Milk and Other Dietary Influences on Coronary Heart Disease

by William B. Grant, Ph.D.

Abstract

While dietary links to ischemic heart disease (IHD) and coronary heart disease (CHD) mortality have been studied for many years, the correlation has not clearly been resolved, especially for older populations. In this paper, a multi-country statistical approach involving 32 countries is used to find dietary links to IHD and CHD for various age groups aged 35+. For IHD, milk carbohydrates were found to have the highest statistical association for males aged 35+ and females aged 65+, while for females aged 35-64, sugar was found to have the highest association. In the case of CHD, non-fat milk was found to have the highest association for males aged 45+ and females aged 75+, while for females 65-74, milk carbohydrates and sugar had the highest associations, and for females aged 45-64, sugar had the highest association. A number of mechanisms have been proposed in the literature that might explain the milk carbohydrate or non-fat milk association. One of the most prominent theories is that animal proteins contribute to homocysteine (Hcy) production; however, milk more than meat lacks adequate B vitamins to convert Hcy to useful products. Lactose and calcium in conjunction with Hcy from consumption of non-fat milk may also contribute to calcification of the arteries.

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Introduction

It is always difficult to find dietary links for chronic diseases since they take a long time to develop. There are five techniques that can be employed: multi-country statistical or ecological approach; case control approach; clinical studies; pathology studies; and animal studies. Each has its strengths and weaknesses.

The multi-country statistical approach has been used in the past as a way to link macronutrients to chronic disease, such as cancer and heart disease, although it has fallen into disuse during the past two decades, having been largely replaced by the case control approach. However, Grant[1] used this approach to find that dietary fat and total calories are high-risk factors for Alzheimer's disease, while fish consumption reduces the risk; and that diet near the time of development of Alzheimer's disease is more important than diet earlier in life. Using the case control approach, Smith et al[2] reported supporting evidence for total calories and diet after the

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Table 1. Rank order correlation coefficients for atherosclerotic coronary heart disease mortality rates for males 55-59 for various elements of national diets for 22 countries.[19]

Diet	Death from ACHD
Animal protein	0.756
Total calories	0.723
Animal fat	0.684
Fat	0.659
Carbohydrates	0.305
Vegetable fat	-0.236
Vegetable protein	-0.430

age of 60, while Kalmijn et al[3] reported supporting evidence for the dietary fat and fish findings. The work is summarized in ref. 4. These results show the high degree of specificity possible in linking diet to chronic disease using the multi-country approach, suggesting its demise was premature.

The advantage of using the multi-country approach is the disease mortality data and sometimes prevalence data are readily available in the literature, as are the dietary supply factors for macronutrients,[5] and very little time or funds are required for the research. The problem with using the multi-country approach is that dietary supply values do not represent exactly what people eat; for example, in the United States, an estimated 25 percent of the consumer food supply is not eaten. However, similar factors likely apply to other countries as well. In addition, confounding variables can affect the results, such as lifestyle factors, quality of medical delivery system, or dietary micronutrients not included in the FAO tables.[5] However, given the number of chronic diseases for which the macronutrient/disease link was first uncovered through the multi-country approach, and the great importance of macronutrients in the etiology of chronic disease, it deserves more attention, and can certainly provide a guide for additional research efforts.

The case control approach is currently the method most commonly used when trying to link diet to chronic disease. In this approach, a defined population is studied, including dietary factors and health problems, and statistical analyses are performed on the data. While this approach permits the study of micronutrients as well as macronutrients, such studies are costly and take years to conduct. More significantly, if important variables are not controlled in the study, wrong conclusions can be inferred from the data (e.g., the finding that increasing dietary fat leads to a reduction in the occurrence of stroke without controlling for dietary sodium).[6] Another problem with the case control approach is that women have generally been excluded from such studies, although this has changed in the past decade or so.

In the clinical approach, a small number of people are given modified diets, and thereafter, changes in body chemistry and disease status are measured. For example, it has been shown that if people remove sucrose from their diet, serum cholesterol can drop from 230 mg/dl to 160 mg/dl in 4 weeks, and that if sucrose is reintroduced into the diet, serum cholesterol levels rise rapidly again.[7]

In the pathology approach, tissues and organs of the deceased are examined to see what happened and to look for evidence of build-up of foreign matter in the tissues. Hcy, for example, is often found in the arterial plaque of those with atherosclerosis.[8,9]

In animal studies, animals that are thought to have some physiological factors in common with humans are fed diets containing suspected agents or injected directly with such agents. There is, however, no guarantee that animals really do mimic humans. Rath,[10] for example, wrote a book on why humans get heart disease but animals don't (his conclusion: They can synthesize vitamin C while humans can't).

