A substitution model of dietary manipulation is an effective means of optimising lipid profile, reducing C-reactive protein and increasing insulin-like growth factor-1

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There are two key methods in which fat intake may be manipulated; the ‘substitution model’ and the ‘reduction model’. However insufficient information is known about the mechanisms of dietary fat reduction in individuals who have successfully reduced their fat intake, to be clear as to which strategy offers the greatest chance of success. Our objective was to ascertain the most effective dietary intervention for improving cardiovascular risk profile. Eighty female volunteers (high fat consumers) were recruited. Each subject was randomly allocated into one of the following groups. Substitution of high-fat foods was made with reduced-fat products, by the reduction of high-fat foods, by a combination of substitution and reduction strategies, or no advice was given. Each intervention lasted 3 months. Anthropometric measures and fasting blood samples were taken at baseline and follow-up. The substitution intervention resulted in weight loss (mean −1·4 (95 % CI −2·4, −0·2) kg) and reduced percentage body fat (mean −1·3 (95 % CI −2·0, −0·5) %). There was no significant weight change with the other interventions. Fasting triacylglycerols (−0·2 (SEM 0·07) mM; P=0·04), cholesterol and C-reactive protein (CRP) levels (0·8 (SEM 0·2) mg/l; P=0·04) fell with the substitution intervention, but not with the other interventions. Insulin-like growth factor-I increased with both substitution and reduction (P=0·02). There was no significant change in fasting insulin or glucose with any intervention. The substitution model of dietary intervention is effective even over a relatively short interval of time in reducing fasting total cholesterol, triacylglycerols and CRP. Although the group size for the present study was small and involved females only, it has significant implications for population intervention strategies.

Dietary interventions: Substitution model: Cardiovascular risk factors: Lipids: C-reactive protein

CVD is a major cause of death worldwide. In the last five decades a great deal of effort has been put into understanding the factors (metabolic, inherited, and lifestyle) that predispose individuals to CVD. High fat intakes have been linked to CHD and obesity for more than 50 years.

Ancel Keys established the cholesterol hypothesis (Fidanza et al. 1970; Grande et al. 1970; Keys, 1975). From this the concept of risk factors for CHD evolved. In the last decade numerous prospective studies have been published identifying hypercholesterolaemia as a major risk factor in predicting coronary events (Anonymous, 1994; Shepherd et al. 1995, Downs et al. 1998; Sever et al. 2003).

There are numerous ways to reduce fat intake (Lawton et al. 1998), but these have often been expensive or too complicated and intensive for widespread public health efforts (Greene & Rossi, 1998). In essence, there are two key methods in which fat intake may be manipulated to successfully reduce levels in the diet. The first is the ‘substitution model’, whereby the substitution of high-fat foods is made with reduced-fat products wherever possible. This method has been reported to be easily adopted and highly acceptable (Markckmann et al. 1994). The second strategy is the reduction of high-fat foods by choosing food types that are intrinsically low in fat, which can be described as the ‘reduction model’ (Hill et al. 1998). Although this method is a popular strategy used to reduce fat in the diet, long-term compliance with such diets is difficult for a variety of reasons; for example it is likely to reduce the palatability of the diet (Walker et al. 1996). In broader terms, the perceived health benefits of a lower fat intake have promoted a proliferation on the market of reduced-fat products.

Abbreviations: CRP, C-reactive protein; DINE, dietary instrument for nutrition education; HOMA, homeostasis model assessment; IGF, insulin-like growth factor; IGFBP, insulin-like growth factor binding protein; RCT, randomised controlled trial.

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In the present study of women identified as high fat consumers, we aimed to compare the efficacy of dietary intervention strategies to reduce fat in modifying established cardiovascular risk factors. These factors included insulin like growth factor (IGF)-1 which has recently been shown to be implicated in the pathogenesis of impaired glucose homeostasis and CVD (Heald et al. 2001; Sandhu et al. 2002) and the acute-phase reactant C-reactive protein (CRP), which is an independent risk factor shown to be strongly predictive of future cardiovascular events (Ridker et al. 2000, 2003). Furthermore we explored the impact of these interventions on anthropometric parameters.

