

The Relationship Between Meat Intake and Cardiovascular Disease

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INTRODUCTION

Dietary patterns are a major factor in the development of coronary heart disease (CHD) and other chronic disorders. Much published research examines the role of dietary fat and cholesterol in the development of CHD. Because meat is a major source of dietary fat and cholesterol, investigators have studied the impact of meat consumption on CHD risk. Data regarding meat consumption per se and CHD risk are limited, however, and it is difficult to differentiate the impact of meat consumption from that of cholesterol and fat. Nevertheless, current recommendations by the American Heart Association emphasize greater consumption of fruits and vegetables, and reduced consumption of meats, especially red meats or non-lean meats¹. These recommendations are based chiefly on findings from studies conducted over the last several decades. In this paper, we review the data on meat consumption and cardiovascular risk, and identify future directions for research.

STUDY DESIGNS USED IN EPIDEMIOLOGIC RESEARCH

Before discussing specific results, it is worth reviewing the types of study designs used in conducting research in humans. Different study designs are associated with different advantages and disadvantages that have implications for the interpretation of results. **Table 1** summarizes the most common types of study designs. Prospective studies and clinical trials yield the best data.

Prospective Studies

Prospective studies enroll large numbers of subjects before the onset of disease and follow subjects forward in time in order to document new cases of the disease as it occurs. A number of risk factors are measured at the beginning of the study, before the disease develops in any subject. At the end of the study, it is possible to determine the risk of developing the disease according to various levels of specific risk factors. In prospective studies putative risk factors are determined *before* the onset of disease, thus establishing a logical temporal association between a risk factor of interest and the disease. This is a major advantage over cross-sectional or case-control study designs. Another advantage of determining the risk factor before disease appears is that *recall bias* is eliminated. Recall bias occurs when subjects over-report their exposure to the risk factor because they suspect an association between that risk factor and the disease of interest. Recall bias is particularly problematic for studies of dietary intake since much of the exposure data, i.e. dietary intake, are determined from recall. Even without recall bias, prospective studies are still subject to misinterpretation due to confounding by other measured or unmeasured factors. Confounding occurs when another factor is associated with both the outcome of interest and the putative risk factor. This three-way association can make it difficult to determine which of the two factors is truly associated with the disease.

Randomized Clinical Trials

In contrast to each of the other study designs, only randomized clinical trials (RCTs) have the ability to determine directly the effect of an exposure or intervention on

disease risk. RCTs assign one group of participants to receive an intervention while another group receives a “control” or comparison intervention. Random assignment of interventions substantially reduces or eliminates the impact of confounding factors and allows researchers to isolate effects of a single factor or intervention. In studies of food consumption, however, there are limitations to our ability to determine the impact of a food (e.g., meat) as opposed to its nutrient constituents (e.g., cholesterol or fat). Furthermore, drastic dietary changes (e.g., elimination of meat from the diet) are not likely to be sustained and thus, are impractical, especially since these dietary changes would have to occur over a long period of time in order for researchers to determine their impact on disease outcomes.

Cross-Sectional and Case-Control Studies

Researchers often use data from cross-sectional and case-control studies to provide a rationale to conduct more definitive prospective studies or clinical trials. Cross-sectional studies examine both disease and potential risk factors at a single point in time. Hence, while an association between the disease and a risk factor may be found, a direct cause-effect relationship cannot be defined. However, based on data from other sources, researchers attempt to infer such a relationship though such an inference cannot be drawn directly from cross-sectional analyses alone.

In case-control studies, risk factors of interest are compared between cases (persons already known to have the disease) and controls (persons without the disease). Again, no temporal associations can be made since all measurements occur at a single point in time. Like cross-sectional studies, causality is inferred, but not proven.

Although an abundance of data from cross-sectional and case-control studies exists regarding meat intake and CHD risk, these data are subject to substantial confounding due to their design. The data are thus “weaker” than data from prospective studies or clinical trials. With this review we will only present data that have utilized the more robust study designs of prospective studies and clinical trials.

