128 | 97 (74–127) | |
| *Nuts* | | | | | | |
| < once per week | 30 | 100 | | 188 | 100 | |
| 1–4 times per week | 21 | 119 (68–210) | NS | 123 | 99 (79–125) | NS |
| ⩾ 5 times per week | 13 | 87 (45–168) | | 72 | 77 (58–101) | |
| *Dietary fibre* | | | | | | |
| 1st tertile | 7 | 100 | | 82 | 100 | |
| 2nd tertile | 14 | 192 (77–479) | NS | 88 | 101 (75–137) | NS |
| 3rd tertile | 17 | 225 (92–553) | | 93 | 98 (73–133) | |
| *Alcohol* | | | | | | |
| 0 or < 1 unit per week | 24 | 100 | | 158 | 100 | |
| 1–7 units per week | 25 | 131 (74–234) | NS | 122 | 88 (69–113) | NS |
| > 7 units per week | 15 | 102 (51–203) | | 108 | 104 (79–135) | |

*2p < 0.05; **2p < 0.01.
Numbers of deaths may not total 64 or 392 because values of the dietary factors were unknown for some subjects.

Death ratios were also computed for all subjects (i.e. including ones with pre-existing disease), but not included in the paper. “The trends for all subjects were similar to those presented for the group with no prior disease except that IHD mortality was significantly lower in the vegetarian/vegan group than in the meat eaters (death rate ratio 63; 95% CI 42–93).”
Some interesting extracts from the paper in the discussion section w.r.t. IHD:

1) “These results may therefore indicate which dietary factors are determinants of IHD mortality when populations comply with current dietary guidelines that emphasise the need to reduce the intake of saturated fatty acids and increase the intake of foods rich in dietary fibre.”
2) “The findings support the hypothesis that the nature and quantity of dietary fat and cholesterol are key determinants of IHD mortality. A gradient of risk is apparent with increasing intake of total animal fat, saturated fat, and dietary cholesterol as well as some of the major food sources of these nutrients.”
3) “Other recent studies have suggested that the deleterious effect of saturated fat and cholesterol is less important than the protective effects of dietary fibre and linolenic acid. However, in the present study there was a wide range of dietary fat intakes, resulting from the inclusion of vegans, vegetarians, semi-vegetarians, and meat eaters. ***Most other cohort studies have involved more homogeneous populations with a relatively narrow range of fat intakes. It is impossible to identify even strong disease associations if there is little variation in a dietary variable in the study population.*** Conversely, the absence of an effect of dietary fibre in our data could be due to the fact that our cohort had average intakes above that observed in other studies and that a gradient of risk is no longer apparent with intakes in this higher range.”
4) “The semiquantitative food frequency questionnaire was a relatively crude instrument, having been designed before the development of the more sophisticated food frequency questionnaires currently employed in large scale epidemiological studies. However, we are confident of its ability to provide reasonable estimates of dietary fat, cholesterol, and fibre. Special attention was given to the food sources of these nutrients as they were of particular interest when the study was planned.”
5) “We were unable to detect a protective effect of either fish intake or alcohol, which have been reported in several other studies. The most likely explanation is a relatively narrow spread of intakes.”
6) “We were not able to examine the potentially protective effects of antioxidant nutrients or of long chain unsaturated fatty acids. When the study started there were no clear hypotheses concerning effects of these nutrients so the questionnaire did not include details of relevant foods.”

Oxford Vegetarian Grading

1) *Overadjustment with Lipids*. **Not applicable**.
2) *Sufficient Test of SFA Guidelines*. **B**. The total kcal intake per day was not calculated. But we can assume typical averages to estimate percentages. Also, SFA intake was only provided for animal sources. But the guidelines advise cutting SFA,

by reducing animal sources - not from plant sources, which are small in comparison. The 1st tertile of animal saturated fat intake for men and women respectively are: 14.6g and 13.6g. Assuming a daily energy intake of 2500 for men and 2000 for women[5], the resulting percentages are: 5.3% and 6.1%. And the range of saturated fat over the 3 tertiles is significant - 2.8 for tertile-3/tertile-1 means.

