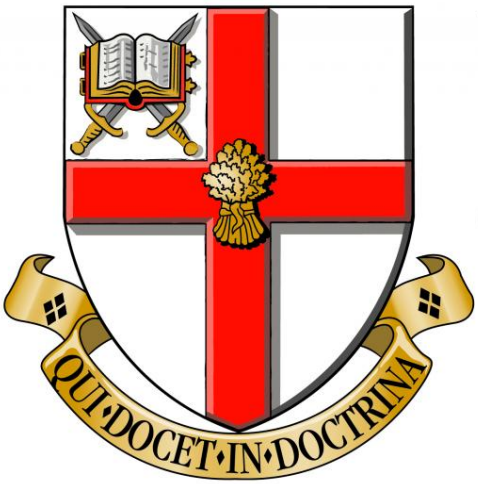

University of Chester

Department of Clinical Sciences & Nutrition

MSc in Cardiovascular Rehabilitation

Module Title: Research project

Module Code: XN7415

Module Tutor: Dr Stephen Fallows

James Carlsson

Assessment number: J10309

Submission date: 30th September 2015

This work is original and has not been submitted previously in support of a degree qualification or other course.

Signed:

Date:

Contents

List of Figures and Tables

List of Appendices

List of Abbreviations

CVD – Cardiovascular disease

CHD – Coronary heart disease

UK – United Kingdom

NI – Northern Ireland

CHO – Carbohydrate

SFA – Saturated fat

TF – Total fat

%TE – Percentage of total energy intake

MI – Myocardial infarction

WHO – World Health Organisation

MONICA- Multinational Monitoring of Trends and Determinants in Cardiovascular Disease

COMA- Committee on Medical Aspects of Food Policy

ONS- Office for national statistics

HSE – Health survey for England

SHS – Scottish Health Survey

DEFRA - Department for Environment, Food and Rural Affairs

DOH – Department of health

NICE – National Institute for Health and Care Excellence

ICD – International Statistical Classification of Diseases and Related Health Problems

LCFS - Living Costs and Food Survey

EFS - Family Expenditure Survey

NFS – National Food Survey

NDNS – National Diet and Nutrition Survey

UK Dietary Guidelines For The Prevention Of Cardiovascular Disease.

Literature Review of available evidence and if it supports current dietary guidelines to reduce Total and Saturated Fat.

Abstract

This paper looks at the history of current United Kingdom dietary guidelines for the prevention of heart disease and evaluates available evidence to support the relationship between saturated fat and coronary heart disease and recommendations to replace energy from a reduction in saturated and total fat intake with carbohydrate.

Results show a lack of support for a reduced fat diet with replacement of energy with carbohydrate. The relationship between saturated fat, total fat and heart disease is inconsistent across studies with evidence pertaining to the UK weak. Further investigation into the relationship is recommended.

Introduction

Cardiovascular disease (CVD) the collective term for diseases of the heart and blood vessels was responsible for 161,252 deaths in the United Kingdom (UK) in 2012 (Townsend, Williams, Bhatnagar, Wickramasinghe, & Rayner, 2014). CVD mortality has been declining and for the first time since 1961 is no longer the overall leading cause of death in the UK (Townsend, Williams, Bhatnagar, Wickramasinghe, & Rayner, 2014).

Coronary heart disease (CHD) accounts for 48% of CVD deaths and remains the largest single cause of death accounting for 73,680 deaths in the UK in 2012 (Townsend, Williams, Bhatnagar, Wickramasinghe, & Rayner, 2014). CHD presents as myocardial infarction (MI), angina, silent ischemia, unstable angina, arrhythmias, heart failure and sudden death, with the most common cause a build-up of atheroma leading to narrowing of vessels and occlusions (Grech, 2003). The estimated cost of CVD to the UK economy was an estimated €18.9 billion in 2014 (Centre for Economics and Business Research, 2014).

Smoking, diabetes, hyperlipidaemia and hypertension are known conventional risk factors (Khot, et al., 2003). In addition to conventional risk factors the INTERHEART study identified abdominal obesity, psychosocial stress, fruit and vegetable intake, physical activity and alcohol consumption, with the nine factors accounting for 90% of CHD risk (Yusef, et al., 2004).

In recent years a number of reviews and meta-analysis have called into question the relationship between Saturated fat (SFA) and CVD (Chowdhury, et al., 2014) (Ramsden, et al., 2013) (Siri-Tarini, Sun, Hu, & Krauss, 2010). It has been suggested by Harcombe et al (2015) that prior to UK dietary guidelines becoming policy evidence from RCTs was lacking, with the authors suggesting dietary guidelines should never have been introduced. The aim of this review is to look at the history of the guidelines and the available evidence to support current UK dietary recommendations with a focus on CHD.

History of Dietary Guidelines in the UK

The first Committee on Medical Aspects of Food Policy (COMA) panel on diet and heart disease was formed in 1970 in response to the 1969 meeting called to discuss the findings of Strom & Jensen (1951) on the effect of diet on CHD (Morgan, 2012) (Bufton M. , 2005) .

The panel took three years and ten drafts to produce their report having considered over 400 papers (DHSS, 1974). The report's recommendations listed in Table 1 were basic with advice to reduce intake of sugar and fat, particularly saturated fat. The basic advice was a result of the panel unable to reach a consensus, expressed by Professor John Yudkin, stating that the report had exaggerated the possible role of dietary fat in causing CHD and had minimised the possible role of dietary sucrose. Due to the lack of consensus the recommendations were not made policy (Bufton M. , 2001).

In 1984 the second COMA report was published having considered over 600 scientific papers and 40 working papers however consensus again was not reached (DHSS, 1984). The objecting member Professor Mitchell strongly disagreed with the assertion that there was a causal link between SFA and risk of heart disease (Bufton & Berridge, 2000). Despite lack of consensus the guidelines, listed in Table 1 issued quantitative dietary recommendations.

It was suggested by the Vice chairman of the National Advisory Committee on Nutrition Education (NACNE) that the 1984 COMA report was created to provide a mechanism for Government to distance themselves from the NACNE 1983 quasi-

official policy proposals, suggesting COMA felt under pressure to produce a report that would be acceptable to Government (Bufton & Berridge, 2000).

The most recent COMA report on diet and heart disease was published in 1994 with no reported dissenters on the panel (DOH, 1994). In 2000 COMA was disbanded and replaced by the Scientific Advisory Committee on Nutrition (SACN) (DOH, 2012). Current dietary guidelines listed in Table 1 are based on the 1994 COMA report.

Table 1: Summary of Dietary Guidelines

	1974 (DHSS, 1974)	**1984 (DHSS, 1984)**	**1994 (DOH, 1994)**
Total Fat	Reduce Intake	35%	35%
Saturated Fat	Reduce intake	15%	No more than 10%
n-6 Polyunsaturated	No increase	No specific recommendation	No increase in average intakes with those consuming >10% TE no further increase.
n-3 polyunsaturated	No increase	No specific recommendation	Increase to 0.2g / day
Monounsaturated Fat	No recommendation	No specific recommendation	No specific recommendation as evidence for LDL reduction is inconsistent
Trans fatty acids	No recommendation	Treated same as SFA but no specific recommendations.	No more than 2% with consideration to reduce intake
Sugar	Reduce intake	No increased intake	No specific advice but COMA Panel on DRV recommended no more than 10% energy from non-milk extrinsic sugars.
Carbohydrates	No recommendation	Panel sees advantage in replacing calories from reduced fat with fibre rich CHO but no specific recommendation.	Complex CHO and sugars in fruits and vegetables should restore energy deficit from reduction in fat. Recommended increase to approx. 50%

Evidence Base for Dietary Guidelines

None of the published COMA reports contain references of the papers considered in the creation of their respective guidelines thus it is not possible to critique the exact literature used. No working papers were found.

Review of the literature

Intervention Trials

Primary Prevention

The non-randomised Finnish Mental Hospital study was the only exclusively primary prevention trial found. The study reported a significantly lower CHD mortality in the experimental modified fat diet in men but not women (Turpeinen, et al., 1979) (Meittinen, et al., 1983). The disproportionate use of the cardio-toxic drug thioridazine in one of the study arms (Ramsden, Hibbeln, Majchrzak, & Davis, 2010) and the inappropriate crossover study design to test CHD, a progressive disease, may have confounded results.

Two Randomised control trials (RCT) tested a fat modified diet using oil filled products to increase PUFA consumption while decreasing SFA intake contained subjects with or without existing CHD (Dayton, Pearce, Hashimoto, Dixon, & Tomiyasu, 1969), (Frantz, et al., 1989).

In the double blinded Minnesota Coronary Survey no significant differences in primary endpoints of CVD mortality or events in either men or women were reported (Frantz, et al., 1989). Similarly the partially blinded male only LA Veterans trial found no significant difference between experimental and control groups in either the CHD

events of sudden death or MI were found. There was however a significant difference when results were pooled with secondary CVD event endpoints (Dayton, Pearce, Hashimoto, Dixon, & Tomiyasu, 1969).

All trials lowered total serum cholesterol levels (TC) in the treatment arms. However there was no effect on total mortality in the Finnish hospital study or LA Veterans trial, which reported higher all-cause mortality in the experimental group. In both of these studies adherence was poor with only half of meals available consumed onsite in the LA Veterans trial. Food eaten off site was considered but not analysed in the same manner. In the Finnish Mental Hospital study only 33% of women and 53% of men were present for the entire study period with meals eaten outside the hospital not accounted for.

No primary prevention trials were found to have tested a reduced fat diet. A summary of the all studies included this review can be found in the appendix.

Secondary Prevention Trials

Four RCTs and one non randomised trial were found which focused on fat modification and one RCT on fat reduction. All studies were of men and not women. Three studies identified were UK based (Rose, Thomson, & Williams, 1965) (Ball, et al., 1965) (MRC, 1968).

The Oslo diet-heart study reported a positive association between CHD and lowering SFA, however only CHD relapses and nonfatal MIs were reduced, there was no difference in overall CHD mortality after eleven years of follow up (Leren, 1970). While

this was the longest running study at 11 years no dietary analysis was completed after five years.

The non-randomised study on young males aged 30-50 (Bierendaum, et al., 1970) reported a lower rate of reinfarctions in the experimental group however the study had many design issues. After one year due to a lack of difference between experimental groups the researchers assumed a lack of compliance so issued frozen meals, however after another six months no difference remained so a control group was added and the two diet groups merged. The control group contained more heavy smokers and more heavy drinkers than the experimental group. In the experimental group the overweight men were put on a calorie control diet, however those in the control were not. The study is the only one to test only younger men when the incidence rate of CHD is lower than older men and given the small sample size significant findings were unlikely.

Reanalysis of data from Woodhill and colleagues Sydney Diet Heart study data reported higher incidence of CHD and CVD mortality in the intervention than control (Woodhill, Palmer, Leelarthaepin, McGilchrist, & Blacket, 1978) (Ramsden, et al., 2013), likewise the corn oil trial found more of the control group remained free of cardiac events than either intervention (Rose, Thomson, & Williams, 1965).

A single trial was identified to have tested the effect of fat reduction and reported no significant difference in coronary relapses or deaths (Ball, et al., 1965) . Like Bierenbaum et al the overweight were put on a weight loss diet with 21% of the control group and 15% of the intervention on a reduced calorie intake. This may have

confounded the results with any effect possibly attributable to weight loss rather than diet.

All studies reported lowered TC in the intervention group however the Corn oil study despite a significant reduction in the first 18 months reported a non-significant change from baseline at study end. The Oslo trial found while TC was higher in those who relapsed with only a difference in groups in men under 60 (Leren, 1970). The MRC Soya trial reported relapses were not related to initial cholesterol level (MRC, 1968).

In all studies total mortality was not reduced in the intervention groups with both the low fat and Sydney trial reporting higher all-cause mortality in intervention groups than control (Ball, et al., 1965) (Ramsden, et al., 2013).

The efficacy of secondary prevention trials to test the effect of TF and SFA on CHD has been questioned with men having suffered an MI likely to make multiple lifestyle changes which may confound findings (Woodhill, Palmer, Leelarthaepin, McGilchrist, & Blacket, 1978).

Observational Studies

Twenty two observational studies were found which included clear data on SFA intake and CHD of which four were of UK participants (Fehily, Yarnell, Sweetnam, & Elwood, 1993), (Mann, Appleby, Key, & Thorogood, 1997), (Boniface & Tefft, 2002), (Morris, Marr, & Clayton, 1977).

Two studies reported a clear positive association between SFA and CHD**,** Mann, Appleby, Key, & Thorogood (1997) reported a positive relationship between saturated animal fat and CHD mortality (P<0.01) in health conscious individuals**.** Kromhout et al

(1995) reported a significant (*P*<0.001) association between SFA with 25 year CHD mortality rate in sixteen cohorts of the Seven Countries study. Although two of the rural Italian cohorts included were analysed by Farchi et al (1989) who reported a significant inverse relationship between SFA and CHD (*P*<0.01).

The Seven Countries study, a 10 year investigation led by Ancel Keys of men aged 40-59 from sixteen cohorts researched CHD in six western countries and Japan. No rationale was given for the countries selected apart from opportunity and practicality with friendships and personal contacts influencing cohort locations (Keys A. , 1980). Keys found median TC strongly related to CHD mortality (r=0.80) but not all cause mortality, with low TC correlated with non CHD deaths. In men without CVD at entry total fat intake (r=0.50) and SFA intake (r=0.84) was correlated with CHD mortality, although intakes varied largely between cohorts**.**

The study had a number of limitations, the American Railroad cohort, the studies largest, failed to reach follow up due to funding issues and the Rome railroad men's final examinations were incomplete which may have affected results.

The lowest CHD mortality reported in Crete and attributed to their dietary habits did not take into account the Greek Orthodox church practice of regular fasting with 60% of the cohort following all fasting periods of the church (Cannon, 2004), (Katerina & Kafatos, 2005).

Ten studies reported no relationship between SFA and CHD (Shekelle, et al., 1981) (Fehily, Yarnell, Sweetnam, & Elwood, 1993), (Pietinen, et al., 1997) (Leosdottir, Nilsson, Nilsson, & Berglund, 2007) (Knekt, et al., 1994) (Kromhout & De Coulander,

1984) (Garcia-Palmieri, et al., 1980) (Morris, Marr, & Clayton, 1977) (Tucker, et al., 2005) (Farchi, et al., 1989).

McGee et al reported a significant association ($P<0.05$) with relative (%TE) SFA intake and CHD but not absolute intake (g) (McGee, Reed, Yano, Kagan, & Tillotson, 1984) , similarly Posner et al found no association overall but when adjusted for energy intake %TE SFA in men aged 45-56 was significantly ($P<0.050$) related (Posner, et al., 1991).

Two of seven studies which included both men and women reported positive associations in women but not men (Jakobsen, Overvad, Dyerberg, Schroll, & Heitmann, 2004) (Boniface & Tefft, 2002), with the latter reporting a significant relationship in only women aged 60-75 ($P<0.01$). CVD in females is known to develop seven to ten years later than in men which may have affected results (Maas & Appelman, 2010). Significant findings in two other studies were affected by age, regardless of gender, Esrey, Joseph, & Grover (1996) only reported a positive association in those aged 30-59 ($P<0.01$) and Xu et al (2006) only in those aged 47-59.

Multivariate analysis removed significance from three studies reporting a positive trend between SFA with CHD (Oh, Hu, Manson, Stampfer, & Willett, 2005) (Ascherio, et al., 1996) (Yamagishi, et al., 2010). Conversely Kushi et al found %TE SFA to be associated with twenty year CHD mortality ($P<0.005$) only after multivariate analysis, despite a non-significant 0.5% difference in SFA %TE intake between men who died of CHD or those without CHD (Kushi, et al., 1985).

