The 2012 University of Cape Town Faculty of Health Sciences centenary debate

“Cholesterol is not an important risk factor for heart disease, and the current dietary recommendations do more harm than good”

Noakes TD, MBChB, MD, DSc, PhD (hc), FACSM, (hon) FFSEM (UK), Emeritus Professor
University of Cape Town, Department of Human Biology and Sports, Science Institute of South Africa, Cape Town

Correspondence to: Timothy Noakes, e-mail: timothy.noakes@uct.ac.za

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Abstract

Our human ancestors thrived on a diet high in fat and protein of animal or fish origin for at least 2.5 million years. Foods with a high-energy content and nutritional density were required for the development of the large, energy-expensive human brain. A reduction in human height and deterioration in our health followed the introduction of agriculture 2 000-12 000 years ago. In 1977, the United States Department of Agriculture (USDA) introduced novel dietary guidelines based on an untested hypothesis of Keys that dietary fat, especially of animal origin, increases the blood cholesterol concentration, “clogging” the coronary arteries and causing heart attacks, i.e. the diet-heart hypothesis.

Here, I use five key arguments to show that those guidelines represent the single greatest error in the long history of medicine:

- Economic considerations drove the adoption of the 1977 USDA dietary guidelines in the absence of proper scientific proof.
- Within five years of their adoption, the rates of type 2 diabetes mellitus and obesity increased explosively, especially in the USA, subsequently spreading across the globe.
- The presence of insulin resistance (IR) explains why large numbers of persons in predisposed populations develop obesity and type 2 diabetes mellitus when following the high-carbohydrate, low-fat (HCLF) diet advocated by the USDA dietary guidelines.
- A low-carbohydrate, high-fat (LCHF) diet reverses all known coronary risk factors in persons with IR, whereas the HCLF diet may worsen many of those factors.
- The multi-million dollar 48 835 persons Woman’s Health Initiative Randomized Controlled Dietary Modification Trial (WHIRCDMT), of which Rossouw was project leader, shows that the USDA dietary guidelines are associated with accelerated disease progression in persons with either established heart disease or diabetes. That study does not support Keys’ diet-heart hypothesis, of which Rossouw continues to be a staunch advocate.

This paper shows why “cholesterol” is not an important risk factor for heart disease, and why the current dietary recommendations that promote a high-carbohydrate and low-fat intake, aimed at reducing blood cholesterol blood concentrations, raise blood glucose and insulin concentrations at the same time and stimulating hunger, have caused the global epidemic of obesity and type 2 diabetes mellitus that will bankrupt the world’s medical services within the next two decades. Seldom have economically-driven “good” intentions produced such calamitous outcomes.

Introduction

Our human ancestors evolved from the tiny Australopithecus africanus (~ 1 m tall, weighing 30 kg) to the substantially taller and heavier modern Homo sapiens over a period of 3.5 million years. This change occurred as hominins became more successful at increasing the quality of the foods they ate, changing from a predominantly vegetarian diet to one containing an increasing amount of animal fat and protein.1-3 The greater consumption of meat occurred as early hominins became the most effective persistence hunters on the planet, able to run large antelope to their exhaustion within 4-6 hours in extreme heat. 4-6 The discovery of fire and the development of cooking7 approximately 1.8 million years ago increased the energy delivery from meat, roots and shoots, reducing the time humans spent chewing their food. Stone-tipped throwing spears were added approximately 500 000 years ago,8 further increasing our human ancestors’ ability to capture large, fat-filled animals, including elephants,9 and in Africa, rhinoceros and hippopotamus.

By the mid 1800s, the Plains Indians of North America, who existed on a diet of bison and little else, were the tallest10 and perhaps the healthiest of all the peoples then populating the earth. In the 1830s, Catlin11 travelled west of the Mississippi River, and painted hundreds of Plains Indians, including Black Dog and Tal-lee, two
Osage warriors, who ate mostly buffalo meat and were both over 1.98 m tall. The arrival of avaricious Europeans, disconnected from the land, foretold the massacre of 60 million bison and the demise of the Plains Indians’ health. Forced to eat the standard American diet, the modern descendants of the Plains Indians are now among the least healthy populations in North America.12 Annually, millions of dollars of public monies are spent trying to “discover” why these first peoples of North America are so unhealthy. Genius is not required to solve that particular riddle.

Xhosa- and Zulu-speaking South Africans experienced a not dissimilar fate. In 1896, the Rhinderpest virus decimated the cattle herds of East and South Africa, forcing our indigenous peoples to migrate to the cities, where they first encountered the standard American diet of highly processed foods, white flour, refined carbohydrates, sugar and processed “vegetable” (actually seed) oils. There was an epidemic increase in obesity and diabetes within the urban black population. The modern descendants of the Xhosa- and Zulu-speaking South Africans experienced a not dissimilar fate. In 1896, the Rhinderpest virus decimated the cattle herds of East and South Africa, forcing our indigenous peoples to migrate to the cities, where they first encountered the standard American diet of highly processed foods, white flour, refined carbohydrates, sugar and processed “vegetable” (actually seed) oils. There was an epidemic increase in obesity and diabetes within the urban black population.

The most recent assault on global health began in the 1950s, largely as a result of the determined endeavours of biochemist, Keys, aided after 1972 by USA President Nixon, that ultimately led to the 1977 USDA dietary guidelines. Political and economic forces, not science, drove the adoption of those dietary guidelines.19-21 Since those forces will continue to intensify in the future, there is little hope that anything short of a people-led uprising will save us from the obesity and type 2 diabetes mellitus tsunami that those forces have unleashed.