**Methods**

**Subjects**

Volunteers were recruited from women who responded to posters displayed in the Leeds General Infirmary and University of Leeds campus, UK. Of the 207 volunteers who initially expressed an interest to enrol in the study, only 132 subjects were eligible (64 %). The remaining subjects were excluded as they were either not classified as high fat consumers according to the dietary instrument for nutrition education (DINE) questionnaire (DiClemente & Prochaska, 1998). Based on a quick assessment of an individual’s diet by adding the scores relevant to the frequency of consumption of the groups of foods to give a total fat score. A total score is calculated and the respondents can be classified as low, medium or high fat consumers. The DINE cut-off point of 25 is effective in predicting high fat consumers. To this end, Jackson et al. (2002) investigated the suitability of the DINE cut-off points for high fat consumers (Jackson et al. 2002). This involved comparing the DINE method to data from the UK Women’s Cohort Study, which used a 217-item food-frequency questionnaire to classify subjects into equal tertiles, based on their reported absolute fat intake (Calvert et al. 1996). By selecting a new cut-off point of 25, the agreement between the DINE and the UK Women’s Cohort Study classification was improved. Therefore, subjects who scored 25 or more using the DINE questionnaire were classified as high fat consumers. It was on the basis of this that the cut-off point of 25 for DINE score was used in the present study.

The group was provided with detailed instructions regarding the replacement of traditional full-fat items with reduced-fat alternatives but to stay on their usual diet. Wherever possible they were not specifically instructed to purchase any particular food items that were not already part of their habitual diet. They were not asked to modify portion size of the food consumed. They were also asked to replace red meats with chicken or fish and to buy lean cuts of meat, where possible. **Reduction.** This group was asked to cut down on high-fat foods and increase foods that are intrinsically low in fat and/or serve smaller portion sizes of high-fat foods. At each meal their aim was to decrease the portion size of foods high in fat and increase fibre-rich foods such as bread, pasta, rice, cereals and potatoes, without adding fat. **Combination.** The aim in this group was to substitute high-fat foods with reduced-fat alternatives and also to cut down on fatty foods and increase fibre-rich food such as bread, pasta, rice, cereals and potatoes and/or serve smaller portion sizes of fatty foods. **Control.** This group was asked to continue with their normal diet and no change was advocated for the period of the study.

No other additional recommendations were made regarding modification of other risk-relevant behaviours. Specifically, participants were specifically asked not to make any alterations in their day-to-day physical activity or exercise regimen.

**Study method and procedure**

**Dietary instrument for nutrition education.** The DINE was used to assess dietary fat intake (Roe et al. 1994). It was designed so that foods with a similar nutrient content and dietary use were grouped together. Scores were assigned to the food groups proportionally to the fat content of a standard portion size (Crawley, 1988). The scores were weighted by the frequency of consumption using four categories, ranging from ‘less than once a week’ to ‘six or more times a week’. The DINE provides a quick assessment of an individual’s diet by adding the scores relevant to the frequency of consumption of the groups of foods to give a total fat score. A total score is calculated and the respondents can be classified as low, medium or high fat consumers. However for randomised controlled trials (RCT), it is essential that the DINE is effective in predicting high fat consumers. To this end, Jackson et al. (2002) investigated the suitability of the DINE cut-off points for high fat consumers (Jackson et al. 2002). This involved comparing the DINE method to data from the UK Women’s Cohort Study, which used a 217-item food-frequency questionnaire to classify subjects into equal tertiles, based on their reported absolute fat intake (Calvert et al. 1996). By selecting a new cut-off point of 25, the agreement between the DINE and the UK Women’s Cohort Study classification was improved. Therefore, subjects who scored 25 or more using the DINE questionnaire were classified as high fat consumers. It was on the basis of this that the cut-off point of 25 for DINE score was used in the present study.
Our subjects completed a pre- and post-intervention DINE questionnaire to assess the changes in fat scores and hence fat consumption over the 3 months.