Tucker et al (2005) found a low intake of SFA was not protective of CHD incidence ($P<0.005$) although each gram of SFA was related to a 7% increased risk of death from

CHD (P<0.001), however SFA intake was grouped with low fruit and vegetable which may have confounded results.

Dietary Reporting

Studies varied in reporting methods with dietary intake being split into subgroups, either by SFA intake or via disease status in the majority with a few such as the Shekelle et al (1981) only reporting the cohorts mean diet.

Dietary SFA intake reported as relative %TE rather than absolute g/day in the Honolulu and Framingham Study affected whether the association with CHD was significant or not (McGee, Reed, Yano, Kagan, & Tillotson, 1984) (Posner, et al., 1991). Posing the question of whether the absolute or relative contribution of SFA or TF that has the greater impact. If SFA were to have a linear dose response, then a greater absolute intake would have a greater impact on disease risk than the relative intake which is influenced by either total energy intake or other dietary macronutrients, unless the influence of SFA intake is interrelated and mitigated by other dietary factors suggested by the fruit and vegetable or fibre intake in the Baltimore study (Tucker, et al., 2005).

Intake of SFA varied across cohorts from 9.2g in Japan (Yamagishi et al 2010) to 78g in Finland (Knekt et al 1994), with the latter reporting no association between SFA and CHD. The high intakes of SFA reported by Knekt et al stand as an outlier with men free from CHD after a 14 year follow up consuming 73g SFA compared to the 78g consumed by men who died of CHD. This may be explained by geographical differences, a non-linear effect of SFA or an unidentified confounder.

Five of twenty two observational studies identified reported a lower energy intake in those with CHD with Boniface & Tefft (2002) suggesting total energy may cause a non-random error. In addition to Boniface & Tefft (2002) lower energy intakes in those with CHD were also reported in the Ireland-Boston Diet-Heart trial (Kushi, et al., 1985), Caerphilly (Fehily, Yarnell, Sweetnam, & Elwood, 1993), Lipid Research Clinics (Esrey, Joseph, & Grover, 1996) and Zutphen studies (Kromhout & De Coulander, 1984).

Methods of recording dietary intake used in the cohort studies raise questions of how well a 24 hour recall , food frequency questionnaire (FFQ) or 7 day diary represents not only the habits of the previous year but also an individual's long term intake when in certain studies up to and over twenty years pass between dietary assessment and study end.

While simple to administer in large scale studies the FFQ has been shown to underreport energy intake and is a poor predictor of both relative and absolute macronutrient intakes (Paul, Rhodes, Kramer, Baer, & Rumpler, 2005). It has also been suggested that the use of FFQ may mask associations, in a pooled analysis of cohort studies a significant relationship between breast cancer and dietary SFA was reported in a seven day food diary intake but not a FFQ (Bingham, et al., 2003). Ten studies of the twenty two were based on a FFQ, three of which validated intake either by interview (Shekelle, et al., 1981), seven day food diary (Leosdottir, Nilsson, Nilsson, & Berglund, 2007) or weighed food diary (Fehily, Yarnell, Sweetnam, & Elwood, 1993).

Five studies assessed diet using a twenty four hour recall (McGee, Reed, Yano, Kagan, & Tillotson, 1984), (Posner, et al., 1991), (Esrey, Joseph, & Grover, 1996), (Xu, et al.,

2006), (Garcia-Palmieri, et al., 1980). Twenty four hour recall has shown similar validity to FFQ with the 7 day diary closest to a weighed dietary record (Bingham, et al., 1997). While it is possible the use of FFQ and twenty four hour recall may have masked findings only four studies using FFQ and one using 24hr recall reported no association between SFA and CHD (Shekelle, et al., 1981) (Fehily, Yarnell, Sweetnam, & Elwood, 1993) (Ascherio, et al., 1996) (Pietinen, et al., 1997) (Garcia-Palmieri, et al., 1980). The lack influence of dietary assessment method and its impact on findings is further questioned by two of four studies using weighed dietary intakes reporting no association between SFA and CHD (Fehily, Yarnell, Sweetnam, & Elwood, 1993) (Morris, Marr, & Clayton, 1977) with Jakobsen, Overvad, Dyerberg, Schroll, & Heitmann (2004) only reporting an association in women.

Only five of twenty two observational studies identified followed up on dietary intake. Shekelle, et al (1981) followed up after one year during a twenty year observation period whereas Oh, Hu, Manson, Stampfer, & Willett (2005) assessed diet five times in the same period. Tucker, et al (2005) followed up diet four times in eighteen years and Knekt, et al (1994) twice in fourteen years. In the Seven Countries study repeated dietary surveys were completed but in only seven of sixteen cohorts (Kromhout, et al., 1995).

Geographical Differences

A study of Japanese living in Hawaii, America and Japan found TC to be higher in America compared to those in Japan despite eating equivalent diets suggesting another factor other than dietary fat. Japanese-Americans who retained a traditional way of life had CHD prevalence as low as observed in Japan suggesting cultural rather

than dietary differences. Those who adopted an American way of life but maintained a traditional Japanese diet had a higher prevalence of CHD than those who had retained traditional culture but adopted an American high fat diet (Marmot & Syme, 1976).

The findings of Marmot & Syme may explain the geographical differences in the study of Irish men, with the men living in Ireland suffering a lower CHD mortality rate than those in Boston, USA despite consuming more SFA as %TE (Kushi et al, 1985).

Reviews and Meta-Analysis

Seven review papers found looked at evidence of dietary fat on CHD, one addressed SFA specifically (Siri-Tarini, Sun, Hu, & Krauss, 2010). Summary of Review findings, inclusion criteria and included papers are listed in the appendix.

Siri-Tarini et al concluded no significant evidence for supporting the association between SFA and risk of CHD in observational studies (Siri-Tarini, Sun, Hu, & Krauss, 2010), although the papers statistical analysis and methodology have been questioned (Stamler, 2010) (Scarborough, Rayner, van Dis, & Norum, 2010) (Katan & Brouwer, 2010).

Similarly Chowdhury et al (2014) who concluded current evidence does not support advice to lower SFA intake and increase PUFA intake received similar criticism (Willett, Stampfer, & Sacks, 2014). The findings of Chowdhury et al are supported by Ramsden et al (2013).

Conversely Mozaffarian et al reported an overall risk reduction of 19% corresponding to 10% reduction in CHD risk per 5% energy replacement of SFA with PUFA (Mozaffarian, Micha, & Wallace, 2010). Study duration was a significant (P<0.017) factor in risk reduction with longer studies showing greater benefits.

The World Health Organisation (WHO) expert consultation report on fats and fatty acids in Human Nutrition (FAO, 2010) was based on the review by Jakobsen et al (2009) and meta-analysis by Skeaff and Miller (2009). Jakobsen et al concluded reducing and replacing SFA with PUFA prevents CHD while Skeaff and Miller concluded available evidence was unsatisfactory.

The Cochrane review on Reduced or modified dietary fat for preventing CVD reported a 14% reduced risk of combined CVD events in any type of dietary fat intervention compared to a control diet (P<0.007) (Hooper, et al., 2012). However the relationship to specific CVD events e.g. MI was not significant. When studies with systematic differences in care between intervention and control groups were removed along with studies with multiple dietary interventions other than just dietary fat then the risk reduction was no longer statistically significant. Differences between subgroups were also non-significant with no difference between modified, reduced or modified and reduced fat trials, all of which individually had no significant relationship with CVD events. Subgrouping results showed combined risk reduction was attributable to modified fat and modified reduced fat studies of at least two years and only in men with a moderate to high risk at baseline, not general population groups. There was no relationship of dietary fat with either total or CVD mortality.

Serum Cholesterol and CHD

The current guidelines recommend a reduction of SFA intake based on the association between SFA and both TC and low density lipoprotein (LDL) cholesterol levels (DOH, 1994). European guidelines suggest a target TC level <5mmol/L and LDL <3mmol/L in

healthy adults (Perk, et al., 2012). There is no official UK target for cholesterol levels (NICE, 2014).

Metabolic ward studies have demonstrated dietary SFA increases serum cholesterol levels (Keys, Anderson, & Grande, 1957) (Hegsted, McGandy, Myers, & Stare, 1965) however SFA intake also increases HDL levels so the HDL to TC ratio remains unaltered (Siri-Tarino P. W., Sun, Hu, & Krauss, 2010).

A number of studies discussed below challenge the association between TC, LDL and CHD as well as the desirability of achieving a low TC level. The World Health Organisation (WHO) Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) set up in to investigate and explain the decline in CHD mortality seen in the 1960's (Kuulasmaa, et al., 2000) failed to report a significant effect of cholesterol on CVD mortality (WHO, 1994).

Results from two studies on CHD hospitalisations observed raised cholesterol in only the minority of cases. Canto et al (2011) reported only 28% of patients hospitalised between 1994 and 2006 with their first MI presented with dyslipidaemia while Sachdeva et al (2009) reported an average admission TC level of 174.4mg/dl (4.5mmol/L), with 56.4% of patients LDL levels < 100mg/dl. (2.6mmol/L). In those without prior CHD or diabetes 72.1% had admission LDL <130 mg/dL (3.4mmol/L) and 41.5% <100 mg/dL (2.6mmol/l). However the authors note lipid levels post MI may not be representative of baseline due to the acute phase response (Sachdeva, et al., 2009).

Observational studies have also questioned the orthodoxy of the cholesterol CHD relationship. The 30 year follow up of the Framingham study found an inverse

relationship between cholesterol levels and an increased risk of CHD and total mortality. For every 1mg drop in cholesterol levels there was an 11% increase in coronary and total mortality (Anderson, Castelli, & Levy, 1987). Castelli noted those with higher SFA and energy intakes had lower TC levels (Castelli, 1992).

The Honolulu Heart Program of 3572 Japanese-American men aged 71-93 years found only a significant relationship with mortality in those who had low serum cholesterol levels at entry and exit (Schatz et al., 2001). Similar findings were reported by Nago et al (2011) noting a clear relationship in Japanese men and women between low TC and increased mortality, with the highest CHD mortality incidence in men with a TC below 4.4mmol/L (Nago, Ishikawa, Goto, & Kayaba, 2011).

In Danish men and women significantly lower all-cause mortality was reported in those with TC levels 5-7.99mmol/L compared to those with TC below 5mmol/L (P<0.001). Participants aged over 50, free of diabetes, CVD and statin use at baseline reported higher than recommended LDL levels (>2.5mmol/L) were similarly significantly protective. Increased Triglyceride levels were linked with increased risk of CHD, particularly in women suggesting guidelines should focus on triglyceride levers rather than lipid levels (Bathum et al., 2013).

Results from a meta-analysis of 61 prospective studies covering 11.6 million person-years at risk in men and women aged 40-89 found a weak positive association between TC and CHD mortality in only those aged 40-69 (Prospective Studies Collaboration, 2007). The association however was significant in those aged 70-79 (P0.04) and 80-89 (P0.0005) contrasting with the findings of both Nago et al (2011) and Schatz et al

(2001). Such findings may be explained by the work of Petursson et al (2012) who suggest cholesterol may act differently as a risk factor for CHD than previously believed with the authors observing a u-shaped curve between TC and CVD in both men and women (Petursson, et al., 2012).

Carbohydrate and CHD

Current guidelines recommend the energy deficit from a reduced fat intake be made up with complex carbohydrate (CHO) and sugars in fruit and vegetables (DOH, 1994).

This advice may have unintended consequences, the 2000 United States (US) dietary guidelines committee noted their advice to increase CHO consumption had corresponded with increasing rates of obesity (Hite et al., 2010).

Only one RCT testing a low fat high CHO diet was identified, reporting no effect on CHD (Ball, et al., 1965). Kuipers et al (2011) suggest a shift in focus from reducing SFA to reducing CHO, particularly high glycaemic (GI) sources as it is shown that a high CHO diet can increase risk of cardiovascular disease (Kuipers et al 2011) with postprandial hyperglycaemia induced by high GI foods suggested to increase CVD risk through oxidative stress (Ludwig, 2002).

A study recording none fasting glucose levels found elevated blood glucose may be causally related to development of CHD (Benn et al., 2012). This is supported by Khaw et al who reported a significantly ($P<0.001$) increased risk of CHD with increased levels of Haemoglobin A1c (Hba1c), an indicator of average blood glucose concentration over the preceding months. In those without diabetes or history of CHD there was a relative

risk (*P*<0.002) of 1.4 for every 1% increase in HbA1c (Khaw, et al., 2004). Both studies findings were independent of diabetes status.

Studies of UK Dietary Guidelines

One RCT testing UK Dietary guidelines was identified, predicting the adherence to recommendations could reduce the risk of fatal CVD by 15% and nonfatal CVD by 30% (Reidlinger, et al., 2015). Those given advice to follow dietary guidelines reported a drop in all lipid levels compared to baseline, with a significant drop in TC and LDL compared to control. The study however had a number of issues; the studies twelve week duration with no CVD endpoints do not show the long term efficacy of the diet. Furthermore comparison with the studies control group is questionable with the group given dietary advice to follow a traditional British diet along with supplemental foods with no rationale for the traditional British diet advice given. Weight loss in the dietary guideline group (1.3KG) and with weight gain (0.6KG) in the control group along with an unequal gender spilt may have also confounded results.

Conclusion

From the evidence considered in this review it is clear there is no consistent link between SFA and CHD although it is clear in certain populations and demographics an association exists. The lack of a consistent association is not however evidence that no relationship exists. Harcombe et al (2015) noted that prior to UK dietary guidelines becoming policy in 1984 evidence from RCTs was lacking, this review supports that assertion.

Since the publication of 1994 guidelines no primary or secondary prevention RCTs on SFA and CHD were found to have been completed. Twelve of twenty two cohort studies identified in this review were completed or had findings published after 1994 with only two reporting a clear association, both with issues discussed in this paper (Mann, Appleby, Key, & Thorogood, 1997) (Kromhout, et al., 1995). No clinical trials of decreased SFA intake and CHD were identified, the 1984 COMA panel noted due to cost such a trial would unlikely to ever be completed (DHSS, 1984).

Limitations of dietary intervention trials may have confounded results. To test the effect of SFA requires the modulation of other nutrients for a diet to remain isocaloric, nutrients which may have an independent effect on CHD risk.

Considering geographical differences in SFA intake and CHD mortality the efficacy of basing UK dietary guidelines on evidence of other countries is questionable. Evidence from within the UK is not convincing. The three secondary prevention trials, all of men reported no significant benefit of fat modification (Rose, Thomson, & Williams, 1965) (MRC, 1968) or reduction (Ball, et al., 1965). No primary prevention control trials were identified to have been completed on UK populations. Similarly evidence from UK based cohort studies were not convincing with only Mann, Appleby, Key, & Thorogood (1997) reporting a clear positive association albeit in health conscious individuals. Boniface & Tefft, 2002 reported an association in women but not men which highlights the need for further investigation of SFA and females, furthermore it suggests that a one size fits all dietary guideline may not be adequate.

It is clear evidence to support the Uk dietary guidelines recommendation to replace energy from SFA with carbohydrates is lacking with only a single study identified to have tested a reduced fat and increased carbohydrate diet (Ball, et al., 1965). The study by Reidlinger et al (2015) is the first to specifically test UK dietary guidelines and a step forward in establisng their efificay however with no endpoints the long term effect has not been established. Furthermore relience on CHD risk factors such as serum lipid levels to calculate risk may be undermined by the evidence considered here which questions the association between cholesterol and CHD.

This review did not consider multiple intervention trials apart from Reidlinger et al (2015) due to inability to isolate the effect of a single nutrient, however it may be that overall diet and lifetyle has a greater effect than reduction of a single nutrient as nutrients are rarely eaten in isolation.

