Ten Cases of Severe, Mostly Rheumatoid, Arthritis Cured by the McDougall Diet

The following are typical examples of the results achieved by people with various forms of inflammatory arthritis who have followed my dietary recommendations strictly.* You can read the short quotes beside the pictures of these people for a glimpse at their lives before the McDougall Diet. There is little need for individual comments about life "after McDougall" because the outcomes are all so similar: complete relief of their inflammatory arthritis. Clicking on the arrows over their pictures leads to comprehensive stories about these real people.

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- Fresca Bean Salad
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Evaluation of Chowdhury Meta-Analysis on the Association of Fatty Acids with Coronary Risk, Part 3

This is part 2 of my review of the Chowdhury meta-analysis study [1] that was published online at the Annals of Internal Medicine on March 18, 2014. The study effectively said that the current guidelines on saturated fatty acid (SFA) intake (<10% of calories from SFA) were not justified by the evidence and should be reconsidered. That led Mark Bittman, the NY Times Magazine's lead food columnist to write, Butter is Back, and said, "Julia Child, goddess of fat, is beaming somewhere. Butter is back, and when you're looking for a few chunks of pork for a stew, you can resume searching for the best pieces — the ones with the most fat." PAGE 14

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Amy Fewel
Rheumatoid Arthritis

"I've had some ups and downs with my health, but when I woke up with such severe pain in my hands that I couldn't lift my son out of his crib in the mornings, it was terrifying. All of a sudden my feet and knees were aching all the time. There were many days when it was difficult for me to get out of bed because I was so fatigued. I had to quit my job because my joints were so inflamed that it was difficult and exhausting to move. For the next nine months, I spent most of my time on the couch due to the pain and fatigue caused by this disease."

Burgess Laughlin
Arthritis, Bursitis, Dermatitis, Iritis, Tendonitis

"When I was 30, one eye became so bloodshot and painful that I nearly lost sight in it. Similar eye episodes (iritis) appeared about 10 more times in the following 28 years. At 45, near the height of my physical fitness activities (ranging from martial arts to running), I began having painful tendons. The problem spread from my hips to my legs and arms. I had to stop running, and sometimes I could not even walk. At one point, when the arthritis spread to other joints, I became so crippled that I began shopping on the Internet for a wheelchair."

Debbie Cockrell
Rheumatoid Arthritis

"My rheumatoid arthritis began in 2008 with pain in my knees, which soon traveled to my elbows and hands. Each day it got a little harder to walk. I felt like the Tin Man from The Wizard of Oz, rusting in place. I could not roll over in bed and, I would wake up crying in terrible joint pain. I could not button clothes or tie my shoes. I was convinced that I was dying. I felt like I had PMS most days, especially within 48 hours after my methotrexate dosage. I would crash so hard and feel so depressed."

Jackie Swoboda
Non-specific Inflammatory Arthritis

"It started gradually then it got to be a 24-hour a day thing where I would fight to see how far I could get without eating a handful of Advil. I had spasms and pain in my back, neck, shoulders, and hips. I was in so much pain I could not sleep. Then I could not go to work because I was so tired. I started getting depressed and it just sort of spiraled from there. I actually considered killing myself."

Juliea Baker
Juvenile Rheumatoid Arthritis

"It started when I was 15 years old with pain in my jaw. I couldn't easily open my mouth to chew. When I was 16 ½ we realized something was very wrong: my knuckles were very swollen and I couldn't make a fist without intense pain; even shaking hands was painful. My right foot was so swollen I couldn't wear a shoe comfortably, and I walked with a limp. I actually told my mom that I thought my foot was broken because it hurt so badly whenever I walked. I was difficult for me to get from class to class because I was limping. I started becoming depressed when I was told there was no cure."

Leslie Crane
Rheumatoid Arthritis

"My hands throbbed with such intense pain that my husband had to stop holding them. In bed, I pulled the blanket up with my teeth. I kept pliers at my desk to pinch the ink cartridge in order to remove it from my printer. My hands wouldn't close into a fist. My hips and shoulders ached so much that there were nights that I could not sleep. My knees were ruining my life. The pain was disabling. I was crippled. My husband had to pull me out of a chair. When he was not around, I chose chairs with arms so that I could push myself up and out with my elbows."

Meredith Fishman
Rheumatoid Arthritis

"In December of 2008, the day after I qualified for the prestigious Boston Marathon (I had been training 3 times a day for almost a year) I was struck down with painful arthritis. Even though I was forced to take many months off from running, I still kept getting "injured." A short time later, I developed inflammation in my jaw, my right hand, and elbow. I practically lived in my orthopedist's office, getting one cortisone shot after another every few weeks in different joints and living on the anti-inflammatory medication for almost a year."

Nicole O'Shea
Psoriatic Arthritis

"As I entered my late thirties, I was struck with crippling psoriatic arthritis. I came to the point where I had unrelenting symptoms with fluctuating levels of pain in both knees and pain and stiffness in many of my other joints and pain in my muscles. At times I could not walk, dress, or bathe myself. I found myself unable to move, and even breathe, without causing jarring, dizzying pain to shoot through my joints. It took about 8 months to get a diagnosis. Having a name for my disease was minor relief, which did not offset the bad news that psoriatic arthritis was a disabling illness with no cure."

Paula Calle
Rheumatoid Arthritis

"It started in one finger and then spread all around my body to my knees, elbows, and ankles. The things I loved to do the most, I could not do. The pain was so terrible that I could not ride my bike. I was not able to open my bottle of shampoo to wash my hair or even open my medication. I was feeling like an old lady. My husband and son were very supportive but they do not feel my pain. Only I know how much pain I have. After using steroids for a long time I was put on methotrexate with bad side effects. I was told I would have to live with this condition for my whole life."

Phyllis Heaphy
Rheumatoid Arthritis

"I began experiencing "traveling" inflammation to various parts of my body: one week it would be in one or two fingers, the next week in one of my wrists, a month later in my shoulder. The turning point was when I spent two days unable to walk. The pain was so intense in the balls of my feet that the slightest pressure was unbearable. I cried as I tried to make my way across the room. The rheumatologist spent almost an hour examining me before giving her diagnosis of mild-to-moderate RA. It sounded like a death sentence"

*These are not simply "best case scenarios." Patients with inflammatory arthritis, not osteoarthritis, should expect similar outcomes. (There are exceptions.) Plus, residual, post-inflammatory changes, including permanent structural damages to the joints, will remain. Otherwise active disease is stopped.

Autoimmune diseases are conditions in which the body produces antibodies that attack its own tissues. "The body attacks itself" in every imaginable place from the top of the scalp to deep inside the bowels. No organ—not the brain, not the liver, not even the heart—is beyond the reach of attack. Assaults on the joints are common, and the majority of these severe inflammatory arthritis conditions are labeled as "rheumatoid arthritis." Even when one or a few body parts are predominantly involved, such as the hands and/or knees, the disease is at the same time affecting the rest of the body (it is said to be systemic) and can be deadly for some people.

COMMON AUTOIMMUNE DISEASES	
Alopecia (hair loss)	Pernicious anemia
Ankylosing spondylitis	Polymyositis
Crohn's disease	Psoriasis
Dermatomyositis	Psoriatic arthritis
Diabetes (type 1)	Relapsing polychondritis
Glomerulonephritis (kidney)	Rheumatoid arthritis
Juvenile rheumatoid arthritis	Scleroderma
Lupus	Thyroiditis (resulting in hypothyroidism)
Multiple sclerosis	Ulcerative colitis
Myasthenia gravis	Uveitis (iritis)
Nonspecific inflammatory arthritis	Vitiligo

Autoimmune disease is one of the ten leading causes of death among women younger than 65 years of age. Interestingly, and without any reasonable explanation, approximately 80% of the cases of autoimmune disease are found in women. Over-the-counter anti-inflammatory medications, such as aspirin and Advil, are mainstays of therapy for relieving pain and stiffness. As the severity progresses, rheumatologists prescribe powerful medications, such as methotrexate and newly marketed biologic agents, to inhibit the immune system's functions. Their benefits are primarily limited to relieving symptoms of the disease (like pain). These agents can have deadly side effects and unbearable financial costs.

Dr. McDougall's Experience with Diet and Inflammatory Arthritis

Over the past 36 years I have learned many valuable lessons about treating inflammatory arthritis. The pain and disability of this disease is often sufficient to cause people to seek help from anywhere and at any price. When their respectable medical doctors with their powerful drugs fail, patients look to alternative medicine and the supplement industry. Along the way most patients ask the experts: "Does diet have anything to do with my arthritis?" With very few exceptions medical doctors and registered dietitians emphatically answer, "NO." In the face of unified resistance, and a past personal medical history littered with

multiple failed attempts for a cure, the patient may become sufficiently motivated to take what seems to be the most drastic step of all, which is to radically change his or her diet.

