

## Invited Commentary

# The Women's Health Initiative. What is on trial: nutrition and chronic disease? Or misinterpreted science, media havoc and the sound of silence from peers?

### Summary

The first results of the Women's Health Initiative dietary intervention trial were published in the USA in February. This is a colossal intervention designed to see if diets lower in fat and higher in fruits, vegetables and grains than is usual in high-income countries reduce the incidence of breast cancer, colorectal cancer, heart disease and other chronic diseases, in women aged 50–79 years. As interpreted by US government media releases, the results were unimpressive. As interpreted by a global media blitz, the results indicate that food and nutrition has little or nothing to do with health and disease. But the trial was in key respects not reaching its aims, was methodologically controversial, and in any case has not produced the reported null results. What should the public health nutrition profession do about such messes?

### The media blitz

'The more we know about nutrition, the less we seem to know... It's enough to make us drown our confusion in a big serving of extra-rich ice-cream'. This editorial in *The New York Times* (NYT) in early February this year typified the beginning of a global media blitz that followed the appearance of the first results published in the *Journal of the American Medical Association* (JAMA) from the Women's Health Initiative (WHI) dietary intervention. This is a vast US trial designed to investigate the effect of diets relatively low in fat and high in fruits, vegetables and grains on the incidence of chronic diseases in older women. These results concerned cardiovascular disease, colon cancer and breast cancer<sup>1–3</sup>.

The study was funded by the National Institutes of Health (NIH) of the US government. An NIH media release on 7 February announcing the results was downbeat. It stated: 'News from the Women's Health Initiative: reducing total fat intake may have small effect on risk of breast cancer, no effect on risk of colorectal cancer, heart disease, or stroke'<sup>4</sup>. On the same day, JAMA posted their media release with much the same tone but with a slight difference: 'Large study shows low-fat diet has little effect on reducing risk of breast cancer, colorectal cancer, or cardiovascular disease in postmenopausal women'.

The following day the NYT chief science reporter Gina Kolata put a negative spin on the results in a front page news lead story, claiming: 'Low-fat diet does not cut health risks, study finds', quoting a senior NIH employee as saying that the study results were 'completely null'. The NYT evidently set the global media agenda. Stories all over the world carried headlines such as: 'Get stuffed', 'Forget all you ever knew about diets', 'Low fat does not reduce disease risk'.

This in turn ignited a prairie fire of nihilistic commentary against the established scientific consensus on food, nutrition and chronic diseases. In Sweden, for example, a daily newspaper accused the government's National Food Administration (NFA) of being hopelessly behind the research frontiers. Swedish morning TV played a popular song '*Who can we trust...*' in the background when referring to the news. Journalists accepted the negative story, and were in many countries not even countered by nutrition experts. In Sweden, the NFA wrote a rapid and adequate response, but this was not always noticed; thus, as late as 17 February, a radio commentator stated that food messages on fat were now more religion than anything else – where you are a believer or non-believer. She asked for someone to tell right from wrong. She evidently had not got the NFA message.

### The intentions and results of the trial

The WHI study is Big Science, no question about that. It has cost 415 million dollars so far, and the dietary modification followed 49 000 subjects for over 8 years. It was conceived and funded by NIH in 1991, to investigate the most common causes of death, disability and impaired quality of life in postmenopausal women. It was heralded as the biggest US prevention trial of its kind, with unique opportunities of supporting public health nutrition policies for and life choices of postmenopausal women.

The dietary intervention aimed to reduce fat intake to 20% of energy, to increase intake of fruits and vegetables to 5 servings a day, and to increase grains to at least 6 servings a day. The women enrolled in the study were 50 to 79 years of age.

The first striking fact about the results of the trial so far is that they do not provide a basis for the media stories; and indeed can be said to be at variance with the NIH and

JAMA media releases. Specifically, they do not show that a low-fat diet has no health benefits.

- The cardiovascular disease paper<sup>1</sup> concludes that the fat reduction was inadequate, as was the increase in fruits and vegetables. Further, the results suggest that women who achieved greater reductions in saturated fat or *trans* fats might be at reduced risk of heart attacks.
- The breast cancer paper<sup>2</sup> concludes that while a statistically significant reduction in this cancer was not seen (the confidence intervals were 0.85 to 1.01), its incidence dropped by 9% in the intervention group.
- The colorectal cancer paper<sup>3</sup> concludes that effects on this cancer in mid to late life cannot perhaps be expected to be seen with the changes of diet achieved within the length of time the subjects were followed.

None of these conclusions indicates that the low-fat message is wrong. Indeed, the breast cancer paper suggests that the message is right and with a longer follow-up, it may have been possible to demonstrate this. The colorectal cancer paper also suggests that greater benefits may be revealed with a longer follow-up, as there were fewer polyps (precancerous lesions) found in the intervention group.