I present five topics that explain the abysmal science and weak logic that has produced this predictable outcome.

Economic considerations drove the adoption of the current dietary guidelines in the absence of any scientific proof

Keys and the origins of the diet-heart hypothesis

The theory that fat in the diet raises the cholesterol blood concentration, which then causes coronary atherosclerosis, leading to coronary heart disease (CHD), is known as the diet-heart hypothesis. (The lipid hypothesis excludes the dietary component, and postulates only that elevated cholesterol blood concentrations cause heart disease. Therefore, they are separate hypotheses.) The diet-heart hypothesis owes its origin to the single-minded vigour of one American biochemist, Keys. In 1953, Keys wrote the following:22

• It is a fact that compared with healthy people of the same age, patients with definite angina pectoris or who have survived a myocardial infarction tend to have blood serum characterised by high cholesterol and certain lipoprotein concentrations, a high cholesterol to phospholipid ratio, and a larger proportion of the total cholesterol in the beta 1-lipoprotein fraction.

• It is a fact that, on average, persons afflicted with diabetes, myxoedema and nephrosis tend to have high cholesterol and the other serum peculiarities mentioned. There is a high incidence of atherosclerosis and degenerative heart disease in those patients.

• It is a fact that in animal experiments, those measures, such as high-cholesterol diets and thyroid suppression, which produce high levels of cholesterol and allied substances in the serum, are also productive of atherosclerosis.

• It is a fact that a major characteristic of the atherosclerotic plaque is the presence of abnormal amounts of cholesterol in that artery. The atherosclerotic plaque consists of 40-70% cholesterol. It is extremely probable that most or all of this cholesterol is derived from the blood.22

In his paper, Keys also published the iconic figure that would define the future of the debate. He showed an apparently linear relationship between the (supposed) fat content of the diet and CHD rates in six countries (Figure 1). He concluded that this association proved by randomised controlled clinical trials (RCTs) in which all observations does not prove causation.21 Causation can only be proved by randomised controlled clinical trials (RCTs) in which all variables, except the one of interest, are held constant. Keys reported on observational studies, not RCTs, on the diet-heart hypothesis.
in his career. As a result, he could never prove that hypothesis “unequivocally”. Thirdly, he spent much of his life defending his theory against the criticism that any number of confounding variables could also explain the associational relationships that he considered to be causal. Fourthly, his dubious research methods, exposed only recently, further undermine the likely validity of this hypothesis. For example, Keys studied populations that had yet to recover from the economic hardships of World War II. He included Greek Orthodox populations during Lent when they abstained from all foods of animal origin. Also, he did not consider the potential health benefits of fasting, and most troublingly is that his conclusions on what constitutes the “Mediterranean diet” were based on an analysis of fasting, and most troublingly is that his conclusions on what constitutes the “Mediterranean diet” were based on an analysis of some of Keys’ associational studies. From the available data for all 22 countries, including the 16 ignored by Keys, they investigated a wide range of possible associational relationships, finally concluding that “the evidence from 22 countries, for which data are available, indicates that the association between the percentage of fat calories available for consumption in the national diets and mortality from arteriosclerotic and degenerative heart disease is not valid. The association is specific, neither for dietary fat nor for heart disease mortality. Clearly, this tenuous association cannot serve as much support for the hypothesis which implicates fat as an aetiological factor in arteriosclerotic and degenerative heart disease”. As a result: “It is concluded that the suggested association between national death rates from heart disease and the percentage of fat in the diet available for consumption cannot at the present time be accepted as valid”.

Similarly, Yudkin were the first to publish a careful rebuttal of Keys’ associational studies. From the available data for all 22 countries, including the 16 ignored by Keys, they investigated a wide range of possible associational relationships, finally concluding that “the evidence from 22 countries, for which data are available, indicates that the association between the percentage of fat calories available for consumption in the national diets and mortality from arteriosclerotic and degenerative heart disease is not valid. The association is specific, neither for dietary fat nor for heart disease mortality. Clearly, this tenuous association cannot serve as much support for the hypothesis which implicates fat as an aetiological factor in arteriosclerotic and degenerative heart disease”. As a result: “It is concluded that the suggested association between national death rates from heart disease and the percentage of fat in the diet available for consumption cannot at the present time be accepted as valid”.

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Firstly, USA President Eisenhower’s heart attack in September 1955 was skillfully orchestrated to prove that Americans were in the midst of a CHD epidemic. In fact, the incidence of CHD in the USA had begun to increase shortly after the end of World War I, and was already peaking in the 1950s at the time of Eisenhower’s heart attack (Figure 3). Within a decade, and even before scientists had begun to institute preventive steps, CHD was already in retreat in the USA. Others argue that the death rates from coronary heart disease had been falling since the early 1900s, and that the cause of this “epidemic” is owing to “frequent reclassifications of heart disease during the past 75 years”.29

41 countries, and that in 15 of the 22 countries studied by Yerushalmy and Hilleboe on which data were available, rising sugar intakes were associated with increased CHD rates (Figure 2). He questioned how a distinction could be made between sugar and fat as the key nutritional factor driving the CHD “epidemic” if consumption rates for both were high in countries with high CHD rates and vice versa. A subsequent 1974 study showed an almost perfect relationship between the amount of sugar in the diets of different nations and their CHD rates.28

Keys also conveniently ignored the evidence that the exponential growth, and then fall, in cigarette consumption, exactly matched changes in CHD incidence in the USA (Figure 3).29

Note that Harper argues that death rates from coronary heart disease were already high in 1900, but were under-reported due to “frequent reclassifications of heart disease during the past 75 years” so that no single risk factor has yet been discovered that tracks changes in coronary heart disease mortality since 1900.