PROSPECTIVE STUDIES

RED MEAT

Data regarding the association between red meat intake and the risk of CHD is conflicting. Several large studies comparing vegetarians to non-vegetarians have found an increased risk of CHD in persons who consume meat (see below). In men, a 2-fold increase in risk was associated with eating beef more than 3 times per week². In the Nurse’s Health Study, women with a higher ratio of red meat to fish and poultry intake had significantly higher risk of CHD although neither red meat alone nor fish alone was significantly associated with harm or benefit after adjusting for other cardiovascular risk factors³. In another study, greater consumption of heme-iron, which is mainly derived from red meat, was associated with a higher risk of fatal and non-fatal CHD events⁴.

One mechanism by which red meat intake could increase CHD risk is by increasing levels of harmful cholesterol levels. Increased total cholesterol has long been associated with increased risk of CHD. Total cholesterol is composed of three main elements: Low-density lipoprotein cholesterol (“LDL cholesterol”), High-density lipoprotein cholesterol (“HDL cholesterol”) and triglycerides. Increased levels of LDL cholesterol and triglycerides in particular have been associated with higher risk of CHD.

LDL cholesterol is therefore called “bad cholesterol”. In contrast, HDL cholesterol has been found to protect against CHD and therefore, increased levels are desirable and therefore is called “good cholesterol”. The reason red meat has the potential to increase CHD risk is because it contains a high proportion of saturated fat. Saturated fat can be converted to both “good” and “bad” cholesterol in the body. Hence, these changes could offset one another resulting in no increase in CHD risk. Conversely, a reduction in total and saturated fat intake may cause a drop in HDL cholesterol that would offset the benefit of a reduction in LDL cholesterol. Furthermore, a large part of the saturated fat in beef is stearic acid, which has little effect on blood lipids⁵. Overall, it appears that the risk of CHD associated with fat intake might, in the end, depend upon the total balance of cholesterol raising saturated fats and cholesterol lowering unsaturated fats. Apart from its effects on cholesterol levels, red meat could contain other elements, such as animal proteins, that might adversely affect CHD risk factors, but this hypothesis has not been proven.

FISH

While red meat intake has most consistently been found to increase the future risk of heart disease, fish intake may have beneficial effects, although data are inconsistent. One hypothesis is that a beneficial effect of fish consumption is due to omega-3 fatty acids contained in fish. Omega-3 fatty acids have a favorable effect on serum lipids and may also reduce the propensity to form blood clots⁶. A reduced clotting tendency could explain why fish consumption tends to be more protective in persons already at high-risk of developing heart disease. In several prospective studies, persons who eat fish have a

reduced risk of developing heart disease, but other studies have shown no impact of fish consumption on CHD risk (**Table 3**). Marckmann et al ⁷ recently performed a systematic review of eleven prospective studies of fish intake and CHD mortality. A total of 116,764 individuals were included in these studies. Four studies were judged to be of high quality based on the design and conduct of the study as well as appropriate adjustment for potential confounding factors. The two largest studies (n = 44,895 and 20,051) were conducted in populations at low-risk for CHD. No protective effect of fish consumption was observed in these studies. Two other high-quality studies were smaller (n = 852 and 1,822) and included individuals at higher risk for CHD. These studies suggested a benefit to fish consumption (i.e., fewer deaths due to CHD). Thus, prospective studies of fish intake are conflicting with regard to the beneficial impact of fish intake on CHD risk and may only be effective in higher risk populations.

Another potential explanation for an apparent benefit of fish intake is that fish intake per se is not responsible for the findings, but is associated with other dietary factors that could themselves influence CHD risk. Since red meat intake may be lower in persons who consume more fish, the decrease in red meat intake could explain the apparent protective effect of fish. Alternatively, some unrecognized harmful substance could be contained within fish in differential amounts leading to conflicting results. In a study of men in Eastern Finland, Salonen et al.⁸ demonstrated that a high intake of mercury from non-fatty freshwater fish was associated with a higher risk of CHD. In another study, increased mercury content in toenails, which is highly associated with fish consumption, was associated with a 2-fold increase in risk of a first heart attack in persons with the highest quintile versus the lowest quintile of mercury content⁹. In

contrast, a study in medical doctors and dentists failed to find an association between mercury content and risk of heart attack even though mercury levels were highly associated with fish consumption¹⁰.