The long term effect of UK dietary guidelines in unknown there is a clear need for further investigation between CHD mortality and dietary trends, if SFA is a major dietary risk factor for CHD then have intakes changed in conjunction with declining CHD mortality and what effect if any have UK dietary guidelines influenced diet.

Word Count: 5228 words

References

Anderson, K., Castelli, W., & Levy, D. (1987). Cholesterol and Mortality 30 Years of Follow-up From The Framingham Study. *JAMA, 257*(16), 2176-2180.

Ascherio, A., Rimm, E., Giovannucci, E., Spiegelman, D., Meir, S., Willett, W., et al. (1996). Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States. *British Medical Journal, 313*(7049), 84-90.

Ball, K. P., Hanington, E., McAllen, P. M., Pilkington, T. R., Richards, J. M., Sharland, D. E., et al. (1965, Sep 11). Low-Fat Diet in Myocardial Infarction. *Lancet*(7411), 501-504.

Bathum, L., Depont, R., Christensen, L. E., Pedersen, P. L., Larsen, J., & Nexoe, J. (2013). Association of lipoprotien levels with mortality in subjects aged 50+ without previous diabeities or cardiovascular disease: A population-based register study. *Scandinavian Journal of Primary Health Care*(31), 172-180.

Benn, M., Tybjaerg-Hansen, A., McCarthy, M., Jensen, G., Grande, P., & Nordestgaard, B. (2012). Nonfasting Glucose, Ischemic Heart Disease,and myocardial infarction: a Mendelian randomisaztion study. *J Am Coll Cardiol, 59*(25), 2356-65.

Bierendaum, M., Fleischman, A., Green, D., Raichelson, R., Hayton, T., Watson, P., et al. (1970). The 5-Year Experience of Modified Fat Diets on Younger Men with Cornoary Heart Disease. *Circulation*(42), 943-952.

Bingham, S., Gill, C., Welch, A., Cassidy, A., Runswick, S., Oakes, S., et al. (1997). Validation of dietary assessment methods in the UK arm of EPIC using weighed records, and 24-hour urinary nitrogen and potassium and serum vitamin C and carotenoids as biomarkers. *International Journal of Epidemiology, 26*, S137-S151.

Bingham, S., Luben, R., Welch, A., Wareham, N., Khaw, K., Day, N., et al. (2003). Are imprecise methods obscuring a relation between fat and breast cancer? *Lancet, 362*(9379), 212-214.

Boniface, D., & Tefft, M. (2002). Dietary fats and 16-year coronary heart disease mortality in a cohort of men and women in Great Britain. *European Journal of Clinical Nutrition, 56*(8), 786-792.

Bufton, M. (2001, October). Coronary heat disease versus BSE: characterising official British expert advisory committees. *Science and Public Policy, 28*(5), 381-388.

Bufton, M. (2005). British Expert Advice on Diet and Heart Disease c.1945-2000. In V. Berridge, *Making Health Policy: Networks in Research and Policy After 1945* (First ed., pp. 125-148). Amsterdam: Rodopi Bv Editions.

Bufton, M., & Berridge, V. (2000). Post-war nutrition science and policy making in Britain c. 1945-1994: the case of diet and heart disease. In D. Smith, & J. Phillips (Eds.), *Food,*

Science, Policy and Regulation in the Twentieth Century: International and Comparative Perspectives (pp. 207-222). London: Routledge.

Cannon, G. (2004). Out of the Christmas Box. *Public Health Nutrition, 8*(7), 987-990.

Canto, J., Kiefe, C., Rogers, W., Peterson, E., Frederick, P., French, W., et al. (2011). Number of Coronary Heart Disease Risk Factors and Mortality in Patients WIth First Myocardial Infarction. *JAMA, 306*(19), 2120-2127.

Castelli, W. P. (1992). Concerning the Possibility of a Nut ... *Arch Intern Med, 152*, 1371-1372.

Centre for Economics and Business Research. (2014, August 28). *The Rising Cost of CVD.* Retrieved August 21, 2015, from Centre for Economics and Business Research: http://www.cebr.com/wp-content/uploads/2015/08/Short-Report-18.08.14.pdf

Chowdhury, R., Warnakula, S., Kunutsor, S., Crowe, F., Ward, H. A., Johnson, L., et al. (2014, March 18). Association of Dietary, Circulating, and Supplement Fatty Acids With Cornary Risk. *Annals of Internal Medicine, 160*(6), 398-406.

Dayton, S., Pearce, M. L., Hashimoto, S., Dixon, W. J., & Tomiyasu, U. (1969). A Controlled Clinical Trial of a Diet High in Unsaturated Fat in Preventing Complications of Atherosclerosis. *Circulation, 40*(SII), 1-63.

DHSS. (1974). *Diet And Coronary Heart Disease.* Department of Health and Social Security. London: Her Majesty's Stationary Office.

DHSS. (1984). *Diet And Cardiovascular Disease* (Vol. 28). London: Her Majesty's Stationery Office.

DOH. (1994). *Report on Health and Social Subjects 46 Nutritional Aspects of Cardiovascular Disease.* London: HMSO.

DOH. (2012, 05 06). *[ARCHIVED CONTENT] Committee on Medical Aspects of Food and Nutrition Policy (COMA) Department of Health - Archive*. Retrieved 08 06, 2014, from The National Archives: http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/ab/Archive/COMA/index.htm

Esrey, K., Joseph, L., & Grover, S. (1996). Relationship between dietary intake and coronary heart disease mortality: lipid research clinics prevalence follow-up study. *Journal of Clinical Epidemiology, 49*(2), 211-216.

FAO. (2010). *Fats and Fatty Acids in Human Nutrition: Report of an Expert Consultation.* Food and Agraculture Organization of the United Nations. Rome: FAO.

Farchi, G., Mariotti, S., Menotti, A., Seccareccia, F., Torsello, S., Fidanza, F., et al. (1989). Diet and 20-y mortality in two rural population groups of middle-aged men in Italy. *American Journal of Clinical Nutrition, 50*(5), 1095-1103.

Fehily, A., Yarnell, J., Sweetnam, P., & Elwood, P. (1993). Diet and incident ischaemic heart disease: the Caerphilly Study. *British Journal of Nutrition , 69*(2), 303-314.

Frantz, I. D., Dawson, E. A., Ashman, P. L., Gatewood, L. C., Bartsch, G. E., Kuba, K., et al. (1989). Test of effect of lipid lowering by diet on cardiovascular risk. The Minnesota Coronary Survey. *Arterioscerosis, Thrombosis, and Vascular Biology, 9*, 129-135.

Garcia-Palmieri, M., Sorlie, P., Tillotson, J., Costas, R., Cordero, E., Rodriguez, M., et al. (1980). Relationship of dietary intake to subsequent coronary heart disease incidence: The Puerto Rico Heart Health Program. *American Society for Clinical Nutrition, 33*(8), 1818-1827.

Grech, E. (2003). Pathophysiology and investigation of coronary artery disease. *BMJ, 326*, 1027-1030.

Harcombe, Z., Baker, S., Cooper, S., Davies, B., Sculthorpe, N., DiNicolantonio, J., et al. (2015). Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review and meta-analysis. *Open Heart, 2*(1), 1-7.

Hegsted, D. M., McGandy, R. B., Myers, M. L., & Stare, F. J. (1965, Nov). Quantitative Efeects of Dietary Fat on Serum Cholesterol in Man. *American Journal of Clinical Nutrition, 17*, 281-295.

Hite, A. H., Feinman, R. D., Guzman, G. E., Satin, M., Schoenfeld, P. A., & Wood, R. J. (2010). In the face of contradictory evidence: Report of the Dietary Guidelines for Americans Committee. *Nutrition Journal, 26*, 915-924.

Hooper, L., Summerbell, C. D., Thompson, R., Sills, D., Roberts, F. G., Moore, H. J., et al. (2012). Reduced or modified dietary fat for preventing cardiovascular disease. *Cochrane Database of Systematic Reviews*(5).

Jakobsen, M., O'Reilly, E., Heitmann, B., Pereira, M., Bälter, K., Fraser, G., et al. (2009). Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. *American Journal of Clinical Nutrition, 89*(5), 1425-1432.

Jakobsen, M., Overvad, K., Dyerberg, J., Schroll, M., & Heitmann, B. (2004). Dietary Fat and Risk of Coronary Heart Disease: Possible Effect Modification by Gender and Age. *American Journal of Epidemiology, 14*(5), 701-706.

Katan, M. B., & Brouwer, I. A. (2010). Saturated fat and heart disease. *American Journal of Nutrition, 92*(2), 459-60.

Katerina, S., & Kafatos, A. (2005). Letter to the Editor: The Seven Countries Study in Crete: olive oil, Mediterranean diet or fasting? *Public Health Nutrition, 6*(8), 666.

Keys, A. (1980). *Seven Countries: A Multivariate Analysis of Death and Coronary Heart Disease.* Cambridge: Harvard University Press.

Keys, A., Anderson, J. T., & Grande, F. (1957). Prediciton of Serum Cholesterol Responses of Man to Changes in Fats in the Diet. *Lancet, 270*(7003), 959-966.

Khaw, K., Wareham, N., Bingham, S., Luben, R., Welch, A., Day, N., et al. (2004). Association of HEmoglobin A1c with Cardiovascular Disease and Mortality in Adults: The European Prospective Investigation into Cancer in Norfolk. *Annals of Internal Medicine*(141), 413-420.

Khot, U., Khot, M., Bajzer, C., Sapp, S., Ohman, M., Brener, S., et al. (2003). Prevalence of Conventional Risk Factors in Patients With Coronary Heart Disease. *JAMA, 299*(7), 898-904.

Knekt, P., Reunanen, A., Jävinen, R., Seppänen, R., Heliövaara, M., Aromaa, A., et al. (1994). Antioxidant Vitamin Intake and Coronary Mortality in a Longitudinal Population Study. *American Journal of Epidemiology, 139*(12), 1180-1189.

Kromhout, D., & De Coulander, C. (1984). Diet, prevalence and 10-year mortality from coronary heart disease in 871 middle-aged men. The Zutphen Study. *American Journal of Epidemiology, 119*(5), 733-741.

Kromhout, D., Menotti, A., Bloemberg, B., Aravanis, C., Blackburn, H., Buzina, R., et al. (1995). Dietary saturated and trans fatty acids and cholesterol and 25-year mortality from coronary heart disease: the Seven Countries Study. *Preventive Medicine, 24*(3), 308-315.

Kuipers, R. S., de Graaf, D. J., Luxwolda, M. F., Muskiet, M., Dijck-Brouwer, D., & Muskiet, F. (2011). Saturated fat, carbohydrates and cardiovascular disease. *The Netherlands Journal of Medicine, 69*(9), 372-378.

Kushi, L., Lew, R., Stare, F., Ellison, C., Lozy, M., Bourke, G., et al. (1985). Diet and 20-Year Mortality from Coronary Heart Disease — The Ireland–Boston Diet–Heart Study. *New England Journal of Medicine, 312*, 811-818.

Kuulasmaa, K., Tunstall-Pedoe, H., Dobson, A., Fortmann, S., Sans, S., Tolonen, H., et al. (2000, Febuary 26). Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. *The Lancet, 355*, 657-87.

Leosdottir, M., Nilsson, P., Nilsson, J., & Berglund, G. (2007). Cardiovascular event risk in relation to dietary fat intake in middle-aged individuals: data from The Malmö Diet and Cancer Study. *European Journal of Cardiovascular Prevention & Rehabilitation, 14*(5), 701-706.

Leren, P. (1970). The Oslo Diet-Heart Study: Eleven-Year Report. *Circulation, 42*, 935-942.

Ludwig, D. S. (2002). The Glycemic Index Physiological Mechanisms Relating to Obesity, Diabeties and Cardiovascular Disease. *Journal Of The American Medical Association, 287*(18), 2414-2423.

Maas, A., & Appelman, Y. (2010). Gender differences in coronary heart disease. *Netherlands Heart Journal, 18*(12), 598-602.

Mann, J., Appleby, P., Key, T., & Thorogood, M. (1997). Dietary determinants of ischaemic heart disease in health conscious individuals. *Heart, 78*, 450-455.

Marmot, M., & Syme, L. (1976). Acculturation and Coronary Heart Disease in Japanese-Americans. *American Journal of Epidemiology, 104*(3), 225-247.

McGee, D., Reed, D., Yano, K., Kagan, A., & Tillotson, J. (1984). Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *American Journal of Epidemiology, 119*(5), 667-676.

Meittinen, M., Turpeinen, O., Karvonen, M. J., Pekkarinen, M., Paavilainen, E., Elosuo, R., et al. (1983). Dietary Prevention of Coronary Heart Disease in Women: The Finnish Mental Hospital Study. *International Journal of Epidemiology, 12*(1), 17-25.

Morgan, P. J. (2012). The Boyd Orr Lecture Back to the future: the changing frontiers of nutrition research and its relationship to policy. *Proceedings of the Nutrition Society , 71*, 190-197.

Morris, J., Marr, J., & Clayton, D. (1977). Diet and heart: a postscript. *British Medical Journal, 2*, 1307-1314.

Mozaffarian, D., Micha, R., & Wallace, S. (2010, March). Effects on Coronary Heart Disease of Increasing Polyunsaturated Fat in Place of Saturated Fat: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *PLoS Medicine, 7*(3).

MRC. (1968). Controlled Trial of Soya-Bean Oil in Myocardial Infarction. *Lancet, 292*(7570), 693-700.

Nago, N., Ishikawa, S., Goto, T., & Kayaba, K. (2011). Low Cholesterol is Associated With Mortality From Stroke, Heart Disease, and Cancer: The Jichi Medical School Cohort Study. *Journal of Epidemiology, 21*, 67-74.

NICE. (2014). *NICE Clinical Guideline CG181 Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease.* National Clinical Guideline Centre.

Oh, K., Hu, F., Manson, J., Stampfer, M., & Willett, W. (2005). Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the nurses' health study. *American Journal of Epidemiology, 161*(7), 672-679.

Paul, D., Rhodes, D., Kramer, M., Baer, D., & Rumpler, W. (2005). Validation of a food frequency questionnaire by direct measurement of habitual ad libitum food intake. *American Journal of Epidemiology, 162*(8), 806-814.

Perk, J., De Backer, G., Gohlke, H., Graham, I., Reiner, Z., Verschuren, M., et al. (2012). European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). *European Heart Journal, 33*, 1635-1701.

Petursson, H., Sigurdsson, J. A., Bengtsson, C., Nilsen, T. I., Philos, D., Getz, G., et al. (2012). Is the use of cholesterol in mortality risk algorithms in clinical guidelines valid? Ten years prospective data from the Norwegian HUNT 2 studyjep_1767 159..168. *Journal of Evaluation in Clinical Practice, 18*, 159-168.

Pietinen, P., Ascherio, A., Korhonen, P., Hartman, A., Willett, W., Albanes, D., et al. (1997). Intake of Fatty Acids and Risk of Coronary Heart Disease in a Cohort of Finnish Men: The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *American Journal of Epidemiology, 145*(10), 876-887.

Posner, B., Cobb, J., Belanger, A., Cupples, A., D'Agostino, R., Stokes, J., et al. (1991). Dietary Lipid Predictors of Coronary Heart Disease in Men. *JAMA, 151*(6), 1181-1187.

Prospective Studies Collaboration. (2007). Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55000 vascular deaths. *The Lancet, 370*, 1829-39.

Ramsden, C. E., Hibbeln, J. R., Majchrzak, S. F., & Davis, J. M. (2010). n-6 Fatty acid-specific and mixed polyusaturate dietary interventions have different effects on CHD risk: a meta-analysis of randomised controlled trials. *British Journal of Nutrition*(104), 1586-1600.