Thus, already in the 1970s, associational evidence linking tobacco and sugar use with the rising incidence of CHD was at least as strong as any postulated link between saturated fat and that disease.

Further growth of the diet-heart hypothesis

The manner in which the diet-heart hypothesis became an institutionalised dogma, immune to disinterested scientific enquiry, has been described in great detail by Taubes, Minger and Teicholz. A few key points are presented here.

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Secondly, the American Heart Association (AHA) did not initially support Keys’ speculative hypothesis based on associational data. In 1957, a 13-page review concluded that “the proposition that the character of the American diet has so changed during the past 50 years as to increase the incidence of coronary vascular disease cannot be supported”.30 Without the addition of any new information, in 1961, the AHA reversed its earlier conclusion, advising Americans at risk of CHD to reduce their consumption of dietary fat and cholesterol, concluding that “this recommendation is based on the best scientific information available at the present time”.31 The sole change between 1957 and 1961 was not the appearance of definitive new evidence. Rather, it occurred after Keys became a key member of the AHA committee.

Thirdly, Keys’ speculative hypothesis could become the singular focus of USA commercial and political interests, only if the two other suspected culprits of the day, cigarettes and sugar, could be made to “disappear”. The formation of the tobacco lobby, i.e. Tobacco Industry Research Committee, in the 1950s specifically to bury concerns about the health dangers of the tobacco habit explains why any possible link between the cigarette habit and CHD (and other diseases) was not pursued.32 Similarly, the formation of the USA Sugar Research Foundation in 1943, subsequently re-named the Sugar Association in 1947, served an identical function.33 As a result, the potential link between sugar and ill health, including CHD, proposed by a group of Afro-English scientists,34,35 including Yudkin,36,37 was effectively silenced. Instead, the Sugar Lobby applied its influence to squeeze Yudkin’s funding sources, causing the premature termination of his research career.37

As a result, the possibility that rising sugar consumption might play a central role in the development of obesity, type 2 diabetes mellitus and CHD has been skilfully buried for the past 70 years. But the book that Yudkin wrote in 197237 survives as a work of genius. Forty years later, his campaign has been revived by Taubes,35 Gillespie38 and Lustig,39-41 among others.42

With the cigarette and sugar hypotheses conveniently concealed from public scrutiny, the path was cleared for the diet-heart and lipid hypotheses to become the unchallenged winners. But while there was clear evidence that the “increase” in CHD incidence occurred at the same time that cigarette (Figure 3) and sugar consumption36 had both increased dramatically, no such increase occurred in the intake of meat, eggs, milk fat or butter (Figure 4). An increase in total fat intake began after 1940 (Figure 5), but was due to an increased intake of polyunsaturated fat, including linoleic acid, not saturated fat. Figure 6 shows that the intake of lard and butter fell dramatically since 1909, whereas the intake of soy bean, shortening
levels seen in the early 20th century, and was sharply distinguished to the conventional interpretation. Thus, “meat consumption in after the Depression when CHD rates were increasing, according to the conventional interpretation.29 Thus, “meat consumption in the USA dropped to unusually low levels in the Great Depression.44 By 1965, it had reached the highest levels in American history”. Note that before 1936, shortening comprised mainly lard, but the lard was replaced with hydrogenated oils incrementally thereafter. Instead, it seems probable that modern Americans began to eat substantially less meat in the 100 years immediately before CHD rates began to increase (Figure 8).44,45 and especially in the 1930s after the Depression when CHD rates were increasing, according to the conventional interpretation.29 Thus, “meat consumption in the USA dropped to unusually low levels in the Great Depression. Consumption rebounded in the 1940s, but it remained well below levels seen in the early 20th century, and was sharply distinguished by income”.44 Importantly, meat intake has always been least in the lowest socio-economic classes, precisely those who suffer the greatest burden of chronic diseases, including CHD.46 Subsequently, “meat consumption began to climb dramatically in the 1950s after the end of the Korean War’s rationing programme.44 By 1965, it had reached the highest levels in American history”. Thus, the conventionally described increase in CHD rates in the USA from 1910-1950 was associated with decreased meat, and hence saturated fat intake from meat, whereas declining rates after the 1960s occurred subsequent to a ~ 50% increase in meat consumption, especially in those in the lowest socio-economic groups. Most of this increase is explained by the rising consumption of white meat, especially poultry (Figure 8).

Therefore, from the outset, the validity of the diet-heart hypothesis, linking the conventionally described rising CHD incidence after 1910 to an increased saturated fat intake from meat especially, is not supported by the evidence, at least in the USA (Figures 4-8). Instead, it would seem to be disproven by this information that is conveniently ignored by advocates of the diet-heart hypothesis.