My 36-years of seeing patients, along with many scientific papers, has lead me to the conclusion that a healthy low fat, vegan diet (the McDougall Diet, for example) dramatically improves and in most cases cures inflammatory arthritis. The diet consumed cannot simply be "vegan" (without animal foods). Meals must be based around unrefined starches with the addition of vegetables and fruits. Vegetable oils (olive, corn, canola, flaxseed, etc.) are strictly forbidden.

When patients first start, I usually recommend that they follow the basic McDougall Diet without wheat or soy foods. (This request is made only for general health reasons because it eliminates refined flours found in breads and cereals, and processed soybeans, including fake meats and cheeses.) A gluten-free diet (no wheat, barley, or rye) is a next reasonable step for anyone not achieving rapid improvements from the basic McDougall Diet. A few people will have to follow the stricter McDougall Elimination Diet (see below). A temporary water-only fast maintained for a few days is the ultimate dietary restriction and is a final step I have resorted to for a few difficult patients.

Benefits for arthritis usually begin to appear within four to seven days of strict adherence to the new diet regime. This is the amount of time required for the bowels to eliminate all of the foods previously consumed. After the remnants of unhealthy foods are emptied from the intestines, the animal-food-derived protein antigens slowly clear out of the bloodstream over the next few days. Products of inflammation, such as the antibodies attacking the body's own tissues, may persist for weeks. Complete resolution of active disease may take as long as four months; only then can the full benefits be appreciated from following the new diet therapy.

Unfortunately, small indiscretions often result in big penalties. That error could be a tiny bite of cheese or a bowlful of oily vegetables. One of my patients had been free of all of her arthritis pain and swelling for four months when she ventured out to a Chinese restaurant. The food served may have been vegan, but the peapods and sprouts were drowning in peanut oil and swimming with questionable ingredients. The next day she was in my office with both knees red, hot, and swollen.

People on medication must keep in contact with their private doctors. As they improve with the new diet regime then their doctors should be recommending, sooner rather than later, reductions and eliminations of medications. Remember, the medications are primarily for symptom relief. The cost of too aggressive reduction of medication is an increase in pain, which can be remedied by restarting the drug regime. Most people, like the ten examples in this article, will be able to stop all medications and live comfortably. The program is essentially cost-free, side effect-free, and risk-free. Of course, patients should consult their healthcare provider before making any changes in their diet or medication, especially if they are ill or on powerful drugs.

THE MCDOUGALL ELIMINATION DIET:

The following foods are allowed without calorie restriction. Portion control (based on a visual estimate) should result in about 80% of the food coming from starches; the remainder will be from vegetables and fruits. Cook all foods thoroughly. Heat breaks down and deactivates proteins and other troublesome components of the food. Boiling and steaming are the healthiest ways to cook.

Starches (all cooked), include:

Brown rice (or white rice)
Sweet potatoes
Winter squash (Acorn, Butternut, Pumpkin, etc.)
Taro (or poi)

Non-starchy green and yellow vegetables (all cooked) include:

Asparagus
Artichoke
Beets
Beet greens
Celery
Chard
Kale
Lettuce
Spinach
String Beans
Summer squash

Almost all other non-starchy yellow, orange, red, green, and purple vegetables are allowed (cooked). Avoid onions, green pepper, cucumbers, and radishes, especially when raw because they can be very troublesome for the stomach, causing indigestion.

Fruits (all cooked) include:

Apricots
Bananas
Berries
Cherries
Papaya
Peaches
Plums
Avoid all citrus fruits, including oranges, grapefruits, tangerines, lemons, limes, etc. and also tomatoes.

Condiments include:

Salt
Sugar

Only common table salt and table sugar are allowed, if not restricted for other health reasons. This means no salad dressings, mustard, lemon juice, vinegar, pepper or other condiments.

Beverages:

Water (sparkling water is OK)

Managing the Elimination Diet:

After one week of being strictly on the new Diet, problems should be ending and the dieter should be feeling much improved. If this is the case, then the dieter can begin adding other foods (those not listed above) back to his or her diet, but only one at a time, in order to determine if any of these cause unpleasant reactions. For testing purposes, each "new" food should be eaten in large amounts three times a day for two days. If the food does not cause a reaction, then the dieter can conclude that this food is not a troublemaker. Most reactions occur within a few hours, but some may not show up for several days. Each food must be tested individually; do not introduce two new foods at once. When there is a reaction to a specific food, the dieter must wait for four to seven days before testing the next item. This interval gives the time required to clear the intestines and to rest the system from that allergy-causing food.

The foods added back during the elimination diet should not be from animal products of any kind or from vegetable oils for general health reasons. No one should follow a diet "more liberal" than the basic McDougall Diet.

Recipes

This month's featured recipes are contributed by Katie Mae, MS of PlantBasedKatie.com.

Along her path, she realized her passion for good health went even deeper when it came to pregnancy and children. In order to best support women before, during and after pregnancy, she was trained as a Post-partum Doula through Natural Resources in San Francisco.

From cooking demos to nutrition presentations to individual coaching, she loves playing with and talking about food. Katie's whole foods cooking style is 100% plant-based, gluten-free, and more importantly, free of sugar, oil and salt. When she's not in the kitchen or talking nutrition, you may find her practicing yoga and meditation, jamming to live music, dancing out in nature or giving into her travel bug.

Sweet Potato Tostadas

3 medium cooked sweet potatoes, mashed
1½ cup cooked black beans (or 1 can drained and rinsed)
2 tablespoons water
½ tablespoon ground cumin
1 teaspoon ground coriander
1 teaspoon garlic granules
½ teaspoon chili powder
1½ cups spinach
6 corn tortillas, oil-free

Preheat oven to 350F. Set freshly cooked and mashed sweet potatoes aside. If the sweet potatoes were cooked previously and are cool, warm them up on the stove top.

In a medium saucepan over medium low heat, add black beans, water cumin, coriander, garlic granules and chili powder. Heat the beans for 5-10 minutes, stirring occasionally.

Lay tortillas in a single layer on a baking tray. Put tortillas in the oven for 3-5 minutes, depending on how soft you want them to be. Remove from oven and lay on a serving plate.

To make a tostada, start with 1 cooked tortilla. First add a thin layer of spinach - about ¼ cup. Then scoop a little of the sweet potatoes onto the spinach. Carefully spread the sweet potatoes across the tortilla. Add about ¼ cup of the black beans on top of the sweet potatoes.

Add your favorite toppings, such as Strawberry Mango Salsa (recipe below) or a delicious guacamole.

Makes 6 tostadas

Fresca Bean Salad

1 can (15 ounces) black beans, drained and rinsed (1½ cups)
1 medium carrot, shredded (about 1 cup)
½ small red onion, minced (about ¼ cup)
1 cup cherry tomatoes, halved
2 tablespoons fresh cilantro, diced
1 avocado, diced
½ lime, juiced
1½ tablespoon garlic granules or powder
1 teaspoon ground cumin
2 generous pinches of cayenne pepper, or to taste

In a large bowl, mix the beans, carrots, onion, tomato cilantro and avocado. Stir in the lime juice and spices. Stir well.

Makes 4 cups

Caramelized Onion & Pepper Quesadillas

¾ cup raw cashews, soaked for 2 hours
½ cup nutritional yeast flakes
1 lime, juiced
½ tablespoon stoneground mustard, no-salt added
¾ cup water
1 yellow onion, sliced thin
1 red bell pepper, sliced thin
1 yellow bell pepper, sliced thin
1½ tablespoons ground cumin
1½ teaspoon chili powder
8 organic 100% corn tortillas, no salt or oil added
2 cups fresh spinach, loosely

packed

Make the cheese sauce: Add the cashews, nutritional yeast, lime, stoneground mustard and water to a blender. Blend until it the sauce is creamy. Set it aside.

Make the onion-pepper filling: Place a sauté pan over medium heat. Add the sliced onion and bell pepper. Stir in the cumin and chili powder. Cover and cook for 5 minutes, stirring occasionally so the veggies don't stick to the bottom of the pan. Then stir in a tablespoon of water and continue cooking uncovered. When the water evaporates stir in another tablespoon of water, continuing to sauté until the onions are caramelized.

Turn the heat to low. Pour the cheese sauce into the onion and peppers. Stir well and then cover with a lid so the mixture doesn't dry out.

Make the first quesadilla: Place a non-stick pan over medium heat. Let it heat for 5 minutes. Then place one of the tortillas into the pan. Set a timer, letting the first side toast for 2 minutes and then flip. Set the timer for another 2 minutes. As you wait, carefully scoop about ¼ of the filling onto the tortilla and spread it evenly, forming a single layer of peppers and onions. Layer ½ cup of spinach across the onions and peppers. Place the second tortilla on top of the spinach.

