A hole in the diet–heart hypothesis?

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Newly published data recovered from a large, randomized, controlled trial conducted >4 decades ago show no difference in mortality between individuals with a diet rich in saturated fat and those with a diet rich in linoleic acid, despite the cholesterol-lowering effect of the latter. These findings challenge the widely accepted diet–heart hypothesis.


The traditional diet–heart hypothesis is that particular dietary components increase blood cholesterol concentrations and that, in turn, elevated blood cholesterol level is causally linked to increased risk of coronary heart disease. Research conducted in the 1960s and 1970s showed that several commonly occurring dietary saturated fatty acids raise total-cholesterol and LDL-cholesterol concentrations, whereas the omega-6 polyunsaturated fatty acid (PUFA) linoleic acid lowers total-cholesterol and LDL-cholesterol concentrations1. Linoleic acid is present in high amounts in vegetable oils such as corn, safflower, soybean, and sunflower oils, and in margarines made from these oils. Linoleic acid is the most prevalent PUFA and omega-6 PUFA in most Western diets. Given their opposing actions on blood cholesterol levels, decreasing intake of saturated fat and increasing intake of PUFAs has been a cornerstone of dietary advice for several decades, with the aim of reducing the risk of cardiovascular disease. Typical advice is to limit saturated fatty acids to <10% of dietary energy and to aim for a PUFA intake (mainly linoleic acid) of 5–10% of dietary energy2,3. Despite commonly held views to the contrary, the effect on coronary heart disease or cardiovascular mortality of replacing dietary saturated fat with linoleic acid without changes in other fatty acids (such as trans or omega-3) has rarely been investigated. Health authorities have instead used blood cholesterol levels as the basis for advice and recommendations.

In 2013, Ramsden et al. published newly recovered results from the Sydney Diet Heart Study4, a randomized, controlled, trial conducted between 1966 and 1973, reporting data on all-cause, coronary heart disease, and cardiovascular disease mortality in middle-aged men (aged 30–59 years) with a recent coronary event who were randomly assigned to a diet rich in linoleic acid or to continuation of their habitual diet rich in saturated fatty acids. Curiously, the data on coronary heart disease and cardiovascular disease mortality from the Sydney Diet Heart Study had never been published. Despite significant lowering of serum cholesterol levels in the linoleic acid group (13%), all-cause mortality and the risk of death from coronary heart disease or cardiovascular disease were higher in the linoleic acid group than in the group with no dietary intervention1. The study called into question the traditional diet–heart hypothesis and the widely accepted advice on healthy eating5. Ramsden et al. have now conducted a second remarkable piece of research, recovering and analysing a set of data of possibly even greater importance than that from the Sydney Diet Heart Study.

The Minnesota Coronary Experiment (MCE) was a double-blind, randomized, controlled trial conducted from 1968 to 1973 including >9,500 men and women aged 20–97 years who were living in a nursing home or in one of six mental-health hospitals in Minnesota, USA. Therefore, unlike the Sydney Diet Heart Study, the MCE included women and elderly participants, although the average age of participants was 52 years. Participants in the MCE were of normal body weight and had normal blood pressure and serum cholesterol concentrations. The participants were randomly assigned to a diet rich in linoleic acid or a control diet. All meals were provided to participants throughout the trial; meals were highly controlled with regard to nutrient content, and were eaten under supervision. The linoleic acid group had meals in which corn oil was used for cooking and was added into many food items, and a corn-oil-based margarine was also used. This replacement resulted in a 50% reduction in dietary saturated fatty acid intake compared with the participant’s habitual diet, and an average increase in linoleic acid intake from 3.4% to 13.2% of dietary energy. Linoleic acid intake in the control group was about 4% of dietary energy. Follow-up duration was 41–56 months, depending on the location. Data were recovered from nine-track magnetic tapes and paper documents. Longitudinal data on serum cholesterol concentrations were available for 2,355 participants who were in the study for at ≥1 year.

Some data from the MCE7 were published in 1989, but for reasons that are not clear, the data on all-cause and coronary heart disease mortality in the participants with known serum cholesterol concentrations at study entry and after ≥1 year of intervention were

Box 1 Practice points

• The diet–heart hypothesis links dietary factors, elevated blood cholesterol levels, and increased risk of coronary heart disease
• Common saturated fatty acids raise blood total-cholesterol and LDL-cholesterol concentrations, whereas the omega-6 fatty acid linoleic acid lowers them; these effects underlie much common dietary advice
• Unpublished data recovered from old randomized, controlled trials testing the effects of replacing saturated fat with linoleic acid confirm cholesterol lowering, but do not support that this lowering reduces mortality
• These data question the diet–heart hypothesis and current dietary advice; more research is required in this area
never published. Likewise, findings from autopsy investigation on participants who died during the study follow-up were never published. In those participants who were followed up for ≥1 year, serum total-cholesterol levels were lowered by an average of 13.8% in the linoleic acid group. This percentage is very close to the value predicted from the equation that estimates the change in serum cholesterol concentration that is expected according to changes in dietary intake of common saturated fatty acids and PUFAs. However, the reduction of serum cholesterol levels was associated with increased, not decreased, risk of death, but no difference was found for all-cause or coronary heart disease mortality between groups.

Nevertheless, the death rates were low, perhaps because many participants were young and had a healthy risk-factor profile. The researchers then used the new data generated from the MCE to update their earlier meta-analysis. This new meta-analysis included a total of five linoleic acid intervention trials to assess coronary heart disease and cardiovascular disease mortality, including the Sydney Diet Heart Study and the MCE. The five trials involved a total of 10,808 participants. This updated meta-analysis indicated no benefit of diets rich in linoleic acid on all-cause or coronary heart disease mortality.

These data from the MCE confirm the well-established observation that replacing dietary saturated fat with linoleic acid lowers blood cholesterol concentration. However, this reduction in cholesterol levels was not associated with reduced mortality from coronary heart disease. Why? One possibility is that the enrichment of LDL particles with linoleic acid makes them more susceptible to oxidation, a process that is involved in the pathogenesis of cardiovascular disease, thereby counteracting the effect of lowering the concentration of LDL cholesterol. Another possibility is that high intake of linoleic acid might have deleterious consequences, such as increasing inflammation, that negate the cholesterol-lowering effect. Whatever the mechanisms involved, these new findings uncovered from the MCE — similarly to the data uncovered from the Sydney Diet Heart Study — argue against the diet–heart hypothesis, the ‘saturated fat bad, omega-6 PUFA good’ dogma, and much of the current dietary advice. However, the findings of these studies cannot be used to argue that lowering total-cholesterol and LDL-cholesterol concentrations by means other than replacing dietary saturated fat by omega-6 PUFAs (for example, through other dietary strategies or by using statins) might not be effective in reducing the risk of coronary heart disease, cardiovascular disease, or death. Furthermore, this study has some limitations. For example, data on intake of trans fatty acids are not available — although the researchers argue that this intake was probably low — and the generalizability of the study findings to populations beyond those institutionalized is not clear. Importantly, the intake of linoleic acid achieved in the treatment group in the MCE is beyond the upper limit of the intake recommended by some health authorities, and is beyond what most individuals in most countries are habitually consuming. Although these data add to the current debate about the healthfulness of different dietary fatty acids10,11 to consider altering the current recommendations for dietary intake of fat and fatty acids seems premature (BOX 1).

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doi: 10.1038/nrcardio.2016.78
Published online 12 May 2016


Competing interests statement
The author declares no competing interests.