The industrialisation of corn production in the USA leads to the 1977 United States Department of Agriculture dietary guidelines

The next key event that drove the global adoption of the diet-heart hypothesis was the 1972 USA presidential election, in which the incumbent, Nixon, was confronted by a losing war in Vietnam, rising food prices, unhappy housewives and a disgruntled farming community. He appointed Butz as Secretary of Agriculture with two orders, namely to increase the wealth of USA farmers, and to bring down the price of food.46 Butz decided that the production of corn on an industrial scale by farmers receiving large government subsidies to cultivate all their available land was the solution to both “problems”. His actions would have momentous effects on global health.

The industrialisation of corn production would be of little value if all of the newly grown corn was not eaten, either by USA citizens or the rest of the world. The challenge was to convince the world that grains and cereals were healthier than the foods high in animal fat and protein that Americans had always eaten.

The key player was Senator McGovern, whose Senate Select Committee on Nutrition and Human Needs developed the first USDA dietary guidelines in 1977. These novel guidelines were based specifically on Keys’ unproven diet-heart hypothesis. They advised Americans to restrict their intake of saturated fats, especially, by eating 8-12 servings of grain and cereals per day. Grains and cereals replaced the butter, lard, cheese, eggs and meat that had been the American staples until then.20

Figure 8: Changes in total meat and red and white meat intake from 1800-2000 in the USA23

and margarine increased steeply over the past century, with a much smaller increase in beef tallow. More recently, data from the USA Nurses’ Health Study show that the intake of high-fat dairy and red meat fell from 1980 and 1990, to be replaced with an increased intake of low-fat dairy and white meat (fish and poultry) (Figure 7).43 This change is associated with the rising incidence of obesity and type 2 diabetes mellitus after 1980 (next section).

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test the hypothesis of alterations in nutritional risk with the diets advocated by their health advisers". He also noted that “less than 20% of patients” with CHD have an “abnormal lipid pattern”. Harper pointed out that “the assumption that cardiovascular diseases may be delayed by the adoption of the dietary goals is speculation” so that “proposals for action, that are based on speculation and conjecture, rather than on critical analysis, are distressing under any circumstances. They are especially distressing when they are proposed by a senate committee for adoption as the basis for federal policy”. Leveille argued that the “committee’s report failed to consider all of the available evidence” and that “there is equally compelling evidence suggesting that the recommended dietary changes would make little or no difference as to the incidence and severity of cardiovascular disease or cancer”. Mann complained that “the level of fat in the diet has not been related causally to any disease, and in particular, not to either obesity or to cancer. Those who contend this are adventurists” because “the amount of saturated fat in the diet has not been shown to be causal for any disease”. He concluded that “the release of this document is a nutritional debacle”. Olson concurred: “I think the proposal is disastrous as there is no evidence at present to justify such a drastic change in the American diet”. He argued that the new guidelines were “not based on scientific evidence” and that “there is no evidence from 10 intervention studies on coronary disease involving 5,000 men and 36,000 man-years of study on the effect of the prudent diet that diet modification will change the mortality rate of this disease”. Schmidt warned: “For anyone to say, ‘Let’s change the nation’s dietary habits, even though we don’t know that doing so will do any good – it can’t do any harm’ is naive. One doesn’t know, and can’t predict, what harm may result. But experience teaches us that we often learn late, even a generation late of harm, that no one could or did predict”. Others argued that “the data demonstrating the concept that the risk of coronary heart disease is a function of serum lipids at any level is no longer valid”.49

Finally, Hegsted, then Professor of Nutrition at the Harvard School of Public Health, presented a more optimistic opinion: “The question to be asked, therefore, is not why should we change our diet, but why not? What are the risks associated with eating less meat, less fat, less saturated fat, less cholesterol, less salt and more fruit, vegetables, unsaturated fat and cereal products, especially wholegrain cereals. There are none that can be identified and important benefits can be expected”. One wonders whether Hegsted would still hold this position.

These guidelines continue to be modified every five years. However, the advice to eat less animal fat and protein and more carbohydrate in the form of grains and cereals remains immutable.50 Instead, the guidelines appear to be driven by the political decision that only the increased production of cereals and grains, and not animal products, would provide sufficient food to sustain the global population explosion.

Recent epidemiological evidence does not support the diet-heart hypothesis

Modern epidemiological data show an inverse relationship between the percentage of saturated fat in the diet and the incidence of heart disease in European countries (Figure 9).51 In fact, Western European countries have among the lowest rates of heart disease in the world, despite high rates of saturated fat intake and higher blood cholesterol concentrations, a phenomenon that has been termed the “European Paradox”. This term replaces the incorrect “French Paradox”. Thus, in 2015, Keys would be unable to produce epidemiological evidence to support his 1957 “unequivocal proof”. Furthermore, meta-analyses show that the amount of fat in the diet does not relate to heart disease risk in individuals.52-58 and that reducing dietary fat intake has not been proven to reduce heart attack risk,59-61 although there is some suggestion from associational studies that replacing saturated fat in the diet with omega-3 polyunsaturated fat may provide some benefit,58 whereas replacement with carbohydrates or omega-6 polyunsaturated fat is more likely to be detrimental.59-61 It is perhaps important to remember that it has never been shown that persons with heart disease eat more saturated fat than those without the disease.52 Even in the revered Framingham study, it was found that “there is a considerable range of serum cholesterol levels within the Framingham study group. Something explains this inter-individual variation, but it is not the diet”.62 Interestingly, this information is from an unpublished manuscript from the Framingham study group discovered by Mann in a basement in Washington DC. Another quotation is: “In Framingham, for example, we found that the people who ate the most cholesterol ate the most saturated fat, ate the most calories, weighed the least, and were the most physically active”.63

The Harvard School of Public Health has recently written:64 “Well, it’s time to end the low-fat myth. The low-fat approach to eating may have made a difference to the occasional individual, but as a nation, it hasn’t helped us to control weight or become healthier”.

