A co-operative trial in the primary prevention of ischaemic heart disease using clofibrate

Sir,
We read with great interest the recent report from the Committee of Principal Investigators on the co-operative trial in the primary prevention of ischaemic heart disease using clofibrate (British Heart Journal, 1978, 40, 1069–1118).

We note with satisfaction that our dietary prevention trial in two mental hospitals near Helsinki (Miettinen et al., 1972) was considered by the Principal Investigators in their Discussion. However, the results of our study were partly misrepresented.

On page 1101 it is stated, correctly, that ‘there was a significant reduction in IHD mortality’ during the experimental diet periods. However, on page 1096 the authors say that ‘mortality from IHD, . . . , was not reduced in . . . primary prevention trials using a diet rich in polyunsaturated fats ( . . . ; Miettinen et al., 1972)’. This statement is in obvious contradiction to the previous one and is false.

On page 1098 it is stated that in our study (Miettinen et al., 1972) there was ‘a non-significant excess in total mortality among the experimental group taking a polyunsaturated fat diet’. This is not true. On the contrary, in our trial total mortality among the experimental groups was not higher but lower than among the control groups. The relevant mortality figures per 1000 man-years were as follows (cf. Table 6, loc. cit.):

<table>
<thead>
<tr>
<th>Diet Period</th>
<th>Hospital N</th>
<th>Hospital K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>34-56</td>
<td>35-12</td>
</tr>
<tr>
<td>Normal</td>
<td>38-78</td>
<td>40-20</td>
</tr>
</tbody>
</table>

Thus in both hospitals total mortality was reduced during the experimental diet periods. The differences, however, failed to reach statistical significance.

On page 1101 the authors refer to the criticisms of our study by Halperin et al. (1973) but, curiously enough, completely ignore our reply (Miettinen et al., 1973). In this reply we showed that the remarks of Halperin and his colleagues were largely unfounded.

On page 1099, where the authors refer to the study of Sturdevant et al. (1973) indicating an increase in the prevalence of gallstones on a diet high in polyunsaturated fat, it might have been relevant also to mention our paper (Miettinen et al., 1976) with the finding that the polyunsaturated fat diet in our trial was not lithogenic.

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References


This letter was shown to the authors of the report who reply as follows:

Sir,
We are grateful for the opportunity to comment on the letter by Miettinen and his colleagues.

They are right in pointing out that there is a contradiction, which we much regret, in our statements concerning the Helsinki Mental Hospitals Study. But there is inconsistency also in the results of the only two large primary prevention trials using polyunsaturated fats to lower plasma cholesterol: coronary mortality appears to have been reduced in the Helsinki Mental Hospitals Study, yet not in the Los Angeles Veterans Administration Study.
Miettinen and colleagues are correct in their statement about total mortality but the point which we wished to stress is that the degree of apparent reduction in coronary heart disease mortality was proportionately greater than that for overall mortality, indicating, therefore, that a slight excess must have occurred in mortality from non-cardiovascular deaths. Indeed, it is relevant to repeat what we said on page 1098: 'Age-adjusted death rates/1000 person-years for malignant neoplasms (5.02 diet v 3.96 control) and 'other diseases' (15.45 diet v 13.03 control) were both greater in men receiving the cholesterol-lowering diet'. It is this marginal excess of non-cardiovascular mortality in the Helsinki Mental Hospitals Study which we believe requires emphasis in view of the significant excess of non-cardiovascular mortality reported in the WHO study.

The same is true for the Los Angeles Veterans Administration Study, where increased mortality from non-cardiovascular causes is also evident when deaths from atherosclerotic events are subtracted from total death figures. This adds support to the findings of the WHO study.

Finally, the question of the degree to which a diet high in polyunsaturated fat is lithogenic will become increasingly clear as more studies are reported. One interesting aspect of the study by Sturdevant et al. (1973) is that lithogenicity increased with the number of consumed meals rich in polyunsaturated fats. The negative findings of Miettinen et al. (1976) need not be in conflict with those reported by Sturdevant et al. (1973), since there is no reason to assume that diets, differently enriched in polyunsaturated fats with different P/S ratios, will all have the same degree of lithogenicity or non-lithogenicity. Committee of Principal Investigators
A co-operative trial in the primary prevention of ischaemic heart disease using clofibrate.

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