Animal Studies on Diet and Atherosclerosis

Kritchevsky[11] reviewed the literature on diet and atherosclerosis with respect to serum cholesterol levels from experiments with animals, as well as some reference to ecological studies involving national data. Both carbohydrates and proteins have been shown many times to raise serum cholesterol levels in animals.

Kritchevsky[12] reviewed the early literature on dietary protein, cholesterol and atherosclerosis in animal studies using rabbits. A number of investigations dating from 1908[13] showed that animal protein (casein) was more atherogenic than plant protein (soy). Similar conclusions are reached in modern-day research.

Case Control Studies

Several recent case control studies are relevant to the present discussion. At least 3 recent case control studies have reported that a high-carbohydrate, low-fat diet offers no more protection against heart disease than does a low-carbohydrate, high-fat diet.[14-16] While these studies do not differentiate between simple and complex carbohydrates, and may not have controlled other confounding variables, they do strike a blow at the conventional wisdom that fat is the primary dietary cause of heart disease. As will be shown below, there are two possible reasons for these results: first, simple carbohydrates are a risk factor for heart disease[17]; and second, milk carbohydrates and non-fat milk are higher-risk factors for heart disease than either simple carbohydrates or saturated fat, and were not controlled in these studies.

Table 2. Correlation coefficients (r) between IHD mortality (1968 or 1969) and commodity consumption in 30 countries in the years 1963-1965.[30]

Variable	Men	Women
Sugar	0.76	0.69
Animal protein	0.75	0.58
Milk	0.72	0.48
Saturated fat (est.)	0.71	0.58
Meat	0.65	0.65
Total fat	0.59	0.39
Eggs	0.56	0.59
Total protein	0.49	0.45
Cigarettes (1953-55)	0.41	0.55
Fish	-0.19	-0.30
Vegetables	-0.39	-0.22
Cereals	-0.58	-0.39

Ecologic Studies of Diet and Heart Disease

Since the multi-country or ecologic approach can involve a large range of dietary values for most macronutrients, and can be done very inexpensively (the data already exist), it is worthwhile to review the history of multi-country studies of dietary links to IHD and CHD.

The earliest ecologic studies are those of Yudkin,[18] and Yerushalmy and Hilleboe.[19] Yudkin found the incidence of IHD could be correlated with intake of animal protein as well as that of fat. Yerushalmy and Hilleboe did a statistical comparison of dietary macronutrients and atherosclerotic CHD mortality rates for men aged 55-59 in 22 countries. They found animal protein, total calories, animal fat, and fat in general to have the highest rank order correlation coefficients (see Table 1), with carbohydrates having a low but positive coefficient.

The next reported study was by Joliffe and Archer.[20] They found saturated fat to be the most important factor accounting for IHD death rates between countries, with animal protein accounting for a large proportion of the variability in the rates.

The multi-country approach was also used in the 1960s for studying CHD, with the finding that sugar was also a risk factor.[21-23]

Table 3. Spearman rank order correlation coefficients for 1986 ischemic heart disease mortality rates for various elements of national diets for 32 countries. The animal protein, milk protein and sweetener values are from 1983; the animal fat is from 1973; cigarettes are from 1972

Age	mcar*	nfm	milk	mpro	mf	af	s	cig	cer
Males									
75+	0.815	0.794	0.668	0.651	0.536	0.669	0.669	0.325	-0.659
65-74	0.852	0.851	0.749	0.732	0.634	0.766	0.639	0.426	-0.692
55-64	0.845	0.842	0.742	0.712	0.634	0.744	0.582	0.472	-0.659
45-54	0.821	0.814	0.718	0.679	0.618	0.728	0.581	0.531	-0.628
35-44	0.675	0.659	0.583	0.530	0.507	0.576	0.463	0.460	-0.449
Females									
75+	0.796	0.728	0.554	0.531	0.400	0.549	0.754	0.291	-0.572
65-74	0.738	0.683	0.522	0.492	0.382	0.596	0.687	0.381	-0.524
55-64	0.675	0.598	0.433	0.393	0.293	0.506	0.704	0.390	-0.456
45-54	0.572	0.476	nss@	nss	nss	0.367	0.725	0.356	-0.371
35-44	nss	nss	nss	nss	nss	nss	0.600	nss	nss