**Food diary records.** To assess dietary intake, each subject completed 4 d food and drink weighed diaries on three occasions; at the start of the study (baseline intakes), after 1 month and post-intervention (after 3 months). All food diaries were reviewed with the subject at the sessions to ensure clarity and completeness and to minimise the degree of under-reporting. This method of dietary assessment involved each subject recording (either weighing or recording in household measures) all foods and drinks consumed over a period of 4 d. It has been reported that using dietary diaries in a study with highly motivated subjects can be a very reliable and valid method of assessing dietary intake (De Castro, 1994). However, there are limitations of this method. There is the possibility of the subjects altering their eating behaviour, the diaries require a high degree of cooperation from subjects, continued motivation is required to complete the diaries accurately, and the diaries are time-consuming for researchers and therefore expensive to use. Additional problems are incurred with accurately recording food intake when meals are consumed outside the home. In addition, it has been estimated that 12 d of weighed food records are required in order to correctly classify subjects’ fat intake, and for the precision to be within 10% (Bingham, 1987). However, expecting volunteers to complete 12 d diaries is unrealistic and 4 d diaries are considered to provide a reasonable compromise between precision and practicality.

Participants were asked to complete the food diaries on 3 weekdays and 1 weekend day at baseline and at the 3-month follow-up.

Analysis of all diet records was performed using the McCance & Widdowson food tables (Holland et al., 1991) in the form of an in-house dietary package (Diet and Nutrition Tool for Evaluation; DANTE).

**Body-weight data.** Body weight was measured before the start of the study and at the end of the intervention. Participants were weighed fasted, in light clothes and without shoes or socks. Body-weight change was calculated for each subject to assess any impact of the intervention. The mean weight change for each group was compared to assess any impact of the intervention. The mean change in percentage body fat for each group was compared to assess any differential effects of the different dietary interventions.

**Laboratory methods.** Fasting blood samples were collected from each subject before the start and at the end of the intervention. These samples were separated by centrifugation, frozen immediately and stored at −40°C. They were analysed for lipid profile, glucose, CRP, intact insulin, IGF-1 and IGF binding protein (IGFBP)-1.

Lipid profile and glucose were measured on Integra 700, an automated analyser used for all the routine biochemistry at Hope Hospital, Salford, UK. Within- and between-assay CV were <2.5% for the measurement of total cholesterol, HDL-cholesterol and triacylglycerols and <2% for the measurement of glucose.

CRP was measured on Immulite by immunometric assay by a high-sensitivity CRP kit supplied by Diagnostic Products Corporation (Los Angeles, CA, USA). It has an analytical sensitivity of 0.1 ng/ml and a functional sensitivity of <0.2 mg/l. The antibody is highly specific for CRP. The method is linear and has good precision with CV of 5–10%.

Insulin was measured by the immunometric method on Immulite with the kit supplied by Diagnostic Products Corporation (Los Angeles, CA, USA). The method has an analytical sensitivity of 0.01 μIU/l (13.9 pmol/l). The intra- and inter-assay CV was <5%. The antibody was highly specific with no cross-reactivity detectable. Insulin sensitivity was calculated by the homeostasis model assessment (HOMA)-sensitivity (S) formula (Matthews et al., 1985).

Baseline IGF-1 was measured by ELISA using the Diagnostic Products Corporation (Los Angeles, CA, USA) Immulite Autoanalyzer. The limit of sensitivity of the assay is 20 ng/ml; within- and between-assay CV is <8%. Fasting circulating IGFBP-1 concentration at baseline was determined by a previously reported antibody-based assay (Westwood et al. 1994) with a detection limit of 3 μg/l and within- and between-assay CV of <8%.

Both biochemical and anthropometric data were analysed for the change in relation to dietary intervention and at both visits for the control group.

**Statistics.** Statistical analyses were carried out using the statistical package SPSS for Windows (release 10; SPSS Inc., Chicago, IL, USA). Non-normally distributed variables were logarithmically transformed before analysis by intervention group. Comparison of the differences between visits by intervention group was carried out by one-way ANOVA across all intervention groups and by paired t tests for comparison of the difference between visits for each individual intervention vs the control group. For univariate correlations
between continuous variables, Spearman correlations were used.