In summary, the original data on which the diet-heart hypothesis were constructed are purely associational and cannot ever prove causation. That almost all subsequent studies of this hypothesis are fatally flawed has been exposed by careful analysis in three recent books.19-21 Teicholz21 concluded that “the advice that comes out of this book is that a higher-fat diet is almost assuredly healthier than
The power of this evidence led *Time* magazine to conclude in its 23 June 2014 issue: “Don’t blame fat. For decades it has been the most vilified nutrient in the American diet. But new science reveals fat isn’t what’s hurting our health”. Instead, the author concludes that it is dietary carbohydrates that are the villain.

Within five years of adoption of the 1977 United States Department of Agriculture dietary guidelines, rates of type 2 diabetes mellitus and obesity increased explosively, especially in Britain and the USA.

The damage caused by the adoption of the 1977 USDA dietary guidelines did not take long to surface. Already by 1994, the adoption of these guidelines was followed by a 6% increase in daily energy intake in men and a 22% increase in women. This is predictable since carbohydrates drive hunger. They do not satiate. This information has been known since at least 1970. After 1980, there was also a dramatic increase in the rates of obesity (Figure 10) and type 2 diabetes mellitus (Figure 11) in the USA, perfectly matching the temporal change in this increased carbohydrate and energy consumption. Interestingly, there is a strong relationship between obesity and diabetes prevalence rates across the world (Figure 12).

This increased calorie intake by persons with IR (next section) would be more than sufficient in explaining the explosive rise in the USA obesity and diabetes rates.

That these two events are linked by both time and plausible biological mechanisms, proves, in my opinion, that “current dietary recommendations do more harm than good”. This also disproves Hegsted’s optimistic predictions of the health benefits that would follow the adoption of the 1977 USDA dietary guidelines.
The presence of insulin resistance explains why large numbers of persons in predisposed populations become obese and develop type 2 diabetes mellitus, when following the high-carbohydrate, low-fat diet advocated by the United States Department of Agriculture dietary guidelines.

Not all humans are created with an equal capacity to metabolise carbohydrate. Instead, a sizable proportion of humans are unable to store the glucose derived from ingested carbohydrate normally in their liver and muscles68-71 and have the condition of IR. Persons with IR convert excess ingested carbohydrate into triglycerides (TGs) in the liver,72 producing non-alcoholic fatty liver disease,73 or export the fat in the blood, raising blood TG concentrations.74 Excess production of hepatic TG reduces high-density lipoprotein (HDL) cholesterol blood concentrations,69,75-79 and increases the production of small, dense LDL cholesterol particles. Persons with an increased number of small, dense LDL cholesterol particles are at threefold greater risk of suffering a heart attack. This risk may,80 or may not,81 be explained by related changes in HDL cholesterol and TG blood concentrations.82 Small, dense LDL cholesterol particles are more damaging because of an increased susceptibility to oxidation.83 Interestingly, the higher rates of CHD cholesterol particles are more damaging because of an increased rate of CHD83. The mechanism by which insulin resistance leads to coronary heart disease87

Figure 14: The mechanism by which insulin resistance leads to coronary heart disease

Table I: The metabolic characteristics of persons with insulin resistance exposed to a high-carbohydrate diet for a prolonged period (decades)

<table>
<thead>
<tr>
<th>Blood parameters</th>
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<tbody>
<tr>
<td>Elevated blood glucose concentrations</td>
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<tr>
<td>Elevated blood insulin concentrations</td>
</tr>
<tr>
<td>Elevated haemoglobin A1c concentrations</td>
</tr>
<tr>
<td>Elevated blood triglyceride concentrations</td>
</tr>
<tr>
<td>Reduced blood high-density lipoprotein cholesterol concentrations</td>
</tr>
<tr>
<td>Increased, small, low-density lipoprotein particles</td>
</tr>
<tr>
<td>Increased blood uric acid concentrations</td>
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<tr>
<td>Increased blood ultra-sensitive C-reactive protein concentrations</td>
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</tbody>
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Table II: Blood risk factors for the development of coronary heart disease

<table>
<thead>
<tr>
<th>Blood parameters</th>
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</thead>
<tbody>
<tr>
<td>Total blood cholesterol concentrations</td>
</tr>
<tr>
<td>Blood ultra-sensitive C-reactive protein concentrations</td>
</tr>
<tr>
<td>Blood fibrinogen concentrations</td>
</tr>
<tr>
<td>Fasting or random blood glucose concentrations</td>
</tr>
<tr>
<td>Blood-glycosylated haemoglobin concentrations</td>
</tr>
<tr>
<td>Blood homocysteine concentrations</td>
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<tr>
<td>Blood high-density lipoprotein cholesterol concentrations</td>
</tr>
<tr>
<td>Blood low-density lipoprotein cholesterol concentrations</td>
</tr>
<tr>
<td>Blood low-density lipoprotein particle size or number</td>
</tr>
<tr>
<td>Blood lipoprotein (a) concentrations</td>
</tr>
<tr>
<td>Blood-fasting insulin concentrations</td>
</tr>
<tr>
<td>Blood omega 6 to omega 3 ratio</td>
</tr>
<tr>
<td>Blood triglyceride concentrations</td>
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<tr>
<td>Blood uric acid concentrations</td>
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</tbody>
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Seldom are these risk factors measured in individual patients for reasons of cost. Rather, the total cholesterol, HDL cholesterol and TG concentrations in the blood are measured. Persons with elevated total cholesterol and TG concentrations, and reduced HDL cholesterol concentrations, are labelled as suffering from atherogenic dyslipidaemia (AD). According to the diet-heart hypothesis, patients with AD must be treated with a low-fat diet and cholesterol-lowering medications (statins) in the belief that this prevents any further progression of coronary atherosclerosis. But this is an unproven theory.101