Ramsden, C. E., Zamora, D., Leelarthaepin, B., Majchrzak-Hong, S. F., Faurot, K. R., Suchindran, C. M., et al. (2013, Feb 5). Use of Dietary Linoleic Acid for Secondary Prevention of Coronary Heart Disease and Death: Evoluation of Recovered Data From The Sydney Diet Heart Study and Updated Meta-analysis. *BMJ, 36*(e8707), 1-18.

Reidlinger, D., Darzi, J., Hall, W., Seed, P., Chowienczyk, P., Sanders, T., et al. (2015). How effective are current dietary guidelines for cardiovascular disease prevention in healthy middle-aged and older men and women? A randomized controlled trial. *American Journal of Clinical Nutrition, 101*(5), 922-930.

Rose, G., Thomson, W., & Williams, R. (1965, June 12). Corn Oil in Treatment of Ischarmic Heart Disease. *BMJ*, 1531-1533.

Sachdeva, A., Cannon, C., Deedwania, P. C., LaBresh, K. A., Smith Jr, S. C., Dai, D., et al. (2009, January). Lipid levels in patients hospitalized with coronary artery disease: An analysis of 136,905 hospitalizations in Get With The Guidelines. *American Heart Journal, 151*(1), 111-117.

Scarborough, P., Rayner, M., van Dis, I., & Norum, K. (2010). Meta-analysis of effect of saturated fat intake on cardiovascular disease: overadjustment obscures true associations. *American Journal of Clinical Nutrition, 92*(2), 458-9.

Schatz, I., Masaki, K., Yano, K., Chen, R., Rodriguez, B., & Curb, D. (2001, August 4). cholesterol and all-cause mortality in elderly people from the Honolulu Heart Program: a cohort study. *The Lancet, 358*, 351-355.

Shekelle, R., Shryock, A., Paul, O., Lepper, M., Stamler, J., Liu, S., et al. (1981). Diet, Serum Cholesterol, and Death from Coronary Heart Disease — The Western Electric Study. *N Engl J Med, 304*, 65-70.

Siri-Tarini, P. W., Sun, Q., Hu, F. B., & Krauss, R. M. (2010). Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *American Journal of Clinical Nutrition, 91*(3), 535-46.

Siri-Tarino, P. W., Sun, Q., Hu, F. B., & Krauss, R. M. (2010, November). Saturated Fatty Acids and Risk of Coronary Heart Disease: Modulation by Replacement Nutrients. *Current Atherosclerosis Reports, 12*(6), 384-390.

Skeaff, C. M., & Miller, J. (2009). Dietary Fat and Coronary Heart Disease: Summary of Evidence from Prospective Cohort and Randomised Controlled Trials. *Annals of Nutrition & Metabolism, 55*, 173-201.

Stamler, J. (2010). Diet-heart: a problematic revisit. *American Journal of Clinical Nutrition, 91*, 497-9.

Strom, A., & Jensen, A. (1951). MORTALITY FROM CIRCULATORY DISEASES IN NORWAY 1940-1945. *Lancet, 257*(6647), 126-9.

Townsend, N., Williams, J., Bhatnagar, P., Wickramasinghe, K., & Rayner, J. (2014). *Cardiovascular Disease Statistics, 2014.* London: British Heart Foundation.

Tucker, K., Hallfrisch, J., Qiao, N., Muller, D., Andres, R., Fleg, J., et al. (2005). The combination of high fruit and vegetable and low saturated fat intakes is more protective against mortality in aging men than is either alone: the Baltimore Longitudinal Study of Aging. *Journal of Nutrition, 135*(3), 556-561.

Turpeinen, O., Karvonen, M., Pekkarinen, M., Mettinen, M., Elosuo, R., & Paavilainen, E. (1979). Dietary Prevention of Coronary Heart Disease: The Finnish Mental Hospital Study. *International Journal of Epidemiology, 8*(2), 99-118.

WHO. (1994, June). Ecological analysis of the association between mortality and major risk factors of cardiovascular disease. The World Health Organization MONICA Project. *International Journal of Epidemiology , 23*(3), 505-516.

Willett, W., Stampfer, M., & Sacks, F. (2014). Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk. *Annals of Internal Medicine, 161*(6).

Woodhill, J. M., Palmer, A. J., Leelarthaepin, B., McGilchrist, C., & Blacket, R. B. (1978). Low Fat, Low Cholesterol Diet in Secondary Prevention of Coronary Heart Disease. *Advances in Experimental Medicine and Biology, 109*, 317-30.

Xu, J., Eilat-Adar, S., Loria, C., Goldbourt, U., Howard, B., Fabsitz, R., et al. (2006). Dietary fat intake and risk of coronary heart disease: the Strong Heart Study. *American Journal of Clinical Nutrition, 84*(4), 894-902.

Yamagishi, K., Iso, H., Yatsuya, H., Tanabe, N., Date, C., Kikuchi, S., et al. (2010). Dietary intake of saturated fatty acids and mortality from cardiovascular disease in Japanese: the Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC) Study. *American Journal of CLinical Nutrition, 92*(4), 759-765.

Yusef, S., Hawken, S., Ounpuu, S., Dans, T., Avezum, A., Lanas, f., et al. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet, 364*(9438), 937-952.

Appendices

Summary Table 1: Primary Prevention Control Trials Which Either Lowered Fat or Replaced Saturated Fat with Polyunsaturated Fat

Name	Author	Score	Subjects (*n*)	Location	Study Design	Blinding	Diet		Adherence	Study Duration	Follow Up	Dietary Analysis	Effect on Cholesterol	Effect on CHD Mortality / Events
							Intervention (%TE)	Control (%TE)						
Minnesota Coronary Survey	Frantz et al 1989		9057 Institutionalised Men (n4393) & Women (n4664) With or without CHD.	U.S.A	Open entry Parallel RCT	Double Blinded	**Treatment** Filled Products 38% Fat 9.2% SFA 14.7% PUFA	**39% Fat** 18.3% SFA, 5.2 % PUFA	Missed meals recorded but data not published	4.5 Yrs.	Mean 1.1 yrs. (384 Days)	Direct Analysis (pre-defined diet)	↓ 14.5% in Treatment Group & 0.7% in Control	No difference between groups after 4.5 YRS in CVD deaths or events
LA Veterans	Dayton et al 1969		846 volunteer men over 55 in domiciliary care with or without CHD	U.S.A	Parallel randomised	Blinded clinical follow up	Filled products 38.9% Fat 38.4% LA PUFA	**Standard diet** 40.1% Fat 10% LA PUFA 90g PRO SFA not listed	49% Experimental Group, 56% Control	8 Yrs.	-	Direct analysis of representative meal	↓12.7% Intervention	No sig difference in primary endpoint of sudden death or MI. Sig difference when pooled with secondary endpoints (p0.01) ↑ CHD deaths in Control but ↑ all cause deaths in experimental group Incidence of cancer ↑exp group. No dif in total deaths.

Finnish Mental Hospital	Turpeinen et al 1979 Miettinen et al 1983		357 Women 461 Men. Middle aged, institutionalised without CHD.	Finland	Non randomised cross over Two Hospitals (N&K) Swapped Diet after 6 YRS. Experimental & Normal Diet.	No	Filled Products 37.7% Fat 9.4% SFA 13.9% PUFA 12.6% TE MUFA 53.1% CHO 14.7% PRO.	36.7% FAT 18.7% SFA 4.7% PUFA 11.4% MUFA 54.1% CHO 14.9% PRO	33% Women and 53% Men present for both parts of the study. Participants only need to be in attendance for 50% of study to be included. Meals outside of hospital not accounted for.	12 year Duration. 6 Years on each diet.	6 YRS	Direct	Sig (P<0.001) ↓ -15% in Men,- 13% in Women on experimental diet from baseline.	No Sig difference in either Male or Female Total Mortality. Sig ↓ CHD Mortality when following diet in men but not women.

Summary Table 2: Secondary prevention fat modification and reduction trials

Name	Author	Score	Subjects (n)	Location	Study Design	Blinding	Intervention	Follow Up	Diet	Dietary Analysis	Effect on Cholesterol	Effect on CHD Mortality / Events
Corn Oil	Rose et al 1965		80 Men aged under 7 with previous MI	UK	Randomised Parallel groups	Partially	Two experimental groups given 80g of oil to consume over three meals in equal doses. Olive Oil (n26), Corn Oil (n28). Control n26. Oil groups given advice to avoid fried foods, fatty meat, sausages, pastry, ice cream, cheese and cakes.	2 Years	Mean 58g olive oil consumed, 64g Corn Oil. Feel to 51g a day in both groups after 18-24 months	Self-administered questionnaire	Corn Oil sig drop in cholesterol during first 18 months (P<0.01) but not sig lower from baseline after 18-24months. No sig dif In Control or Olive Oil groups.	After two years 75% of Control remained free of cardiac events compared to 57% of Olive Oil and 52% Corn Oil participants.
Oslo Heart Study	Leren 1970		412 Men 30-64 with Prior MI (Control n206, Intervention n206)	Norway	Parallel randomised Open Entry	Blinded outcome assessment	**Intervention** Dietary advice aimed at lowering serum cholesterol. Advice to consume diet low in animal fat and cholesterol while high in vegetable oils	5 years and 11 years	Not Clear. No dietary assessment after 5 YRS	7-14 day weighed assessment of 17 dieters	17.6% lower in intervention from baseline after 5 YRS vs 3.7% lower in Control	At 5 YRS sig ↓ major CHD relapses (p0.05) in intervention group, no sig dif in non-fatal MI. At 11 years Sig ↓ MI mortality. Overall CHD & Total mortality not sig dif.
MRC 1965 London Low Fat	A Research Committee 1965		264 men aged <65 Yrs. recently recovered from MI	UK	Randomised Parallel groups		Intervention group prescribed low fat diet with 45g Fat. Control Usual Diet with 110-130g Fat. Overweight given calorie controlled diet (21% Control, 15% Intervention)	Mean 3 Yrs.		Weighted Food diary once a week on different days for first 7 weeks then once a month	44mg/dl drop in intervention from baseline. 25mg/dl drop in control.	No sig difference between groups in relapses or deaths. 1.9% risk reduction in intervention group. 0.2% difference in event rate between groups. All-cause mortality higher in intervention

Name	Author	Score	Subjects (n)	Location	Study Design	Blinding	Intervention	Follow Up	Diet	Dietary Analysis	Effect on Cholesterol	Effect on CHD Mortality / Events
												(18.6%) vs control (16.26)
MRC Soya	MRC 1968		393 Men under 60YRS recently recovered from first MI	UK	Randomised Parallel groups, open entry	blinded assessment	**Intervention** (n199) diet low in SFA with 85g Soya bean oil daily. **Control** (n194) usual diet	2 - 6.75 YRS Mean 3.5YRS		Weight food diary	Experimental diet ↓ SC during first six months from 272 to 213mg/100ml. (22%fall) Control group fell 6%**.**	No significant difference in relapse of CHD deaths. Relapses not related to initial cholesterol level.
Sydney Diet Heart Study Rozanlucis	Ramsden et al 2013 Woodhill et al 1978		458 Men aged 30-59 with recent coronary event	Australia	RCT, parallel groups	single	**Intervention:** advice to limit SFA intake to less than 10% TEI and increase PUFA to 15% TEI using safflower oil & safflower margarine. **Control** no advice	Median 39months		7 day food logs completed three times in the first year and every six months	12 month sig drop in TC (*P*<0.001) in intervention compared to control (-13.3%vs-5.5%)	All-cause mortality in intervention group was 17.6% vs 11.8% in control group *P*<0.05). CHD mortality sig (*P*<0.036) higher in intervention (16.3%) vs control group (10.1%)
Young Males	Bierenbaum et al 1967		200 Men aged 30-50 with documented CHD & Confirmed previous MI	USA	Non randomised Parallel groups		Two Intervention groups; **Diet 1** (n50) 1oz corn & safflower oil mix. 27.8% TE Fat (5.5%SFA, 9.3% MUFA, 14.1% PUFA), 20..4% PRO, 51.8% CHO. **Diet 2** (n50) 1oz Coconut Oil & Peanut Oil mix 28.2% FAT(9.6% SFA, 13.2%MUFa,	Study Changed at 1Yr due to lack of difference in TC. After 18 Months Control Group added & Diet groups merged.		Interview	No sig difference between Diets. Both Diets lowered TC in first year.	Rate of MI recurrence lower in experimental group (merged diet groups)

Name	Author	Score	Subjects (n)	Location	Study Design	Blinding	Intervention	Follow Up	Diet	Dietary Analysis	Effect on Cholesterol	Effect on CHD Mortality / Events
							3.3%PUFA) 20.7% PRO, 51.1% CHO. Control (n100) Usual Diet.					

Summary Table 3: Cohort Study Summary Table

Study / Review	Study Name	Population	CHD Status at Baseline	Location	Size	Mean Diet		Dietary Analysis	Follow up Dietary Analysis?	Average Follow up	Results	SFA linked with CHD?
						Energy (Kcal)	FAT % Total Energy (TE)					
Shekelle et al 1981	Western Electric	Random sampling of men aged 40-55	Without	USA	n5397	3183	Baseline SFA 16.7% PUFA 3.8%	FFQ & Interview with Nutritionist	At 1 year	20YRS	PUFA inversely associated with CHD death risk (p0.10). DC positively associated with CHD death risk. SFA linked with TC.	No
Paul et al 1963	" "											
McGee et al 1984	Honolulu Heart	Men of Japanese ancestry living in Honolulu.	Without	USA	n8006	2303	Total Fat 33.7% (83g) SFA 12.3% (31.8g) PUFA (15.4g)	24hr recall	None	10YRS	Total CHD (*P*< 0.05) & MI or CHD Death (P<0.001) associated With relative but not absolute intake of either total or SFA fat. Multivariate analysis removed significance of %TE SFA with total CHD or angina however still associated along with total fat with MI or CHD death (*P*<0.001).	g/day NO %TE YES
Kushi et al 1985	Ireland-Boston Diet-Heart	Brothers aged 30-60Yrs of Irish ancestry or	With &Without	USA & Ireland	N1508	Ireland 4033 Boston 3099	Ireland TF 37.6%, SFA 17.7%,PUFA 2.1%	FFQ	None	20YRS	%TE SFA related to CHD mortality (p0.005). No sig difference in SFA or PUFA consumption between men	Yes

Study /	Study Name	Population	CHD	Location	Size	Mean Diet		Dietary	Follow	Average	Results	SFA linked
		origin living in Boston or Ireland.				First Generation 2946	Boston TF 38.9%, SFA 16.9%, PUFA 2.6%. First Generation TF 38.9%, SFA 15.9%, PUFA 3.5%				without CHD and CHD deaths. Brothers living in Ireland lower CHD mortality than in Boston.	
Posner et al 1991	Framingham	Men aged 45-65 from the Framingham study.	Without	USA	N813	2643 (age adjusted)	Aged 45-55 TF 39.7% (118.4g), SFA 15.2% (45.3g) Aged 56-65 TF 38.3% (109.3g) SFA 14.8% (42.4g)	24hr Recall	none	16YRS	Men Aged 45-56 Energy adjusted %TE SFA significantly associated with CHD (p0.050) but not unadjusted, multivariate or absolute intake. Men aged 56 or more no relationship between SFA or TF & CHD.	Yes in men aged 45-56 when adjusted for energy as %TE but not g/day. NO in others.
Fehily et al 1993	Caerphilly	Men living in Caerphilly	With &Without	UK	N2512	Non-CHD 2313 CHD 2179	Non-CHD Animal Fat 29.5%, CHD 29.7%. Total Fat Non-CHD 40.1%,CHD 40.9%	FFQ, 30% completed 7d weighed food diary.	None	5YRS	No significant relationship between CHD and either Total or Saturated (Animal) fat.	No
Ascherio et al 1996	Health Professionals Follow Up	Health professionals aged 40-75 without diagnosed CVD or diabetes in 1986	Without	USA	N43757	NA	SFA First quintile 7.2% - fifth quintile 14.8%. Total Fat First quintile 23.9%- fifth quintile 39.1%	FFQ	None	14YRS	Age adjusted significant relationship between SFA & MI (p0.002) and CHD mortality (p0.0001). Multivariate analysis removed significance.	No
Mozaffarian et al 2005	" "											
Mozaffarian et al 2006												
He 2003	" "14 Yrs. follow up											
Esrey et al 1996	Lipid Research	Men and women aged	Without	USA	N4546		SFA Intake CHD Death 40.8g 30-	24hr recall	None	12YRS	Significant relationship between %TE SFA intake and	**YES** in 30-59 age