Results

Demographic data

The demographic data were similar in the four dietary intervention groups as shown in Table 1. There were no significant differences between any of the groups in age or ethnicity, baseline weight, BMI, smoking status or measured metabolic parameters.

Stage of change scores

There was no significant difference found between the groups in the stages of change questionnaire. Self-reported stage of change score was approximately 3 in each intervention group. This indicates that the subjects classified themselves in the preparation phase; they believed they were not eating a low-fat diet but had tried to reduce their fat intake and were prepared to continue trying over the next 6 months.

Weight and percentage body-fat changes

In Table 2 we have shown $P$ values for comparison of difference between visits 1 and 2 for the ANOVA across all intervention groups ($P^a$) and for the comparison of difference between visits 1 and 2 for each intervention v. the control group ($P^b$).

For the substitution group there was a significant reduction in weight (mean $-1.4$ (95% CI $-2.4$, $-0.2$) kg; $P=0.03$ for comparison of change with the control group). However, there was no significant weight change with the other interventions: reduction ($-0.4$ (95% CI $-1.3$, $0.4$) kg; NS for comparison of change with the control group); combination (0 (95% CI $-1.5$, $1.5$) kg; NS for comparison of change with the control group).

Table 1. Age and anthropometric and metabolic data at baseline

(Arithmetic mean values and 95% confidence intervals)

<table>
<thead>
<tr>
<th></th>
<th>Substitution group</th>
<th>Reduction group</th>
<th>Combination group</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39-1 37-2, 44</td>
<td>44-5 37-2, 52</td>
<td>43-8 49-7, 38</td>
<td>45 38-7, 52-3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30-4 27-3, 35-5</td>
<td>30-0 27-1, 32-9</td>
<td>32-0 28-8, 35-1</td>
<td>32-0 28-8, 35-1</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>35-0 30-1, 39-1</td>
<td>35-3 31-5, 39-2</td>
<td>36-6 33-1, 40-1</td>
<td>31-8 28-1, 35-5</td>
</tr>
<tr>
<td>White European (n)</td>
<td>19</td>
<td>19</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Other ethnic group (n)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DINE score</td>
<td>42-6 37-2, 48-1</td>
<td>35-4 32-2, 38-6</td>
<td>42-6 35-7, 49-5</td>
<td>35-4 30-2, 40-6</td>
</tr>
<tr>
<td>SOC score</td>
<td>3-1</td>
<td>2-8</td>
<td>2-8</td>
<td>3-1</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>4-9 44-5, 53</td>
<td>5-2 4-8, 5-6</td>
<td>4-9 4-4, 5-4</td>
<td>5-2 4-6, 5-8</td>
</tr>
<tr>
<td>Triacylglycerol (mg/dl)</td>
<td>1-4 1-0, 1-7</td>
<td>1-3 1-0, 1-6</td>
<td>1-4 1-0, 1-7</td>
<td>1-0 0-8, 1-2</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>2-9 2-5, 3-3</td>
<td>3-2 2-8, 3-6</td>
<td>3-0 2-5, 3-4</td>
<td>3-2 2-8, 3-7</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>4-1 2-3, 6-0</td>
<td>2-7 1-4, 4-0</td>
<td>3-5 2-1, 4-8</td>
<td>3-3 0-4, 6-0</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>4-9 46-5, 5-3</td>
<td>5-4 4-7, 5-6</td>
<td>5-0 4-3, 5-6</td>
<td>4-8 4-4, 5-3</td>
</tr>
<tr>
<td>Insulin (pmol/l)</td>
<td>87-1 62-2, 112-0</td>
<td>64-6 41-0, 88-2</td>
<td>90-7 67-1, 114-2</td>
<td>68-1 58-5, 67-8</td>
</tr>
<tr>
<td>IGF-1</td>
<td>173-3 145-7, 201</td>
<td>171-2 129-4, 213</td>
<td>190-5 147, 234-1</td>
<td>195-4 153-4, 237-3</td>
</tr>
<tr>
<td>IGFBP-1</td>
<td>28-5 15, 42-1</td>
<td>30-4 16, 44-3</td>
<td>27-1 9-2, 45</td>
<td>28-0 21-7, 34-4</td>
</tr>
</tbody>
</table>

DINE, dietary instrument for nutrition education; SOC, stage of change; CRP, C-reactive protein; IGF, insulin-like growth factor; IGFBP, insulin-like growth factor binding protein.