A recent publication evaluated the ability of some of these risk factors to predict the future risk of a heart attack or stroke102 in a population of 165 544 individuals, of whom 10 132 developed heart disease and 4 994 suffered a stroke. Table III lists those risk factors in order of their predictive power, measured as the hazard ratio (HR). The higher the HR, the greater the ability of that factor to predict future risk in that study.

Table III: The relative importance, based on the hazard ratio, of the different risk factors for coronary heart disease102

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Hazard ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>2.04 (1.76-2.35)</td>
</tr>
<tr>
<td>Age</td>
<td>1.87 (1.73-2.02)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.79 (1.66-1.94)</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>1.31 (1.26-1.37)</td>
</tr>
<tr>
<td>Total cholesterol concentration</td>
<td>1.22 (1.17-1.27)</td>
</tr>
<tr>
<td>Triglyceride concentration</td>
<td>1.19 (1.15-1.23)</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol concentration</td>
<td>0.83 (0.78-0.87)</td>
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Total blood cholesterol concentration was among the least important risk predictors since an elevated blood cholesterol concentration increases the risk of a future heart attack by only 21%, little better than the risk associated with elevated blood TG concentrations (19%), or low HDL cholesterol concentrations (17%). In contrast, age alone predicts an increased risk by 87%, whereas the presence of diabetes increases the risk by 104%. Other studies show that the majority of persons in the USA with a heart attack have normal blood cholesterol concentrations, but elevated blood TG concentrations103 (in fact, the Framingham study was the first to show this),104 and that blood TG concentrations, not total or LDL cholesterol concentrations, in persons with type 2 diabetes mellitus, are the best predictors of CHD risk.105 It was found in the Framingham study that “90% of the total cholesterol levels measured were ineffectual (by themselves) in predicting the risk of CHD in a general population. Indeed, twice as many individuals who had a lifetime total cholesterol level of less than 200 mg/dl (5.2 mmol/l) had CHD, compared with those who had a total cholesterol level greater than 300 mg/dl (7.8 mmol/l)”.105

Additional published findings that conflict with the lipid hypothesis are that a study has not yet shown a significant relationship between pre-morbid blood cholesterol concentrations and the extent of coronary atherosclerosis at autopsy.106,107 Nor do blood cholesterol concentrations predict the coronary artery calcium volume (CACV) score, by far the best predictor of future risk of a cardiac event,108 because groups with the highest and the lowest CACV scores have identical ranges of blood cholesterol concentrations.109 This latter study is perhaps the strongest evidence that disproves the lipid hypothesis, although the authors fastidiously avoid drawing that conclusion.

Thus, the question: “If total blood cholesterol concentration is such a relatively poor predictor of heart attack risk, is it likely to be the sole important factor causing heart disease, as is the focus of this debate?”

In summary, these data show that the total blood cholesterol concentration is a poor predictor of future heart attack risk (Table III), confirming that “cholesterol is not an important risk factor for heart disease”. Instead, both diabetes and metabolic syndrome, which are disorders of carbohydrate, not fat, metabolism, are the single most important risk factors for a heart attack. What is it about diabetes and metabolic syndrome that makes them so dangerous?

The concept of hyperglycaemic hyperinsulinaemic atherogenic dyslipidaemia

In contrast to what Keys wrote in 1953, diabetics do not have higher blood cholesterol concentrations than those without the disease.108 Thus, higher rates of arterial damage in diabetics cannot be due to higher blood total cholesterol concentrations. Something else must be involved.

The best predictors of heart attack risk in those with an abnormal carbohydrate metabolism are the blood TG concentrations,82 and the blood glycosylated haemoglobin (HbA1c) concentrations,110,111 a measure of the average 24-hour blood glucose concentrations over the previous three months. Similarly, blood TG, but not other lipid markers, are associated with magnetic resonance imaging markers of cerebral small vessel disease.112

Thus, the Norflor arm of the European Investigation into Cancer and Nutrition Study (EPIC-Norflor study)110 found an essentially linear increase in the relative risk of developing a heart attack with increasing HbA1c concentration (Figure 15), such that an HbA1c concentration greater than 7% (a value considered to be acceptable in persons with type 2 diabetes mellitus eating a high-carbohydrate diet, according to the current guidelines for treating diabetes) increases the risk of a heart attack more than sevenfold, that is, by more than 700%. Compare this to the ~ 20% increased risk associated with an elevated blood cholesterol concentration (Table III). This relationship was “independent of age, body mass index, waist to hip ratio, systolic blood pressure, serum cholesterol concentration, cigarette smoking, and a history of cardiovascular disease”.111 The authors concluded that their findings “support the need for randomised trials of interventions to reduce haemoglobin A1c concentrations in persons without diabetes". Restricting dietary carbohydrate intake is currently the only proven physiological method of reducing the HbA1c concentration, especially in those with IR and diabetes.113
The manner in which elevated blood glucose concentrations cause arterial damage was fully described by Brownlee in his 2004 Banting lecture.114

The ages at which persons with different random blood glucose concentrations are likely to develop ischaemic heart disease or myocardial infarction were determined in another publication from the EPIC study.115 It was shown in the study that there is a graded effect of the blood glucose concentration, so that the lower the glucose concentration, the older the age at which the risk of a heart attack begins to rise (Figure 16).