* mcar = milk carbohydrates, nfm = non-fat milk, milk = milk calories, mpro = milk protein, mf = milk fat, af = animal fat, s = sweeteners, cig = cigarettes, cer = cereals.
@ not statistically significant at the p = 0.05 level

Keys[24,25] seems to have made the case that animal fat should be considered a much more important CHD risk factor than sugar, with Walker[26] echoing the sentiment against sugar. However, the conclusions were based only on studying CHD mortality among men, and limited to those between the ages of 40 and 59. Reiser[27] conducted a critical examination of the literature linking saturated fat to serum cholesterol concentration and found a number of problems with the studies, primarily conducted in the 1950s and 1960s, including those of Keys et al.[28,29] Armstrong et al[30] were able to show that sugar had the highest statistical association with IHD mortality rate for 30 countries (Table 2), but this finding seems to have been largely ignored. See the discussion in ref. 31.

Seely[32] used 24 countries for male CHD mortality rates from the latest years available (1975-1978) along with 11 dietary macronutrients, plus cigarettes. Milk products in various forms were found to have the highest association. For the three items judged to be most important, simple correlation coefficients (r) were found as follows: unfermented milk protein, $r^2 = 0.882$; sugar, $r^2 = 0.707$; and saturated fats, $r^2 = 0.610$. For females, data from 21 countries were used, with similar results, with milk protein predominating.[33] (Note that r^2 is generally taken as the fraction of the data explained by the model, e.g. r^2 of 0.61 means 61% of the data reviewed correlates with the model.)

Seely[34] extended this work using CHD mortality rates for 21 countries in 1983. For diet-disease lag times of 4 and 8 years, oats were found to have the highest associations with CHD mortality rates (r^2 as high as 0.778) for males in 10-year age groupings from 45-74 years, but for 12- and 16-year lags, milk proteins were found to have the highest associations (r^2 as high as 0.785). For women 45-54 with a 16-year lag time, sugar had the highest association ($r^2 = 0.426$), while for women 65-74 and an 8-year lag, oats were found to have the highest association ($r^2 = 0.760$), with milk fats and milk protein not far behind ($r^2 = 0.676$ and 0.664, respectively). While there are possible mechanisms to explain the milk-CHD connection, no mechanism was suggested for oats.

Gey et al[35] reported an inverse correlation between plasma vitamin E and IHD mortality rate based on a multi-country study involving 16 European study populations. For each population, approximately 100 apparently healthy men aged 40-49 were studied for plasma vitamin E. Regional IHD mortality rates for males aged 40-59 were used as well. Inverse correlations (r^2) between 0.62 and 0.73 were found.

Bolton-Smith and Woodward[36] studied approximately 8,000 men and women in Scotland primarily between the ages of 40 and 59 for dietary associations with CHD. The most significant finding was an odds ratio of 1.21 for those in the highest quintile for lactose intake.

A recent epidemiologic study of Hcy in men aged 40-49 from 11 countries, found a significant association ($r^2 = 0.50$, $p<0.05$) for CHD mortality rate and plasma total Hcy.[37] The lowest CVD mortality rates (170-210 cases/100,000) were found in Japan and France; they had near the lowest Hcy values (7-8 μmol/L). The highest Hcy value was found in Finland (10.7 μmol/L), which also had the highest CVD mortality rate (550 cases/100,000). It should be pointed out that while statistical association is relatively high, it probably would be higher if people over the age of 75 were studied (see below) and if only those with CHD, not CVD were included, since the link between Hcy and stroke has not been demonstrated.