* Other ethnic group refers to South Asian, African Caribbean or African ethnic origin.

Table 2. Baseline and post-intervention measurements and change between baseline and post-intervention measurements (post-intervention–baseline)$†$

(Mean values and 95% confidence intervals)

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n 80)</th>
<th>Post-intervention (n 69)</th>
<th>Mean change (n 69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>Mean 95% CI</td>
<td>Mean 95% CI</td>
<td>Mean 95% CI</td>
</tr>
<tr>
<td>Substitution</td>
<td>82-7 75-2, 88-9</td>
<td>81-3 70-6, 84-2</td>
<td>-1-4</td>
</tr>
<tr>
<td>Reduction</td>
<td>82-7 75-5, 89-8</td>
<td>82-3 74-7, 89-8</td>
<td>-0-4</td>
</tr>
<tr>
<td>Combination</td>
<td>88-0 79-2, 96-8</td>
<td>87-9 76-8, 97-2</td>
<td>0-0</td>
</tr>
<tr>
<td>Control</td>
<td>72-6 62-7, 82-5</td>
<td>72-8 60-8, 84-1</td>
<td>0-2</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>35-9 32-1, 39-8</td>
<td>34-6 29-2, 36-6</td>
<td>-1-3</td>
</tr>
<tr>
<td>Substitution</td>
<td>35-4 31-7, 39-1</td>
<td>35-7 32-9, 39-7</td>
<td>0-3</td>
</tr>
<tr>
<td>Reduction</td>
<td>37-4 34-1, 40-8</td>
<td>38-1 34-1, 42-4</td>
<td>0-7</td>
</tr>
<tr>
<td>Control</td>
<td>31-8 28-1, 35-5</td>
<td>31-0 26-4, 34-9</td>
<td>-0-8</td>
</tr>
</tbody>
</table>

* For details of subjects and procedures, see Table 1 and p. 810.
† Overall test comparing differences between visits 1 and 2 by intervention group (one-way ANOVA).
‡ Comparing differences between visits 1 and 2 for each intervention group v. the control group ($t$ test).
comparison of change with the control group); control (0·2 (95% CI −0·7, 1·0) kg; NS for comparison of change with the control group).

A similar effect was seen for percentage body fat, with the substitution group having a significant reduction in percentage body fat (−1·3 (95% CI −2·0, −0·5) %; P=0·01 for comparison of change with all other groups). No significant change was seen in the other two intervention groups: reduction group (0·3 (95% CI −0·9, 1·5) %); combination group (0·7 (95% CI −0·4, 1·8) %); control group (−0·8 (95% CI −1·5, 0·1) %). There was a trend for the substitution intervention to cause a reduction in percentage body fat when compared with the control group (P=0·06).

Fat intake

There was no difference in total fat or saturated fat intake at baseline between the groups (data not shown). There was an overall significant difference between the groups and change in DINE score after 3 months (P<0·01). The substitution group showed the greatest change with a decrease in the mean DINE score of 24 (95% CI 17, 31) (P<0·01). The other groups also showed a significant decrease in DINE score: reduction group (13 (95% CI 8, 17); P<0·01); combination group (20 (95% CI 12, 27); P<0·01); control group (4 (95% CI 0, 7); P=0·03).

Biochemical data

Fasting triacylglycerols (change of −0·2 (SEM 0·07) mmol/l; P=0·04) fell with the substitution intervention as did CRP levels (0·8 (SEM 0·2) mg/l; P=0·04 (−24·3 (SEM 8) %) (Fig. 1), but not with the other interventions. There was a trend for fasting cholesterol to fall with substitution (−0·3 (SEM 0·08) mmol/l; P=0·06) but not with the other interventions (Fig 1(b)). No significant change in HDL-cholesterol was seen with any intervention.

