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 (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). 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), 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).

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’.

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’. 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 WHIRCDMT 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 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. The low-fat diet also worsened glucose control in women with diagnosed diabetes, 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). 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).

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 diabetes.
Effects of dietary linoleic acid – 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. 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. The mechanisms by which oxidised omega-6 PUFA may initiate and promote atherosclerosis is understood. In contrast, n-3 PUFAs (from fish, certain vegetables and pasture-raised ruminants) appear protective.

### Statin Use and History of CVD

<table>
<thead>
<tr>
<th>Statin Use</th>
<th>Intervention</th>
<th>Comparison</th>
<th><strong>p-value for interaction</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>862 (0.58)</td>
<td>1344 (0.60)</td>
<td>0.81</td>
</tr>
<tr>
<td>Yes</td>
<td>138 (1.49)</td>
<td>203 (1.45)</td>
<td></td>
</tr>
<tr>
<td>History of CVD (MI, CABG/PCI or stroke)</td>
<td>806 (0.53)</td>
<td>1292 (0.57)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

**Favours intervention**

![Figure 1. Extracted from Howard et al. (2013)](image)

This month in the SAMJ …

**Richard van Zyl-Smit** qualified at the University of Cape Town (UCT) in 1996. He is head of the Lung Clinical Research Unit at the UCT Lung Institute and an honorary consultant pulmonologist at Groote Schuur Hospital. After completing his pulmonology training in 2007, he completed a PhD investigating the effects of tobacco smoking on human immune responses to mycobacterial infection. He directs the smoking cessation services at Groote Schuur Hospital as well as being actively involved in asthma, chronic obstructive pulmonary disease (COPD) and tuberculosis research.

**Brian Allwood** is an honorary consultant pulmonologist and senior lecturer in the Division of Pulmonology at the University of Cape Town (UCT). He received his undergraduate degree from the University of the Witwatersrand and completed his training as a specialist physician (2008) and consultant pulmonologist (2012), at Groote Schuur Hospital. He also attained a Masters in Public Health in Clinical Research from UCT (2012), and is currently completing his PhD at the UCT Lung Institute in Tuberculosis and Chronic Obstructive Pulmonary Disease. Apart from research, he remains committed to South Africa’s healthcare problems, and has a strong interest in clinical medicine, improvement in medical services as well as teaching.

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