CRITIQUE

The Women's Health Initiative Randomized Controlled Dietary Modification Trial: An inconvenient finding and the diet-heart hypothesis

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One goal of the US$700 million Women's Health Initiative Randomized Controlled Dietary Modification Trial was to determine whether post-menopausal women who adopted what was regarded as a 'heart healthy' low-fat diet, high in vegetables, fruits and grains, reduced their risk of developing cardiovascular disease. The trial substantially favoured the outcome in the intervention group, who also received an intensive nutritional and behaviour education programme not offered to the control group. These studies neatly disprove the diet-heart hypothesis since adoption of 'heart healthy' eating not only failed to influence future cardiac events in the healthy but it increased such events in the unhealthy and worsened diabetic control in those with type 2 diabetes mellitus.

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One goal of the US$700 million Women's Health Initiative Randomized Controlled Dietary Modification Trial (WHIRCDMT) was to determine whether post-menopausal women who adopted what was regarded as a 'heart healthy' low-fat diet, high in vegetables, fruits and grains, reduced their risk of developing cardiovascular disease (CVD). The trial substantially favoured the outcome in the intervention group, who also received an intensive nutritional and behaviour education programme not offered to the control group.

The conclusion after 8.1 years of study was that: '… a reduced total fat intake and increased intake of vegetables, fruits, and grains did not significantly reduce the risk of [coronary heart disease] (CHD), stroke, or CVD in postmenopausal women and achieved only modest effects on CVD risk factors' (p. 655).[1] However, the abstract notes that these conclusions apply only to women who were healthy at the start of the trial since it excludes 'participants with baseline CVD (3.4%)'. It is not clear whether the inclusion of these unhealthy women would have altered the overall conclusion.

The study's only statistically significant finding, reported on the seventh page of the published manuscript (p. 661),[1] has yet to enter the scientific discourse: 'The H(azard)R(atio) for the 3.4% of women with CVD at baseline was 1.26 (95% CI, 1.03-1.54)'.

This shows that women with diagnosed CVD at the start of the trial who adopted the 'healthy heart' low-fat eating option had a risk of developing future cardiovascular complications that was 26% higher than that of the non-intervention group. This finding is not discussed and a key line of text is missing from Fig. 3 (Fig. 1).[1]

In the press release reporting the study findings, neither Dr Elizabeth G Nabel, the former Director of the National Heart, Lung, and Blood Institute nor Dr Jacques Rossouw, the project leader, mentioned this result. Dr Nabel is reported to have said: 'The results of this study do not change established recommendations on disease prevention. Women should continue to … work with their doctors to reduce their risks for heart disease including following a diet low in saturated fat, trans fat and cholesterol'.[2]

The project leader's opinion was: 'This study shows that just reducing total fat intake does not go far enough to have an impact on heart disease risk. While the participants' overall change in [low-density lipoprotein (LDL)] 'bad' cholesterol was small, we saw trends towards greater reductions in cholesterol and heart disease risk in women eating less saturated and trans fat'.[2] However, this explanation is false for three reasons.

First, the prognosis of women with diagnosed CVD worsened when they ate the 'heart healthy' low-fat diet that would produce 'favourable' changes in 'bad' cholesterol. Second, the focus of this uniquely expensive study was to measure outcomes, not changes in biological markers. The latter could have been done with a far less expensive trial. Third, the project leader's statement confirms that the WHIRCMDT was not designed to test a null hypothesis. Instead, the inconvenient finding supporting the null hypothesis was promoted as evidence for a false-negative finding on the grounds that the intervention did 'not go far enough'.

