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# Contribution of specific dietary factors to CHD in US females

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## Abstract

*Objective:* To estimate dietary cholesterol contribution to CHD risk among US females, relative to other dietary risk factors.
*Design:* A risk apportionment model was applied to apportion CHD risk shares among the lifestyle and dietary risk factors.
*Setting:* The model was implemented using relative risks from the Nurses' Health Study and data on CHD risk factors and consumption from the National Health and Nutrition Examination Survey 1999–2002.
*Subjects:* US females aged 25 years or older.
*Results:* On average, poor diet contributes 20% of the CHD risk relative to obesity, inactivity and smoking, of which *trans* fat intake contributes 2·9%, dietary cholesterol 1·5% and 16% is due to low consumption of nutrients, i.e. MUFA (1·5%), PUFA (1·7%), marine *n*-3 fatty acids (2·7%), α-linolenic acid (1·1%), dietary fibre (2·4%), vitamin $B_6$ (4·1%), vitamin C (0·5%) and folate (1·8%).
*Conclusions:* Reducing *trans* fat and dietary cholesterol intakes could lead to CHD reduction, but greater risk reduction may be achieved by improving intakes of heart-healthy nutrients currently deficient in US females' diets. Total diet consideration is essential in any CHD risk reduction strategy.

**Keywords**
Dietary cholesterol
Coronary heart disease
Risk factors
NHANES
Risk apportionment model

Despite the multiple risk factors including older age, male gender, genetic, race, smoking, inactivity, overweight, diet, high blood pressure, high blood cholesterol and diabetes mellitus, a major focus of CHD risk reduction has been on dietary cholesterol. However, recent epidemiological evidence has raised questions about the relationship between dietary cholesterol, plasma cholesterol levels and CHD risk[1–4].

The Health Professionals' Follow-up Study (HPFS) showed no association between dietary cholesterol and CHD risk among male subjects[2]. At the highest quintile of intake (422 mg/d) the relative risk (RR) was 1·03 (95% CI 0·81, 1·32). A non-significant association between dietary cholesterol and CHD risk was observed among females in the Nurses' Health Study (NHS). There was a slight increase in CHD risk for all quintiles of cholesterol intake ($P$ for trend = 0·24)[2].

In the present paper the dietary cholesterol contribution to CHD risk among US females aged 25 years or older was derived using RR estimates from the NHS and data on intake and CHD risk factors from the National Health and Nutrition Examination Survey (NHANES) 1999–2002. A risk apportionment model[5] was applied. The egg cholesterol share of CHD risk was also ascertained.

## Methods

### *Model*

A proportional weight risk apportionment model was used to calculate the contribution of risk factors to the overall CHD risk. Techniques to calculate the proportionate contribution of causal factors to a disease risk and their application to a public health setting were reviewed by Barraj *et al.*[5]. The 'proportional weights model' is a better model when the additivity assumption of the combined risk does not hold[5]. This model estimates assigned share ($AS_i$) associated with the $i$th risk factor ($RR_i$ denotes the relative risk associated with the $i$th risk factor) as:

$$AS_i = \Bigg\{ (RR_i - 1) + \sum_{j \neq i} w_{i|j}[(RR_i - 1)(RR_j - 1)] + \sum_{j \neq i} \sum_{\substack{k \neq i \\ k \neq j}} w_{i|jk}[(RR_i - 1)(RR_j - 1)(RR_k - 1)] + \cdots + w_{i|1\ldots n}[(RR_1 - 1)\cdots(RR_n - 1)] \Bigg\} \Big/ RR_1 \cdots RR_n - 1$$

where

$$w_{i|j} = \frac{RR_i - 1}{RR_i + RR_j - 2},$$

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$$w_{i|jk} = \frac{\mathrm{RR}_i - 1}{\mathrm{RR}_i + \mathrm{RR}_j + \mathrm{RR}_k - 3}$$

and

$$w_{i|1\ldots n} = \frac{\mathrm{RR}_i - 1}{\sum_j (\mathrm{RR}_j - 1)}.$$

In the present study, the model was implemented as follows:

1. Stratify the US females aged 25 years or older based on their common risk attributes (diet, obesity, exercise and smoking) using NHANES 1999–2002 data[6].
2. Within each stratum, apply the model to calculate the diet share of CHD risk, using a 'diet score', relative to obesity, exercise and smoking.
3. Within each stratum, apply an apportionment model with only the dietary factors to estimate specific dietary shares of CHD risk.
4. Within each stratum, estimate the fraction of dietary cholesterol from egg foods and apply this fraction to the dietary cholesterol share of CHD risk to calculate the egg share.

## Data

The following data for the lifestyle and diet risk factors and associated RR were used to implement the model.