VEGETARIAN DIETS

Much of the data on the health effects of vegetarian diets comes from studies in Seventh-Day Adventist populations. A recent study that combined results from 5 large prospective studies showed that vegetarians have about a 25% lower risk of heart disease than non-vegetarians¹¹. Although there is wide variation, it should be noted that the average Seventh-day Adventist vegetarian does not consume a low-fat diet. Estimates from studies of Seventh-day Adventists show average fat consumption of 100.5 g/d in vegetarians and 102.2 g/d in non-vegetarians¹². The difference between these groups was in the type of fat consumed. Vegetarians consumed a greater proportion of unsaturated fats than non-vegetarians. Thus, a low-fat diet may be less important than avoidance of saturated fats, which in the U.S. are primarily from animal sources. In contrast, very-low-fat diets such as those consumed by vegans do not clearly reduce total or cause-specific mortality below the rates seen in the more liberal vegetarians, although more evidence is needed¹².

It is important to note that vegetarians may have lower disease risk because of their lack of meat consumption, but it is also possible that this protection could be due to increased consumption of fruits, vegetables, or nuts. Vegetables, fruit, grains, and nuts contain phyosterols and unsaturated fats that lower harmful blood cholesterol concentrations. In addition, they contain a number of antioxidants (eg, tocopherols,

ascorbate, carotenoids, saponins, and flavonoids) that may reduce the risk of heart disease by preventing the oxidation of LDL cholesterol, and may also reduce the risk of cancer by preventing oxidative damage to nucleic acids and other cellular components¹³.

DIETARY PROTEIN

In addition to differences in fatty acid composition between meats and plant foods, there is growing interest in the potential impact of dietary protein on disease risk. Unfortunately, few studies have examined the independent effect of protein intake on cardiovascular disease risk. Most prospective studies of dietary protein intake and CHD risk factors are difficult to interpret because they did not account for other important dietary factors often associated with higher protein intake, namely greater intake of dietary fat^{14,15}. Vegetable protein has been associated with reduced risk of CHD¹⁶, but it is not clear if this is independent of total caloric intake and other dietary factors. In one well controlled prospective study in healthy women, increased dietary protein intake from animal or vegetable sources was not associated with an increase risk of ischemic heart disease¹⁷. This study did suggest, however, that at the same level of fat and calorie intake, increased dietary protein relative to carbohydrate intake is associated with a non-significant reduction in ischemic heart disease risk. These results must be viewed with caution, however, because an increase in protein intake from animal sources is frequently accompanied by an increase in saturated fat and cholesterol, and may have adverse effects in people with kidney disease or osteoporosis.

Few clinical trials have addressed the impact of protein on cardiovascular disease risk. Observational studies have identified an inverse relationship between protein intake

and blood pressure¹⁸, but most clinical trials of protein and blood pressure have lacked sufficient statistical power to detect small, but important, changes in blood pressure. Hence, it is unclear whether increased animal protein is associated with CHD risk. More studies are needed to determine the strength of this association.

CLINICAL TRIALS

Trials of dietary interventions examining effects on cardiovascular end-points such as death, myocardial infarction and stroke, are uncommon compared to pharmacologic interventions. This is because there are often insurmountable logistical problems of cost and compliance with large-scale dietary studies. In fact, despite substantial evidence from observational studies that meat intake increases the risk of developing ischemic heart disease, there are no clinical trials that have directly tested the impact of a vegetarian diet compared to an omnivorous diet on major cardiovascular disease endpoints. Instead, most dietary studies of major cardiovascular disease endpoints have been designed to test the effect of the type or amount of dietary fat on cardiovascular disease outcomes. In order to achieve their goals, however, most studies of dietary patterns recommended a reduction in meat intake, especially red meat, as part of an overall dietary change that included reduced saturated fat intake from meat, dairy and other sources. Hence, these studies can provide some indirect evidence of the potential impact of meat reduction, but do not directly test the effect of meat consumption per se.