Even within the normal range of blood glucose concentrations (5.0-5.5 mmol/l), heart attack risk rises with increasing blood glucose concentration, so that persons with fasting blood glucose concentrations at the upper limit of the normal range have a 50% higher risk of suffering a heart attack than those with blood glucose concentrations of 5.0 mmol/l.116 However, absolute risk at these low HbA1c values is extremely low.

Other markers of metabolic syndrome and IR (Table I) include elevated blood insulin and TG concentrations, and reduced HDL cholesterol concentrations, with an increased number of small, dense LDL cholesterol particles. The key recent finding described in the next section is that all these risk factors are modified in the same direction by a diet rich in carbohydrates, and in the reverse direction, by a diet low in carbohydrates and higher in fat and protein.

All the metabolic features of the hyperglycaemic hyperinsulinaemic atherogenic dyslipidaemia alter together, worsening on a high-carbohydrate diet and improving on a high-fat diet

According to the traditional model, a high-fat diet promotes arterial damage by causing AD. But according to the hyperglycaemic hyperinsulinaemic atherogenic dyslipidaemia model, a high-carbohydrate diet causes arterial damage by producing changes in almost all of the risk factors listed in Table III.

The suppressed work of Phinney and Volek117-119 has clearly established that all the known risk factors alter in the same direction in response to a dietary change, improving on the LCHF diet, or either worsening or improving less on the high-carbohydrate diet promoted by the USDA dietary guidelines. Twenty-five RCTs75,120-144 have now established the superiority of the LCHF over the HCLF diet.

Figure 17 provides a summary of the findings from the most complete study by Volek et al,143 in which patients with metabolic syndrome were studied while eating either a high-fat or high-carbohydrate diet. All risk factors improved on the high-fat diet, whereas they changed less, or worsened, on the high-carbohydrate “prudent” diet. Importantly, blood glucose, insulin and TG concentrations, and the number of small, dense LDL cholesterol particles increased on a low-fat diet, but were reduced on the LCHF diet, as were apolipoprotein B blood concentrations. Similarly, blood HDL cholesterol concentrations increased on the low-carbohydrate diet, but were reduced on the low-fat diet. Other studies have reported similar findings,145,146 especially the effect of high-carbohydrate diets in increasing the atherogenic small, dense LDL particles.146-148

As a result, the prevalence of the atherogenic pattern B, comprising increasing numbers of these atherogenic particles, is an inverse function of the percentage of fat in the diet (Figure 18).147

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As a result, the prevalence of the atherogenic pattern B, comprising increasing numbers of these atherogenic particles, is an inverse function of the percentage of fat in the diet (Figure 18).147
population of older women who followed the USDA dietary guidelines. The goal of the WHIRCDMT study was to determine whether or not a heart hypothesis, of which Rossouw continues as a staunch advocate, is associated with accelerated disease progression in persons with either established heart disease or type 2 diabetes mellitus. This study does not support Keys’ diet-heart hypothesis, of which Rossouw continues as a staunch advocate.

The multi-million dollar 48 835-person Woman’s Health Initiative Randomized Controlled Dietary Modification Trial, of which Rossouw was project leader, shows that the United States Department of Agriculture dietary guidelines are associated with accelerated disease progression in persons with either established heart disease or type 2 diabetes mellitus. This study does not support Keys’ diet-heart hypothesis, of which Rossouw continues as a staunch advocate.

The goal of the WHIRCDMT study was to determine whether or not a population of older women who followed the USDA dietary guidelines would reduce their risks of colorectal and breast cancers, as well as heart disease. For the study, 48 835 postmenopausal women were encouraged to either adopt the USDA dietary guidelines by reducing their fat intake, and eating more vegetables and grains, or to continue eating their usual diet. Women in the intervention group also received an “intensive behavioural modification programme” comprising 18 group sessions in the first year, followed by quarterly maintenance sessions for the next seven years. The control group only received a copy of dietary guidelines for Americans. As a result, any positive outcomes in the intervention group could not be ascribed purely to dietary change, since the intervention group received additional interventions not shared by the control group.

The study found that eating according to the USDA dietary guidelines did not reduce the risk of cancers of either the colorectum or breast. This is predictable if both cancers are associated with low-fat, high-carbohydrate diets, or rich in omega 6 polyunsaturated fats, of the type promoted by the 1977 USDA dietary guidelines. The authors concluded that the avoidance of weight gain reduced the risk for developing these cancers. Given that high-carbohydrate diets cause weight gain in persons with IR, it would have been more logical for the authors to postulate that high-carbohydrate diets explain the co-existence of obesity with colorectal and breast cancers in persons with IR.

The main reported finding of the WHIRCDMT study on heart disease was that “a reduced total fat intake and increased intake of vegetables, fruit and grains did not significantly reduce the risk of CHD, a stroke or CVD in postmenopausal women, and achieved only modest effects on CVD risk factors”. In reality, this study, published after the USDA dietary guidelines were first released, found that these eating guidelines were without any health benefits in postmenopausal women. The warnings expressed by the experts in 1977 quoted earlier, have proven to be correct.