### *Lifestyle factors*

The American Heart Association (AHA) has identified exercise, BMI below 25 kg/m$^2$, avoidance of smoking, moderate alcohol intake, and a diet low in *trans* fat and glycaemic load, high in fibre, marine *n*-3 fatty acids (FA) and folate, with a high ratio of PUFA to SFA, as important lifestyle factors to prevent CHD in women. Demographic, smoking, exercise, anthropometric and dietary data were abstracted and recoded from NHANES 1999–2002 to create the following dichotomous categories.

1. Exercise: responses to questions on vigorous or moderate physical activity over the previous month were recoded into 'heavy' and 'moderate'.
2. Smoking: participants were classified into current smokers and former/non-smokers.
3. Obesity: participants were classified into two categories, BMI $\geq$ 25 kg/m$^2$ or BMI $<$ 25 kg/m$^2$.
4. Diet score: this was calculated using the 24 h food-recall data. The scoring mimicked the approach described by Stampfer *et al.*[7] and used intakes of *trans* fat, cereal fibre, dietary folate, glycaemic load and PUFA:SFA ratio. A diet score was derived and categorized into quintiles. Higher quintile scores are indicative of a 'prudent' diet, e.g. low intake of *trans* fat, high intakes of fruits, vegetables and fibre, higher intake of chicken and fish relative to red meat and/or higher PUFA:SFA ratio[7]. Quintiles 1, 2 and 3 are categorized as poor diet and quintiles 4 and 5 as good diet.

Based on these categories, US females were stratified into groups with similar modifiable lifestyle risk factors.

### *Intakes*

Daily nutrient and cholesterol intakes were estimated using 24 h consumption data for NHANES 1999–2002 and food nutrient contents from the US Department of Agriculture's (USDA) National Nutrient Database[8]. The fraction of dietary cholesterol from egg foods was determined using USDA–Environmental Protection Agency food recipes[9]. Only foods containing whole eggs or egg yolk were considered.

### *Estimated relative risks*

A number of studies have estimated RR for CHD risk factors, but there is variability among them with respect to study size, geography, population, adjustment for confounders and design. To ensure consistency and avoid using RR for a risk factor that could have been confounded by other factors, only multivariate-adjusted RR from the NHS were used. The NHS was chosen because it is among the largest investigations of risk factors for chronic diseases in women, with long follow-up periods and carefully collected information. NHS data on the association between CHD and smoking, obesity, exercise and diet reported by Stampfer *et al.*[7] were used (Table 1).

Estimated RR values for specific dietary factors were also derived from the NHS. A number of publications on diet factors and CHD risk from the NHS were found in the published literature. Estimated RR and intakes for most of these studies are summarized in the Appendix. The apportionment model was limited to ten dietary factors: cholesterol, marine *n*-3 FA, PUFA, MUFA, *trans* fat, α-linolenic acid (ALA), dietary fibre, folate, vitamin $B_6$ and vitamin C. The rationale for this selection and the exclusion of SFA from the model are as follows.

1. SFA was not included because no association with CHD was observed in the NHS subjects (RR = 1·00,

**Table 1** Lifestyle risk factors and relative risks (RR) included in the risk apportionment model, US females aged 25 years or older

| Factor | | RR* |
|---|---|---|
| Diet | Poor diet (quintile 1, 2 & 3) *v.* good diet (quintile 4 & 5) | 1·46 |
| Smoking | Current smoker *v.* former or non-smoker | 3·33 |
| Obesity | BMI $\geq$ 25 kg/m$^2$ *v.* $<$25 kg/m$^2$ | 1·35 |
| Exercise | Physical activity $<$3·5 h/week *v.* $\geq$3·5 h/week | 1·24 |

*Extrapolated from Stampfer *et al.* (2000)[7].

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**Table 2** Dietary factors, intakes and interpolated relative risks (RR) included in the risk apportionment model*, US females aged 25 years or older

| Dietary factor | Daily intake (NHANES 1999–2002) | Interpolated RR | *P* | Reference |
|---|---|---|---|---|
| Cholesterol | 227·70 mg | 1·17 | 0·24 | Hu *et al.* (1997)[2] |
| Marine *n*-3 fatty acids | 0·07 g | 1·27 | <0·01† | Hu *et al.* (2002)[12] |
| α-Linolenic acid | 0·84 g | 1·14 | 0·5 | Hu *et al.* (1999)[15] |
| *Trans* fat | 2·49 % of energy | 1·29 | 0·01† | Oh *et al.* (2005)[10] |
| PUFA | 5·49 % of energy | 1·19 | 0·004† | Oh *et al.* (2005)[10] |
| MUFA | 12·66 % of energy | 1·17 | 0·19 | Oh *et al.* (2005)[10] |
| Dietary fibre | 14·30 g | 1·25 | 0·07 | Wolk *et al.* (1999)[14] |
| Folate | 363·70 μg | 1·20 | 0·003† | Rimm *et al.* (1998)[13] |
| Vitamin $B_6$ | 1·57 mg | 1·38 | 0·004† | Rimm *et al.* (1998)[13] |
| Vitamin C | 84·80 mg | 1·08 | 0·52 | Osganian *et al.* (2003)[16] |

NHANES, National Health and Nutrition Examination Survey.
*All outcomes: fatal + non-fatal CHD.
†Statistically significant.