A reduction in saturated fat and a relative increase in poly- or monounsaturated fats is a common pattern for most dietary clinical trials (**Table 4**) On the whole, these

studies suggest that a reduction in dietary saturated fat and cholesterol could result in a substantial reduction in cardiovascular disease events. Of particular interest in these studies is the finding that significant reductions in cardiovascular disease events can be achieved without substantial changes in the total amount of fat consumed. Rather, the quality of dietary fat, i.e., reduced saturated and trans-saturated fats, appears to confer more benefit. Depending on the definition of the outcome, a diet reduced in saturated fat and cholesterol, and relatively increased in polyunsaturated fat has been shown to reduce the risk of coronary events from 23% to 73% in persons with pre-existing disease or at high-risk of developing disease.

We would expect the risk reduction to be less in persons who are at average or low risk of disease. One study conducted among middle-aged men in a Finnish mental hospital demonstrated a 43% reduction in coronary events with a diet low in total and saturated fat¹⁹, but a similar study in women failed to show statistically significant differences²⁰. Still, in one large primary prevention trial (a trial conducted in persons without CHD) total fat consumption was relatively unchanged, but the intervention diet contained a higher ratio of polyunsaturated to saturated fat and no statistically significant reductions in cardiovascular events occurred after 4.5 years of follow-up²¹. An important potential limitation of these studies is their relatively short length of follow-up, given the fact that participants in these studies did not have a history of cardiovascular disease at baseline.

In the majority of the preceding studies that showed a significant benefit from a low-saturated fat diet, the dietary changes were accompanied by reductions in cholesterol levels. However, a recent eleven-year follow-up of the Lyon Diet Heart Study showed a

72% reduction in cardiac death and non-fatal myocardial infarction in persons consuming a Mediterranean-type diet compared to persons consuming a prudent Western-type diet despite the fact that there was no difference in LDL, HDL or total cholesterol levels between the groups^{22,23}. The Mediterranean diet substitutes animal fat with polyunsaturated vegetable oil and replaces meat, butter and cream with fish, legumes, bread, fruits and vegetables. Total fat intake was similar in both groups. In the same study, the Mediterranean diet group had a higher intake of fiber, likely indicating higher consumption of fruits and vegetables. Thus, the risk reduction in the Lyon Diet Heart Study cannot be attributed to beneficial effects on serum lipids or cholesterol per se, but appear to implicate dietary factors, like increased fiber consumption, or increased consumption of certain types of fatty acids (e.g. unsaturated relative to saturated fatty) independent of their effects on absolute serum lipid levels. In addition, a recent study conducted in India demonstrated that a diet with features of the Mediterranean diet (increased whole grains, nuts, fruits and vegetables) also substantially lowered CHD risk²⁴.

Clinical trials of fish consumption are sparse. Interestingly, advice to increase fish intake in one study was associated with a statistically significant 29% reduction in death from all causes in persons with a prior history of myocardial infarction, but was not associated with a statistically significant reduction in the incidence of recurrent heart attack and death from ischemic heart disease²⁵. In the same study, advice to reduce fat intake was not associated with any benefit, perhaps because the amount of cholesterol reduction from reduced fat intake was very modest (3-4%).

In summary, there is limited evidence from clinical trials on the impact of reduced meat intake on cardiovascular disease events. Existing evidence suggests that a diet reduced in saturated fat and increased in polyunsaturated fats substantially reduces heart disease risk. Since saturated fat is mainly obtained from animal products in the U.S., it stands to reason that reduced meat intake, especially red meat, might reduce the risk of heart disease. This hypothesis, however, has not been directly tested. Moreover, it is not clear from existing evidence whether reduced intake of lean meats would confer the same benefit. Finally, findings from one major clinical trial support the hypothesis that fish intake may be beneficial.

LIMITATIONS AND ALTERNATIVE HYPOTHOSES

One major limitation to the available evidence regarding meat consumption and the risk of CHD is the difficulty in separating out the potential harmful effect of meat consumption and the potential beneficial effect of fruit, vegetable and fish consumption. Nutritional epidemiologists often do not have the luxury of being able to compare groups of people whose diet *only* differs by the presence, type or amount of meat consumed. Rather, when conducting analyses of prospective studies, it is more common for researchers to stratify study participants according to these parameters and statistically adjust for other factors that may be associated with them, such as physical activity, smoking, body weight, and other dietary factors. This method of analysis, however, does not reflect the “real world” in the sense that people often have patterns of eating and lifestyle, rather than choosing to omit or add a single dietary factor. With regard to meat consumption, the major limitation in clinical trials has been the lack of direct evidence

implicating meat consumption per se in the development of cardiovascular disease. Because of major practical and logistical issues surrounding such a trial, it is unlikely that such a study will be undertaken. The best evidence regarding risk associated with meat consumption will likely be indirect evidence from clinical trials and large prospective studies.