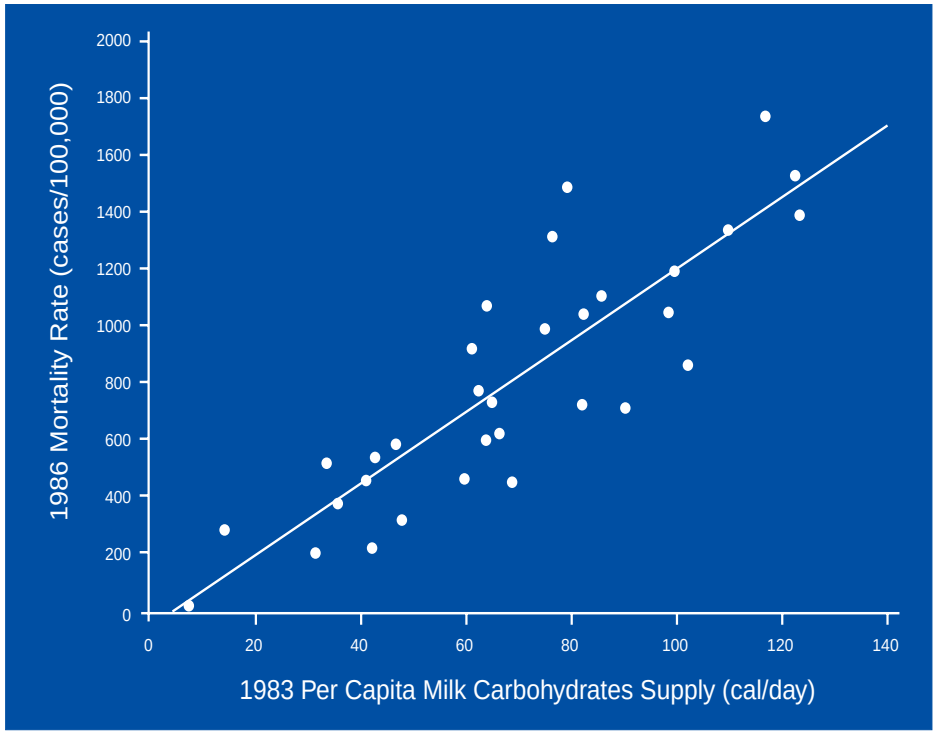
Dietary links to IHD were recently reexamined[17] with the finding that for males age 45-74, animal fat was the primary dietary risk factor, while for females age 55-74, simple sugars were the primary risk factor. Neither animal protein nor milk were considered in that analysis, which turns out to be a weakness in that particular study.

The Present 32-Country Ecological Study

In the study reported here, statistical analyses were rerun for IHD using 32 countries (Footnote 1)**.** Several countries were excluded for which the data points were more than 2 standard deviations away from the mean of the regression for CHD and the highest associative factors for males age 75+. These include four Eastern European countries[38] as well as Argentina and Paraguay. It is thought that non-dietary factors, such as quality of health care, play roles in elevating the CHD mortality rates in the excluded countries.

The same epidemiologic data[39] and dietary supply data source[5] as in ref. 17 were used with animal protein, cereals, meat protein, milk calories, carbohydrates, fat, and with protein, non-fat milk, and cigarettes[40] added.

Figure 1. Ischemic heart disease mortality rates, males aged 65-74[39] vs. milk carbohydrates



The lag between dietary supply and mortality was varied between 1973 (animal fat, animal protein, milk protein) and 1983 (animal protein, milk, and sweeteners, including all simple sugars beyond what are found in whole foods, such as fruit).

The Spearman rank order correlation coefficients (SROCC), a measure of statistical association, are given for IHD in Table 3, and for milk carbohydrates in Table 4. Non-fat milk (determined by taking nine times the milk fat [grams] from total milk calories) and milk carbohydrates (non-fat milk less 4 times milk protein [grams]) have the highest SROCC values for males of all ages and females aged 65+, while sugar has the highest SROCC values for females aged 35-64. However, non-fat milk has SROCC values very near those for milk carbohydrates. Animal fat has higher SROCC values than does sugar for males aged 35-74, with the situation reversed for females aged 35+, in agreement with the results presented in ref. 17. Cereals have strong inverse SROCC values for both males and females. It should be noted that the macronutrient with the highest SROCC value is most likely to have a causal relation to heart disease. Those with lower SROCC values could have them either because of association with the highest-value macronutrient or because of some causal relationship. Statistics alone are not able to distinguish between these two possibilities.

Table 4. Spearman rank order correlation coefficients for various macronutrients with respect to milk carbohydrates

Macronutrient	SROCC
Non-fat milk	0.950
Milk calories	0.846
Milk protein	0.817
Milk fat	0.740
Animal fat	0.723
Sweeteners	0.571
Cigarettes	0.451
Cereals	-0.645

The regression results are in Table 5 and Figure 1. The F value (t^2, student-t test) is used to determine whether any multi-linear regressions are statistically significant. Increasing the number of degrees of freedom by adding variables almost always increases the regression coefficient, r, so looking for the highest r value is not a sufficient test of a more statistically-significant association. It was found that the macronutrients with the highest SROCC values also had the highest r values. In addition, no multi-linear regression yielded statistically-more-significant values than for the single linear regressions.