Circulating IGF-1 rose significantly with the substitution (31 (SEM 17) ng/ml) and reduction interventions (19 (SEM 10) ng/ml) (P=0·02) (Fig. 2). No change was found with IGFBP-1. There was no significant change in fasting insulin, fasting glucose or HOMA-S with any intervention between visits 1 and 2.

Correlations between measured metabolic and anthropometric variables

IGF-1 levels were inversely associated with serum triacylglycerols, cholesterol and CRP concentrations and also with fasting glucose levels. IGF-1 correlated negatively with BMI and percentage body fat. A lower level of fasting IGFBP-1 was associated with higher CRP, fasting glucose and percentage body fat. As previously reported, IGFBP-1 correlated negatively with BMI and insulin (Table 3).

There was a strong positive relationship between CRP and fasting glucose, insulin, BMI and percentage body fat. CRP was not associated significantly with cholesterol or triacylglycerols levels. Reduction in weight positively correlated with reduction in triacylglycerols (Spearman’s ρ 0·27; P=0·03) and cholesterol level (ρ 0·27; P=0·03) (Figs. 3 (a) and (b)).

Discussion

In the present study we have determined that the substitution model of dietary intervention is effective even over a relatively short interval of time in reducing weight, percentage body fat and fat consumption (as measured by the DINE questionnaire), together with fasting serum concentrations of triacylglycerols and CRP with a consequent improvement in cardiovascular profile.

The reduction seen in CRP is of a similar order to that seen in a recent study in which male dyslipidaemic subjects were given 15 ml linseed oil (rich in α-linoleic acid and with a high n-3:n-6 fatty acid ratio) per d and a reduction of 38% in CRP was achieved (Rallidis et al. 2003). The recently published study of Kaaks et al. (2003) in forty-nine women showed no change in circulating IGF-1 and an increase in IGFBP-1. However, they used a reduction...
rather than a substitution model of dietary intervention, involving reductions in the intake of total fat and refined carbohydrates and an increase in the dietary ratio of $n$-3:$n$-6 plus saturated fatty acids.

Despite continuing recommendations to reduce fat intake and several national bodies highlighting the health risks, the UK population average intake of dietary fat still remains high. It is clear that the present strategies for modifying population fat intake are not as successful as public health nutritionists would desire. Thus there is a need for further interventions to promote successful dietary change (Department of Health, 1999). A number of systematic reviews have been carried out on the effects of advice concerning low-fat diets (Pirozzo et al. 2003) and the effects of a reduction or modification in dietary fat intake on CVD (Hooper et al. 2001). Reducing fat intake is a specific lifestyle change and need not necessarily be associated with weight reduction per se. In a recent meta-analysis of low-fat diets, Astrup et al. (2000) concluded that dietary fat restriction prevented weight gain in participants of normal weight and produced weight loss in overweight participants. The systematic review by Pirozzo et al. (2003) assessed the effects of advice about low-fat diets as a means of achieving sustained weight loss. This review focused primarily on participants who were overweight or clinically obese and were dieting for the purposes of weight reduction. They concluded that in overweight or obese individuals who are dieting for the purpose of weight reduction, low-fat diets are as efficacious as other weight-reducing diets for achieving sustained weight loss but not more so. Hooper et al. (2001) stated that there is a small but potentially important reduction in cardiovascular risk with the reduction or modification of dietary fat intake, seen particularly in trials of longer duration.

The use of low-fat foods has been reported to be easily adopted and highly acceptable, and to be one of the most effective approaches to reduce fat intake (Keenan et al. 1996). The present study confirmed for the first time using an RCT that in this British population the substitution model was most effective. A combination of strategies has also been considered likely to offer the best chance of successfully reducing levels of fat in the diet. However, in the present study this was not the case. Perhaps, this model may have proved difficult to comply with due to the greater complexity of the messages regarding dietary change. The absence of a significant difference

Table 3. Associations between measured metabolic and anthropometric variables† (Spearman correlations)