Once the timer goes off or the bottom side is toasted, use a large spatula to carefully flip the entire quesadilla. Toast the second side of the tortilla for 2-3 minutes.

When the quesadilla is done transfer it to a plate. Repeat this process with the remaining filling to make a total of 4 quesadillas. Note that subsequent quesadillas may require less cooking time because the pan will be hotter. You may want to turn the heat down slightly after the first couple. Slice the quesadillas into triangular pieces and serve with toppings of your choice.

Serves 4

Strawberry Mango Salsa

1 cup strawberries, diced
1 cup mango, diced
2 tablespoons white onion, minced
2 tablespoons jalapeno, seeded and minced
2 tablespoons fresh cilantro, diced
1 lime, juiced

In a medium bowl, combine strawberries, mango, jalapeño,

onion, cilantro and lime juice. Mix well. Serve immediately or chill in refrigerator.

Makes 2¼ cups

Fry-less Refried Beans

1 yellow onion, chopped
2 jalapenos, seeded and chopped
3 cups cooked pinto beans (or 2 cans drained and rinsed)
¾ cup water
½ tablespoon garlic granules

Place a non-stick pan or stainless steel saucepan over low-medium. Add onion and jalapenos. Cover with lid to keep the moisture in the pan. Stir occasionally to prevent sticking. After 5 minutes transfer the onion and jalapeno to a blender.

Add beans and water to the blender. Blend until beans have a creamy consistency.

Transfer the blended bean mixture to a sauce pan. Cook on low-medium heat for 20 minutes, stirring occasionally. Careful not too turn the heat too high because air pockets will form, pop and splash pinto beans. The beans will thicken as they cook – the cooking time will depend on your desired consistency. Serve in tacos or as a side dish.

Makes 3½ cups

Tempeh & Broccoli Rojo

½ small yellow onion, diced
3 cups broccoli florets
1½ cups corn
2½ cups dried chili sauce (separate recipe)
3 ounces tomato paste
8 ounces tempeh, diced
1 tablespoon dried oregano
1 lime, juiced
1 avocado, chopped

Place a medium-size sauté pan or pot over medium heat. Add onion,

broccoli and corn and cover with lid. Cook for 3 minutes, stirring occasionally so the vegetables don't stick to the bottom of the pan.

Add the chili sauce, tempeh, oregano and lime juice. Once the sauce comes to a boil turn heat down to medium-low and remove the lid. Cook for 10 minutes. Remove from heat and stir in avocado. Serve immediately.

Makes 5-6 cups

Dried Chile Hot Sauce

3-6 dried New Mexico chiles
2½ cups water
½ small yellow onion
1 tablespoon garlic granules

Add all ingredients to a high-speed or standard blender. Blend until smooth. Stores in the fridge for up to 2 weeks.

Makes 2½ cups

Evaluation of the Chowdhury Meta-Analysis on the Association of Saturated Fatty Acids with Coronary Risk, Part 3

They "*can't see the forrest for the trees*"[1]

Fred Pollack
May 31, 2014

About Fred

I live with my wife, Iris, in Miami Beach. We are both 66. 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.

This is the concluding chapter (i.e. part 3) of my review of the Chowdhury meta-analysis study [1] that was published online at the Annals of Internal Medicine on March 18, 2014. The study effectively said that the current guidelines on saturated fatty acid (SFA) intake (<10% of calories from SFA) were not justified by the evidence and should be reconsidered. That led Mark Bittman, the NY Times Magazine's lead food columnist to write, Butter is Back, and said, *"Julia Child, goddess of fat, is beaming somewhere. Butter is back, and when you're looking for a few chunks of pork for a stew, you can resume searching for the best pieces — the ones with the most fat."*

From my own extensive reading of the medical/nutritional research, I doubted Chowdhury's conclusion, and thus was compelled to do an in-depth review. And, the only way to do this is to *read and analyze all **20** of the SFA intake studies* that were used in the Chowdhury meta-analysis. I have now completed that analysis, writing up each and every one. The result is a 100+ page document that you can download the PDF, by clicking supplement.

The purpose of this newsletter article is to provide an overall summary of my analysis. Section 1 will provide the big picture (i.e. the forest), including a very brief overview of just 3 of the studies that are illustrative of the big picture view. Section 2 will highlight the common flaws present in almost all of the 20 studies. Section 3 will provide a brief synopsis and grading of each of the 20 studies. And, of course, the last section is the conclusion.

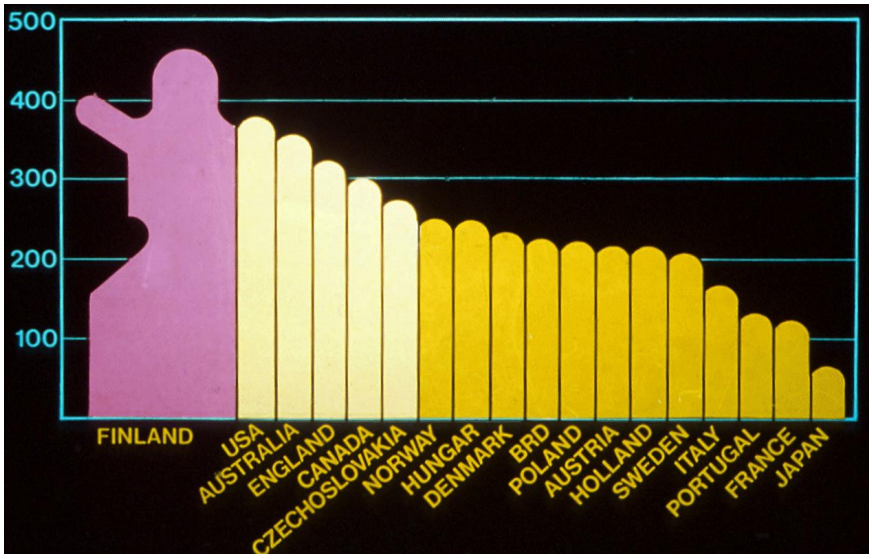
Big Picture

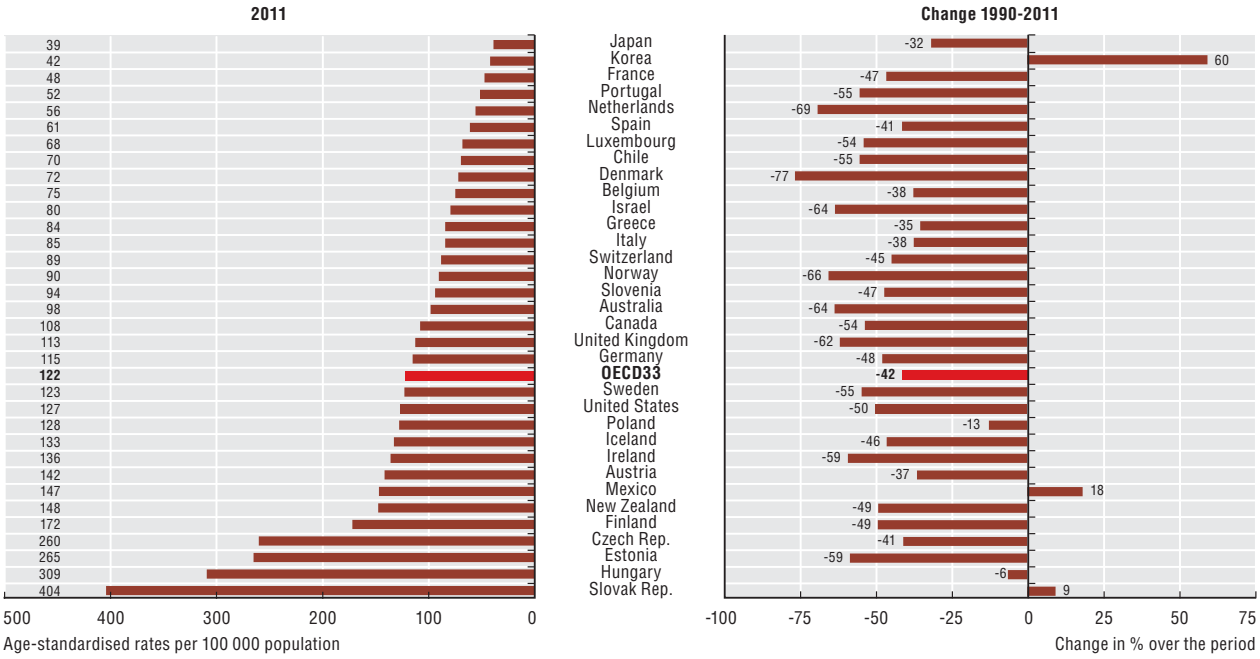
In part 2 (McDougall April Newsletter), I began with a chart from Finland that showed Coronary Heart Disease (CHD) mortality for men in 1973 from various countries. Here is that same chart again (top of the next page). Note that Finland has the highest CHD mortality and Japan has the lowest. But what about the most recent data. Below is the most recent data from OECD 2013 Health at a Glance Report, measuring Ischemic Heart Disease Mortality (IHD)[2] for

[1] Meaning: http://www.englishclub.com/ref/esl/Idioms/American/can_t_see_the_forest_for_the_trees_149.htm.