In fact, there were a number of negative findings from the WHIRCDMT. The leanest women at the start of the trial gained weight on the low-fat diet[3] and those with the least insulin resistance at the start of the trial were at greater risk of developing type 2 diabetes mellitus (DM) if assigned to the low-fat diet.[4] The low-fat diet also worsened glucose control in women with diagnosed diabetes,[5] a finding that 'agrees with some, but not all, previous studies evaluating the effects of high- and low-carbohydrate diets in persons with diabetes' (p. 83).[1] The authors concluded: '… caution should be exercised in recommending a reduction in overall dietary fat in women with diabetes unless accompanied by additional recommendations to guide carbohydrate intake' (p. 84).[1]

In fact, these studies neatly disprove the diet-heart hypothesis since adoption of 'heart healthy' eating not only failed to influence future cardiac events in the healthy but it increased such events in the unhealthy and worsened diabetic control in those with type 2 DM.

The recently (February 2013) recovered data from the Sydney Diet Heart Study[6] confirm that a key component of the 'healthy heart' diet

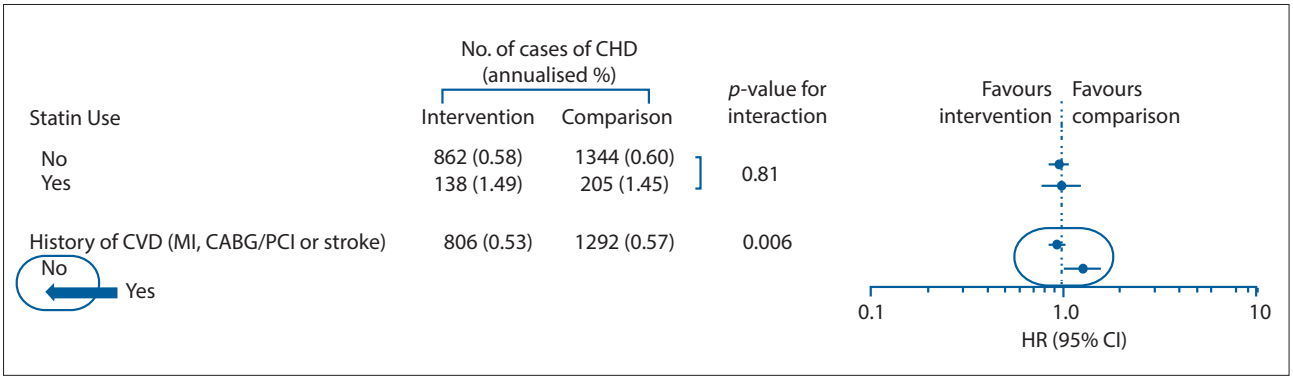

Fig. 1. Extracted from Howard et al.[1] *(Fig. 3). The figure compares the coronary heart disease (CHD) outcome in the intervention (low-fat 'heart healthy' eating) and comparison (usual eating) groups according to 15 different variables, 2 of which are shown here. Note that for statin use there are 2 lines of information indicating either use (Yes) or non-use (No) of statins. But for the 'history of cardiovascular disease (CVD)' group there is a missing line of text for those women with CVD at the start of the trial (Yes). Note that the hazard ratio (HR) for the missing Yes line favours the usual eating, comparison group indicating that women with CVD at the start of the trial had a more favourable outcome if they did not adopt the low-fat 'heart healthy' diet. This is the only significant finding reported in that paper. MI = myocardial infarction; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.*

– replacing dietary saturated fatty acids (SFA) with polyunsaturated fatty acids (PUFA), specifically n-6 PUFA linoleic acid – 'increased rates of death from cardiovascular disease, coronary heart disease and all cause mortality compared to a control diet rich in SFA from animal fats and common margarines' (p. 4).[6] As in the WHIRCDMT, the active intervention produced adverse outcomes even though it lowered blood cholesterol concentrations. Analysis of all published trials of primary and secondary interventions with n-6 PUFA linoleic acid confirms adverse outcomes approaching statistical significance (p. 4).[6] The mechanisms by which oxidised omega-6 PUFA may initiate and promote atherosclerosis is understood.[6] In contrast, n-3 PUFAs (from fish, certain vegetables and pasture-raised ruminants) appear protective.

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