0·94, 0·96, 1·04 and 0·97 for quintiles 1 to 5 of exposure as a percentage of energy, respectively)[10]. Given that the RR for all quintiles are at unity, had SFA been included in the model, no CHD risk would be apportioned to SFA as a risk factor.

2. Although the association between dietary cholesterol and CHD is not statistically significant in the NHS, it is listed as a risk factor by the AHA[11] and is a focus of the present study, so it was included.
3. The associations between CHD and low intake of marine *n*-3 FA[12], PUFA[10], folate[13], vitamin $B_6$[13] and dietary fibre[14], and high intake of *trans* fat[10], were statistically significant among NHS subjects and were included.
4. While not statistically significant for non-fatal CHD, the association between fatal CHD and low ALA[15] intake was significant in the NHS and was included.
5. Although the associations between CHD and MUFA and vitamin C were not statistically significant, an inverse relationship between increasing intake and CHD risk was observed (MUFA: RR = 1·22, 1·15, 1·16, 1·11 and 1·00 for quintiles 1 to 5 as a percentage of energy, respectively[10]; vitamin C: RR = 1·16, 1·06, 1·00, 0·98 and 1·00 for quintiles 1 to 5 of exposure, respectively[16]). Thus MUFA and vitamin C were included.

The daily intakes for these ten factors were developed using NHANES 1999–2002 data and the associated RR were extrapolated from the quintiles of intakes and RR reported in the NHS study (Table 2).

## Results

### *Diet and lifestyle factors*

The prevalence of poor diet, inactivity, obesity and smoking among US females aged 25 years or older was determined using the NHANES 1999–2002 data. Over 82 % of females (>77 million) have >1 lifestyle risk factor. The most common mutually exclusive combinations of lifestyle factors are presented in Table 3. Approximately 68 % (>52 million) US females have poor diet as a risk factor, with 8 % having poor diet as the only modifiable factor and 60 % having combinations of >2 modifiable factors.

Diet contribution to CHD risk varies depending on the presence/absence of other CHD risk factors. The current study focuses on the diet and lifestyle factors while ignoring health status and non-modifiable factors such as age and genetics. When diet is examined as a whole, its share of CHD risk is 13 % when obesity, inactivity and smoking risk factors are also present and 65 % when inactivity is the only other risk factor present. When diet is the only risk factor (8 % of the females) its share of the CHD risk is 100 %. On average, poor diet contributes about 20 % of the CHD risk among US females aged 25 years or older (Table 3).

### *Specific dietary factors*

Of the 20 % dietary share of CHD risk, relative to obesity, inactivity and smoking, current consumption of *trans* fat contributes 2·9 %, dietary cholesterol 1·5 % and the remaining 16 % is due to low consumption of desirable nutrients such as MUFA (1·5 %), PUFA (1·7 %), marine *n*-3 FA (2·7 %), ALA (1·1 %), dietary fibre (2·4 %), vitamin $B_6$ (4·1 %), vitamin C (0·5 %) and folate (1·8 %; Fig. 1).

Based on the NHANES 1999–2002 intake data, dietary cholesterol in 82 % of US females averages 227·7 mg/d. Cholesterol intake in females with poor diet ranges from 227·8 to 258·2 mg/d. Those with poor diet and having >1 modifiable risk factor represent 68 % of this group. Cholesterol intake ranges from 152·2 to 233·8 mg/d for females without poor diet (Table 4).

Among females with poor diet, cholesterol has the lowest CHD risk share (1·14 %) when obesity, inactivity and smoking are also present, and the highest risk share (7·79 %) when poor diet is the only risk factor (Table 4). Given the current cholesterol intake among US females, dietary cholesterol CHD risk share, relative to the other nine factors included in the model (*trans* fat, MUFA,

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**Table 3** Lifestyle factors and CHD risk shares, US females aged 25 years or older

| | Presence and percentage share of CHD risk† | | | |
|---|---|---|---|---|
| Population with risk factors* (%) | Smoking | Inactive | BMI ≥ 25 kg/m$^2$ | Poor diet |
| 8·1 | | | | (100) |
| 3·9 | | (34·8) | | (65·2) |
| 14·2 | | | (43·2) | (56·8) |
| 11·7 | | (22·6) | (33·3) | (44·1) |
| 7·0 | (83·6) | | | (16·4) |
| 4·0 | (78·1) | (7·1) | | (14·8) |
| 9·6 | (75·8) | | (10·2) | (14·0) |
| 9·4 | (72·0) | (5·9) | (9·2) | (12·9) |
| 6·8 | | | ✓ | |
| 5·7 | | | | |
| 4·4 | | ✓ | ✓ | |
| 2·4 | | ✓ | | |
| 4·9 | ✓ | | ✓ | |
| 4·2 | ✓ | | | |
| 2·4 | ✓ | ✓ | ✓ | |
| 1·3 | ✓ | ✓ | | |
| | | | Average | 20·3 % |

*Total weighted *n* is 77 129 836 (~82 % of US females in the National Health and Nutrition Examination Survey 1999–2002).
†✓ = present; ( ) = CHD risk share.