[2] IHD and CHD are used interchangeably.

CHD Mortality per 100,000 men in 1973





2011, including both men and women. The chart next to it, also shows the changes by country since 1990. Going back to the 2009 OECD Health at a Glance Report, you can see the IHD mortality data for 2006, as well as a graph for rates going back to 1980 for the OECD average plus a few select countries.[3] For the countries in which the 20 studies took place, I wanted to go back to 1970. So, I've included a table from OECD Health at a Glance from 2003 for just these countries.[4]

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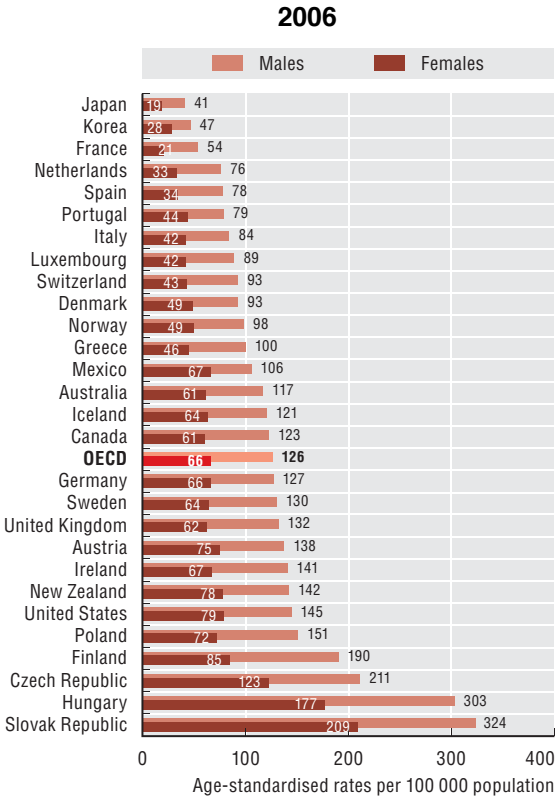
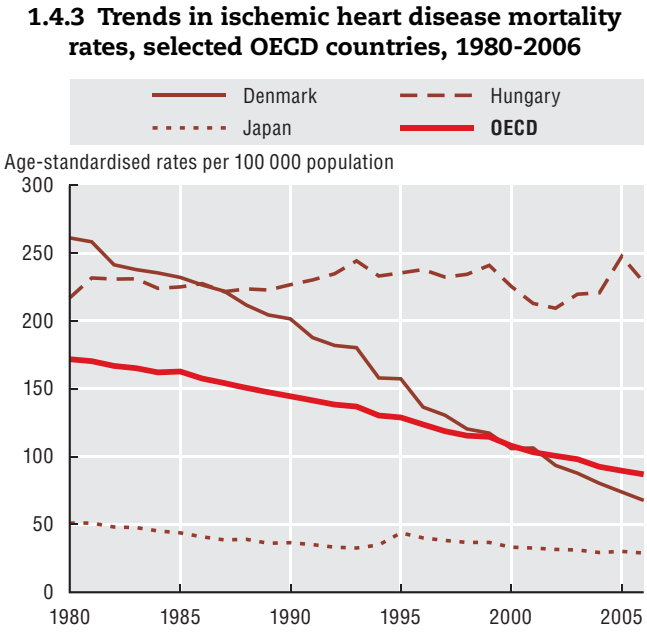
[3] Note that the graph on the right is not quite comparable to the table on the left. The graph is "age-standardised to the 1980 OECD population."

[4] From table 1.15 (page 98 of the PDF).





IHD Mortality per 100,000

standardized to the OECD standard population (1980)
Finland and Japan 1999 data is actually 2000 data.

Men	1970	1980	1990	1999	Women	1970	1980	1990	1999
Canada	412	322	214	164		218	159	108	81
Denmark	371	366	282	172		200	180	141	83
Finland	451	411	344	244		188	169	155	115
Greece	92	115	129	115		45	44	60	51
Japan	78	68	49	51		46	40	28	26
Sweden	364	388	261	182		209	188	116	83
United Kingdom	373	367	295	207		171	162	142	99
United States	481	330	228	194		266	169	122	110

The two key points in all this data is: (1) The vast difference in IHD mortality rates in countries; and, (2) the significant decrease in IHD mortality since 1970. Right now, I want to focus on the first point.

In the OECD countries there are 3 dietary patterns that are often described: (1) Northern European (e.g. Finland, Sweden, UK, USA) - high in animal products, and low in fruits, vegetables, and legumes; (2) Mediterranean (e.g. Greece, Italy, France, Spain) - lower in animal products and higher fruits, vegetables, and legumes; and, (3) Asian (e.g. Japan, Korea, China) - much lower in animals, higher in legumes, and higher in grains (i.e. rice). W.r.t. saturated fat intake, it is highest in the Northern-European style and lowest in the Asian.

18 of the 20 studies in the Chowdhury meta-analysis on SFA-intake involved just a single country. The other 2 involved 2 countries, but with comparable diet patterns. 19 of the 20 involved a homogenous study population, i.e. eating effectively the same diet. In other words, there is a relatively small variation in SFA intake in each of these 19 studies. In addition in 18 of the 19 studies, dietary input is only assessed at the beginning of the study, and the assumption is made that the subjects do not change their diets over the study period, which is, in most cases, over 10 years. And, the assessment of an individual's diet at the beginning of these studies is subject to significant human error in judgement.

Thus, given the homogenous population in 19 studies, it is not surprising to find relatively little effect on diet in each of these studies. Two types of a meta-analysis could be envisioned:

1. **Combining study populations**. If all the studies were constructed in the same manner (e.g. same food frequency questionnaire, same lifestyle parameter input, and same output - e.g. CHD mortality), then all the subjects could be combined into one super-study. This would assure a very large range of SFA-intake (from about 5% to 30% of SFA-intake as percent of total energy consumed).
2. **Combining Statistics**. If the studies are totally different, as is the case with these 20 studies, it is not possible to do (1). Instead you just combine the statistical outcomes.

I'll illustrate the difference in these 2 approaches by an *extreme* example. Suppose we have 2 studies to measure the effect of increasing altitude w.r.t. mortality. Both studies divide their study populations into quintiles (fifths). Study 1 uses altitudes from 2,000 to 10,000 feet in 2,000 ft increments. Study 2 uses altitudes 30,000 to 42,000 ft also in 3,000 ft increments. Each study, by itself, shows no effect from increased altitude (i.e. in study 1, all lived[5], and in study 2, all died). Thus, each study reported that there was no statistically significant difference in outcomes between quintiles 5 and 1 (study 1: 10,000 vs 2,000; study 2: 42,000 vs 30,000). If we simply *combine statistics* from these 2 studies, we conclude that there is no effect of increasing altitude on mortality.

At this point, you should be thinking, "Surely, Fred, the 19 studies and the Chowdhury analysis could not be this bad or even close. I'll show you the data, and let you be the judge. In the Japan study (JACC), the mean intake of SFA was 14.4 g with a standard deviation (SD) of ~3 g. Whereas in the Finnish KIHD study, it was 55 g with an SD of 12 g. Even after adjustment for SFA-intake as % of Energy intake, quintile 1 of the KIHD study (i.e. mean of lowest fifth of

[5] Actually, 5% of quintile 5 (10,000 ft) died, but after adjustment for age, lung function, BMI, and sense-of-humor, this was no longer statistically significant.

SFA-intake) would still be higher than that of the JACC study's quintile 5 (i.e. mean of highest fifth of SFA-intake).

Both the Japanese study and the Finnish KIHD study reported no harm of increased SFA intake. Here are the specific numbers reported by Chowdhury in his meta-analysis for both of these studies, plus the mortality rate for men from IHD in 1990 and 1999 (from the table of OECD data)[6]:

	RR	95% CI	1990	1999
JACC (Japan)	0.99	(0.77,1.28)	49	51
KIHD (Finland)	0.92	(0.74,1.14)	344	244

An RR (Relative Risk) of >1.00 indicates increased risk of IHD mortality with increased SFA intake. <1.00 indicates benefit. But to reach statistically significance, the confidence interval needs to be above 1.00 for harm, or below 1.00 for benefit. Thus, both Japanese and Finish studies indicated a very slight benefit to increased SFA-intake, but this did not reach statistical significance.