<table>
<thead>
<tr>
<th>Triacylglycerol</th>
<th>Cholesterol</th>
<th>CRP</th>
<th>Glucose</th>
<th>Insulin</th>
<th>IGF-1</th>
<th>IGFBP-1</th>
<th>BMI</th>
<th>Percentage body fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triacylglycerol</td>
<td>1·00</td>
<td>0·435**</td>
<td>0·204</td>
<td>0·159</td>
<td>0·445**</td>
<td>−0·367**</td>
<td>0·157</td>
<td>0·300**</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1·00</td>
<td>−0·038</td>
<td>0·129</td>
<td>0·068</td>
<td>−0·341**</td>
<td>0·000</td>
<td>0·064</td>
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<tr>
<td>CRP</td>
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<td>0·241**</td>
<td>0·339**</td>
<td>−0·251**</td>
<td>−0·285*</td>
<td>0·605*</td>
<td>0·614**</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>1·00</td>
<td>0·355**</td>
<td>−0·311**</td>
<td>−0·322**</td>
<td>0·373**</td>
<td>0·371**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>1·00</td>
<td>−0·189</td>
<td>−0·580**</td>
<td>0·655**</td>
<td>0·555**</td>
<td>0·555**</td>
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<td></td>
</tr>
<tr>
<td>IGF-1</td>
<td>1·00</td>
<td>0·014</td>
<td>−0·017***</td>
<td>−0·278*</td>
<td>−0·346**</td>
<td>−0·346**</td>
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<tr>
<td>IGFBP-1</td>
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<td>0·607**</td>
<td>−0·537***</td>
<td>0·027</td>
<td>0·027</td>
<td>0·027</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>1·00</td>
<td>0·927**</td>
<td>0·927**</td>
<td>1·00</td>
<td>1·00</td>
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<td></td>
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</tr>
</tbody>
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CRP, C-reactive protein; IGF, insulin-like growth factor; IGFBP, insulin-like growth factor binding protein.

*P < 0·05; **P < 0·01.
† For details of subjects and procedures, see Table 1 and p. 810.
between the change in percentage body fat for the substitution intervention v. the control group is in our view a type 2 error related to sample size. The control group subjects were not given any specific advice about alteration in diet or activity levels. There was no change in intake of total fat or saturated fat in the control group during the study (data not shown).

As scientific evidence mounts for recommendations of a low-fat diet, there is a pressing need for more effective and less costly dietary change interventions. Little is known about how dietary interventions modify fat intake in the free-living population. This is because most of the previous studies that have observed a reduction in fat intake have focused on experimental manipulation of fat intakes in the laboratory setting, have been carried out over short periods of time and have used intensive and repeated group education, which can be extremely time-consuming (Gorbach et al. 1990). However, in the present study we have shown that such modifications reduce the intake of fat in free-living populations within the UK.

A reduction of fat is likely to reduce the palatability of the diet, which has been found to be an important barrier to adopting such diets (Lloyd et al. 1995). Our finding that the reduction and combination models did not result in any significant change in lipid or CRP levels suggests that compliance with these interventions was poorer than with the substitution model. The combination model may have proved difficult to comply with due to the greater complexity of the messages regarding dietary change. The reduction model, where high-fat foods are omitted from the diet and replaced by other food groups such as fruit and vegetables or bread and potatoes, is a popular strategy promoted in much of the available dietary literature on reducing fat intake (Kristal et al. 1992). The evidence presented here strongly supports the adoption of the substitution model because of its greater efficacy.

Fig. 3. (a) Scatterplot of change in weight v. percentage change in fasting serum cholesterol ($r^2$ 0.11). (b) Scatterplot of change in weight v. percentage change in fasting serum triacylglycerols ($r^2$ 0.09).
Although not all individuals who consume a high-fat diet are fat (Cooling & Blundell, 2000), it may be that dietary fat is a particular risk factor for obesity in a susceptible sub-population or phenotype (Astrup et al. 1994). In the present study, the utilisation of the DINE questionnaire to identify high fat consumers combined with the effectiveness of the substitution dietary intervention model in reducing CRP and increasing IGF-1 levels is particularly important. This is because of the close association of high CRP with obesity (Festa et al. 2001) and low circulating IGF-1 with the subsequent development of impaired glucose handling (Sandhu et al. 2002).