Study /	Study Name	Population	CHD	Location	Size	Mean Diet		Dietary	Follow	Average	Results	SFA linked
	Clinics	30 and above					59YRS, 32.7g 60-79YRS Living 37.7g 30-59YRs 29.9% 60-79YRS				CHD mortality in men and women aged 30-59 (P<0.01) but not in those aged 60-79. Similar association for total fat.	group. **No** in 60-79 age groups.
Mann et al 1997	Oxford Vegetarian	Vegetarian men & women and their meat eating friends and family aged 16-79Yrs.	With & Without	UK	N10802	NA	First tercile SFA intake: Men 14.6g, Women 13.7g. Third Tertile Men 41g, Women 38.1g	FFQ	None	13YRS	Saturated animal fats intake associated with CHD mortality (P<0.01). *Overall mortality half of national average.	YES
Pietinen et al 1997	Alpha-Tocopherol …	Male smokers aged 50-69 free of diagnosed CVD at baseline	Without	Finland	N 21930	NA	First quintile TF 83.2g, SFA 34.7g. -Fifth quintile TF 121.6g, SFA 67.5g.	FFQ	None	6YRS	No association between SFA or total fat with risk of CHD death.	NO
Boniface and Tefft 2002	Health & Lifestyle Survey	Men and women aged 40-75 randomly selected from Health & lifestyle survey	Without	UK	N2676	NA	NA	FFQ	None	16YRS	SFA not related to risk of CHD death in men but was in older women aged 60-75Yrs (p0.0023). SFA was linked with death from other causes in women 40-59Yrs (p0.0041) and 60-75Yrs (p0.0010)	Yes in Women No in Men
Jakobsen et al 2004	Glostrup Multi Centre	Men and women aged 30-71Yrs	Without	Denmark	N3686	Men 1576 -3248 Women 1194 – 2436	Women SFA intake lowest tercile 14.1% to 24.8% highest tercile. Men SFA intake 14.5% to 24.8%. Women TF 36.6% to 54.4%. Men 37.4% to 55.1%.	7day weighed food diary (n3553) or interview (n244).	None	16YRS	No association with either total or any type of fat with risk of CHD. In Women 5% increase in SFA resulted in 36% increased risk of CHD.	Yes in Women No in Men
Leosdottir et al 2007*	Malmo	Middle aged Men and women	Without	Sweden	N28098	Men 2425 to 2808 women	Men SFA 12.7% lowest quartile to 20.9%	7day food diary and FFQ	None	8YRS	No significant association between SFA, total fat or PUFA intake with risk of a	NO

Study /	Study Name	Population	CHD	Location	Size	Mean Diet		Dietary	Follow	Average	Results	SFA linked
						1834 to 2164	highest. Women 12.8% to 21.3%. TF Men 31.8% to 47.7%. Women 30.8% to 46.1%. Men PUFA 5.5% to 7.1%, Women 5.1% to 6.8%.				CVD event	
Wallstrom 2012	" "											
Oh et al 2005	Nurses Heart Study	Female nurses aged 30-55 free of CVD and diabetes	Without	USA	N78778	Based on SFA quintiles Lowest 1698 to 1721.	SFA lowest quintile 10.1% - highest 17.6%. TF 28.3% to 44%. PUFA 4.1% - 7.4%.	FFQ	5 times	20YRS	Age adjusted positive trend with SFA intake (p0.0001) or Total fat intake (p0.001) with CHD risk. Multivariate analysis removed significance.	YES & NO
Albert 2005	" "											
Iso 2001	" "											
Hu et al 1997	Nurses' Health Study DIETARY FAT INTAKE AND THE RISK OF CORONARY HEART DISEASE IN WOMEN											
Hu et al 1999												
Tucker et al 2005	Baltimore Longitudinal	Men aged 34-80Yrs	Not Clear	USA	N501	Non-CHD 2213. CHD Death 2178.	Non-CHD SFA 12.3% CHD Death 13.8%.	7 day food diary	4 times	18YRS	Low SFA intake not protective of CHD incidence (p0.005). Each gram of SFA related to 7% increased risk of CHD death (*P*<0.001) however results grouped with low Fruit and vegetable intake*.	NO*
Xu et al	Strong Heart	American	Without	USA	N2938	Aged 47-	Aged 47-59	24hr recall	none	8YRS	No relationship between SFA	NO overall

Study /	Study Name	Population	CHD	Location	Size	Mean Diet		Dietary	Follow	Average	Results	SFA linked
2006		Indians aged 45-74 without CHD at baseline				59 NON-CHD 1916, CHD 1940. Aged 60-79 NON-CHD 1709, CHD 1672.	**NON-CHD** TF 35.8%,SFA 12.1% (26.1g) **CHD** TF 36.9%, SFA 12.6% (27.7g) Aged 60-79 **NON-CHD** TF 34.2%, SFA 11.6% (22.4g). **CHD** TF 33.9%, SFA 11.5% (21.9g)				and CHD Overall. Higher intake of SFA, total fat and MUFA associated with higher CHD mortality in those aged 47-59 (p0.01)	YES in participants aged 47-59
Yamagishi et al 2010	JACC - Japan Collaborative	Men and women aged 40-79 free from CHD	Without	Japan	N 58453	Men lowest by SFA quintile 1607, Highest 1592. Women lowest 1309 to highest 1283	Men lowest quintile SFA 9.2g/day to highest 20.3g/day. Women 9.4g/day to 19.9g/day.	FFQ	none	14	SFA not associated with CHD mortality. Age and sex adjusted relationship between SFA and risk of CVD (*P*<0.001) and MI (p0.03). Multivariate analysis removed significance of SFA and MI and lowered relationship between SFA and CVD (p0.05).	Yes but not CHD mortality.
Knekt et al 1994	Antioxidant Vitamin Intake and Coronary Mortality in a Longitudinal Population Study	Men and women aged 30-69	Without	Finland	N 5133	Men CHD 3106, Alive 2990. Women CHD 2127, Alive 2169.	Men CHD TF 136g/day, SFA 78g/day. Alive TF 129g/day, SFA 73g/day. Women CHD TF 92g/day, SFA 53g/day. Alive TF 88g/day, SFA 50g/day.	Interview	Twice	14	SFA not related to CHD mortality	NO
Farchi et al 1989	7 countries Italy Rural 20yr mortality	Two Rural Italian Men cohorts from the Seven countries study aged	Without	Italy	N1536	Alive 2900 All Cause Death 2869 CHD Death 2697	Alive TF 28.5% (90.8g), SFA 9% (28.9g). CHD Death TF 26% (76.9g), SFA 8% (23.8g)	? Dietary history method	None	15	SFA protective against CHD mortality and total mortality. SFA intake significantly different between survivors and those who died of CHD (*P*<0.01).	NO

Study /	Study Name	Population	CHD	Location	Size	Mean Diet		Dietary	Follow	Average	Results	SFA linked
		45-64Yrs					All Cause Death TF 26.7% (83.5g) SFA 8.5% (26.9g)					
Kromhout et al 1984	Zutphen	Men aged 40-59	Without	Netherlands	N871	CHD 2531 Non-CHD 3055	CHD SFA 16% (45.4g) Non-CHD 17.6% (59.6g)	Dietician interview with spouse	None	10	SFA intake significantly lower in men who developed CHD (p0.002).	NO
Oomen et al 2001	Zutphen											
Oomen 2001	Zutphen											
Streppel 2008	Zutphen											
Gordon et al 1981	Three Study Summary Honalulu, Framingham, Puerto Rico	See individual studies.										
Garcia-Palmieri et al 1980	Puerto Rico Heart Health (PRHH)	Urban and Rural Men aged 45-64	Without	Puerto Rico	N8218	**Non-CHD** Urban 2413, Rural 2353. **CHD** Urban 2305, Rural 2241	**Non-CHD** Urban TF 36.6% (99g), SFA 13.5% (37g) Rural TF 32.2% (86g) SFA 12.6% (33g) **CHD** Urban TF 38% (98g), SFA 13.6% (36g). Rural TF 32.3% (81g) SFA 13.1% (33g)	24hr recall	None	6	No difference in SFA intake between men with or without CHD.	NO
Morris et al 1977	Diet and heart: a postscript London 1956	Men aged 30-67	Without	UK	N337	Range 1860-4440	Range of TF 30-56% SFA NA	7 day weighed diary	None		No relationship between SFA or Total fat and CHD	NO
Kromhout et al 1995	Dietary Saturated	Men aged 40-59 from	Not Clear	Various	N12763	See Full Paper	See Full Paper Table 1. SFA	Weighed food diary	Yes in 7 of 16	25	SFA (P<0.001) & total fat (P<0.05) linked with CHD 25	YES

Study /	Study Name	Population	CHD	Location	Size	Mean Diet		Dietary	Follow	Average	Results	SFA linked
	and *trans* Fatty Acids and Cholesterol and 25-Year Mortality from Coronary Heart Disease: The Seven Countries Study	16 cohorts of the seven countries study.				Table 1	Range 10.1g to 88.6g	of 1-7 days.	cohorts		year mortality rate	
Kromhout et al 1989	Food consumption patterns in the 1960s in seven countries											

Summary Table 4: Systematic reviews & Meta-analysis

Author & Year	Stated aim of review	Funding	Number Papers Cited	Study Selection	Conclusion
Chowdhury et al (2014)	To Surmise evidence about associations between fatty acids and coronary disease	British Heart Foundation, Medical Research Council, Cambridge Institute for Health Research Biomedical Research Centre and Gates Cambridge.	76, 32 Observational Studies of Fatty Acids from dietary intake, 17 observational studies of fatty acid biomarkers. 27 RCT's of fatty acid supplementation.	Prospective, observational studies with >1 YR follow up. RCT which recorded coronary outcomes as endpoint.	Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats.
Siri-Tarino et al (2010)	To surmise the evidence related to the association of dietary saturated fat with risk of CHD, stroke and CVD in prospective epidemiological studies	National Dairy Council, National centre for research resources.	21 cohort studies , (16 on CHD and 8 on Stroke)	Prospective cohort studies which specifically evaluated SFA with CVD measured dietary SFA, fatal or non-fatal CVD events but not CVD risk factors, Healthy participants at baseline.	Prospective epidemiological studies show no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD.

Author & Year	Stated aim of review	Funding	Number Papers Cited	Study Selection	Conclusion
Jakobsen et al 2009	To investigate associations between energy intake from MUFAs, PUFAs and CHO with CHD risk while assessing potential effect of age and sex	National Heart, Lung and Blood institute, Danish Heart Foundation. Danish Medical Research Council	11 cohort studies	Inclusion Criteria: published follow up study with >150 coronary events, avaibliity of usual diet, validated dietary assessment method. Excluded were subjects <35 Yrs., any previous history of CVD, diabetes or cancer and extreme energy intake.	Associations suggest that replacing SFAs with PUFAs rather than MUFAs or CHO prevents CHD over a wide range of intakes.
Ramsden 2013 (Ramsden, Hibbeln, Majchrzak, & Davis, 2010)	Examine effects of PUFA interventions on risk of CHD	Life insurance medical research fund of Australia and New Zealand. National institutes of health.	8 RCT on PUFA intervention on secondary prevention.	Randomised trials which increased PUFA in place of SFA reporting non-fatal MI, CHD deaths and/or Total deaths. Excluded if CHD risk disproportionate in study arms; or dietary information necessary to classify experimental diets As either 'n-6 specific PUFA' or 'mixed n-3/n-6 PUFA' was not available.	Finds no benefit of cardiovascular benefit in linoleic acid interventions trials
Skeaff & Miller 2009	To assist the expert consultation group to make evidence-based recommendations about fat, fatty acids and human health.	Not clear	28 Cohort, 9 Control trials	Low fat or PUFA-SFA interventions with CHD endpoints	"Available evidence from cohort and RCT trials is unsatisfactory and unreliable to make judgment about and substantiate the effects of dietary fat on risk of CHD"
Mente et al 2009	To systematically evaluate dietary exposures and CHD using Bradford Hill criteria, determine which RCTs on dietary exposure support findings of prospective cohort studies and which exposures have insufficient evidence.	No external funding	EXLUDED AS Multifactorial		
Cochraine Hooper et al 2012	To assess the effect of reduction and/or modification of dietary fats on mortality, cardiovascular mortality, cardiovascular morbidity and individual outcomes including myocardial infarction, stroke and cancer diagnoses in randomised clinical trials of at least 6 months duration.	Cochraine		Inclusion criteria, randomised and appropriate control group; Stated aim of intervention was reduction or modification of intake of dietary fat or cholesterol unless intervention was specifically omega 3, trials non multifactorial, adults with or without CVD, intervention at least 6months, included mortality or CVD morbidity.	"findings are suggestive of a small but potentially important reduction in cardiovascular risk on modification of dietary fat, but not reduction of total fat, in longer trials"
Mozaffarian et al 2010	To asses impact of increase PUFA consumption as replacement for SFA on CHD endpoints	National Heart, Lung and Blood Institute & Chicago Community Trust Searle Scholar award	8	RCTs which increased PUFAs for at least 1 year without any other intervention, had an appropriate control group, reported sufficient data to calculate risk estimates with standard errors for effects on hard CHD events. Observational, non-randomised and omega 3	Findings provide evidence that consuming PUFA in place of SFA reduces CHD events in RCTs.

Author & Year	Stated aim of review	Funding	Number Papers Cited	Study Selection	Conclusion
				dominant studies excluded. Not limited to primary or secondary trials.	