But now look at the difference in IHD mortality rates (per 100,000 for men) for 1990 and 1999 (the most applicable dates for these 2 studies - on average about a 6X difference). And, as I noted above, the Finnish/KIHD SFA-intake per day for men (in grams) was about ~4X that of Japanese/JACC men. After adjustment for total energy intake, this difference was about 2.5X.

Thus, from looking at the homogenous studies (i.e. 19 of the 20 in the Chowdhury meta-analysis), it is very difficult to conclude anything about diet that might explain the huge IHD mortality rate differences, whether it be SFA-intake, or some other nutrient or lifestyle variable.

And, there are a lot more problems with the 20 studies than just the homogenous aspect, and I'll get to those soon. But first, what about that 1 study that was not homogenous?

The non-homogenous one was the Oxford-Vegetarian study that I described in part 1 (in McDougall March 2014 newsletter). I'll briefly describe it here just to complete this picture.[7]

Using the above extreme analogy, this one study used altitudes in increments of 7,000 ft, beginning at 7,000 ft, and thus, had a range of 7,000 to 35,000 ft.

Although participants of the Oxford-Vegetarian study 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

[6] The KIHD study only used men.

[7] Details also available in my full report of each of the 20 studies.

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." Meat-eaters made up over 50% of the study group.

The mean SFA-intake for men was ~27.4 g, with a standard deviation of ~13 g.[8] Thus, this study has a much larger range than either the Japanese/JACC study (14.4, SD:3) and the Finland/KIHD study (55g, SD:13g). Note the difference of SD as percent of mean: almost 50% for the Oxford-Vegetarian study, but just about 20-25% for the JACC and KIHD studies.

Thus, the Oxford-Vegetarian study has a range of SFA-intake that overlaps the JACC study higher-half and the KIHD study lower-third.[9]

The Oxford-Vegetarian study (and the Chowdhury meta-analysis) reported an RR of 2.77, with 95% CI (1.25 - 6.13). This implies that a man in the highest third of animal SFA-intake has 2.77 times the risk as a man in the lowest third animal SFA-intake. And, since the confidence interval is >1.00, this was statistically significant.

The authors of the Oxford-Vegetarian study had the best summary on my point about homogeneity of studies: "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."***

The other approach to seeing the big picture with SFA-intake is to look what happened in Finland overt time. This was presented in part 2 (April McDougall newsletter). The CHD death rate in Finland over a 35 year period dropped 80%. Three-fourths of this (60%) was explainable by a reduction in risk factors. About two-thirds of that was due to the major drop in serum cholesterol, and that was due principally to the drop in SFA intake from 22% of energy intake (i.e. calories) to 13%.

Key messages:

1. There is huge difference in IHD mortality rates between countries, e.g.in 2011, the rate in Finland was 4.4X the rate of Japan. But a study involving a homogenous population does

[8] One of the flaws in this study is that it only reported on SFA-intake from animal sources. Total SFA-intake is likely to be a little higher. Another flaw is that the study does not report on total energy intake. So, no estimates of % of SFA-intake of energy. The UK NHS estimates the average calorie intake of men at 2500 kcal/day. I suspect it is somewhat lower in this study's population.

[9] The amount of overlap is just an approximation on my part, using a back-of-the-envelop calculation.

not provide sufficient differences to determine relationships between dietary intake and outcome. 19 of the 20 studies in the Chowdhury meta-analysis had this problem.
2. Of the 20 studies, the KIHD Finland study had one of the highest SFA-intakes - a mean of ~2.5X (as percent of calories/day) that in the Japanese/JACC study, which had the lowest. But due to the homogeneity problem, neither showed a relationship to SFA intake.
3. The one study of the 20 (the Oxford-Vegetarian one) that did not have the homogeneity problem did show a statistically significant harmful effect of increased SFA-intake, RR: 2.77, with a 95% CI of (1.25, 6.13).
4. Finland's 35-year experience of reducing IHD mortality by 80%, and the associated drop in SFA-intake from 23% to 13% is telling.

The Other Problems

In Part 1, I described the criteria that I would be using to grade the different studies. These were based, at that time, on the 9 studies that I had read by then. I am going to repeat their description here, with very minor changes:

1) *Over-adjustment with Lipids*. As the Chowdhury paper notes including an adjustment for serum lipids (i.e. serum cholesterol) may act as a potential mediator between fatty acids and coronary heart disease. Thus, the meta-analysis tried to include the most adjusted results that did not include an adjustment for serum lipids. However, as Chowdhury notes, 6 of the 20 studies included in the meta-analysis did include adjustment for serum lipids, because adjustments without it were not available. In other words, in my opinion, these 6 studies should have been excluded, but were not. But not quite true. In my reading and analyses of the 20 studies, there were actually 8, whose multivariate adjustments included serum lipids; i.e. really 8 of the 20 should have been excluded.
2) *Sufficient Test of SFA Guidelines*. Most studies divide the study population into fifths (quintiles), fourths (quartiles), or thirds (tertiles). Other studies just provide a mean and a standard deviation. To test the validity of the ≤10% of energy from SFA intake, it would be appropriate to have 20-33% meeting the SFA intake guidance, and have the SD (standard deviation) at least 33% of the mean. 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.* I covered this problem in the previous section. But I should also note that there is a spectrum in this.
4) *Food/Lifestyle Questionnaire.* This involves a Food Frequency Questionnaire (FFQ), as well as a Lifestyle one about health status, medications, exercise, smoking habits, etc. In 19 of the 20 studies,[10] 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. many also have an exam (e.g. an ECG to exclude participants that may have a pre-existing

[10] The exception is the Nurses Health Study.

heart condition and not know it, a blood glucose test to exclude those with diabetes, a blood pressure measurement, since BP is known risk factor for IHD, and should be an adjustment factor in analysis). Some studies are very diligent in gathering the initial data. Some are quite poor. Nevertheless, over the period of time that 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 some of 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 or measure blood pressure at the beginning of the study.
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 Over-adjustment or under-adjustment. For example, consider a study that adjusts for dietary cholesterol - that is likely to be an over-adjustment due to its correlation with SFA-intake. Similarly, when the adjustments include all fatty acids, that may also result in over-adjustment. Under-adjustment can be due to missing data, e.g. TFA. For example, substituting margarine (with TFA) for butter reduces SFA intake, but may have worse CHD outcomes; and, many studies realized this problem too late to do anything about it. In the Japanese/JACC study, hypertension was determined by a yes/no question (versus a measurement). This underestimated the percent of hypertension by ~3X. So, this likely resulted in under adjustment. And, there are many factors that I found that were unique to specific studies that may or may not be factors in others (e.g. mercury, iron, arsenic, salt). But even in specific studies where there should have been adjustments for these, there wasn't.
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.***" Anyone following Dr. Michael Greger, who reviews the latest in nutrition research on his free website knows this to be the case. Consider one somewhat humorous/bizarre example of interaction. in researching the Glostrup/Denmark study, I came across this study of men in Copenhagen, Denmark, 1996 BMJ article. Consider a group of men, all with LDL ≥ 203 mg/dl. "those who did not drink alcohol had ***five times the risk*** of ischaemic heart disease compared with those who consumed three alcoholic beverages or more a day." So, if you have sky high cholesterol, and don't want to change your diet, a rather high intake of alcohol would seem to be a better choice than a statin. But note that alcohol intake was not significant factor in subjects with lower LDL cholesterol.[11]

[11] This is just meant as a humorous story about interactions, in this case a high animal SFA diet and alcohol. It is really meant as an illustration of how studies that just look at nutrients (vs food) can lead one to rather strange results.

Having now looked at all 20 studies, I've noticed a 2 other problems with some of them that need to described.

Age

Almost all studies exclude subjects with a pre-existing heart condition and diabetes. The former may just be a survived heart attack (determined by asking the patient or hospital records). It can also involve asking if the patient if he/she experiences angina. In a few studies, it also involved an ECG to detect a possible silent heart attack that the patient was unaware of. Diabetes is determined by asking the patient and also taking blood and measuring blood glucose levels. A level of 120 or above would exclude the patient from the study.

Some studies only include middle-age subjects (e.g. 45-59) at study entry. Many others include older subjects (e.g. up to 79). In a few of these, middle-aged and elder subjects were evaluated separately. In such studies, increased SFA-intake was often statistically associated with increased IHD in the middle-aged, but not the elderly.

Why?

The exclusion is at the beginning of the study. Arteriosclerosis is a life-long pursuit. The individuals eating the worst diet (e.g. high in SFA-intake, cholesterol intake, low fruits and vegetables) and worse lifestyle (e.g. smoking, lack-of-exercise) are the ones most likely to be excluded from the study, due to signs of CHD and/or diabetes. Genetics may also be a factor. Thus, a person in the elder group (e.g. aged 60 to 75, with a mean age of 66) that doesn't have any signs of heart disease or diabetes at the start of the study is more likely to die from other causes than would otherwise be.