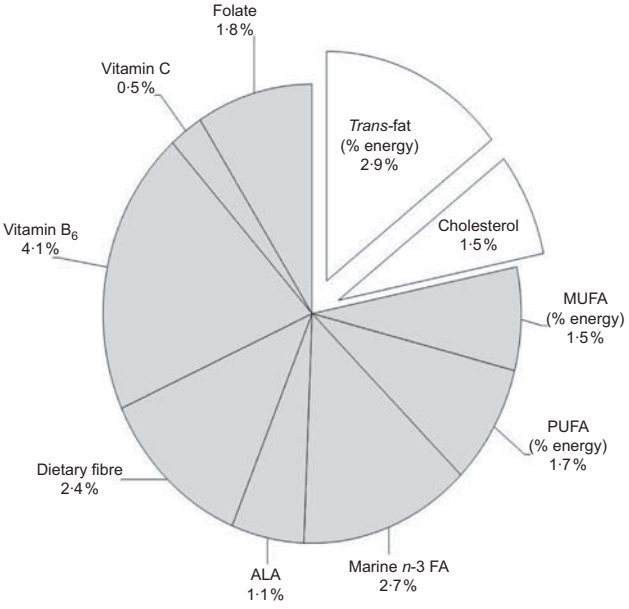


**Fig. 1** Relative risk (RR) contribution of specific dietary factors among US females aged 25 years or older. Total dietary CHD risk share is ~20 %. Specific dietary factor risk share is based on average intake and RR when compared with reference intake: cholesterol (227·7 mg/d *v.* 132 mg/d); marine *n*-3 fatty acids (FA; 0·07 g/d *v.* 0·24 g/d); α-linolenic acid (ALA; 0·838 g/d *v.* 1·36 g/d); dietary fibre (14·3 g/d *v.* 22·9 g/d); vitamin $B_6$ (1·57 mg/d *v.* 4·4 mg/d); vitamin C (84 mg/d *v.* 209 mg/d); folate (363·7 μg/d *v.* 696 μg/d); *trans* fat (2·5 % of energy *v.* 1·3 % of energy); MUFA (12·7 % of energy *v.* 18 % of energy); PUFA (5·49 % of energy *v.* 7·4 % of energy)

PUFA, marine *n*-3 FA, ALA, dietary fibre, vitamin $B_6$, vitamin C and folate) and other lifestyle risk factors (obesity, inactivity, smoking), averages 1·5 %.

As a sensitivity analysis, the apportionment model was implemented with dietary cholesterol as the principal dietary factor (ignoring other dietary factors). In this case, dietary cholesterol was used instead of the overall diet score in the apportionment model and its contribution to CHD risk was assessed relative to obesity, inactivity and smoking. This analysis provides an upper-bound estimate of dietary cholesterol share of CHD risk, approximately 1·9 %.

Foods containing whole egg and/or egg yolk contribute 20–28 % (average 25 %) of dietary cholesterol for US females aged 25 years or older (Table 4). The egg CHD risk share when restricted to those with 'poor diet' (~68 % of the US females included in the present analysis) ranges from 0·27 % to 1·96 % (average 0·8 %). When all females are considered the egg CHD risk share is 0·4–0·5 %.

## Discussion

Epidemiological studies consistently have shown a close association between CHD risk and diets high in total fat, SFA and cholesterol, and low in fibre and PUFA[17,18]. In the present study, when genetics and age were ignored, a poor diet contributed approximately 13 % to 65 %, depending on whether smoking, obesity and inactivity were present. On average, the dietary share of CHD risk, relative to other lifestyle factors, was approximately 20 % for US females aged 25 years or older.