In these participants, baseline lipid levels were significantly below those at which intervention would conventionally be deemed necessary (Wood et al. 1998), although they did reflect average population values and, even so, significant changes were observed. This would suggest that the substitution model has potential utility for improving fasting lipids in individuals with a dyslipidaemic profile according to accepted definitions.

The positive cross-sectional associations between CRP and fasting glucose, fasting insulin, BMI, and percentage body fat are in accordance with results from the Insulin Resistance and Atherosclerosis Study where strong associations were found between CRP and measures of body fat (BMI, waist circumference), insulin resistance and fasting insulin (Festa et al. 2000). We have recently shown that IGF-1 and CRP independently contribute to variation in insulin sensitivity (Heald et al. 2003a) with low IGF-1 levels being associated with elevated circulating CRP. The negative correlations here between IGF-1 and CRP and between IGF-1 and other markers of cardiovascular risk concur with this and also with the finding that a low circulating IGF-1 is associated with the increased risk of diabetes and myocardial infarction (Vaessen et al. 2001). Although lower circulating IGFBP-1 levels are well known to be associated with a more adverse cardiovascular risk profile (Janssen et al. 1998), the very strong relationship between low IGFBP-1 and percentage body fat found in the present study is further evidence for a profound impact of increasing adiposity on IGFBP-1 production, an association that was independent of circulating insulin levels.

The significant increase in IGF-1 with both the substitution and reduction of dietary saturated fat is intriguing in the view of the potential long-term benefits of increased circulating IGF-1 on insulin sensitivity and cardiovascular risk (Heald et al. 2001, 2003a), although we did not see any measurable changes in HOMA-S in the present short-term study. IGF-1 production by hepatocytes is known to be up regulated by insulin at the level of hepatic gene transcription (Phillips et al. 1991; Pao et al. 1992). One possible mechanism for the increase in circulating IGF-1 seen in the present study may be a reduction in hepatic portal non-esterified fatty acid concentration which in turn results in improved insulin sensitivity at the liver (Cruickshank et al. 2001) and so improved responsiveness of hepatocytes to hepatic portal insulin.

Health promotion strategies have been devised to encourage a reduction in fat consumption by the population. Much of the research in dietary intervention has focused on the experimental manipulation of fat intakes in the laboratory setting and over short periods of time (Caputo & Mattes, 1992; Foltin et al. 1992a,b; Blundell et al. 1993). There remain important issues concerning longer-term adherence to dietary intervention strategies, which are relevant when the results of structured studies are generalised to the population at large (White et al. 1992). It is also pertinent to explore motivations behind changes in fat consumption at an individual level and the impact that dietary intervention has from a psychological perspective. This is the first RCT to explore the effectiveness of the two main methods of reducing fat in the diet; substitution with reduced-fat products or reduction of total fat.

Although the present study was a small-scale RCT, RCT are the best way of measuring the efficacy of intervention because of their ability to minimise bias and avoid false conclusions. A second strength of the study was the multiple measures of dietary change. The random assignment of subjects to different intervention groups was a good way of achieving a balance between the groups for the known and unknown factors that influence outcome (Stephenson & Imrie, 1998). The inclusion of a control group greatly aided the interpretation of the results. The limitations of the present RCT include feasibility and relevance to the real world, which are factors in most study designs. It was not feasible to examine the maintenance of changes beyond 3 months within the present study and it is not necessarily generalisable to the general population as the participants were high fat consumers at baseline assessed by the DINE questionnaire, were highly motivated and had an interest in health to inspire them to volunteer for research studies.

In conclusion, the efficacy of the substitution intervention in reducing body weight, total fat and energy consumption, fasting cholesterol and triacylglycerols and CRP in the study is important in that this model could potentially be applied to a larger population sample. Furthermore, the previously described relationships between IGF and IGFBP levels and macronutrient intake (Hellenius et al. 1995; Heald et al. 2003b) suggest that IGF bioavailability may be modifiable by dietary intervention. Thus the present findings have important preventative and therapeutic implications for managing disease risk within the population in the future.

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References

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