How does this age/exclusion problem affect the Chowdhury's meta-analysis? Two ways.

First consider the studies that broke up the study population into 2 age groups (middle and elder), and that increased SFA-intake was a significant risk factor for IHD in the middle-aged population, but not the elder one. In this case, Chowdhury's meta-analysis will only use the combined population, which usually doesn't show a significant statistical effect for increased SFA-intake.

Now consider a study that doesn't divide the age groups, and has a study population of both middle and elderly. In my view, if the mean age of the study population is around

55 and the age cut-off is 70 or higher, this has the same problem as the 1st example - we just don't get to see if there is an association with the middle-aged. One example of this is the Malmo/Sweden study which had an age range of 44 to 79 with a mean of 58 y. Another is the Japan/JACC study, with an age range of 40 to 79 with a mean of 57 y.

End Points

In some studies, the only end point was *death*. In others, it was *incidence* of IHD, e.g. AMI (acute myocardial infarction), or a procedure (e.g. a bypass or a stent put in) or another ECG done at the end of the study or the patient reporting angina pectoris. And some reported both, i.e. death and incidence. Chowdhury had the preference in the meta-analysis for incident rates, but in the studies that only reported on death, the meta-analysis would use that.

But is this fair in a meta-analysis? Consider a study that reports both, and with CHD death reports a statistically significant relationship with increased SFA-intake, but there isn't one with incidence. Chowdhury only uses the latter. Is that reasonable? Clearly, it takes more work for the researchers to look at incidence. Death is much easier to monitor. In other words, if the researchers were lazier, the results used in the meta-analysis would have been different.

And 10 of the 20 studies report incidence, and the other 10 just death.

Even More Problems

Just the general problems are more than enough to really disqualify all of the 20 studies, even the Oxford-Vegetarian one (e.g. see my grading of it in Part 1 or the supplement).

There are a few studies that I spent way too much time on, e.g. the KIHD/Finland study (see part 2), the JACC/Japan study (1st one in my analysis supplement), and the Strong Heart Study/American-Indians, digging up a lot of additional-related information to these. I don't see how these 3 papers passed a peer review process. In each of these, there was information that should have been in the paper and other related studies referenced. The omissions appear blatant.

Key Learnings

This section will try and summarize key points of each of the 20 studies. The Siri-Tarino et al paper [2] was another meta-analysis that looked at SFA intake relationship to IHD, and came

to essentially the same conclusion as the Chowdhury paper. All of Siri-Tarino's 16 referenced studies are a proper subset of the 20 that Chowdhury referenced. They used a slightly different methodology in adapting the reported results in these 16 studies, so their RR's and CI for the same study are sometimes different. Along with my terse analysis of each of the 20 studies, I'll give you the scoring used in the Chowdhury/Siri-Tarino meta-analyses.

First though is a table summarizing all 20 studies: the scoring (RR, 95% CI) of each of the studies by both the Chowdhury and Siri-Tarino meta-analyses. The RR's in **bold** are the ones that reached statistical significance. The rest of the columns (labeled 1 to 8, A, E) are my grading of each of the studies. Below the table is the key for it.

		Chowdhury		Siri-Tarino											
Study	**Country**	**RR**	**CI**	**RR**	**CI**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**A**	**E**
JACC	Japan	0.92	(0.74, 1.14)			N	F	F	F	F	D	F	C	T	D
KIHD	Finland	0.99	(0.77, 1.28)			N	F	F	D	D	D	F	F	M	D
SHS	USA	1.09	(0.84,1.42)	1.91	(0.31, 11.84)	Y	C	F	F	F	F	D	F	T	I
Oxford-Veg	UK	**2.77**	(1.25, 6.13)	**2.77**	(1.25, 6.13)	N	B	B	D	C	C	C	B	M	D
EPIC-Greece	Greece	3.10	(0.99, 9.63)			N	C	F	C	D	D	D	B	T	D
MALMO	Sweden	**0.83**	(0.70, 0.99)	0.95	(0.74, 1.21)	N	F	F	C	C	B	D	D	T	I
BLSA	USA	1.22	(0.31, 4.77)	1.22	(0.31, 4.77)	N	C	C	B	D	D	C	C	T	I
Glostrup	Denmark	1.26	(0.87, 1.82)	1.03	(0.66, 1.60)	N	F	F	D	D	F	D	F	S	I
WES	USA	1.07	(0.98,1.17)	1.11	(0.91, 1.36)	Y	F	F	F	C	D	D	F	M	D
Euroaspire	Finland	1.00	(0.68, 1.46)			Y	D	F	C	C	D	F	F	T	I
HPFS	USA	1.07	(0.88, 1.29)	1.11	(0.87, 1.42)	N	B	C	C	C	C	B	C	T	I
HLS	UK	1.04	(0.97, 1.11)	**1.37**	(1.17, 1.60)	N	F	F	F	F	D	D	F	S	D
LRC	US/Can	**1.14**	(1.01, 1.27)	0.97	(0.80, 1.18)	Y	C	D	D	D	D	D	F	S	D
IIHD	Israel	0.90	(0.65, 1.24)	0.86	(0.56, 1.35)	Y	F	B	D	D	F	D	F	T	D
NHS	USA	0.98	(0.79, 1.21)	0.97	(0.74, 1.27)	N	D	D	B	C	D	C	F	M	I
HHS	USA	1.00	(0.68, 1.47)	0.86	(0.67, 1.12)	Y	B	D	F	C	D	D	D	T	I
FRAM	USA	1.04	(0.97, 1.11)	0.92	(0.68, 1.24)	Y	D	F	F	C	D	D	F	S	D
ATBC	Finland	0.90	(0.78, 1.03)	0.93	(0.60, 1.44)	N	F	F	D	B	D	D	F	T	I
IBDH	US/Ireland	1.07	(1.00, 1.14)	1.33	(0.95, 1.87)	Y	F	D	D	C	D	D	D	T	D
Caerphilly	UK	0.92	(0.78, 1.09)	1.57	(0.56, 4.42)	N	F	F	D	D	D	F	D	M	I

Key for Grading

Columns 2 through 8, are graded **A** (Excellent) to **F** (Bad). Analysis of each study with the rationale for the grading of each is in the supplement.

1) *Overadjustment with Lipids*. **Y**es or **N**o.
2) *Sufficient Test of SFA Guidelines*.
3) *Homogeneity.*
4) *Food/Lifestyle Questionnaire*.
5) *Missing Data in the Study.*
6) *Missing Data in the Paper*.
7) *Confounders*.
8) *Food vs. Nutrients*.
A) *Age.* **M** - study population is middle-aged; **S** - study population is both middle-aged and elderly, and analysis is done of each cohort; **T** - study population is both middle-aged and elderly, but analysis is only done as a combined cohort.
E) *End-Point.* ***D*** - IHD death; **I** - IHD incident.

Below, I've provided some of the interesting information about each study. My long analysis of each study is in the supplement.

Japan Collaborative Cohort Study (JACC)

- In 2011, Japan's rate of IHD mortality was 31% of the USA's rate and 23% of Finland's.
- The JACC SFA-intake was 1/3 to 1/2 of that seen in almost all the other studies.
- For men, only the highest quintile of SFA-intake exceeded the ≤10% of energy recommendation.
- Homogenous study population, e.g. 2.5g of SFA separated adjoining quintiles.
- Serious flaws in baseline data, e.g. underestimation of hypertension by ~3X.
- Japanese low-IHD rate is not due to fruit, vegetable, and bean intake. In a different paper using same study group, upper quartile of each <1 serving/day.
- 3 likely confounders (sodium, mercury, and arsenic) not mentioned or included in the study.

Kuopio Ischaemic Heart Risk Factor (KIHD) Study

- Data (Food, lifestyle, blood-work, etc) collected only at beginning of study.
- Failed to disclose dramatic changes in Finnish diet during the 14.6 y study period in the paper.
- Failed to disclose significant confounders (Trans-fats, mercury, excess body iron).
- When I say, "Failed", I mean that they knew, and blatantly omitted relevant data in the paper.
- One-day's internet research on the KIHD study would have been sufficient for any one to reject this study from a meta-analysis. Why didn't Chowdhury et al?

Strong Heart Study (SHS) of American Indians

- Over-adjustment. In the multivariate analysis, adjustments (w.r.t. SFA-intake) included serum cholesterol, dietary cholesterol, and PUFA (i.e. polyunsaturated fat) intakes. Thus, not surprising that SFA-intake did not reach statistical significance w.r.t. *CHD incidence*.

- But surprisingly (given the over-adjustments), SFA-intake for 47-59 y cohort did reach statistical significance for CHD mortality, RR: **5.17** (CI: 1.64, 16.36) - highest quartile of SFA-intake vs lowest quartile. This was higher than any of the other 20 studies.