Inconsistencies observed in the existing data could reflect real differences in risk attributable to differential intake of meats, residual confounding from other unmeasured or imperfectly measured factors associated with both the risk of CHD and meat intake (e.g. smoking, physical activity) or benefits from foods used to replace calories from reductions in meat intake. While issues of residual confounding can be dealt with by improved research and analytical methods, the latter explanation is more difficult to refute. Because of the inherent complexities in identifying particular nutrients or foods responsible that may increase risk of CHD, researchers have recently begun to focus on more global dietary patterns rather than specific foods. Studies of dietary patterns test the hypothesis that combinations of foods and their nutrients, rather than individual constituents within the diet, confer disease risk. In assessing the impact of a dietary pattern, these studies acknowledge the vast and complex array of interactions among dietary constituents. Recent large prospective studies examining “prudent” dietary patterns consisting of reduced meat intake and increased intake of fruits and vegetables have shown that this dietary pattern is associated with reduced risk of cardiovascular disease events²⁶⁻²⁸ 26 While these studies cannot determine which individual dietary components account for the reduced risk, they do offer a practical and more realistic assessment of the effect of the overall diet on CHD risk.

SUMMARY

On the whole, the existing data strongly suggest that replacement of saturated fat in the diet with poly- or mono- unsaturated fats reduces the risk of CHD. While this does not necessarily implicate meat intake in the development of CHD, a practical means of achieving this goal is to reduce intake of meat, particularly red meat. The benefit of a low-saturated fat / high poly- or mono- unsaturated fat diet is most consistently observed in persons at higher risk of CHD. In contrast, fish intake may protect against the development of heart disease, especially in high-risk individuals, but data are inconsistent and recent studies suggest that heavy metals contained in the environment of fresh-water fish may increase CHD risk. A beneficial impact of fish intake may be attributable to the increased omega-3 fatty acid content of fish, which could have wide-ranging cardio-protective properties.

Table 1. CHARACTERISTICS, ADVANTAGES AND DISADVANTAGES OF EPIDEMIOLOGICAL STUDY DESIGNS

Study Design	Characteristics	Advantages	Disadvantages
Cross Sectional	Putative risk factors for the disease and the presence or absence of the disease are measured at a single point in time.	<ul style="list-style-type: none"> • Can examine a number of factors and their association with disease. 	<ul style="list-style-type: none"> • Cannot establish a temporal association between an exposure and the disease. • Cannot conclusively exclude the possibility that other factors associated with meat intake could explain observed associations.
Case-Control	Putative risk factors for the disease are measured in persons already known to have the disease (cases) and in persons known to be free of the disease (controls) at a single point in time.	<ul style="list-style-type: none"> • Can examine a number of factors and their association with disease. 	<ul style="list-style-type: none"> • Cannot establish a temporal association between an exposure and the disease. • Cannot conclusively exclude the possibility that other factors associated with meat intake could explain observed associations. • Persons with the disease are subject to “recall bias”.
Prospective	Putative risk factors are assessed <i>before</i> the onset of disease and subjects followed for the development of disease.	<ul style="list-style-type: none"> • Can establish a temporal association between a risk factor and the disease, i.e. exposure to the risk factor is known to have occurred before the development of the disease. • No “recall bias” 	<ul style="list-style-type: none"> • Cannot conclusively exclude the possibility that other factors associated with meat intake could explain observed associations.
Randomized Clinical Trial	Directly tests the effect of the factor of interest on the risk of disease, by randomly assigning subjects to alternative interventions that include or exclude the factor. Subjects are then followed for the development of disease.	<ul style="list-style-type: none"> • Can establish a temporal association between a factor and the disease. • No “recall bias” • Reduces or eliminates confounding from other factors not tested in the intervention. 	<ul style="list-style-type: none"> • Logistically difficult. • Costly. • Typically can only assesses the effect of one or two factors on disease risk.