While the relationship between overall diet and CHD is consistent, the evidence on dietary cholesterol is not always clear[18]. Recent epidemiological evidence has raised questions about whether limiting dietary cholesterol intake would lead to any significant reduction in CHD risk[1,3,4,19]. Cholesterol feeding studies demonstrating that dietary cholesterol increases both LDL and HDL cholesterol, with little change in the LDL:HDL ratio,

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**Table 4** CHD risk shares for dietary and egg cholesterol, US females aged 25 years or older

| Lifestyle factors | Population with risk factors* (%) | Dietary cholesterol (mg/d) | Dietary cholesterol CHD risk share (%) | | Cholesterol from egg foods (%) | Egg cholesterol CHD risk share (%) | |
|---|---|---|---|---|---|---|---|
| | | | | Sensitivity analysis | | | Sensitivity analysis |
| Poor diet | 8·15 | 243·7 | 7·79 | 7·79 | 25·18 | 1·96 | 1·96 |
| Poor diet & inactive | 3·90 | 227·8 | 4·74 | 2·99 | 26·73 | 1·27 | 0·80 |
| Poor diet & overweight | 14·16 | 239·9 | 4·42 | 2·65 | 24·17 | 1·07 | 0·64 |
| Poor diet & smoking | 7·02 | 241·5 | 1·28 | 0·56 | 22·39 | 0·29 | 0·13 |
| Poor diet, inactive & overweight | 11·69 | 236·2 | 3·44 | 1·78 | 26·59 | 0·91 | 0·47 |
| Poor diet, inactive & smoking | 4·03 | 249·8 | 1·23 | 0·53 | 22·46 | 0·28 | 0·12 |
| Poor diet, overweight & smoking | 9·58 | 248·8 | 1·16 | 0·49 | 26·90 | 0·31 | 0·13 |
| Poor diet, overweight, inactive & smoking | 9·38 | 258·2 | 1·14 | 0·48 | 23·92 | 0·27 | 0·11 |
| No modifiable risk factor | 5·71 | 188·1 | 0·00 | 4·72 | 21·94 | 0·00 | 1·04 |
| Inactive | 2·38 | 227·0 | 0·00 | 2·99 | 27·64 | 0·00 | 0·83 |
| Overweight | 6·84 | 233·8 | 0·00 | 2·38 | 27·89 | 0·00 | 0·67 |
| Smoking | 4·24 | 197·8 | 0·00 | 0·28 | 24·98 | 0·00 | 0·07 |
| Inactive & overweight | 4·40 | 226·5 | 0·00 | 1·40 | 23·96 | 0·00 | 0·33 |
| Smoking & inactive | 1·28 | 152·2 | 0·00 | 0·08 | 19·99 | 0·00 | 0·02 |
| Smoking & overweight | 4·89 | 243·2 | 0·00 | 0·44 | 27·48 | 0·00 | 0·12 |
| Smoking, inactive & overweight | 2·36 | 228·9 | 0·00 | 0·33 | 25·01 | 0·00 | 0·08 |
| Average | | 227·7 | 1·5 | 1·9 | 24·8† | 0·4 | 0·5 |

*Total weighted *n* is 77 129 836 (~82 % of US females in the National Health and Nutrition Examination Survey 1999–2002).
†Based on weighted individual estimates.

provide some explanation for the lack of findings of an association between dietary cholesterol and CHD[20]. Epidemiological studies also show a very limited effect of cholesterol intake on plasma lipoprotein, while PUFA and SFA intakes are found to closely relate to plasma lipoprotein concentrations[1].

In the NHS, an association between dietary cholesterol and CHD risk was observed, but the relationship was not statistically significant ($P$ for trend = 0·24). Nevertheless, assuming that the observed relationship was true and applying the RR associated with dietary cholesterol from the NHS to US females aged 25 years or older, the CHD risk share of current dietary cholesterol is 1·5 % (upper-bound estimate: 1·9 %), as compared with the 2·5 % share from current intake of t*rans* fat (as a percentage of total energy) and the 16 % share from current deficiency in heart-healthy nutrients such as marine *n*-3 FA, PUFA, ALA, dietary fibre, vitamins $B_6$ and C, and folate. These results suggest that while reducing *trans* fat and cholesterol intake could lead to CHD risk reduction, a greater reduction of CHD risk may be achieved with improving intakes of currently deficient heart-healthy nutrients. Thus, consideration of total diet is essential in evaluating CHD risk reduction strategies.

Egg foods contributed between 20 % and 28 % of the total dietary cholesterol, corresponding to 0·4–0·5 % of CHD risk among US females (0·8 % in females with poor diet). It should be noted that published studies do not find any association between CHD and egg consumption[3]. The public health significance of egg consumption should be examined in the context of its benefits, since one single, large egg supplies 12 % of the daily value for protein and other nutrients, including vitamins A, $B_6$, $B_{12}$, D, folate, Fe, P and Zn. Beneficial effects have also been attributed to functional contents in egg yolk, i.e. choline, lutein and zeaxanthin.

The present study did not model CHD risk shares attributed to dietary factors for US adult males because data from the HPFS did not show any statistically significant association between specific dietary factors and CHD risk, with the exception of dietary and cereal fibres, Fe and alcohol consumption. The data for males from the HPFS are summarized in the Appendix.