### What's wrong with the trial?

The full media release<sup>4</sup> of the results so far describes some shortfalls of the WHI. The following text describes some more problems with the study.

#### *Failure to achieve its aims*

None of the aims of the study were met. This does not invalidate the study, but means that its results should be treated with caution. The intervention fell far short of its target for fat, fruits and vegetables, and made almost no impression on consumption of grains.

#### *A wrong question was asked*

In the case of heart disease, any result of a reduction in total fat intake would have been surprising. It has been generally agreed for decades that the significant factor is not quantity fat but quality of fat. If the intervention had achieved a substantial increase in consumption of vegetables, fruits and grains (preferably in whole form) it could have been expected to have an effect, but it failed in this aim.

#### *Impressive results were unlikely*

The average age of the women at entry was 62.3 years. At that age a relatively modest change in diet, amounting (as mentioned in an *NYT* article) to not a lot more than no butter on bread and no cream cheese on bagels, might be expected to have a modest effect – which in the case of breast cancer incidence, it did. Further, if the dietary (and other) determinants of heart disease and cancer begin

relatively early in life, as is evident, an intervention so late in life might be expected to have a negligible effect – as in the case of heart disease and colorectal cancer. Furthermore, of course, the results from a study on a distinct age and gender group cannot be automatically generalised to the population at large.

#### *Problems with dietary assessment*

Registration of intake is always problematic due to underreporting of unhealthy foods, and in this case it seems plausible that the intervention group would tend to report a healthy diet. This bias, together with a massive registration fatigue, suggests that the actual changes made by the intervention group were even smaller than reported. One of the specific dietary assessment issues is the use of food-frequency questionnaires (FFQs), as described in more detail below.

#### *The FFQ controversy*

It is possible that the WHI and other large intervention trials designed to identify relationships between food, nutrition and chronic diseases are fatally flawed. Their standard tool for dietary assessment is the FFQ, a simple, self-administered technique. This has the great advantage of being cheap. But more precise methods of recording actual food intake, such as those used in the massive European Prospective Investigation into Cancer and Nutrition, show highly significant associations, notably between fat, saturated fat and breast cancer, that are not shown when the cruder FFQ method is used<sup>5</sup>.

In a paper published last year, senior US investigators, supporting their European colleagues, stated 'Although painful to admit, it is possible that epidemiologists have been deluded in their acceptance of food frequency questionnaires' in large studies of diet and cancer, and urge that all results from such studies be treated with great circumspection<sup>6</sup>. The message is that null or unimpressive findings from studies using FFQs may well be an artefact caused by measurement error.

FFQ or no FFQ is not the issue here. The important thing is that any study of this type needs to be able to state with some confidence that the intervention group consumed diets different in specified nutritional quality from the comparison group. But in the case of the WHI this cannot be done. The rather minor differences between the intervention and comparison group could in large part be due to underreporting and misreporting. This is of course highly problematic, and calls for utmost caution in the interpretation of results.

#### *The folate intervention*

During the course of the study, what can be described as another intervention took place in the USA. This was the fortification of commonly consumed foods with folate, introduced in 1998, which according to the WHI colorectal cancer paper had the effect of raising total average

individual daily folate intake by around 300 µg or about 50% over baseline. Given the hypothesised protective role of folate in some chronic diseases, it is remarkable that this possible confounding factor was not mentioned as such in any of the papers.

### What should we do?

It is perhaps not realistic to expect the funders and representatives of such a vast and costly study to emphasise the possible flaws in its design, its inappropriate question, its controversial methodology and its meagre effectiveness as an intervention; although independent commentators need not be inhibited.

This aside, the negative official interpretation put on the study, and the nihilistic initial media coverage, were extraordinary; so much so as even to suggest some ideological motivation to discount the value of healthy diets in the prevention and control of major chronic diseases and to discredit the established public health nutrition consensus.

A similar issue occurred after publication of a major study on obesity and mortality<sup>7</sup> in the USA in 2005. On that occasion, a symposium was called at Harvard to counter the inaccurate and misleading interpretation of the study in scientific journals and the media. One recommendation was that findings of major studies liable to cause controversy be subject to additional peer review before publication. But as now, this was after the main event. The damage was done.

What can be done in future? The authors of this commentary believe that the WHI trial, and its interpretation, warns of a crisis for public health nutrition. The profession, with allies, should build and maintain an independent international body geared not only to make rapid responses but also to anticipate publication of research that needs proper analysis and commentary. We suggest this be discussed at a special session at the I World Congress on Public Health Nutrition, taking place this coming September in Barcelona<sup>8</sup>. Anyone attending the congress who is interested in joining such a discussion should contact the corresponding author.

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