Summary Table 5: Observational Studies listed in Reviews. FU Follow up YR Years

Study / Review	Study Name	Siri-Tarino et al 2001	Jokobsen et al 2009	Chowdhury et al 2014 SFA Cohort Studies (20)	Skeaff & Miller 2009	Skeaff & Miller 2009 WITH Listed SFA Intake SUPP Table 7
Shekelle et al 1981	Western Electric	X		X	X 19Yr FU	x
Paul et al 1963	" "				X 4Yr FU	X
McGee et al 1984	Honolulu Heart	X		X	X (also Gordon et al 1981)	X (also Gordon et al 1981)
Kushi et al 1985	Ireland-Boston Diet-Heart	X		X	x	x
Posner et al 1991	Framingham	X		X	x	x
Fehily et al 1993	Caerphilly	X		X	x	x
Goldbourt et al 1993	Israeli IHD	X	x	X	x	x
Asherio et al 1996	Health Professionals Follow Up	X	x	X	x	x
Mozaffarian et al 2005	" "			X		
Mozaffarian et al 2006					X	
He 2003	" "14 Yrs follow up			X		
Esrey et al 1996	Lipid Research Clinics	X		X	x	x
Mann et al 1997	Oxford Vegetarian	X		X	x	x
Pietinen et al 1997	Alpha-Tocopherol …	X	x	X		x
Boniface and Tefft 2002	Health & Lifestyle Survey	X		X	x	x
Jakobsen et al 2004	Glostrup Multi Centre	X	x	X		
Leosdottir et al 2007*	Malmo	X		X		
Wallstrom 2012	" "			x		
Oh et al 2005	Nurses Heart Study	X		X	X	x
Albert 2005	" "			X	X	
Iso 2001	" "			X		
Hu et al 1997	Nurses Health Study DIETARY FAT INTAKE AND THE RISK OF CORONARY HEART DISEASE IN WOMEN		X		X	x

Study / Review	Study Name	Siri-Tarino et al 2001	Jokobsen et al 2009	Chowdhury et al 2014 SFA Cohort Studies (20)	Skeaff & Miller 2009	Skeaff & Miller 2009 WITH Listed SFA Intake SUPP Table 7
Hu et al 1999					x	
Tucker et al	Baltimore Longitudinal	X		X	x	x
Xu et al 2006	Strong Heart	x		X	x	x
Erkkila 2003	Euroaspire			x	x	
Trichopoulou 2006	EPIC Greece			x		
Yamagishi et al 2010	JACC - Japan Collabortive			x		
Folsom et al 1997	ARIC Atherosclerosis Risk in communities		X			
Yamagishi et al 2008	""				x	x
Wang, Folsom, Eckfeldt 2003	""					x
Laaksonen 2005	Kuopio IHD			x		
Fraser et al 1992	Adventist Health Study		X			
Knekt et al 1994	Antioxidant Vitamin Intake and Coronary Mortality in a Longitudinal Population Study		X			
Kushi et al 1996	DIETARY ANTIOXIDANT VITAMINS AND DEATH FROM CORONARY HEART DISEASE IN POSTMENOPAUSAL WOMEN		X			
Hallmans et al 2003	Northern Sweden Health and Disease Study Cohort		X	Not included in SFA but circulating FA		
Liu et al 2002	Womans Health Study (WHS)		x			
Farchi et al 1989	7 countries Italy Rural 20yr mortality				x	x
Khaw et al 1987	California					
Kromhout et al 1984	Zutphen				x	X
Oomen et al 2001	Zutphen			Not included in SFA but Omega 3	X	
Oomen 2001	Zutphen			" "	X	
Streppel 2008	Zutphen			" "		
Gordon et al 1981	Three Study Summary Honalulu, Framingham, Puerto Rico				X Framingham X Honolulu X Cites both for PRHH	X Framingham X Honolulu xPRHH
Garcia-Palmieri et al 1980	Puerto Rico Heart Health (PRHH)				x	x
Miettinen et al 1982	Nested case control				X	x

Study / Review	Study Name	Siri-Tarino et al 2001	Jokobsen et al 2009	Chowdhury et al 2014 SFA Cohort Studies (20)	Skeaff & Miller 2009	Skeaff & Miller 2009 WITH Listed SFA Intake SUPP Table 7
Morris et al 1977	Diet and heart: a postscript London 1956				x	x
Tanasescu et al 2004	Dietary fat and cholesterol and the risk of cardiovascular disease among women with type 2 diabetes					
Kromhout et al 1995	**Dietary Saturated and *trans*Fatty Acids and Cholesterol and 25-Year Mortality from Coronary Heart Disease: The Seven Countries Study**				x	x
Kromhout et al 1989	**Food consumption patterns in the 1960s in seven countries**					
Salonen et al 1985	Nested case control					x
Ohrvall et al 1996						x
Albert et al 2002						x
Jakobsen et al 2003	MONICA-1 & MONICA-II					x

Summary Table 6: Control Trials Included in Reviews MF Modified fat, RF Reduced Fat, R&MF Reduced and Modified fat

Study/Review	Popular Study Name	With or Without CHD.	Sex	Mozaffarian et al 2010	Chowdhury (27 total 8 PUFA for SFA	Skeaff & Miller 2009 (taken from Supp Table 18 RCT FAT MODIFIED DIETS	Ramsden et al 2013 Taken from Supplement	Hooper 2012 Cochraine	
								Analysis 1.3 Combined CVD Events	Analysis 1.2 CVD Mortality
Dayton 1969	LA Veterans	With & Without	M	x	X	X (P/S Events)	X	X (MF)	
MRC 1968 (Morris et al)	MRC Soya Oil	With	M	X	X	X (P/S Deaths) (P/S Events)	X	X (MF)	X (MF)
Leren 1970	Oslo Diet-Heart	With	M	X	X	X (P/S Deaths) (P/S Events)	X		
Leren 1996	" "							X (MF)	X (MF)
Turpeinen 1979	Finnish Mental Hospital (Men)	Without	M	X	X Combined results	X (P/S Deaths) (P/S Events)			
Miettinen 1983	Finnish Mental Hospital (Women)	Without	W	X		X(P/S Deaths) (P/S Events)			
Frantz 1989	Minnesota Coronary Survey	Without	M&W	X	X	X (P/S Events)	X (Splits study into M&W)	X (Splits study into M &W)	X (Splits study into M &W)
Burr 1989	DART	With (Multi)		X	X	X (P/S Deaths) (P/S Events)	X (excluded from main analysis)	X (R&MF)	X (R&MF)
Watts 1992	S.T.A.R.S	With (Multi)		X	X* 1994 paper	X (P/S Deaths) (P/S Events)	X	X (R&MF)	X (R&MF)
Rose et al 1965	London Corn Oil	With	M			X (P/S Events)	X	X (MF)	X (MF)
Ramsden et al 2013	Sydney Diet Heart Revisited	With	M		X		X		
Ball et al 1965	London Low Fat **Low-fat** diet in myocardial infarction	With	M			X (LOW FAT)		X (RF)	X (RF)
De Lorgeril et al 1999	Lyon Diet Heart Study					X (not listed in main paper)			
Howard et al 2006	Women's Health Initiative	With & Without (Multi)	W			X (LOW FAT)		X (RF) Split into With & Without CVD	X (RF) Split into With & Without CVD
Tuttle et al 2008	THIS-DIET					X (not listed in main paper)			
Houtsmuller 1979								X (MF) (Diabetics)	
Sondergaard 2003								X (R&MF) All on Statins	X (R&MF)
MeDiet 2002								X (R&MF) Breast Cancer	

Study/Review	Popular Study Name	With or Without	Sex	Mozaffarian et al 2010	Chowdhury (27 total 8 RHEA for	Skeaff & Miller 2009 (taken from Sunn Table 18 RCT	Ramsden et al 2013	Hooper 2012 Cochraine	
Premier 2003								X (RF) Multiple Intervention High Blood Pressure	
NDHS 1968	National Diet Heart Study							X(MF & R&MF) Feasibility trial	
Black 1994								X (RF) Skin Cancer	X (RF)
Ley 2004								X (RF) Diabetics	X (RF)
Moy 2001								X (RF) Hypercholesterolemia	
DO-IT 2006								X (RF) Omega 3 Supplementation	X (RF)
WHEL 2007									X (R&MF) Breast Cancer

Research Paper:

Trends in Saturated Fat, Total Fat and Coronary Heart Disease in the United Kingdom 1950-2010: Does the evidence support current dietary guidelines.

Word count : 4153

Journal Choice: The journal chosen if this paper were to be published is Open Heart, an open access online journal co-owned by the British Medical Journal and British Cardiovascular Society. The journal has published a number of papers on the relationship between saturated fat and coronary heart disease and has a stated aim to be open and have maximum impact on research progress and patient care while ensuring free access.

Abstract

Background and aims

The aim of this study was to evaluate the relationship between saturated fat, total fat and coronary heart disease (CHD) at United Kingdom (UK), national and regional level and to establish if available data supports current dietary guidelines for the reduction of total and saturated fat intake.

Methods

Data was sought pertaining to historical trends in dietary intake, CHD mortality and associated measures within the UK. Trends were then analysed to establish if a relationship, if any existed between measures.

Results

Results show that from a peak in 1978 male CHD mortality to 2010 fell by 79% in men and 83% in women. In the same period relative saturated fat intake fell by 4.6% and total fat by 3.4%. Analyses showed at the UK population level there was a consistent significant positive association between saturated fat intake and coronary heart disease mortality in men and women between 1972 to 2010 ($P<0.01$). The relationship between total fat intake and CHD was less consistent as were associations at national and regional level. There was no association between saturated fat intake, total fat intake and CHD prevalence.

Conclusion

The results of this study support current population dietary guidelines however the disparity between the percentage change between saturated and total fat intake compared to the decline in CHD mortality over time questions the impact saturated fat has on CHD. It is clear further research is needed.

Introduction

Coronary heart disease (CHD) is the leading single cause of death in the United Kingdom (UK) accounting for 73,680 deaths in 2012 (Townsend, Williams, Bhatnagar, Wickramasinghe, & Rayner, 2014). Interest in the relationship between total fat intake (TF), saturated fat consumption (SFA) and CHD after World War Two in the UK led to the development of a Committee on Medical Aspects of Food Policy (COMA) panel on diet and CHD and publication of dietary guidelines (DHSS, 1974) (Bufton, 2005).

Current dietary guidelines for the prevention of cardiovascular disease (CVD) were published in 1994 and recommend the reduction of the percentage total energy intake (%TE) of TF to 35%TE and SFA to 10%TE due to evidence suggesting lower intakes may lower risk of CHD, lower cholesterol levels and prevent obesity (DOH, 1994).

In recent years the relationship between SFA and CHD has been questioned (Chowdhury, et al., 2014), (Siri-Tarino, Sun, Hu, & Krauss, 2010), (Harcombe, et al., 2015). The purpose of this study is to evaluate this relationship in the UK at a national and regional level and to establish if available data supports current dietary guidelines.

Method

Data collection

Historical diet and age specific mortality and population data pertaining to the UK was identified using searches of the Office for National Statistics (ONS), World Health Organisation (WHO), Department of Health (DOH) and Department for Environment, Food and Rural Affairs (DEFRA).

UK, England & Wales, Northern Ireland (NI) and Scottish mortality and population data were collected from the WHO cause of death database (World Health Orginization, 2015). UK mortality data was available for the years 1950 to 2010 apart from 1998 to 2000. International Statistical Classification of Diseases and Related Health Problems (ICD) codes for CHD used were as follows: ICD-7 A081, ICD-8 A083, ICD-9 410-414 and ICD-10 I20-I25 (Moran, et al., 2012). The age range was selected to cover those most at risk of preventable CHD with 40 the age from which the National Institute for Health and Care Excellence (NICE) recommend CVD risk is reviewed (NICE, 2014) and deaths below the age of 75 considered premature (Townsend, Williams, Bhatnagar, Wickramasinghe, & Rayner, 2014).Regional mortality and population data was provided by the ONS (ONS, 2014) (ONS, 2013).

Dietary intakes were sought to match against available mortality data. Household UK dietary intakes were available from the National Food Survey (NFS) between 1950 and 2000 (DEFRA, 2013). Combined household and eating out intakes were available for 2001-2010 from the Family Expenditure Survey (EFS) and Living Costs and Food Survey (LCFS) (DEFRA, 2014) and at national and regional level (DEFRA, 2015). As England & Wales mortality was combined the mean dietary data from the two countries was used.

CHD prevalence was available for England from the Health Survey for England (HSE) (HSE, 2012) and Scotland Health Survey (SHS) (SHS, 2013). Age specific UK total cholesterol (TC) trends were not identified so age standardised estimates for men and women aged over 25 were taken from the Global Health Observatory Data Repository

(WHO, 2014). Where datasets contained data that predated available country level dietary intakes UK dietary data was used for consistency.

Statistical analysis

Corresponding age specific mortality and population data for male and females aged 40-74 was extracted from collected data using Microsoft Excel 2010 and calculated into a per 100,000 mortality rate. This was done by dividing gender age specific CHD mortality by corresponding age and gender population and multiplying by 100,000.

Data which failed to achieve normality of distribution was analysed using Spearman's rank correlation (r_s). Normally distributed data was analysed using Persons moment correlation (r). Correlations were performed using SPSS (Version 22.0). Correlations were compared against the Cohen & Holliday (1996) classification to assess the strength of relationship (Cohen & Holliday, 1996).

Results

UK Trends

Historical trends for SFA%TE, TF%TE and CHD are shown in figure 1, in the UK CHD mortality in those ages 40-74 peaked in 1978 in males at 710 deaths per 100,000, female mortality also spiked in 1978 at 275 deaths per 100,000 second only to a peak of 288 deaths per 100,000 deaths recorded in 1951. From 1978 Male CHD mortality declined by 79% to 149 deaths per 100,000 in 2010. Female CHD mortality dropped by 83% from 1978 and 84% from 1951 to 47 deaths per 100,000 in 2010. From 1978 to 2010 relative TF intake decreased by 3.4% and SFA by 4.6%.

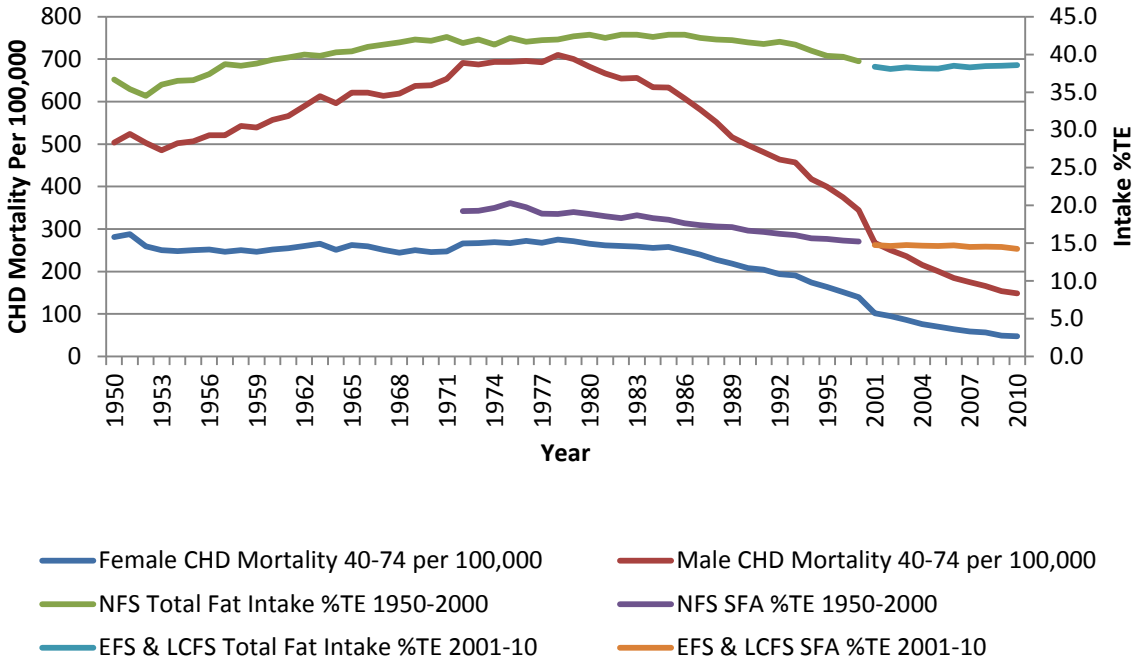

Figure 1: Trends in dietary SFA%, TF%TE and CHD mortality in the UK 1950 to 2010

Mean intakes and mortality rates for the UK and constituent countries are listed in Table 1 and correlations displayed in Table 2. From 1950 to 1997 there was a significant modest correlation in men (r_s =0.49,*P*<0.01) and low correlation in women (r_s =0.34,*P*<0.01) between CHD and absolute total fat intake (g) . From 1972 to 1997, the time period where SFA intake from the NFS is available, the relationship changed to very high in both men (r_s=0.94, *P<0*.01) and women (r_s= 0.93, *P*<0.01). The significance and strength of correlation remained during the EFS and LCFS survey 2001 to 2010. The relationship between relative TF%TE intake was less strong apart from a significant high correlation (*P*<0.01) when spanning NFS, EFS and LCFS surveys in men 1950 to 2010 and both men and women 1972 to 2010. Both relative and absolute

intakes of SFA were significantly highly to very highly correlated with CHD mortality (*P*<0.01).