For CHD, SROCC values were first determined as for IHD. The results are given in Table 6, with the values for non-fat milk in Table 7. The primary difference is that non-fat milk is found to have the highest SROCC values for males aged 45+. In addition, a number of macronutrients are found to be inversely associated with CHD for females aged 35-44. The only gender and age group for which oats were found to be statistically significant was females aged 65-74, but the F value with oats is statistically the same as without.

The regression results for CHD are given in Table 8 and Figure 2. Again, the macronutrients with the highest SROCC values yielded the highest r values for simple linear regressions, and no multi-linear analyses yielded F values higher than for the simple linear regressions. Note that while the regression

Footnote 1. Countries included in the CHD mortality studies: Australia, Austria, Belgium, Canada, Chile, Costa Rica, Cuba, Denmark, Ecuador, England/Wales, Finland, France, West Germany, Greece, Hong Kong, Italy, Japan, South Korea, Mexico, Netherlands, New Zealand, Norway, Panama, Portugal, Singapore, Spain, Sri Lanka, Sweden, Switzerland, Uruguay, United States, and Venezuela. Eastern European countries were omitted since they had CHD mortality rates higher than can be attributed primarily to diet,[38] likewise for Argentina and Paraguay.

line passes very near the origin for IHD, there is a zero-non-fat milk supply intercept near 1100 cases/year (the same intercept was found for females aged 75+). This implies that a significant portion of CHD mortality among males aged 75+ are likely not related to dietary non-fat milk.

Descriptions of the statistics for milk carbohydrates and non-fat milk in the national per capita dietary supplies of the 32 countries studied are given in Table 9.

Thus, the statistical results of the present study confirm the finding in ref. 17 that sugar is important in the etiology of heart disease for middle-aged females, and the results of the studies in refs. 30, 32-34 that the non-fat components of milk are important in the etiology of heart disease for both males and females.

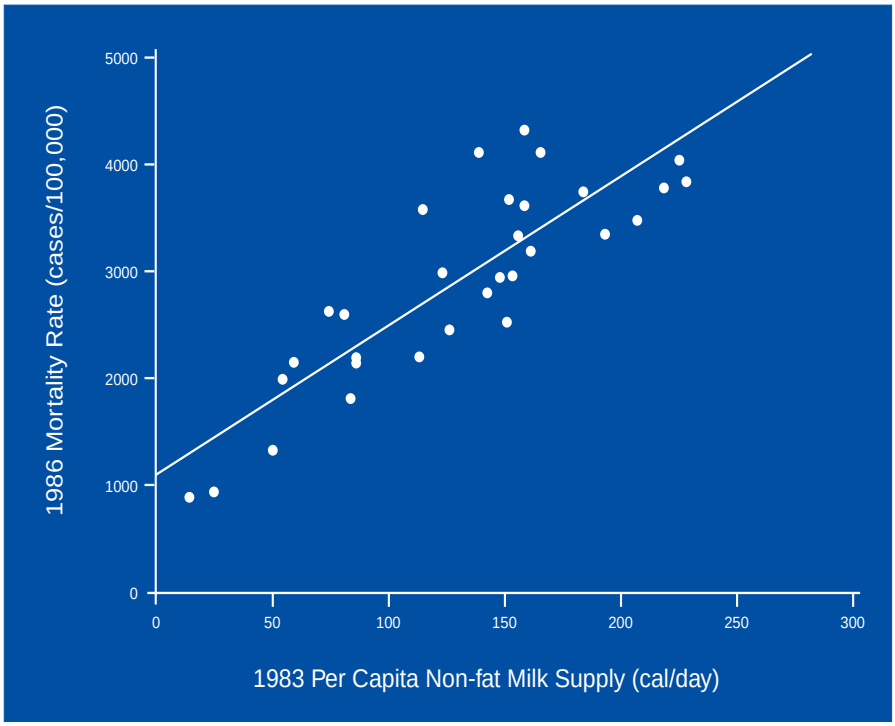
Discussion

Cardiovascular disease is primarily caused by atherosclerosis. A number of theories have been advanced regarding its causes.[11,12,42,43] While cholesterol is an important risk factor for IHD early in life, its importance declines with age. Law et al[41] report that decreasing serum cholesterol in men by 0.6 mmol/l (about 10%) was associated with a decrease in incidence of IHD of 54 percent at age 40 years, decreasing to 19 percent at age 80 years, which is consistent with the SROCC values for non-fat milk and milk carbohydrates vs. animal fat CHD in Table 7. In this discussion, a number of mechanisms that could link milk carbohydrates and milk protein to IHD and CHD are discussed.