The Oxford Vegetarian Study

- This was the only study that involved a study population with a non-homogenous diet. As the authors note, "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"
- As reported by both Chowdhury and Siri-Tarino, highest tertile of SFA-intake had **2.77** times the risk of CHD mortality compared to the lowest third (CI: 1.25, 6.13).
- The highest tertile of **egg-intake had 2.68** times the risk of CHD mortality compared to the lowest tertile (CI: 1.19, 6.02).

Diabetics from the Greek Arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Greece)

- Chowdhury's scoring did not report statistical significance; however, but the EPIC-Greece paper reports that a 10 g increase in SFA-intake resulted in a RR of **1.93** (CI:1.08, 3.42) for CHD deaths.
- Also from the EPIC-Greece paper, "***one egg (40 g)*** [per day] ***increases*** *the risk of death overall threefold and the* ***risk of coronary death more than fivefold.***"

MALMO (Sweden) Study

- Homogenous population, with high SFA-intake. From the Malmo paper, ". . 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.
- The Chowdhury scoring notes a benefit for higher SFA-intake that was statistically significant. And, one can see this by just looking at the numbers in tables. But here is what the paper says, "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)." In other words, including fiber in the multivariate analysis resulted in an over-adjustment.

Baltimore Longitudinal Study of Aging (BLSA)

- The Chowdhury/Siri-Tarino scoring indicate no statistically significant benefit with lower SFA-intake, but . . from the BLSA paper:
- Men consuming either a low-SFA diet or a high FV [fruit and vegetable] diet, but not both, had a 64-67% lower risk of CHD mortality (P<0.05) relative to those doing neither.
- ***Men consuming both a low-SFA diet and a high FV diet had a 76% lower risk of CHD mortality (P<0.001), relative to those doing neither.***
- Authors conclude (last sentence of abstract): "These results confirm the protective effects of low SF and high FV intake against CHD mortality. In addition, they extend these findings by demonstrating that the combination of both behaviors is more protective than either alone, suggesting that their beneficial effects are mediated by different mechanisms."

Glostrup Multi-centre Study (Glostrup)

- This study used a different mode of analysis than any of the other studies.
- "In the models used, total energy and protein intake were fixed. Differences in intake of energy from fat thus reflected complementary differences in intake of energy from carbohydrates." The evaluation

was the risk of CHD according to intake of 5% higher level of energy from dietary fat, and thus 5% lower energy from carbohydrates. Results could be looked at 4 ways: sex (men, women) and age (young: <60 y, old: ≥60 y)
- The mean SFA intake of all participants was ~20% of energy. The mean of the lowest 10% (decile) in SFA intake was ~14%, and the median of the highest decile in SFA intake was ~25%.
- Of the 4 groups, one did reach statistical significance w.r.t. increased **SFA intake with younger (<60 y) women, RR: 2.68, 95% CI: (1.40, 5.12)**, as noted in the abstract of the paper. For these younger women, total fat and MUFA intake also reached statistical significance (both harmful), but this was likely due to the strong correlation with SFA intake.
- Why didn't younger men also see this effect? The paper suggests the possibility that, ". . .intakes of complementary carbohydrates were qualitatively different between the genders. In the present study, only types of fat, but not types of carbohydrates, were considered."

Western Electric Study (WES)

- "When the risk of death from CHD was analyzed in terms of the component dietary variables, it was inversely related to intake of polyunsaturated fatty acids and positively related to intake of dietary cholesterol. The amount of saturated fatty acids in the diet was not significantly associated with the risk of death from CHD, although there was a slight but consistent tendency for risk to increase from the low third to the high third of the distribution. Other base-line variables significantly related (P<0.001) to risk of death from CHD in this multivariate analysis were age, systolic blood pressure, cigarette smoking, and *serum cholesterol* concentration."
- The failure of SFA intake to show statistical significance is likely do to over-adjustment (e.g. serum cholesterol being included).

Finnish Cohort of EUROASPIRE (European Action on Secondary Prevention through Intervention to Reduce Events) Study

- This study is about secondary prevention of CAD with a focus on n-3 Fatty Acids, using a Finnish cohort.
- Various dietary nutrient variables w.r.t. various end-points. The only one that reached statistical significance was SFA-intake w.r.t. **all-cause mortality**: **1.57** (1.13, 2.17).
- Virtually all patients were on cardiovascular drugs, and serum cholesterol was included in the adjustments.

Health Professionals Follow Up (HPFS) Study

- A large study of male health professionals of ages 40 to 75 followed for 6.1 years.
- For CHD incidence (i.e. combined fatal CHD and myocardial infarction incidence), SFA-intake did not reach statistical significance. And, this is what Chowdhury and Siri-Tarino put in their analysis.
- But for CHD **mortality**, the HPFS paper reports an RR of **2.21** (CI:1.38, 3.54) comparing highest quintile of **SFA-intake** to lowest one.
- When fiber is added to this adjustment, the RR drops from 2.21 to **1.72** (CI: 1.01, 2.90) - so still statistically significant. In general, people who eat less saturated fat, eat more whole plant-based foods that have fiber. In fact, in the HPFS study the mean fiber intake in quintile 1 of SFA-intake was ~50% higher than that in quintile 5 (26.2 g/d vs. 16.2).

Health and Lifestyle Survey (HLS) in Great Britain

- Siri-Tarino scoring indicated a statistical signifiant harmful effect for SFA-intake, whereas Chowdhury did not.

- From the HLS paper, using their multivariate analysis for relative risk of CHD death, a 100g/wk increase in SFA-intake results in an RR for women of 1.40 (CI: 1.09, 1.79). But the results for men are 1.00 (0.86, 1.18). Why?[12]
- This study only looks at grams of fat intakes, it doesn't adjust for fat (any type) as percent of energy consumed as do the other studies. As the HLS paper says, "A potential source of non-random error arises from the lack of an adjustment for total energy intake of the participants (Willett, 1990). Any apparent effect on CHD risk of dietary fat could, in principle, be due to the effect of total energy intake. . . . Therefore, not adjusting dietary fats for total energy intake could be expected to reduce their apparent effects on CHD, leading to the relative risks for fat reported in this paper being underestimates." Thus, I don't understand why this was included in both the Siri-Tarino and Chowdhury meta-analysis.

Lipid Research Clinics (LRC) Prevalence Follow-up Study

- Chowdhury indicated a statistical harm to increased SFA intake 1.14 (1.01, 1.27), whereas Siri-Tarino did not.
- The study population was separated into 2 age groups: 30-59 and 60-79 y. There were no statistically significant relationships w.r.t. nutrient intake (other than alcohol) in the 60-79 y cohort. The multivariate analysis included adjustments for *serum cholesterol*.
- W.r.t. the 30-59 age group, the paper included this observation, "Our estimates indicate coronary risk reductions of 4%, **10%**, and 9% for a **1% reduction** in total fat, **saturated fat**, and monounsaturated fat, respectively, among 30 to 59 year olds. For example, a decrease in total fat intake from 39.8% (the mean of the sample of 30 to 59 year olds) to 30% (currently recommended levels) would translate into an estimated risk reduction of 34% (relative risk 0.66, 95% confidence interval 0.47-0.91), which is comparable to the estimates obtained from the Framingham Heart Study."

Israeli Ischemic Heart Disease (IIHD) Study

- As the IIHD paper notes, *"Weak associations of long-term coronary mortality with the dietary intake patterns of fatty acids, as reported at baseline, were probably fully mediated by the effect of the diet on serum cholesterol."*
- Thus, the only interesting data point in the IIHD paper is the association of total serum cholesterol and CHD mortality: an increase of 40mg/dl is associated with an increased risk of CHD death of 1.29 (1.20, 1.39).