TABLE 2. PROSPECTIVE STUDIES OF MEAT INTAKE AND RISK OF CARDIOVASCULAR DISEASE			
	EXPOSURE	COMPARISON	FINDINGS
Burr, et al. 1982. ^{*29}	Any meat	Vegetarian vs. Non-vegetarian	SMR 0.97 (0.81, 1.16)
Burr et al, 1988. ³⁰	Any meat	Vegetarian vs. Non-vegetarian	SMR 0.43 (no confidence intervals given)
Snowdon, et al. 1984. ²	Beef	No beef vs. > 3 tpw	~ 3 fold increased risk of fatal CHD in men age 45-64 years who ate beef compared to non-beef eaters.
Frentzel-Beyme, et al. 1988. ³¹	Any meat	Vegetarian vs. Non-vegetarian	SMR 0.45 (0.22, 0.95)
Snowdon, et al. 1988. ^{*32}	Any meat	Vegetarian vs. Non-vegetarians	SMR 0.74 (0.63, 0.88)
Beeson, et al. 1989. ³³	Any meat	Vegetarian vs. Non-vegetarian	SMR 0.62 (0.53, 0.73)
Chang-Claude, 1992. ³⁴	Any meat	Vegetarian vs. Non-vegetarian	SMR 0.39 (0.29, 0.51) [men] SMR 0.46 (0.35, 0.60) [women]
Thorogood, et al. 1994. ³⁵	Any meat	Vegetarian vs. Non-vegetarian	Unadjusted SMR, 0.38 (0.30, 0.46) Adjusted SMR, 0.72 (0.47, 1.10)
Mann, et al. 1997. ³⁶	Any Meat	Vegetarian & Vegan vs. Non-vegetarian	Adjusted SMR, 0.63 (0.42, 0.93)
Hu, et al. 1999. ³	Red Meat	RR per 1 serving / day	Age-adjusted RR, 1.43 (1.35 – 1.65) Multivariate adjusted RR, 1.09 (0.91, 1.30)
Key, et al. 1999. ^{11 **}	Any Meat	Vegetarian vs. Non-vegetarian	SMR 0.66 (0.55 – 0.79)

† SMR = Standardized Mortality Ratio, RR = relative risk.

* Results included in study by Key et al., 1999.

**This study was a meta-analysis of 5 separate studies evaluating the impact of vegetarian diets on CHD risk.

TABLE 3. PROSPECTIVE STUDIES OF FISH INTAKE AND RISK OF CARDIOVASCULAR DISEASE

tpm/tpw: times per month / week.	AVERAGE FISH INTAKE	COMPARISON	RELATIVE RISK (95% CI)
Kromhout, 1985. ³⁷ d}	20 g/d	≥ 40 g/d vs. none	0.39 (0.13 – 0.55)
Vollset, 1985. ³⁸ d}	NA	≥ 25 tpm vs. 0-4	1.48 (NA)
Lapidus, 1986. ³⁹	NA	NA	No association
Norell, 1986. ⁴⁰	NA	High vs. Low	0.85 (0.69 – 1.06)
Ascherio, 1995. ⁴¹	37 g/d	≥ 6 tpw vs. < 1 tpm	1.14 (0.86 – 1.51)
Kromhout, 1995. ⁴²	14 g/d	Any vs. none	0.47 (0.28 – 0.79)
Morris, 1995. ⁴³	2.1tpw	≥ 5 tpw vs < 1tpw	0.90 (0.40 – 1.80)
Salonen, 1995. ⁴⁴	46.5 g	≥ 30 g/d vs. <30	1.87 (1.13 – 3.09)
Rodriguez, 1996. ⁴⁵	NA	≥ 2 tpw vs. < 2 tpw	No association
Davligus, 1997. ⁴⁶	~ 25 g	≥ 35 g/d vs. 0	0.62 (0.40 – 0.94)
Mann, 1997. ³⁶	NA	≥ 1 tpw vs. 0	1.23 (0.70 – 2.17)
Pietinen, 1997. ⁴⁷	0.4 g ω-3 Fatty Acids /d	5 th quintile vs. 1 st	1.30 (1.01 – 1.67)
Albert, 1998. ⁴⁸	2.5 tpw	≥ 1 tpw vs. < 1 tpw	0.48 (0.24-0.96)
Gartside, 1998. ⁴⁹	NA	> 1 tpw vs. 0	0.92 (0.77 – 1.10)
Oomen, 2000. ⁵⁰	~ 28 g/d	≥ 40 g/d vs. 0	1.08 (0.76 – 1.53)