Table 1: Mean diet and CHD mortality

	Male CHD Mortality Ages 40-74 per 100,000	Female CHD Mortality Ages 40-74 per 100,000	TF (g)	TF (%TE)	SFA (g)	SFA (%TE)
UK						
NFS 1950-1997	576.3 ± 93.9	243.6 ±33.3	103.48 ±12.33	40.46 ±2.56	-	-
NFS SFA 1972-1997	584.0 ±118.3	233.7 ±41.9	96.13 ±10.80	41.68 ±0.94	41.38 ±7.42	17.81 ±1.51
NFS, EFS & LCFS 1950-2010	511.3 ±167.7	213.8 ±72.9	-	40.10 ±2.12	-	-
NFS SFA, EFS & LCFS 1972-2010	477.3 ±202.2	188.4 ±82.6	-	40.76 ±1.71	-	16.92 ±1.94
EFS & LCFS 2001-2010	199.8 ±41.4	70.7 ±19.0	96.69 ±1.63	38.35 ±0.18	36.85 ±1.05	14.61 ±0.18
England & Wales*						
EFS & LCFS 2001-2010	194.3 ±41.2	67.4 ±18.3	97.55 ±2.11	37.14 ±0.24	37.22 ±1.44	14.17 ±0.15
Scotland						
EFS & LCFS 2001-2010	252.8 ±45.4	100.2 ±23.7	97.07 ±1.92	36.78 ±0.35	37.86 ±23.66	14.34 ±0.26
Northern Ireland						
EFS & LCFS 2001-2010	207.1 ±39.1	77.5 ±19.5	97.63 ±3.29	36.79 ±0.34	37.61 ±1.58	14.18 ±0.30
***Mean combined England & Wales diet**						

Table 2: Correlation between dietary SFA, TF and CHD Mortality

	Time Period	Male CHD Mortality Ages 40-74 per 100,000	Female CHD Mortality Ages 40-74 per 100,000
Total Fat	**UK**		
g	NFS 1950-1997	r_s=0.49**	r_s =0.34*
	NFS 1972-1997	r_s =0.94**	r_s =0.93**
	EFS & LCFS 2001-2010	r=0.89**	r=0.89**
	England & Wales		
	EFS & LCFS 2001-2010	r=0.84**	r=0.85**
	Scotland		
	EFS & LCFS 2001-2010	r=0.16	r=0.10
	Northern Ireland		
	EFS & LCFS 2001-2010	r=0.27	r=0.35
Total Fat	**UK**		
%TE	NFS 1950-1997	r_s =0.64**	r_s =0.12
	NFS, EFS & LCFS 1950-2010	r_s =0.71**	r_s =0.34**
	NFS 1972-1997	r_s =0.50**	r_s =0.49*
	NFS SFA, EFS & LCFS 1972-2010	r_s =0.78**	r_s =0.77**
	EFS & LCFS 2001-2010	r=-0.59	r=-0.58
	England & Wales		
	EFS & LCFS 2001-2010	r=-0.30	r=-0.29
	Scotland		
	EFS & LCFS 2001-2010	r=-0.18	r=-0.29
	Northern Ireland		
	EFS & LCFS 2001-2010	r=-0.15	r=-0.89
SFA	**UK**		
g	NFS 1972-1997	r_s =0.95**	r_s=0.94**
	EFS & LCFS 2001-2010	r=0.94**	r=0.94**
	England & Wales		
	EFS & LCFS 2001-2010	r=0.89**	r=0.89**
	Scotland		
	EFS & LCFS 2001-2010	r=0.75*	r=0.71*
	Northern Ireland		
	EFS & LCFS 2001-2010	r=0.53	r=0.59
SFA	**UK**		
%TE	NFS 1972-1997	r_s =0.96**	r_s=0.96**
	NFS, EFS & LCFS 1972-2010	r_s=0.98**	r_s=0.98**
	EFS & LCFS 2001-2010	r=0.80**	r=0.81**
	England & Wales		
	EFS & LCFS 2001-2010	r_s =0.67*	r_s =0.67*
	Scotland		
	EFS & LCFS 2001-2010	r_s =0.62	r_s =0.62
	Northern Ireland		
	EFS & LCFS 2001-2010	r=0.62	r=0.64*
	**Significant to *P*<0.01 *Significant to *P*<0.05		

National Trends

Between 2001 and 2010 CHD mortality fell in all countries within the UK. In England and Wales male CHD mortality fell 45% from 262 to 144 deaths per 100,000, female CHD mortality fell 54% from 98 to 45 deaths per 100,000. In the same period relative SFA intake fell by 0.54%TE to 13.8%TE with absolute intake declining by 11% from 39.3g to 35.0g. TF rose by 0.2%TE to 37.4%TE but absolute intake fell 7% from 102.4g to 95.2g. In Scotland Male CHD mortality fell by 40% from 320 deaths per 100,000 to 193, female CHD mortality fell by 49%, from 137 to 70 deaths per 100,000. During this time SFA intake fell by 0.7%TE to 13.7%TE and absolute SFA by 5% from 38.9g to 36.8g. In Northern Ireland CHD male mortality fell by 40% from 271 to 162 deaths per 100,000, female CHD mortality fell 53% from 114 to 53 deaths per 100,000. SFA intake fell 0.8%TE to 13.5%TE and absolute intake by 13% from 39.7g to 34.5g. TF intake fell by 0.2%TE to 36.2%TE with absolute intake declining by 9% from 101.5g to 92.4g.

Absolute TF (g) but not %TE was significantly highly correlated with CHD in males and females in England and Wales (P<0.01). TF was not significantly correlated with CHD in Scotland of NI.

Table 2 shows absolute and relative SFA intake were significantly highly correlated with male and female CHD mortality in England & Wales (P<0.01) and with absolute intakes in Scotland (P<0.05). There was a significant (P<0.5) modest correlation between CHD and SFA %TE in females but not males in NI.

Differences within the UK

Table 3 shows CHD mortality and dietary TF and SFA intake at UK, national and regional level in 2010. Scotland had the highest CHD mortality but has a lower relative TF and SFA intake than the UK as a whole. The South East of England had the lowest mortality rate however had a higher relative intake of TF and SFA than Scotland. Conversely absolute intake of TF and SFA are higher in Scotland than both the South East and UK overall.

Table 3: CHD Mortality, TF and SFA intake in the UK, constituent countries and regions of England in 2010

	Male 40-74 CHD Mortality Ages 40-74 Per 100,000	Female CHD Mortality Ages 40-74Per 100,000	Total Fat (%TE)	Total Fat (g)	SFA (%TE)	SFA (g)
UK	149	47	38.6	95.2	14.2	35.1
Scotland	193	70	36.3	97.5	13.7	36.8
England & Wales*	144	45	37.4	95.2	13.8	35.0
NI	162	53	36.2	92.4	13.5	34.5
North East	165	48	36.6	91.0	13.8	34.3
North West	176	62	38.0	95.1	13.8	34.6
Yorkshire and The Humber	163	57	37.4	94.8	13.8	35.0
East Midlands	148	46	37.0	94.8	13.9	35.7
West Midlands	154	47	37.1	92.0	13.4	33.1
East of England	127	40	37.3	101.0	13.9	37.7
London	120	37	38.0	91.3	13.4	32.1
South East	115	32	37.7	94.9	14.2	35.7
South West	124	35	37.6	100.6	14.0	37.5
Mean	149.2	47.7	37.34	95.05	13.81	35.17
SD	±23.2	±10.9	±0.69	±3.16	±0.28	±1.59
***Mean Combined England & Wales Diet**						

At UK, national and regional level show there was no significant correlation between SFA, TF and CHD mortality in 2010. In females there was a high negative correlation

between female CHD and absolute TF intake when combining UK, national and regional data. At a national level there was a high correlation between absolute but not relative SFA intake, absolute TF intake was negatively correlated with CHD in both males and women. At regional level there was a low correlation between SFA, TF and CHD.

Impact of Guidelines

Table 4 shows recommended intakes from 1974 (DHSS, 1974), 1984 (DHSS, 1984) and 1994 (DOH, 1994) guidelines for SFA%TE and TF%TE were not met. Prior to the publication of the first COMA guidelines on diet and CHD there was a significant very high correlation as shown in Table 5 between TF% intake and male but not female CHD mortality (r=0.91, $P<0.01$). Between the 1974 guidelines and 1984 guidelines there was significant modest relationship between SFA %TE and female CHD mortality (r=0.66, $P<0.05$). Between the 1984 and 1994 guidelines both male and female CHD mortality was very highly correlated with SFA%TE and TF%TE intake ($P<0.01$). From the publication of the 1994 guidelines to 2010 a significant very high correlation remained between male and female CHD with SFA%TE but not TF%TE ($P<0.01$).

Table 4: Mean UK CHD Mortality Ages 40-74 per 100,000 and percentage TF and SFA intake						
	Male CHD Mortality Ages 40-74 Per 100,000	**Female CHD Mortality Ages 40-74 per 100,000**	**TF %TE**	**TF Guideline**	**SFA %TE**	**SFA Guideline**
Pre 1974 Guidelines 1950-1974	581.9 ±65.2	256.8 ±11.0	39.33 ±2.33	-	-	-
Between 1974 & 1984 guidelines	680.1 ±23.8	265.7 ±6.1	42.16 ±0.41	Reduce	19.05 ±0.64	Reduce
Between 1984 & 1994 guidelines	531.0 ±75.2	219.9 ±8.5	41.83 ±0.62	35%	17.00 ±0.85	15%
Current Guidelines 1994-2010*	252.4 ±94.2	95.4 ±44.1	38.76 ±0.74	35%	14.85 ±0.43	10%

*2001-2010 dietary data includes eating out

Table 5: Correlation between UK CHD Mortality Ages 40-74 per 100,000, TF and SFA			
	Gender	**TF %TE**	**SFA%TE**
Pre 1974 Guidelines 1950-1974	Male	r =0.91**	-
	Female	r_s =-0.14	-
Between 1974 & 1984 guidelines	Male	r=-0.51	r=0.66*
	Female	r=-0.55	r=0.60
Between 1984 & 1994 guidelines	Male	r=0.93**	r=0.99**
	Female	r=0.94**	r=0.99**
Current Guidelines 1994-2010	Male	r_s=0.40	r=0.97**
	Female	r_s=0.40	r=0.97**
****Significant to *P*<0.01** ***Significant to *P*<0.05**			

Prevalence

Table 6 shows prevalence of CHD from the HSE and SHS. In England CHD prevalence has risen while both UK TF%TE and SFA%TE have fallen. In Scotland prevalence has fluctuated in men and fallen in women while Scottish dietary SFA%TE has fallen. TF%TE like male prevalence has fluctuated. Prevalence of CHD was higher in Scotland than England in 2003 with a lower intake of SFA and TF consumed in Scotland. Similarly mean prevalence although spanning different years was higher in Scotland with a lower mean intake of TF%TE and SFA%TE.

Table 6: CHD Prevalence , SFA and TF in England and Scotland in adults aged 16+								
England	**1994**	**1998**	**2003**	**2006**	**2008**	**2009**	**2010**	**Mean**
Male %	6.0	7.1	6.4	6.5	-	-	-	6.50 ±0.45
Female %	4.1	4.6	4.1	4.0	-	-	-	4.20 ±0.27
UK TF %TE	40.5	38.8	38.3	38.5	-	-	-	39.03 ±1.00
UK SFA %TE	15.6	15.2	14.8	14.7	-	-	-	15.08 ±0.41
Scotland	**1994**	**1998**	**2003**	**2006**	**2008**	**2009**	**2010**	**Mean**
Male %	-	-	8.2	-	6.9	7.4	7.5	7.50 ±0.54
Female %	-	-	6.5	-	5.6	5.2	5.2	5.63 ±0.61
TF%TE	-	-	36.8	-	37.0	37.1	36.3	36.80 ±0.36
SFA%TE	-	-	14.5	-	14.3	14.1	13.7	14.15 ±0.34

Neither relative SFA nor TF were significantly correlated with CHD prevalence. There was a high non-significant correlation between Scottish CHD prevalence and SFA%TE intake in women (r=0.82) but not men. In England there was a negative modest correlation between TF and CHD prevalence (r=-0.58).

Saturated Fat and Cholesterol

There was a very high significant correlation between SFA %TE intake from the NFS, EFS and LCFS surveys (mean 16.15%TE ±1.50) with both male (mean 5.75mmol/l ±0.27, r=0.99, *P*<0.01) and female (mean 5.72mmol/l ±0.28, r=0.98, P<0.01) cholesterol levels between 1980 to 2009.

Discussion

The results of this study show a significant correlation between trends in SFA intake and CHD mortality in males and females aged 40-74 at a UK population level. The association is less consistent across nations although a relationship still exists. At a regional level there was a weak relationship between SFA or TF intake and CHD. The

association between TF and CHD however is less clear with the strength of the relationship dependent on time frame and gender. These findings are supported by Keys who reported a high correlation between CHD and SFA (r=0.84) but only a modest correlation with between TF (r=0.50) in the Seven countries study (Keys A. , 1980).

The lack of association between regions may be due to the lack of available age specific mortality data with the single year comparison used not necessarily representative of longer term trends. Furthermore the smaller sample size and variation in population size may have confounded results. The 1974 COMA panel noted the unexplained existence of regional differences in CHD mortality within the UK should prove cautionary in any application to the nation as a whole of advice based on the results of any dietary trial (DHSS, 1974).

The relationship between TF and CHD between 1950 and 1997 is far weaker than between 1972 and 1997, the period that SFA intake is recorded consistently. This can be explained by the fact CHD mortality was still rising from 1950 and not peaking until 1978. Differences in mean intakes over the period may also have affected the relationship with a higher absolute intake yet lower %TE intake between 1950 and 1997 than 1972 and 1997, thus suggesting a difference in energy intake which was not examined in this study. This may also explain why between 1972 and 1997 absolute TF intake shows only a modest correlation with CHD yet a very high correlation with TF %TE. The disparity between absolute and relative intakes on significance has been reported in other studies (Posner, et al., 1991) (McGee, Reed, Yano, Kagan, & Tillotson, 1984). Differences over time could be the result of a lag time between reduction of fat

and CHD with studies suggesting a lag time of five, ten or even twenty five years (Law, Wald, & Thompson, 1994), (Kuulasmaa, et al., 2000), (Rose, 1982), (Law & Wald, 1999).

While the findings of the study show a positive correlation between SFA and CHD and to a lesser extent TF and CHD it does not demonstrate a causal link, it does show however that over time SFA and TF intakes have fallen along with CHD mortality rates. The disparity between the 79% decline in CHD mortality in males and 83% in females from 1978 to 2010 compared to a 4.6% reduction in dietary SFA and 3.4% in TF intake over the same time period may undermine the veracity of association between SFA and CHD. This is supported by the non-association reported between CHD and SFA in UK observational studies (Fehily, Yarnell, Sweetnam, & Elwood, 1993), (Morris, Marr, & Clayton, 1977). However positive associations have been reported in the UK in health conscious men and women (Mann, Appleby, Key, & Thorogood, 1997) and in women aged 40 to 75 (Boniface & Tefft, 2002). A limitation of this study is that dietary data is not gender or age specific nor does it give information on socio economic status which may have affected results, although no clear pattern in TF or SFA and income was reported in the National Diet and Nutrition Survey (NDNS) (Public Health England, 2014).