Nurses' Health Study (NHS)

- Only 1 of the 20 studies that had follow-up questionnaires on diet/lifestyle - every ~4 years. NHS paper used was from 2005 - reporting on 20 years (1980 to 2000)
- Excluded from study at start: ~2% for history of cardiovascular disease, and 5% for ***hypercholesterolemia***. This was the only study of the 20 that excluded people with high cholesterol. And, these were the more likely ones to develop CHD.
- From 1980 to 1998, as percent of energy, decreases in total fat (39% to 29%), SFA (15.6% to 9.4%), MUFA (16.0% to 11.5%), and TFA (2.2% to 1.6%); and, PUFA increased (5.3% to 5.6%).
- In the analysis, to represent long-term dietary patterns, they used cumulative average method. Thus, in the analysis, the median energy intake percent for SFA, ranged from 10.1% for quintile 1 to 17.6% for quintile 5. Thus, this is a homogenous study population w.r.t. SFA-intake.
- NHS paper shows 2 kinds of analysis: Age-adjusted and multivariate in comparing various fat intakes (quintile 5 to quintile 1). The multivariate includes a boat-load of adjustments (besides what you

[12] "Men are from Mars, women are from Venus?"

would expect): the other fats (not being measured), cereal fiber, fruits and vegetable, dietary cholesterol, aspirin use, multivitamin, vitamin E supplement use, protein, etc.
- In the Age-adjusted analysis, all RR's for various fat-types reach statistical significance. But after this multivariate analysis, it disappears for total fat, SFA, and MUFA; but it remains for TFA and PUFA. In fact, PUFA looks better under the multivariate: from 0.80 (0.69, 0.94) to 0.75 (0.60, 0.92). Whereas, SFA goes from 1.52 (1.30, 1.79) to 0.97 (0.73, 1.27). The last number corresponds to the numbers used by Chowdhury and Siri-Tarino meta-analysis.
- The implication is adding ~0.75 TBS of Safflower oil (~75% Linoleic acid) to a diet, without reducing anything else would have a net benefit in reducing CHD risk. For example, this would move someone in quintile 1 of PUFA into quintile 5. Sounds crazy (and I think it is), and no one would suggest this right? Wrong: http://researchnews.osu.edu/archive/saffoil.htm.
- In multivariate analysis by age (<65 and older), benefit of increased PUFA was not statistically significant in older women, RR:0.96 (0.66, 1.39).
- In multivariate analysis by BMI (<25 and higher), benefit of increased PUFA was not statistically significant in the <25 BMI cohort, RR: 0.91 (0.67, 1.26).
- Going back to a 1997 NHS paper, covering 14 years of the study: "***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).***" The 2005 paper did not have this kind of analysis.
- The 1997 paper also provided an additional multivariate analysis, one that did not include the other fats. PUFA only reached statistical significance in the multivariate+other-fats model.

The Honolulu Heart Study

- Study of ~7,000 men of Japanese ancestry living in Oahu. Age 45 to 68 y. Examined in 1965-1968 and followed for 10 years. Prevalent cases of CHD, stroke, or cancer excluded. Negative outcomes fell into 2 categories: (1) severe: CHD death or myocardial infarction; (2) moderate: angina pectoris or coronary insufficiency. Total CHD was a combination of both.
- Chowdhury and Siri-Tarino used Total CHD (i.e. severe + moderate). Multivariate analysis included *serum cholesterol*. So no statistically significant scores for SFA-intake.
- All baseline numbers in the paper are reported as mean ± SD (std. deviation).
- SFA-intake as percent of calories: 12.3% ± 4.0. Implies a good test for SFA-intake recommendation.
- When just the severe category is considered, ***higher increased intakes of SFA, total fat, and protein were significantly and directly related to the 10-year incidence of myocardial infarction or CHD death (P<0.01) with the multivariate analysis (which included serum cholesterol).***
- With just the Age adjustment increased total fat and SFA intakes were even more strongly related to the severe category (P<0.001).

The Framingham (FRAM) Study

- A sub-study of the much larger Framingham study. About 800 men divided into 2 approximately equal cohorts, (45-55 y and 56-65 y). Negative outcome was evidence of CHD disease (CHD death, myocardial infarction, agina pectoris, or coronary insufficiency). Multivariate analysis *included adjustments for serum cholesterol*. Started in 1966-1969, and followed for 16y.
- All baseline numbers in the paper are reported as mean ± SD (std. deviation).
- In the 45-55 yr cohort, in the multivariate model, "total fat intake and monounsaturated fatty acid intake had a significant, independent association with the 16-year incidence of CHD [P<0.01]. Saturated fatty acid intake was *marginally significant* [P = 0.052]." "In men aged 56 years and older, none of the dietary lipid variables was associated significantly with the 16-year incidence of CHD morbidity and mortality." Thus, combining both cohorts, it is not surprising that Chowdhury and Siri-Tarino reported no statistical significance w.r.t. SFA-intake.

- But there is a Part 2 to the FRAM paper. This compared men at the mean-level of total fat, MUFA, and SFA to those at upper-end of NCEP guidelines, i.e. 39.7%/30%, 16.2%/10%, and 15.2%/10%. In the 45-55y cohort, the relative risk (RR), with 95% CI, for each was: total fat, 0.71 (0.56, 0.90); MUFA, 0.64 (0.48, 0.87); and **SFA, 0.78 (0.61, 1.00). Thus, SFA was *marginally significant.*** But this is with the multivariate analysis that *includes adjustments for serum cholesterol*.

ATBC Study

- The original purpose of this study was to determine if giving Alpha-Tocopherol and/or Beta-Carotene supplements to *Finnish men smokers aged 50-69* would reduce their cancer risk. With the data collected they realized that they could use the collected data to assess the risk of CHD based on intakes of specific fatty acids. There were 6.1 years of follow-up from 1985-1988.
- Men in the top quintile of TFA (trans-fatty acid) had a multivariate risk of Coronary death of 1.39 (1.09, 1.78) as compared to men in the lowest quintile.
- The intake of omega-3 fatty acids from fish was also directly related to the risk of coronary death in the multivariate model, 1.30 (1.01, 1.67) for men in the highest quintile of intake compared with the lowest.
- There was **no association between intakes of saturated** or c/s-monounsaturated fatty acids, linoleic or linolenic acid, or dietary cholesterol and the risk of coronary deaths.
- The dietary questionnaire exaggerated the range of intakes of all nutrients. From the validation study, the range of SFA-intake was actually 57% narrower.
- Last sentence of paper: "The selective nature of this cohort (***middle-aged, smoking men eating a diet high in fat***) warrants relatively cautious extrapolation to other populations."

The Ireland-Boston Diet Heart (IBDH) Study

- Study consisted of ~1,000 men (30-69 y) followed for 18 years starting in the early 1960's. 3 cohorts, but since the CHD death rates were similar, they were combined.
- The multivariate analysis included *serum cholesterol*. But even with this, increased SFA-intake (harmful) and fiber-intake (helpful) were marginally statistically significant (P=0.05).
- Missing from the study: physical activity and diabetes indication.
- Based on dietary information, this was a homogenous population that also had a high smoking rate (mean of ~1.7 packs/day).
- Most interesting observation in the IBDH paper (general, not applicable to the study itself):
  *"The principal nutritional change that has occurred since the early 1900s has been a **decrease** in the consumption of **dietary carbohydrates**, not including sugar, of about **45 per cent** during the period **1909 to 1976**. In contrast, changes in the consumption of dietary lipids have been much smaller. **Assuming that the rise in death rates from coronary heart disease was real, the changes in dietary levels of complex carbohydrates match the rise more closely than the changes in dietary lipid levels.**"*

Caerphilly Study

- The study population consisted of 2,423 men, ages 45-59, from small towns in of South Wales, England (Caerphilly and 5 adjacent towns - total population, 41,000) in the early 1980's. Data determined at the beginning of the 5-yr study: a one-time self-administered food-frequency questionnaire and an examination including an ECG.
- No measurement of blood pressure, or indication of hypertension. No measurement of glucose, or indication of diabetes. No information of physical activity.
- The homogenous study population had little dietary differences.
- No statistically significant relationship of CHD incidence with any nutrient - not surprising given length of the study and homogenous study population.

Conclusion

A meta-analysis study seems to have instant credibility. Why? Because the lead-in sentence sounds so compelling, e.g. something like, "we combined the results of 15 studies involving over 200,000 people, and found that . . . ." Sounds extremely credible, doesn't it?

But my background is computer science, and one of the common acronyms is GIGO - Garbage In, Garbage Out. So, I thought a bit about this in the context of the Chowdhury and Siri-Tarino meta-analyses. What if the studies used in a meta-analysis aren't very good? What if, the choice of studies, or the data selected from the studies involves some flaws?

GIGO is the fundamental problem in this case as well. None of the 20 studies is good. Only 1 of the 20 had the possibility of being a good study (the Oxford-Vegetarian one), and even that one had flaws.

What are Chowdhury and co-authors, and Siri-Tarino and co-authors trying to do? If they are truly interested in trying to explain the relationship between diet/lifestyle and IHD, what is their hypothesis for explaining the current 4X difference in IHD death rates between Japan and Finland?

I really don't understand their motives. Unfortunately this kind of thing occurs in other endeavors as well. First read this recent excerpt from a Nobel Laureate's blog of a few week's ago (I'll tell you by who and fill in the blank below):

> "So why are people busy trying to come up with stories in which the opposite happens? Yes, if you work hard enough at it you can produce a model for perverse outcomes (that's pretty close to a theorem). But what empirical motivation is there for doing all of this?
>
> What I think happened here was actually that some _____ said something silly, not out of deep conviction, but because they weren't really thinking about what their equations meant; and that rather than back off, they have now spent the past few years trying to justify their initial claims. But there's no reason to take this stuff seriously."

The missing noun is "economists". And, the author is Paul Krugman, and here is a link to that particular post, from May 17, 2014, "Interest Rates and Inflation and Evidence."

References

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