Homocysteine

As first noted by McCully in 1969,[44] Hcy plays an important role in the etiology of heart disease through its role in the development of atherosclerosis.[8,9,45] Hcy is derived from the amino acid methionine, more common in animal proteins than in vegetable proteins, and can be converted back to methionine with the help of folic acid and vitamin B_{12}. It can also be eliminated from the body through the action of vitamin B_6.[9] Those who have elevated levels of Hcy are generally found to be deficient in the B vitamins,[46-48] which can be overcome by vitamin supplementation.[49-52] The results of the Nurses' Health Study[48] suggest folate and vitamin B6 are much more important than vitamin B12 in controlling homocysteine levels. Both folate and vitamin B12 are

Figure 2. Ischemic heart disease mortality rates, males aged 75+[39] vs. non-fat milk supply[5]



involved in converting homocysteine back to methionine,[9] and, in the Nurses' Health Study, dietary folate was sufficient. A number of recent papers have examined or reviewed the mechanisms involved.[9,53-57] It appears that Hcy may alter lipoprotein(a), an atherogenic lipoprotein,[58] so as to increase the reactivity of the plasminogen-like apolipoprotein(a) portion of the molecule.[59] Some epidemiologic studies of elevated Hcy with age[60] and diet[61] have been reported. Homocysteine has also been associated with a number of other diseases.[62-64]

The fact that milk protein becomes strongly associated with IHD or CHD only after age 65 for females suggests the human body is less well adapted to deal with it as the body ages. Reference 54 discusses what changes might take place with age that might be involved.

Table 5. Highest regression results for 1986 ischemic heart disease mortality rates for 32 countries. $p<0.001$.

Age	Macronutrient	r^2	F*
Males			
75+	milk carbohydrate	0.689	66.40
65-74	milk carbo.	0.739	85.16
55-64	milk carbo.	0.678	63.07
45-54	milk carbo.	0.610	47.00
35-44	milk carbo.	0.434	23.01
Females			
75+	milk carbo.	0.656	57.30
65-74	milk carbo.	0.567	39.34
55-64	sugar	0.508	31.00
45-54	sugar	0.582	41.85
35-44	sugar	0.489	26.78

* $F = t^2$, student-t test

Table 6. Spearman rank order correlation coefficients for 1986 coronary heart disease maortality rates for various elements of national diets for 32 countries as in Table 3.

Age	mcar	nfm	milk	mpro	mf	af	s	cig	cer
Males									
75+	0.820	0.852	0.794	0.783	0.717	0.717	0.673	0.396	-0.755
65-74	0.841	0.859	0.783	0.766	0.692	0.800	0.559	0.449	-0.692
55-64	0.760	0.781	0.705	0.674	0.613	0.733	0.479	0.409	-0.636
45-54	0.666	0.671	0.587	0.559	0.509	0.629	0.421	0.471	-0.495
35-44	0.348	nss	nss	nss	nss	nss	nss	nss	nss
Females									
75+	0.797	0.787	0.712	0.690	0.649	0.633	0.666	0.435	-0.650
65-74	0.648	0.619	0.488	0.466	0.388	0.571	0.640	0.448	-0.504
55-64	0.492	0.410	nss	nss	nss	nss	0.600	nss	nss
45-54	nss	nss	nss	nss	nss	nss	0.469	nss	nss
35-44	-0.37	-0.45	-0.51	-0.52	-0.48	-0.55	nss	nss	nss

Other Factors Related to Non-Fat Milk

A number of investigators have reported finding elevated levels of bovine substances in the arteries of people with atherosclerosis. Whether these findings indicate causality is not clear. However, the fact there are statistical associations between bovine substances and atherosclerosis further substantiates the ecological study findings of high associations between non-fat milk or milk carbohydrates and CHD and IHD mortality. Several of these studies are discussed here.