The major weakness of this study is the dietary data used. The NFS was completed by a single diary keeper and made no account for food or drink purchased outside the home or without the diary keepers knowledge whereas in the EFS and LCFS diaries were kept by all household members (DEFRA, 2013). While adjusted historical intakes were available from 1974 to account for potential underreporting in the NFS the data

was not used as the adjustment made the assumption the level of underreporting was constant despite the intake of commonly underreported foods less common in 1974 (DEFRA, 2013). The reduction in SFA and TF intake shown in this study is validated by data from the NDNS which also has recorded a decline (Department of Health, 2011). No account for food wastage or underreporting was made in this study which may have confounded results, analysis of NDNS data estimated 25% of male and females underreported (Rennie, Coward, & Jebb, 2007).

A number of factors have influenced the decline in CHD mortality rates, It has been suggested that 58% of the decline in CHD is due to reductions in major risk factors with smoking alone accounting for 48% with the remaining 42% of the decline due to improved treatments (Unal, Critchley, & Capewell, 2005). Similar findings for the effect of improved treatment on CHD have been reported in Scotland and England (Bajekal, et al., 2012) (Hotchkiss, et al., 2014). This is supported by the increase in prescriptions and surgical interventions in past decades, in England alone prescriptions to treat diseases of the circulatory system rose from 46,252 in 1981 to 285,530 in 2010, in the UK the number of coronary artery bypass (CABG) surgeries and Percutaneous coronary interventions totalled 105,662 compared to 2,297 coronary artery bypasses in 1977 (Townsend, Williams, Bhatnagar, Wickramasinghe, & Rayner, 2014)

Comparison of countries within the UK demonstrates variations in CHD mortality, it has been suggested much of the mortality gap between England and Scotland is due to non-dietary factors with SFA intake across the countries having very little impact on

variation in mortality rates (Scarborough, Morgan, Webster, & Rayner, 2011). Geographical differences have been shown in other studies (Kushi, et al., 1985) (Marmot & Syme, 1976) which may explain differences between countries of the UK.

The evidence supporting the introduction of UK dietary guidelines has been questioned (Harcombe, et al., 2015), to address this sub analysis of trends was carried out to assess the impact of each edition of dietary guidelines and the evidence before and since. Results were mixed but trends since the publication of current (DOH, 1994) and previous guidelines (DHSS, 1984) support the association between SFA%TE and TE with the significance remaining despite a drop in mean SFA intake over time. The association between SFA and CHD was however weaker prior to guidelines becoming policy in 1984 which may support the findings of Harcombe et al.

A recent randomised control trial demonstrated following current guidelines reduces risk of heart disease (Reidlinger, et al., 2015) however it is clear recommendations have not been met yet CHD has continued to decline, would it be expected that a further reduction in SFA and TF result in a further decline?. The only trial identified to have tested a reduced fat diet reporting a null association with the low fat diet described as unpleasant (Ball, et al., 1965). The lack of adherence to recommendations may question if they are achievable or desirable, especially for those a low risk of CHD. If guidelines continue not to be met then perhaps a switch from population advice to a more targeted approach aimed at those at high risk may be more appropriate.

Considering the relationship between SFA and TF with CHD mortality it would be expected that a similar reduction in CHD morbidity may be seen. The findings of this

study however dispute this although long term data at a UK level was not found which may have influenced results. This relationship can in part by explained by a higher survival rate resulting in an increase in prevalence (Davies, Smeeth, & Grundy, 2007) increasing the burden of the disease (Allender, Scarborough, O'Flaherty, & Capewell, 2008). It has been suggested that better diagnostic techniques may have increased diagnosis rates and thus prevalence (Lampe, Morris, Whincup, Walker, Ebrahim, & Shaper, 2001). Furthermore improvements in diagnosis may explain the rise seen in CHD mortality up to the 1970's (Lozano, Murray, Lopez, & Satoh, 2001).

Long term data on TC levels was limited; the findings of this study demonstrate a significant positive correlation between TC and SFA%TE which supports the guideline advice to reduce SFA however the data used was not age specific which may have affected results. For this reason the relationship between CHD mortality and TC was not included in this study. There is evidence however that questions the association between TC and CHD (Prospective Studies Collaboration, 2007) (Bathum et al., 2013) (Schatz et al., 2001).

A further limitation of the study is its clinical application, food choices were not analysed as the most recent COMA dietary guidelines (1994) do not recommend consumption or reduction of specific foods to meet targets. The lack of information pertaining to ethnicity and socioeconomic status information is not just a limitation of this study with the quality and availability of data relating to CHD in the UK criticised for being inadequate considering it is the largest cause of death (Unal, Critchley, & Capewell, 2003).

The main strength of this study is its simplicity using available data to evaluate the relationship between TF, SFA and associated factors with CHD. Whereas observational studies such as Kushi et al (1985) assessed individuals diet at baseline without follow up in a twenty year study the strength of this study is it looks at continued intakes and although data used is at a population not individual level it would be expected that the relationship still be valid and potentially more appropriate when evaluating population guidelines.

Conclusion

The results of this study support current population dietary guidelines to reduce SFA and TF show differences in regions and countries and the differences in intake over time compared to the CHD question the association between SFA, TF and CHD. It is clear further research is needed and it would be recommend dietary guidelines updated in light of continued non adherence and continued decline of CHD in the UK.

Word count : 4153

References

Allender, S., Scarborough, P., O'Flaherty, M., & Capewell, S. (2008). Patterns of coronary heart disease mortality over the 20th century in England and Wales: Possible plateaus in the rate of decline. *BMC Public Health, 8*(148).

Bajekal, M., Scholes, S., Love, H., Hawkins, N., O'Flaherty, M., Raine, R., et al. (2012). Analysing Recent Socioeconomic Trends in Coronary Heart Disease Mortality in England, 2000–2007: A Population Modelling Study. *PLOS Medicine, 9*(6).

Ball, K. P., Hanington, E., McAllen, P. M., Pilkington, T. R., Richards, J. M., Sharland, D. E., et al. (1965, Sep 11). Low-Fat Diet in Myocardial Infarction. *Lancet*(7411), 501-504.

Bathum, L., Depont, R., Christensen, L. E., Pedersen, P. L., Larsen, J., & Nexoe, J. (2013). Association of lipoprotien levels with mortality in subjects aged 50+ without previous diabeities or cardiovascular disease: A population-based register study. *Scandinavian Journal of Primary Health Care*(31), 172-180.

Boniface, D., & Tefft, M. (2002). Dietary fats and 16-year coronary heart disease mortality in a cohort of men and women in Great Britain. *European Journal of Clinical Nutrition, 56*(8), 786-792.

Bufton, M. W. (2005). British Expert Advice on Diet and Heart Disease c.1945-2000. In V. Berridge, *Making Health Policy: Networks in Research and Policy After 1945* (First ed., pp. 125-148). Amsterdam: Rodopi Bv Editions.

Chowdhury, R., Warnakula, S., Kunutsor, S., Crowe, F., Ward, H. A., Johnson, L., et al. (2014, March 18). Association of Dietary, Circulating, and Supplement Fatty Acids With Cornary Risk. *Annals of Internal Medicine, 160*(6), 398-406.

Cohen, L., & Holliday, M. (1996). *Practical Statistics for Students: An Introductory Text.* London: Paul Chapman Publishing.

Davies, A., Smeeth, L., & Grundy, E. (2007). Contribution of changes in incidence and mortality to trends in the prevalence of coronary heart disease in the UK: 1996 2005. *European Heart Journal, 28*(1), 2142-7.

DEFRA. (2013, January 3). *Defra, UK - National Food Survey.* Retrieved August 6, 2015, from The National Archives: http://webarchive.nationalarchives.gov.uk/20130103014432/http://www.defra.gov.uk/statistics/files/defra-stats-family-food-nfs-nutshist.xls

DEFRA. (2013, January 4th). *Family food methodology.* Retrieved August 15th, 2015, from The National Archives: http://webarchive.nationalarchives.gov.uk/20130103014432/http://www.defra.gov.uk/statistics/files/defra-stats-foodfarm-food-methodology-nfsadjust-121214.pdf

DEFRA. (2014, December 11). *Family food datasets.* Retrieved August 6, 2015, from Gov.uk: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/383452/UKInt-11dec14.ods

DEFRA. (2015, December 11). *Family food datasets*. Retrieved August 8, 2015, from Gov.uk: https://www.gov.uk/government/statistical-data-sets/family-food-datasets

Department of Health. (2011, July 21). *National Diet and Nutrition Survey: Headline results from Years 1 and 2 (combined) of the rolling programme 2008-9 - 2009-10.* Retrieved August 6, 2015, from Gov.uk: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216485/dh_128556.pdf

DHSS. (1974). *Diet And Coronary Heart Disease.* Department of Health and Social Security. London: Her Majesty's Stationary Office.

DHSS. (1984). *Diet And Cardiovascular Disease* (Vol. 28). London: Her Majesty's Stationery Office.

DOH. (1994). *Report on Health and Social Subjects 46 Nutritional Aspects of Cardiovascular Disease.* London: HMSO.

Fehily, A., Yarnell, J., Sweetnam, P., & Elwood, P. (1993). Diet and incident ischaemic heart disease: the Caerphilly Study. *British Journal of Nutrition , 69*(2), 303-314.

Harcombe, Z., Baker, S., Cooper, S., Davies, B., Sculthorpe, N., DiNicolantonio, J., et al. (2015). Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review and meta-analysis. *Open Heart, 2*(1), 1-7.

Hotchkiss, J., Davies, C., Dundas, R., Hawkins, N., Jhund, P., Scholes, S., et al. (2014). Explaining trends in Scottish coronary heart disease mortality between 2000 and 2010 using IMPACTSEC model: retrospective analysis using routine data. *BMJ, 348*.

HSE. (2012, December 20). *Health Survey for England - 2011, Trend tables [NS].* Retrieved August 9, 2015, from http://www.hscic.gov.uk/catalogue/PUB09302/HSE2011-Adult-trend-tbls.xls

Keys, A. (1980). *Seven Countries: A Multivariate Analysis of Death and Coronary Heart Disease.* Cambridge: Harvard University Press.

Kushi, L., Lew, R., Stare, F., Ellison, C., Lozy, M., Bourke, G., et al. (1985). Diet and 20-Year Mortality from Coronary Heart Disease — The Ireland–Boston Diet–Heart Study. *New England Journal of Medicine, 312*, 811-818.

Kuulasmaa, K., Tunstall-Pedoe, H., Dobson, A., Fortmann, S., Sans, S., Tolonen, H., et al. (2000, Febuary 26). Estimation of contribution of changes in classic risk factors to trends in

coronary-event rates across the WHO MONICA Project populations. *The Lancet, 355*, 657-87.

Lampe, F., Morris, R., Whincup, P., Walker, M., Ebrahim, S., & Shaper, A. (2001). Is the prevalence of coronary heart disease failing in British men? *Heart, 86*, 499-505.

Law, M. R., Wald, N. J., & Thompson, S. G. (1994, Feb 5). By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *BMJ, 308*(6925), 367-372.

Law, M., & Wald, N. (1999, May 29). Why heart disease mortality is low in France: the time lag explanation. *BMJ, 318*(7196), 1471-1480.

Lozano, R., Murray, C., Lopez, A., & Satoh, T. (2001). *Miscoding and misclassification of ischaemic heart disease mortality.* Geneva: WHO.

Mann, J., Appleby, P., Key, T., & Thorogood, M. (1997). Dietary determinants of ischaemic heart disease in health conscious individuals. *Heart, 78*, 450-455.

Marmot, M., & Syme, L. (1976). Acculturation and Coronary Heart Disease in Japanese-Americans. *American Journal of Epidemiology, 104*(3), 225-247.

McGee, D., Reed, D., Yano, K., Kagan, A., & Tillotson, J. (1984). Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *American Journal of Epidemiology, 119*(5), 667-676.

Moran, A., Oliver, J., Mirzaie, M., Forouzanfar, M., Chilov, M., Anderson, L., et al. (2012). Assessing the Global Burden of Ischemic Heart Disease. *Global Heart, 7*(4), 315-329.

Morris, J., Marr, J., & Clayton, D. (1977). Diet and heart: a postscript. *British Medical Journal, 2*, 1307-1314.

NICE. (2014, July). *Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease.* Retrieved September 17, 2015, from NICE: http://www.nice.org.uk/Guidance/CG181/Evidence

ONS. (2013, April 30). *Population Estimates for England and Wales, Mid-2002 to Mid-2010 Revised (Subnational).* Retrieved August 8, 2015, from The Office for National Statistics: http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-forengland-

ONS. (2014, October 3). Personal Communication: Regional Mortality Statistics Request.

Posner, B., Cobb, J., Belanger, A., Cupples, A., D'Agostino, R., Stokes, J., et al. (1991). Dietary Lipid Predictors of Coronary Heart Disease in Men. *JAMA, 151*(6), 1181-1187.

Prospective Studies Collaboration. (2007). Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55000 vascular deaths. *The Lancet, 370*, 1829-39.

Public Health England. (2014, May 14). *National Diet and Nutrition Survey: results from Years 1 to 4 (combined) of the rolling programme for 2008 and 2009 to 2011 and 2012.* Retrieved September 16, 2015, from Gov.uk: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/310995/NDNS_Y1_to_4_UK_report.pdf

Reidlinger, D., Darzi, J., Hall, W., Seed, P., Chowienczyk, P., Sanders, T., et al. (2015). How effective are current dietary guidelines for cardiovascular disease prevention in healthy middle-aged and older men and women? A randomized controlled trial. *American Journal of Clinical Nutrition, 101*(5), 922-930.

Rennie, K., Coward, A., & Jebb, S. (2007). Estimating under-reporting of energy intake in dietary surveys using an individualised method. *British Journal of Nutrition, 97*(6), 1169-1176.

Rose, G. (1982, May 29). Incubation period of coronary heart disease. *BMJ, 284*(6329), 1600-1601.

Scarborough, P., Morgan, R., Webster, P., & Rayner, M. (2011). Differences in coronary heart disease, stroke and cancer mortality rates between England, Wales, Scotland and Northern Ireland: the role of diet and nutrition. *BMJ, 1*(1), 1-7.

Schatz, I., Masaki, K., Yano, K., Chen, R., Rodriguez, B., & Curb, D. (2001, August 4). cholesterol and all-cause mortality in elderly people from the Honolulu Heart Program: a cohort study. *The Lancet, 358*, 351-355.

SHS. (2013, September 24). *SHeS Trend Tables 2012.* Retrieved August 8, 2015, from The Scottish Government: http://www.gov.scot/Topics/Statistics/Browse/Health/scottish-health-survey/Publications/Trendtables12

Siri-Tarino, P., Sun, Q., Hu, B. F., & Krauss, R. M. (2010). Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *American Journal of Clinical Nutrition , 91*(3), 535-46.

Townsend, N., Williams, J., Bhatnagar, P., Wickramasinghe, K., & Rayner, J. (2014). *Cardiovascular Disease Statistics, 2014.* London: British Heart Foundation.

Unal, B., Critchley, J. A., & Capewell, S. (2005, March 9). Explaining the Decline in Coronary Heart Disease Mortality in England and Wales Between 1981 and 2000. *Circulation, 109*, 1101-1107.

Unal, B., Critchley, J., & Capewell, S. (2003). Missing, mediocre, or merely obsolete? An evaluation of UK data sources for coronary heart disease. *Journal of Epidemiology and Community Health*(57), 530-535.

WHO. (2014). *WHO Methods And Data Sources For Country-Level Causes Of Death 2000-2012 Global Health Estimates Technical Paper WHO/HIS/HSI/GHE/2014.7.* Department of Health Statistics and Information Systems. Geneva: World Health Orginisation.

World Health Orginization. (2015). *Cause of Death Query online*. Retrieved August 6, 2015, from World Health Orginization: http://apps.who.int/healthinfo/statistics/mortality/causeofdeath_query/