There are several key limitations with the findings from the present study. A major consideration concerning the risk apportionment model is the selection of risk factors and estimated RR. Different risk shares may have been derived if dietary factors other than the ten considered were included or if RR from other cohorts were used, e.g. populations with different education levels or without the health knowledge of NHS participants. The associations between CHD and glycaemic load score and vegetable oil intake were statistically significant in the NHS but were not incorporated in the present study. Vegetable oil intakes were not extractable from the NHANES data and the lack of a consistent method to replicate the glycaemic load score were reasons for their exclusion. Both α- and β-carotene were found to be associated with CHD in the NHS; however, because of the controversy about potential cancer effects, they were not incorporated in the model. Further, since SFA was not included in the model (not shown to be associated with CHD in the NHS), the risk shares of the ten diet factors studied could have been overestimated. If RR for SFA were >1 and incorporated, the CHD risk shares for the ten factors included here would be lowered.

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Moreover, the RR estimates from the NHS were based on consumption data collected using an FFQ. Random and systematic errors are present in FFQ-derived intake estimates, with random error resulting in an attenuation of the RR estimates and systematic error (from under- or over-reporting by consumers) leading to overestimation of the RR. The effect of random variation is typically larger than that of systematic error; however, when multiple factors are included the estimated effect could be biased in either direction[21].

In conclusion, while the NHS was considered the best option for the risk apportionment model because it is a large study with long-follow-up periods and carefully collected information, and the RR estimates were multivariate-adjusted, application of the NHS data in a risk apportionment model is not without limitations. Interpretation of findings from the present study should be made in the context of the underlying data and over-interpretation should be avoided.

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## Appendix

### *Estimated relative risks for dietary factors from the Nurses' Health Study and the Health Professionals' Follow-up Study*

Estimated relative risks (RR) for the dietary risk factors (cholesterol, SFA, etc.) were derived from the Nurses' Health Study (NHS). The following publications were found and reviewed: three publications examined the impact of 'total' diet on CHD risk, four evaluated the impact of 'whole foods' on CHD risk, and twelve assessed the impact of specific macro/micronutrients, fats, cholesterol, etc. on CHD risk. Specifically, Hu *et al.*[1] and Fung *et al.*[2] showed that the 'prudent' diet was associated with a lower CHD risk. Stampfer *et al.*[3] used a diet score to assess diet quality and found that a high diet score was associated with lower CHD risk. Of the four publications that examined the association between 'whole foods' and CHD risk using data from the NHS, two studies[4,5] found no association between coffee or egg consumption and CHD. The other two studies found an inverse association between CHD and intake of fruits and vegetables, green leafy vegetables, vitamin-C-rich fruits and vegetables, and nuts[6,7]. A large number of studies[8–27] examined the association between several macro- and micronutrients, fats, cholesterol intakes and CHD risk. The estimated RR and the quintiles of intakes for most of these studies are summarized in Table A1.

The present study did not model the share of CHD risk attributed to dietary cholesterol and other dietary risk factors for US adult males because data from the Health Professionals' Follow-up Study (HPFS) did not show any statistically significant association between specific dietary factors and CHD risk, with the exception of dietary and cereal fibres, Fe and alcohol consumption (Table A2). Among the males in the HPFS, a slight increase in CHD risk in the upper (5th) quintile of *trans* fat intake was observed; however, the relationship is not statistically