Ross et al[65] reported ectopic xanthine oxidase (X-O) was found in elevated amounts in atherosclerotic plaques. It is postulated there is an enzyme-induced alteration of the phospholipid composition of the cell membrane, inducing serious inflammation or perfusion of the arterial endothelium or the myocardium. Bovine milk ingestion is a major source of the X-O enzyme.

Annand[66] suggested heat-denatured bovine immunoglobulin (BGG) may be a major risk factor in the pathogenesis of atherosclerosis. A number of mechanisms

linking BGG to atherosclerosis were presented, including binding to platelets, perhaps organizing thrombosis; promoting the release of histamines, providing a link to anaphylaxis; binding to calcium; and blocking the metabolism of cholesterol, thus promoting hyperlipidemia.

Seely[67,68] made the case that excess dietary calcium in Western countries is a major cause of arterial disease. One possible action of calcium in the cardiovascular system is to calcify the soft tissues, leading to increased hypertension and a greater burden on the heart. Arterial plaque is very calcium rich.[9] Ganong[69] mentions lactose increases calcium absorption, and Segall[70,71] argues that lactose is the important factor in plaque formation. Thus, non-fat milk, with calcium and lactose, may contribute significantly to increased calcification of the arteries. Seely suggests reducing calcium intake by decreasing foods such as milk, or adding more grains, rich in phytic acid which converts dietary calcium into insoluble phosphates. This idea receives support from animal studies showing calcium antagonists inhibit the development of atherosclerosis,[72] as well as the strong inverse statistical relationship between cereals and CHD and IHD mortality rates (see Tables 3 and 6).[73]

In summary, a number of mechanisms have been suggested that would link non-fat milk to IHD and CHD, especially as one ages. In addition, a number of studies have found bovine milk components in atherosclerotic plaque. Given the strong statistical link between milk carbohydrates, non-fat milk and heart disease in this study as well as those by Seely,[32-34] much more attention should be given to the study of the link between dietary bovine milk and heart disease.

Table 7. Spearman rank order correlation coefficients for various macronutrients with respect to non-fat milk.

Macronutrient	SROCC
Milk carbohydrates	0.950
Milk calories	0.944
Milk protein	0.940
Milk fat	0.859
Animal fat	0.808
Sweeteners	0.571
Cigarettes	0.486
Cereals	-0.718

Sugar

The mechanism linking sugar to heart disease seems primarily to be the production of triglycerides. Excess sugar, in the form of fructose directly or from sucrose, metabolizes to triglycerides, leading to large increases in serum triglycerides[74] and is incorporated predominantly into very low density lipoprotein (VLDL)cholesterol.[75] Both elevated triglycerides and VLDLs are risk factors for CHD. Simple sugars also cause a host of other problems, such as hyperglycemia, hypoglycemia, hypoxia, and impaired immune system response, all of which can lead to cardiovascular problems.[76] Simple sugars also replace foods rich in vitamins and minerals, and sugar metabolism involves several B vitamins. A deficiency in three B vitamins is linked to elevated plasma Hcy levels.[46] Finally, sucrose, in particular the fructose moiety of the sucrose molecule, as well as fructose itself, may induce oxidative damage through increased glycation of proteins (associated with complications of diabetes) and cross-linking of tissue proteins.[77] A full discussion of sugar and its relation to heart disease is beyond the scope of this investigation and can be found in a previous article by this author.[17]

Fish

Fish consumption has been found to lower the CHD mortality rate.[79] This can be related to both a lowering of plasma lipids, lipoproteins, apoproteins,[79] and homocysteine.[80]

Gender-Based Differences

The findings of gender-based differences in CHD mortality rates in the

Table 8. Highest regression results for 1986 coronary heart disease mortality rates for 32 countries. p<0.001 unless otherwise noted.

Age	Macronutrient	r^2	F*	p
Males				
75+	non-fat milk	0.753	91.21	
65-74	non-fat milk	0.724	78.87	
55-64	non-fat milk	0.545	35.94	
45-54	non-fat milk	0.335	15.13	
Females				
75+	non-fat milk	0.666	59.69	
65-74	sugar, oats	0.652	27.16	
65-74	milk carbo	0.475	27.12	
65-74	sugar	0.474	27.02	
55-64	sugar	0.398	19.80	
45-54	sugar	0.181	6.63	0.015

