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From The Heart

Let's bust the myth of the role of saturated fat in heart disease

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There is universal scientific acceptance that trans-fats—found in many fast foods, bakery products, and margarines—increase the risk of cardiovascular disease through inflammatory processes.[1] But "saturated fat" is another story. The mantra of removing saturated fat to reduce risk for CVD has dominated dietary advice and guidelines for almost four decades. Yet scientific evidence shows that this advice has paradoxically increased our risk for CVD. Furthermore, the government's obsession with levels of total cholesterol, which has led to the overmedication of millions of people with statins, has diverted our attention from the more egregious risk factor of atherogenic dyslipidaemia.

Saturated fat has been demonised ever since Ancel Keys' landmark Seven Countries study paper in 1970.[2] This concluded that there was a correlation between incidence of coronary heart disease and total cholesterol, which then correlated with the percentage of calories provided by saturated fat. But correlation is not causation. Nevertheless, we were advised to "reduce fat intake to 30% of total energy and a fall in saturated fat intake to 10%."[3] The aspect of dietary saturated fat that is believed to have the greatest influence on CVD risk is elevated LDL-cholesterol concentrations; yet the reduction in LDL (low density lipoprotein) from reducing saturated fat intake appears to be specific to large buoyant (Type A) particles, when in fact it is the small dense (Type B) LDL particles (responsive to carbohydrate intake) that are implicated in CVD.[4] Indeed, recent prospective cohort studies have not supported any significant association between saturated fat intake and risk of CVD;[5] instead, saturated fat been found to be protective. The source of the saturated fat might be important. Dairy foods are exemplary providers of vitamins A and D. As well as a link between vitamin D deficiency and a significantly increased risk of cardiovascular mortality, calcium and phosphorus found commonly in dairy foods may have antihypertensive effects that may contribute to inverse associations with CVD risk.[6][7][8] One study revealed that higher concentrations of plasma trans-pamitoleic acid, a fatty acid mainly found in dairy foods, was associated with higher HDL (high density lipoprotein), lower triglycerides, lower CRP,

Comment [JA1]: But Footnote 5 says: diet. Existing epidemiologic studies and clinical trials support that substituting polyunsaturated fat for saturated fat is more
beneficial for CHD risk than exchanging carbohydrates for saturated fat in the diet, as described further elsewhere

Comment [JA2]: Can you comment on National Dairy Council Sponsorhip/oversight of publications related to benefit and/or lack of harm of dairy products? For example "Metabolic origins and clinical significance of LDL heterogeneity" Berneis KK and Krauss RM, J Lipid Research, 2002. This is Footnote 79 of your footnote 5. In my opinion, the inancial relationships should be mentioned.

reduced insulin resistance, and lower incidence of diabetes in adults.[9] Red meat is anothermajor source of saturated fat. Consumption of processed meats but not red meat has been associated with CHD and diabetes mellitus, which may be explained by nitrates and sodium as preservatives in the former.[10]

Fat has received notoriety based on its higher calorie content per gram in comparison with protein and carbohydrate. However, work by biochemist Richard Feinman and nuclear physicist Eugene Fine on thermodynamics and the metabolic advantage of different diet compositions demonstrated that the body did not metabolise different macronutrients in the same way.[11] Kekwick and Pawan carried out one of the earliest obesity experiments,, published in the *Lancet* in 1956. They compared groups consuming diets of 90% fat vs 90% protein vs 90% carbohydrate and revealed that the greatest weight loss was in the fat consuming group.[12] The authors concluded that the "composition of the diet appeared to outweigh in importance the intake of calories." Most recently the calorie is not a calorie theory has been further substantiated by a recent *JAMA* study, which revealed that a "low fat" diet showed the greatest decrease in energy expenditure, an unhealthy lipid pattern, and increased insulin resistance in comparison with a low carbohydrate and low glycaemic index diet.[13] In the United States, percentage calorie consumption from fat has declined from 40 to 30% in the past 30 years (although absolute fat consumption has remained the same), yet obesity has rocketed. One reason: when you take the fat out, the food tastes awful. The food industry compensated by replacing saturated fat with added sugar. Scientific evidence is mounting that implicates sugar as a possible independent risk factor for the metabolic syndrome (the cluster of hypertension, dysglycaemia, raised triglycerides, low HDL, and increased waist circumference).