Table 4. Clinical Trials of Cardiovascular Disease

Study	Population	Intervention Diet	Length of Intervention	Outcome	Results
Research Committee. Low fat diet in myocardial infarction; a controlled trial. (1965). ⁵¹	264 men under 65 years of age with history of MI.	Reduced total fat (40 g/day). Reduced animal fats primarily.	5 years	Recurrence of MI or coronary death	NE
Oslo Diet Heart Study Eleven year report, (1970). ⁵²	412 men age 30-64 with history of MI.	Reduced saturated fat, cholesterol and increased in polyunsaturated fat	11 years	Total, CHD and, CHD + stroke mortality.	23% reduction in coronary events (fatal MI), but no change in total cardio vascular disease or overall survival.
Sydney Diet Heart Study, (1978). ⁵³	458 men with CAD.	Reduced saturated fat, cholesterol and increased in polyunsaturated fat	2-7 years	CHD events or coronary death.	NE
Finnish Mental Hospital Study, (1979). ¹⁹	676 hospitalized men age 34-64 in two hospitals.	Diet low in saturated fats and cholesterol and relatively high in polyunsaturated fats. 34% of total calories from fat.	6 years	EKG changes and coronary deaths.	43% reduction in EKG changes consistent with MI or deaths from coronary disease.
Finnish Mental Hospital Study, (1983). ²⁰	591 hospitalized women age 44-64 in two hospitals.	Diet low in saturated fats and cholesterol and relatively high in polyunsaturated fats. 34% of total calories from fat.	6 years	EKG changes and coronary deaths.	NE

Minnesota Coronary Survey, 1989. ²¹	4,393 institutionalized men and 4,664 women. ²¹	Reduced saturated fat, cholesterol and increased in polyunsaturated fat	4.5 years	CHD events and all-cause mortality.	NE
The Diet and Reinfarction Trial (DART), 1989. ²⁵	2,033 men with history of MI.	Three intervention groups: 1. Advised to reduce fat intake and an increase the ratio of polyunsaturated to saturated fat, 2. Advised to increase fatty fish intake 3. Advised to increase cereal fibre intake.	2 years	Total mortality, recurrent MI and coronary death.	29% reduction in 2 year all-cause mortality in fish-advice group. No overall effect of fiber. No overall effect of reduced saturated to polyunsaturated fat intake.
Indian Heart Study, 1992. ⁵⁴	406 patients with history of acute MI, possible MI or angina.	Advised increase fruits and vegetables	1 year	Total cardiovascular disease mortality and non-fatal MI.	40% reduction in cardiovascular mortality and 38% reduction in non-fatal MI.

Lyon Heart Study, 1994. ²²	605 individuals with history of MI.	Mediterranean Diet vs. low-fat diet. The Mediterranean diet substitutes animal fat with polyunsaturated vegetable oil and replaces met, butter and cream with fish, legumes, bread, fruits and vegetables. Total fat intake was similar in both groups.	5 years	CHD events and coronary death.	73% reduction in CHD death and non-fatal MI.
Indo-Mediterranean Heart Study, 2002. ²⁴	1000 individuals with angina, myocardial infarction or CHD risk factors.	National Cholesterol Education Program (NCEP) step I diet vs. Indo-Mediterranean diet (higher in fruits, vegetables, nuts, whole grains, and lower in total and saturated fat, cholesterol) Note: Two-thirds of all participants in both groups were vegetarian at baseline.	2 years	Fatal or non-fatal CHD events, sudden cardiac death and combined endpoints	Risk reductions associated with Indo-Mediterranean diet compared to NCEP step 1 diet: Total events: 52% reduction Non-fatal CHD: 53% reduction Fatal CHD event: 33% reduction (not statistically significant) Sudden cardiac death: 67% reduction.

NE = No Effect of the intervention.

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