**Table A1** Specific dietary risk factors and relative risks (RR) from the Nurses' Health Study

| | Quintile of intake | | | | | | |
|---|---|---|---|---|---|---|---|
| Dietary factor | 1 | 2 | 3 | 4 | 5 | *P* | Reference (outcome) |
| α-Linolenic acid (g/d) | 0·71 | 0·86 | 0·98 | 1·12 | 1·36 | 0·5 | Hu *et al.* (1999)[5] |
| RR | 1·18 | 1·08 | 1·11 | 1·20 | 1·00 | | (IHD, not CHD, non fatal) |
| SFA 12 : 0 to 18 : 0 (% of energy) | 9·5 | 11·4 | 12·8 | 14·5 | 17·2 | 0·47 | Hu *et al.* (1999)[5] |
| RR | 1·00 | 0·82 | 0·87 | 1·05 | 1·04 | | (IHD, not CHD, non fatal) |
| Marine *n*-3 fatty acids (g/d) | 0·03 | 0·05 | 0·08 | 0·14 | 0·24 | <0·01* | Hu *et al.* (2002)[12] |
| RR | 1·45 | 1·35 | 1·14 | 1·00 | 1·00 | | (fatal + non fatal CHD) |
| Vegetable fat (% of energy) | 5·4 | 8·8 | 11·2 | 13·5 | 17·2 | 0·009* | Hu *et al.* (1997)[8] |
| RR | 1·00 | 0·82 | 0·96 | 0·82 | 0·67 | | (fatal + non fatal CHD) |
| Cholesterol (mg/d) | 132 | 163 | 188 | 217 | 273 | 0·24 | Hu *et al.* (1997)[8] |
| RR | 1·00 | 1·15 | 1·08 | 1·24 | 1·17 | | (fatal + non fatal CHD) |
| *Trans* fat (% of energy) | 1·3 | 1·6 | 1·9 | 2·2 | 2·8 | 0·01* | Oh *et al.* (2005)[13] |
| RR | 1·00 | 1·08 | 1·29 | 1·19 | 1·33 | | (fatal + non fatal CHD) |
| PUFA (% of energy) | 4·1 | 5·0 | 5·6 | 6·3 | 7·4 | 0·004* | Oh *et al.* (2005)[13] |
| RR | 1·33 | 1·31 | 1·11 | 1·12 | 1·00 | | (fatal + non fatal CHD) |
| MUFA (% of energy) | 10·6 | 12·5 | 13·8 | 15·3 | 18·0 | 0·19 | Oh *et al*· (2005)[13] |
| RR | 1·22 | 1·15 | 1·16 | 1·11 | 1·00 | | (fatal + non fatal CHD) |
| SFA (% of energy) | 10·1 | 11·9 | 13·3 | 14·8 | 17·6 | 0·93 | Oh *et al.* (2005)[13] |
| RR | 1·00 | 0·94 | 0·96 | 1·01 | 0·97 | | (fatal + non fatal CHD) |
| Total fat (% of energy) | 28·3 | 32·6 | 35·6 | 38·7 | 44·0 | 0·49 | Oh *et al.* (2005)[13] |
| RR | 1·00 | 0·94 | 0·91 | 0·98 | 0·92 | | (fatal + non fatal CHD) |
| Vitamin C (mg/d) | 61 | 94 | 121 | 152 | 209 | 0·52 | Osganian *et al.* (2003)[14,15] |
| RR | 1·16 | 1·06 | 1·00 | 0·98 | 1·00 | | (fatal + non fatal CHD) |
| Lutein & zeaxanthin (μg/d) | 1194 | 2099 | 2897 | 3938 | 6316 | 0·42 | Osganian *et al.* (2003)[14,15] |
| RR | 1·11 | 1·00 | 0·90 | 0·87 | 1·00 | | (fatal + non fatal CHD) |
| β-Carotene (μg/d) | 1720 | 2633 | 3528 | 4843 | 7639 | 0·05* | Osganian *et al.* (2003)[14,15] |
| RR | 1·35 | 1·20 | 0·93 | 1·20 | 1·00 | | (fatal + non fatal CHD) |
| α-Carotene (μg/d) | 209 | 341 | 456 | 711 | 1518 | 0·04* | Osganian *et al.* (2003)[14,15] |
| RR | 1·25 | 1·16 | 1·14 | 1·00 | 1·00 | | (fatal + non fatal CHD) |
| Vitamin E (IU/d) | 2·6 | 3·6 | 4·4 | 5·4 | 7·7 | 0·99 | Stampfer *et al.* (1993)[17] |
| RR | 1·00 | 1·04 | 0·87 | 1·14 | 0·95 | | (fatal + non fatal + bypass) |
| Cereal fibre (g/d, energy-adjusted) | 2·2 | 3·1 | 3·8 | 4·9 | 7·7 | <0·01* | Wolk *et al.* (1999)[19] |
| RR | 1·52 | 1·61 | 1·08 | 1·15 | 1·00 | | (fatal + non fatal CHD) |
| Dietary fibre (g/d, energy-adjusted) | 11·5 | 14·3 | 16·4 | 18·8 | 22·9 | 0·07 | Wolk *et al.* (1999)[19] |
| RR | 1·30 | 1·27 | 1·19 | 1·13 | 1·00 | | (fatal + non fatal CHD) |
| Folate (μg/d) | 158 | 217 | 276 | 393 | 696 | 0·003* | Rimm *et al.* (1998)[16] |
| RR | 1·45 | 1·25 | 1·25 | 1·13 | 1·00 | | (fatal + non fatal CHD) |
| Vitamin $B_6$ (mg/d) | 1·1 | 1·3 | 1·7 | 2·7 | 4·4 | 0·002* | Rimm *et al.* (1998)[16] |
| RR | 1·49 | 1·37 | 1·28 | 1·31 | 1·00 | | (fatal + non fatal CHD) |
| Glycaemic load score (energy-adjusted) | 117 | 145 | 161 | 177 | 206 | <0·0001* | Liu *et al.* (2001)[27] |
| RR | 1·00 | 1·01 | 1·25 | 1·51 | 1·98 | | (fatal + non fatal CHD) |

*Statistically significant.