3) *Homogeneity.* **B.** I didn't give it an **A** because the meat-eaters were a healthier group than average from the UK.
4) *Food/Lifestyle Questionnaire*. **D**. No follow-up over the mean 13.3 year follow-up. And, as noted in the paper, the semi-quantitative FFQ was a relatively crude instrument.
5) *Missing Data in the Study.* **C**. As one example, No trans-fat data. Another is that they did not do any blood work, e.g. cholesterol and glucose.
6) *Missing Data in the Paper*. **C**. The paper did not present the characteristics by SFA tertile. Also, the paper only presented animal sources for fat. And, no data on MUFA and PUFA was presented.
7) *Confounders*. **C**. Since the characteristics per SFA tertile were not presented, it is difficult to say if there may have been confounders or not. However, this was a healthy study group (e.g. w.r.t. BMI, smoking, alcohol). So, confounders are less likely.
8) *Food vs. Nutrients*. **B**. They did identify and present data for the foods highest in saturated fat (e.g. Meat, eggs, milk, cheese). But it would have been useful to see many other foods or categories, e.g. poultry, legumes, whole grains, processed foods. To calculate fat and cholesterol, they must have this data. So, it is likely they didn't present it, because it wasn't significant.

Based on the above grading, I think this is a worthwhile study to include in the meta-analysis.

**Nurses Health Study (NHS)**

This study is referenced by both Chowdhury and Siri-Tarino. They both reference the same 2005 paper [8]. But there is also a 1997 paper on this study that has other useful additional information [9]. Here are the SFA scores from Chowdhury and Siri-Tarino:

| | RR (95% CI) |
|---|---|
| Chowdhury | 0.98 (0.79, 1.21) |
| Siri-Tarino | 0.97 (0.74, 1.27) |

I don't have time to present the details of the NHS papers to provide a detailed analysis. That will be in the revision.

One aspect of the dietary guidelines is the recommendation on how to reduce SFA, i.e. to replace it with plant sources of polyunsaturated fat (PUFA). And, here is an excerpt from the 1997 NHS article:

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[5] From UK's NHS, http://www.nhs.uk/chq/pages/1126.aspx?categoryid=51

*"Replacing 5 percent of energy from saturated fat with energy from unsaturated fats was associated with a 42 percent lower risk (95 percent confidence interval, 23 to 56 percent; P=0.001)."*

Shortly, after the Chowdhury article was available on the internet, some of the same authors of the NHS papers (e.g. Drs. Willet and Stamfer from the Harvard School of Public Health) posted a comment. Here is a related excerpt:

"Further, the authors did not mention a pooled analysis [10] of the primary data from prospective studies, in which a significant inverse association between intake of polyunsaturated fat (the large majority being the N-6 linoleic acid) and risk of CHD was found. Also, in this analysis, substitution of polyunsaturated fat for saturated fat was associated with lower risk of CHD. Chowdhury et al. also failed to point out that most of the monounsaturated fat consumed in their studies was from red meat and dairy sources, and the findings do not necessarily apply to consumption in the form of nuts, olive oil, and other plant sources. Thus, the conclusions of Chowdhury et al. regarding the type of fat being unimportant are seriously misleading and should be disregarded."

Summary

Based on my initial analysis, Chowdhury has not chosen "good" studies to back up his claim, and few are applicable to Chowdhury's claim w.r.t. the dietary guideline for Saturated Fat intake. I will be improving and expanding my analysis to cover all 20 of the studies that Chowdhury cites. I expect that this will take a few weeks due to other Obligations.

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## Featured Recipes

Caroline Graettinger, PhD of Garden Dish is on a quest to vanquish her family history of heart-disease, diabetes, and dementia. After a series of family health scares, culminating in her own in 2003, Caroline embarked on a new plan for life – and health – a plant-healthy diet! We are pleased that Caroline has agreed to share some of her favorite recipes with us.

**Chickpea Pot Pie Lasagna**

This is pot pie meets lasagna, and is good "company" food. It looks and tastes like you worked on it all day, but with no-boil, lasagna noodles, it goes together easily.

Servings: 4

Ingredients

Chickpea Broth
water - 6 cups
cooked chickpeas - 1 cup

Pot Pie Filling
celery, chopped - 2 stalks
onion, chopped - 1/2 medium
carrot, chopped - 1 medium
white button mushrooms, sliced - 1 8 oz pkg
cooked chickpeas - 2 cups
red potatoes, chopped - 3 medium
peas, fresh or frozen - 1 cup
dried thyme - 1 tsp
dried sage - 1 tsp
white wine - 1/4 cup
soy milk, plain and unsweetened - 1/2 cup
cornstarch - 1 Tbs

Lasagna noodles
whole wheat, no-boil (oven ready) lasagna noodles - 9

Instructions
Preheat the oven to 350 °F.

In a blender, puree the chickpea broth ingredients. Set aside.
Add the celery, onion, carrot, and mushrooms to a large pot over medium heat. Cover and cook until tender, about 5 minutes.