For the previous generation, CVD existed in isolation. Now, two-thirds of those admitted to hospital with a diagnosis of acute myocardial infarction really have metabolic syndrome—but 75% of these patients have completely normal total cholesterol.[14] Maybe this is because total cholesterol isn't really the problem?

The Framingham heart study sanctified total cholesterol as a risk factor for coronary artery disease, making statin drugs the second most prescribed medication in the United States, and driving a multi-billion dollar global industry. In the UK 8 million people take statins regularly, up from 5 million 10 years ago. With 60 million prescriptions per year, is it not strange that there has been no demonstrable effect on heart disease trends during this period?[15] Despite the mantra that high cholesterol is a significant risk factor for coronary artery disease, several independent population studies in healthy adults have revealed that

Comment [JA3]: This statement is not correct. See figures 1.9a and 1.9b of your footnote 15. Age standardised mortality rates for CVD have gone down dramatically. This is not to say that the decline was due to statins, but the decline should be acknowledged.

low total cholesterol is associated with both cardiovascular and non-cardiac mortality, suggesting that high total cholesterol is not a risk factor in a healthy population.[16][17][18]

A recent "real world" study of 150<thin>000 patients prescribed statins published in *Annals of Internal Medicine* revealed "unacceptable" side effects, including myalgia, gastrointestinal upset, sleep and memory disturbance, and erectile dysfunction in 20% resulting in discontinuation of the drug.[19] This is massively at odds with the major statin trials that report significant side effects of myopathy or muscle pain in only 1 in 10<thin>000.

A meta-analysis of predominantly industry-sponsored data reveals that in a low-risk group over 60 taking statins, the number needed to treat (NNT) to prevent cardiovascular events in one year is 450.[20] The strongest evidence base for statins are in secondary prevention where all patients post-myocardial infarction are prescribed maximum-dose therapy irrespective of total cholesterol based upon statins' anti-inflammatory or pleiotropic (coronary plaque stabilising) effects. In this group the NNT is 83 for mortality over a 5 year period. That doesn't mean each patient benefits a little; rather 82 will receive no benefit.[21] The fact that no other cholesterol lowering drug has demonstrated mortality benefit supports the hypothesis that the benefits of statins are independent of its effects on cholesterol.

Adopting a Mediterranean diet after a heart attack is almost three times more powerful in reducing mortality than is taking a statin. The recently published Predimed RCT was stopped early after showing that the Mediterranean diet achieved a 30% improvement in cardiovascular events in high-risk individuals compared with a "low fat" diet.[22]

Pharmacotherapy can assuage the symptoms, but can't alter the pathophysiology. Physicians need to embrace prevention as well as treatment. The greatest improvements in morbidity and mortality have been due not to personal responsibility, but rather to public health. It is time to bust the myth of saturated fat's role in heart disease.

1 Wallace S, Mozaffarian D. Trans-fatty acids and non lipid risk factors. Curr.Atheroscler. Rep. 2009;11:423.

2 Keys A (ed). Coronary heart disease in seven countries. Circulation1970: 41(Supp): 1-211.

3 Committee on Medical Aspects of Food Policy. Diet and Cardiovascular Disease: Report of the Panel on Diet in Relation to Cardiovascular Disease. 1984

4 Musunuru K, Atherogenic Dyslipidaemia: Cardiovascular Risk and Dietary Intervention. Lipids. 2010 October; 45(10): 907–914.