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**Table A2** Dietary risk factors and multivariate-adjusted relative risks (RR) from the Health Professionals' Follow-up Study, adult males

| | Quintile of intake | | | | | | |
|---|---|---|---|---|---|---|---|
| Dietary factor | 1 | 2 | 3 | 4 | 5 | *P* | Reference (outcome) |
| Marine *n*-3 fatty acids (g/d) | 0·07 | 0·15 | 0·24 | 0·34 | 0·58 | 0·48 | Ascherio *et al.* (1995)[20] |
| RR | 1·00 | 1·00 | 0·92 | 0·86 | 1·09 | | (fatal + non-fatal CHD) |
| Cholesterol (mg/d) | 189 | 246 | 290 | 338 | 422 | 0·48 | Ascherio *et al.* (1996)[21] |
| RR | 1·00 | 0·86 | 0·98 | 0·94 | 1·03 | | (fatal + non-fatal CHD) |
| *Trans* fat (g/d) | 1·5 | 2·2 | 2·7 | 3·3 | 4·3 | 0·2 | Ascherio *et al.* (1996)[21] |
| RR | 1·00 | 1·12 | 1·12 | 1·12 | 1·21 | | (fatal + non-fatal CHD) |
| SFA (g) | 17 | 21 | 24 | 27 | 33 | 0·69 | Ascherio *et al.* (1996)[21] |
| RR | 1·00 | 1·01 | 0·84 | 0·90 | 0·96 | | (fatal + non-fatal CHD) |
| Total fat (g/d) | 53 | 64 | 72 | 78 | 89 | 0·42 | Ascherio *et al.* (1996)[21] |
| RR | 1·00 | 1·00 | 1·05 | 1·07 | 1·02 | | (fatal + non-fatal CHD) |
| Linoleic acid (g/d) | 7·6 | 9·6 | 11 | 12·6 | 15·4 | 0·89 | Ascherio *et al.* (1996)[21] |
| RR | 1·00 | 1·21 | 1·12 | 1·10 | 1·04 | | (fatal + non-fatal CHD) |
| α-Linolenic acid (g/d) | 0·8 | 0·9 | 1·1 | 1·2 | 1·5 | 0·07 | Ascherio *et al.* (1996)[21] |
| RR | 1·00 | 1·00 | 0·97 | 0·98 | 0·8 | | (fatal + non-fatal CHD) |
| Fe (mg/d, energy-adjusted) | 11 | 13 | 15 | 18 | 37 | 0·02* | Ascherio *et al.* (1994)[22] |
| RR | 1·39 | 1·54 | 1·53 | 1·31 | 1·00 | | (fatal + non-fatal CHD) |
| Mg (mg/d) | 264 | 305 | 336 | 371 | 427 | 0·19 | Al-Delaimy *et al.* (2004)[23] |
| RR | 1·16 | 1·17 | 1·08 | 1·06 | 1·00 | | (fatal + non-fatal CHD) |
| Vitamin C (mg/d) | 92 | 149 | 218 | 392 | 1162 | 0·98 | Rimm *et al.* (1993)[24] |
| RR | 1·00 | 1·08 | 1·32 | 1·26 | 1·25 | | (fatal + non-fatal CHD + bypass) |
| Vitamin E (IU) | 4·3 | 7·6 | 8·8 | 10·2 | 11·1 | 0·11 | Rimm *et al.* (1993)[24] |
| RR | 1·27 | 1·39 | 1·61 | 1·23 | 1·00 | | (fatal + non-fatal CHD + bypass) |
| Cereal fibre (g/d, energy-adjusted) | 2·2 | 3·7 | 5·0 | 6·8 | 9·7 | 0·01* | Rimm *et al.* (1993)[24] |
| RR | 1·00 | 0·96 | 0·88 | 0·86 | 0·71 | | (fatal + non-fatal CHD + bypass) |
| Dietary fibre (g/d, energy-adjusted) | 12·4 | 16·6 | 19·6 | 23·0 | 28·9 | 0·004* | Rimm *et al.* (1993)[24] |
| RR | 1·56 | 1·58 | 1·50 | 1·44 | 1·00 | | (fatal + non-fatal CHD + bypass) |
| Alcohol (g/d) | 0 | 2·50 | 9·95 | 22·45 | 40·00 | 0·04* | Mukamal *et al.* (2003)[25]; Mukamal *et al.* (2006)[26] |
| RR | 1·00 | 0·92 | 0·52 | 0·32 | 0·70 | | (fatal + non-fatal CHD) |

*Statistically significant.

significant (*P* for trend = 0·2). Non-statistically significant inverse associations between intakes of α-linolenic acid, Mg and vitamin E and CHD were also observed. In particular, no association between CHD and any of the quintiles of dietary cholesterol, total fat, SFA and marine *n*-3 fatty acids was found among the HPFS subjects. The multivariate-adjusted RR estimates were approximately unity even at the highest (5th) quintile of intake (Table A2). Incorporating dietary factors with RR of 1 into the apportionment model would apportion 0% share of the CHD risk for these factors. Based on these results, it would appear that diet and dietary fats do not seem to have a significant impact on CHD risk in adult males.

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