Stir in the remaining filling ingredients except the cornstarch. Dissolve the cornstarch in 1 Tbs of cold water and stir into the chickpea mixture. Add 1 1/2 cups of the chickpea broth (stir well before using), cover, and cook over medium heat for 30 minutes, or until the potatoes are tender and the filling is hot and thick. If you'd like your mixture to be thicker, use an immersion blender for a few seconds to puree some of the filling, or blend about two cups of the mixture in a blender and stir it back into the pot. Salt to taste.

To create the lasagna layers, spread 1/4 cup of the filling on the bottom of a 9"x9" baking dish. Lay down 3 of the lasagna noodles, overlapping slightly, and spread 1/3 of the filling on top. Repeat with the other layers, ending with the chickpea filling on top. Cover tightly with parchment paper and aluminum foil. Bake at 350 °F for 15 minutes. Remove the aluminum and parchment paper, and bake another 15 minutes to lightly brown the top.
Remove from the oven and allow to cool about 5 minutes before serving.

Nutrition Information
Nutrition (per serving): 454 calories, 70% calories from carbohydrates, 18% calories from protein, 9% calories from fat, 16.6g fiber.

**Quick Stuffed Portobello Mushrooms**

Servings: 4

Ingredients
portobello mushroom caps - 8 large
frozen brown & wild rice with corn, carrots, and peas - 3 10 oz pkgs
tomato sauce - 2 cups
pizza or Italian seasoning mix - 1 Tbs

Instructions
Preheat the oven to 375 °F. Line a baking sheet with parchment paper.

Gently wipe the mushroom caps with a paper towel to remove any dirt. Place the caps, gills side up, on the baking sheet.

Cook the rice and veggie blend according to the package directions. Scoop 1/2 cup of the rice blend onto each mushroom cap.

Spread 1/2 cup of the tomato sauce on top of the rice, and sprinkle with the pizza seasoning.
Bake in the preheated oven for 30 minutes.

Nutrition Information
Nutrition (per serving): 421 calories, 79% calories from carbohydrates, 14% calories from protein, 7% calories from fat, 12g fiber.

**Rustic Gnocchi**

You don't need to peel potatoes or strong-arm them through a potato ricer to make gnocchi that's more tender than any you can buy at the grocery store. Little bits of potato in the pasta are part of its rustic charm. Appreciate the zen that is rustic gnocchi.

Servings: 5

Ingredients
red skin potatoes, skins left on - 25 oz
soy milk, plain and unsweetened - 1/4 cup
whole wheat flour - 4 cups
oil-free pasta sauce - 1 26 oz jar

Instructions
Prick the skins of the potatoes with a fork and place on a microwave-safe plate. Microwave on High for 10-15 minutes, times will vary depending on the power of your microwave and the size of your potatoes. Check occasionally to see if the potatoes are tender by inserting a sharp knife into the center of each potato. Smaller potatoes will cook faster so you can remove them once they are tender and continue cooking the larger potatoes.

When all the potatoes are done, cut them into bite-size pieces - this will make them easier to mash. Using your electric mixer, beat the potatoes on medium speed for about 1 minute, pour in the soy milk, then continue beating until creamy, about 2 minutes. Small bits of potato and skins will remain intact, and that's ok.

While mixing on medium-low speed, gradually add the whole wheat flour until well incorporated.

Start a large pot of water to boil. On a work surface lightly dusted with flour, roll out half the dough to about 1/4" thick. Using a sharp knife or pizza wheel, cut the dough into triangles of desired size. Drop them into the boiling water and wait until they float to the surface before removing them to a strainer to drain. Repeat with the remaining dough.

Serve topped with your favorite sauce.

Nutrition Information
Nutrition (per serving): 514 calories, 84% calories from carbohydrates, 13% calories from protein, 3% calories from fat, 17.3g fiber.

**Thick and Creamy Taco Soup**

Is this a soup, a stew, or a chowder? It's thick and creamy for sure, and with hearty, stick-to-your ribs flavor.

Servings: 5

Ingredients
frozen blend of corn, black beans, chopped onions, and chopped peppers (southwest blend) - 1 12 oz pkg
pinto beans, drained and rinsed - 1 15 oz can
fat-free refried beans - 1 cup
tomato sauce - 1 15 oz can

taco seasoning (adjust to your taste) - 1-2 tsp
water - 6 cups
whole wheat orzo pasta - 116 oz pkg

Instructions
Dry saute the onion-pepper blend in a soup pot over medium heat until tender, about 3-5 minutes. If needed, add a tablespoon or two of water to prevent sticking.

Stir in the rest of the ingredients, cover, and cook until the pasta is just tender, about 10-15 minutes, Salt to taste.

Nutrition Information
Nutrition (per serving): 532 calories, 78% calories from carbohydrates, 15% calories from protein, 7% calories from fat, 11.4g fiber.