Comment [JA4]: I assume this is based on

Comment [JA5]: Webfigure 1 of the Appendix. NNT is 345 per year for 60-70 (<5% risk per 5 years), but 178 for > age 70. Combining these two requires a bit of arithmetic to calculate the denominator of each cell by diving the events that occurred by % per annum and then dividing again by 4.0 (which equals the median number of years duration of the low risk (<5% risk over 5 years) study participants in studies. If this is not clear, perhaps Trevor would show you the legend to the figure in our upcoming article.

Comment [JA6]: Treatment not based on pleiotropic effect. This is one theory about the mechanism of benefit, but certainly not proven.

Comment [JA7]: A bit more complicated than that. NNT to prevent recurrent heart attack is 38. However, there is no evidence that total serious adverse events are reduced, so the 1 out of 38 patients who avoided a heart attack had another unspecified serious illness in its place.

Comment [JA8]: This is a stretch, I believe a weak and tangential argument in support of pleiomorphic effect.

5 Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. Am J Clin Nutr. 2010;91:535–46

6 Alonso A, Nettleton JA, Ix JH, de Boer IH, Folsom AR, Bidulescu A, Kestenbaum BR, Chambless LE, Jacobs DR Jr. Dietary phosphorus, blood pressure and incidence of hypertension in the atherosclerosis risk in communities study and the multi-ethnic study of atherosclerosis. Hypertension 2010; 55:776-84.

7 Sacks FM, Willett WC, Smith A, Brown LE, Rosner B, Moore TJ. Effect on blood pressure of potassuim, calcium, and magnesium in women with low habitual intake: Hypertension 1998;31:131-8.

8 Geleiijnse JM, Kok FJ, Grobee DE. Blood pressure response to changes in sodium and potassium intake: A metaregression analysis of randomised trials. J Hum Hypertens. 2003;17:471-80.

9 Mozaffarian D, Cao H, King IB, Lemaitre RN, Song X, Siscovick DS, Hotamisligil GS. Trans. – palmitoleic acid, metabolic risk factors, and new-onset diabetes in U.S adults: A cohort study. Ann Intern. Med. 2010;153:790-9.

10 Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke and diabetes mellitus: a systematic review and meta analysis. Circulation 2010;121:2271-83.

11 Richard Feinman and Eugene Fine. A calorie is a calorie violates the second law of thermodynamics. Nutr J. 2004;3:9

12 Kekwick A, Pawan GL Calorie intake in relation to body-weight changes in the obese**.** Lancet 1956 Jul 28;271(6935):155-61.

13 Cara B. Ebbeling, Janis F. Swain, Henry A. Feldman, William W. Wong, David L.Hachey, Erica Garcia-Lago, David S. Ludwig, Effects of Dietary Composition on Energy Expenditure During Weight-Loss Maintenance JAMA. 2012;307(24):2627-2634

14 http://newsroom.ucla.edu/portal/ucla/majority-of-hospitalized-heart-75668.aspx

15 British Heart Foundation. Trends in coronary heart disease, 1961-2011. BHF, 2011. www.bhf.org.uk/publications/view-publication.aspx?ps=1001933

16 Nago N, Ishikawa S, Goto T, Kayaba K. Low cholesterol is associated with mortality from stroke, heart disease, and cancer: the Jichi Medical School Cohort Study. J Epidemiol. 2011;21:67–74.

17 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3247776/

18 Simes RJ. Low cholesterol and risk of non-coronary mortality. Aust N Z J Med. 1994;24:113–119.

19 Zhang H, Plutzky J, Skentzos S, Morrison F, Mar P, Shubina M, et al. Discontinuation ofstatins in routine care settings. *Ann Intern Med* 2013;158:526-34.

20 Cholesterol Treatment Trialists' (CTT) Collaborators, Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet2012;380:581-90

21 http://www.thennt.com/nnt/statins-for-heart-disease-prevention-with-known-heart-disease/

22 Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med* 2013;368:1279-90.