United States receive further support in the cardiovascular disease mortality rates for this country, which include CHD as well as stroke. During the time frame 1979-1995, male mortality has declined from 500 thousand/year (k/yr) to 455 k/yr, while female mortality has increased from 470 k/yr to just over 500 k/yr.[81] If we assume that those concerned about CHD heeded the warnings about fat as a likely cause and tried to consume foods with less fat, they may have increased their consumption of

Table 9. Statistical description of the milk carbohydrate and non-fat milk supply values in the national dietary supplies for 1983

Macronutrient	Mean (cal/day)	Range (cal/day)
Milk carbohydrate	68.7+30.0	8.0-123.1
Non-fat milk	133.0+60.3	13.6-244.3

sugar, since many low-fat foods simply replace fat calories with sugar calories. Per capita animal fat supply that would have affected the outcome has remained nearly constant in the United States, while sugar supply has increased about 9 percent during the period. The tendency to consume low-fat, high-sugar foods would benefit men, but not women.

An unresolved issue in those findings is the gender-based difference in response to dietary macronutrients for those aged 35-74. Barker et al[82] showed Type A personality (high-stress) women prefer sugar while Type A men prefer calories, fat, and protein; however, the food preference differences between American men and women for all age groups in the early 1980s was not very large. For adults age 25-44, men derived 17 percent of their calories from sugar while women derived 19 percent of their calories from sugar, with both deriving 42-43 percent of their calories from fat.[83] For those over the age of 65, the results were similar, although women derived 21 percent of their calories from sugar compared with 19 percent for men.

A more likely explanation is that because of the importance of milk production by women, hormones such as estrogen and other physiological adaptations to milk production are able to manage not only lipids but also proteins and lactose in a manner which does not adversely affect the cardiovascular system during the childbearing years.[84] Indeed, estrogen replacement therapy for postmenopausal women leads to approximately a 50 percent reduction in coronary events.[85] However, sucrose and fructose are not required for lactation. Fructose readily metabolizes to triglycerides and can enter the blood plasma directly or through incorporation in the liver into VLDL cholesterol.

Summary

While these statistical results seem to be robust, i.e., they have high statistical significance and are generally repeated using different data sets, by themselves they do not prove causality. In order to demonstrate causality, criteria such as those laid out by Hill[86] have to be satisfied. These include mechanisms, linear dose/response relation, consistent through a large

number of varied populations, verified by clinical experiments, etc. While it is beyond the scope of this paper to establish whether the relations between non-fat milk and sugars are definitely causal for atherosclerotic heart disease, they seem to satisfy the criteria, having been discussed in the literature for years. The issue probably won't be resolved until the results are confirmed through case control studies. However, given the mounting evidence that non-fat milk and sweeteners likely contribute to atherosclerosis along with animal fat, interested persons might want to start making dietary changes now in anticipation of confirmation of the findings presented here.

These findings strongly suggest that to reduce the risk of CHD mortality among males of all ages and females above the age of 65, non-fat milk consumption should be reduced and vitamin B supplementation[87] should be increased. Consumption of simple sugars should be reduced by females below the age of 74, and probably by males and females of all ages.

A question that cannot be resolved with ecological studies is to what extent macronutrients other than those with the highest statistical correlations with the particular disease should be considered risk factors for the disease. As shown in Tables 3, 4, 6 and 7, the SROCC values for IHD and CHD for macronutrients with weaker statistical associations than milk carbohydrates or non-fat milk are lower by approximately the ratio of the SROCC values for the macronutrients with respect to milk carbohydrates or non-fat milk. The other macronutrients could be merely confounding factors, or they could play a role, especially if the primary macronutrients are reduced in or absent from the diet.

The ecological statistical results presented here, present strong evidence for dietary non-fat milk playing an important role in the etiology of heart disease.[30,32-34] A number of animal studies have also shown milk to be atherosclerotic.[11,12] The author is not aware of any studies showing that non-fat milk or milk carbohydrates are not strongly associated with heart disease, most likely because milk is generally not considered a risk factor for heart disease, and, therefore, is not studied in conjunction with heart disease. A number of putative mechanisms have been identified that could make the link between non-fat milk consumption and heart disease, with unopposed Hcy production being most prominent among them. The fact that heart disease mortality rates remain high despite years of claiming that cholesterol is the primary risk factor for heart disease resulting in subsequent dietary reductions of fat and cholesterol in the general population, supports the idea that heart disease is not adequately understood by the medical system. It is strongly urged that additional research into the relation between milk and sugar consumption and heart disease be studied using case control, clinical, and pathological approaches.

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