Properly interpreted, this finding indicates that women with established heart disease at the start of the trial had a 26% increased risk of developing further cardiac complications if they adopted the USDA dietary guidelines. By showing that postmenopausal women with heart disease were at a lower risk of developing subsequent cardiac complications if they continued to eat more fat and fewer vegetables, fruit and grains, the study essentially disproves the diet-heart hypothesis. For how can a diet designed to prevent heart disease be associated with a worsening of the condition in those who are the most vulnerable because they already have the disease?

As I have described in detail elsewhere, this finding was not discussed further in the abstract, the discussion or the conclusions of that paper. In addition, a key line of text was missing from a table.
When challenged to explain these errors and omissions, the authors dismissed the only significant finding in their study as “likely to be a chance finding” because “there is no biological basis for expecting a different outcome in this (ill) subgroup, as shown in cholesterol-lowering trials on women with prior disease”. Thus, an inconvenient outcome that the authors disliked was ignored because of their certainty that this adverse result had no currently known biological basis. But this explanation is unacceptable.

For example, the authors failed to reference the Estrogenic Replacement and Atherosclerosis (ERA) Trial, which found that coronary atherosclerosis progressed significantly more rapidly over a three-year period in postmenopausal women eating the equivalent of the WHIDMT low-fat “prudent” diet. A higher carbohydrate intake accelerated coronary artery disease progression, as did the substitution of dietary saturated fat with polyunsaturated fat. In contrast, postmenopausal women eating the most saturated fat, and the least carbohydrates and polyunsaturated fat, showed no progression of coronary atherosclerosis, even though that group included a significantly higher proportion of current smokers. As expected, women eating the most saturated fat also had significantly higher serum HDL cholesterol and lower serum TG concentrations, as well as lower total cholesterol to HDL cholesterol ratios.

These findings, the subject of an accompanying editorial, predict that the clinical manifestation of coronary heart disease should increase in participants in the WHIDMT eating the low-fat “prudent” diet. When Howard et al found this, their responsibility was to explain why the conclusions from the Estrogenic Replacement and Atherosclerosis (ERA) trial were not relevant to their discovery. Instead, they ignored that research, choosing rather to advance their deceptive “biologically implausible” argument.

Eminently plausible biological explanations for this inconvenient finding in the WHIRCDMT would include the favourable changes in blood HDL cholesterol and TG concentrations measured in the ERA trial, together with the evidence that a HFLC diet reduces the blood concentration of small, dense LDL cholesterol particles, which, when oxidised or glycated, are considered particularly atherogenic.

The WHIRCDMT also found that although the higher carbohydrate intake of the intervention diet did not influence blood glucose control in women without diabetes, it caused a progressive worsening of control in those with type 2 diabetes mellitus. This finding “agrees with some, but not all, previous studies evaluating the effects of high- and low-carbohydrate diets in persons with diabetes”, forcing the authors to conclude that “caution should be exercised in recommending a reduction in overall dietary fat in women with type 2 diabetes mellitus, unless accompanied by additional recommendations to guide carbohydrate intake”. That diets with a high glycaemic load are associated with an increased risk of the development of type 2 diabetes mellitus is well established in the literature. In truth, the authors of both papers should have stated the obvious, namely that their findings indicate that persons with established heart disease or diabetes should be mandated to eat a higher-, not lower-fat, diet, in order to limit further progression of their disease.

A final study confirms this interpretation, at least in type 2 diabetes mellitus. In October 2012, an 11.5-year study on the combined effects of regular exercise and the USDA dietary guidelines in persons with type 2 diabetes mellitus, was terminated as “pointless” when it was established that these interventions were no more effective in slowing the progression of arterial damage than doing nothing. This confirms that type 2 diabetes mellitus is a determined disease that will not be beaten by simple measures, and certainly not by a diet rich in blood glucose and insulin-raising carbohydrates.

In summary, the WHIRCDMT, of which Rossouw was the “project director”, has clearly established that eating according to the USDA dietary guidelines is associated with an increased risk of the development of the complications of heart disease and of type 2 diabetes mellitus. Rossouw’s findings from the most expensive low-fat diet RCT yet undertaken, fatally damage his favoured diet-heart hypothesis.

**Conclusion**

The diet-heart hypothesis has its origins in an associational epidemiological study, and was driven by commercial interests in the absence of evidence from properly designed randomised controlled clinical trials. However, associational studies cannot ever prove causation, regardless of how frequently they are advanced as “definite” evidence. Today, the evidence is clear. Fat in the diet does not relate to the risk of heart disease. Rather, there is accumulating evidence that it is the exposure of susceptible individuals with IR to a high-carbohydrate diet for 10 or more years that produces obesity, diabetes and metabolic syndrome, and through these diseases, to an increased susceptibility to CHD.

It follows that the only way to counter the epidemic increases in all these diseases is to promote the consumption of diets with a reduced carbohydrate content, most especially in those with IR and metabolic syndrome.

On the evidence presented in this article, those who continue to prescribe or to promote “balanced” high-carbohydrate diets to such individuals are guilty of at best, ignorance; at worst, medical negligence. It is only a matter of time before a major class action will be instigated by patients with IR whose health has suffered as a result of following this wholly inappropriate advice.

**Declaration**

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**References**


