Cognitive Impairment, Cardiovascular Disease Risk and Selected Nutrient Intake in a sample of 50 year old Cantabrians

by

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Preface

The Canterbury Health Ageing and Life Course (CHALICE) study is a longitudinal study investigating the health of 50 year olds living within the Canterbury District Health Board area. The study began in 2009 and aims to investigate physical, psychological and cognitive health amongst a cohort of 1000 participants over their life course. This thesis investigates relationships between cardiovascular disease risk, cognitive health and selected nutrients in the first 200 participants of the CHALICE study.

As part of this thesis, the candidate:

- Interviewed study participants.
- Was responsible for checking returned food and beverage diaries for any omissions or foods requiring clarification, and formulated questions for the interviewers to obtain the required information from participants.
- Entered food and beverage diaries into the nutrient analysis programme
- Was responsible (with two other MDiet students) for quality control of food and beverage diary data.
- Exported data from the nutrient analysis programme and created a database of all available nutrients.
- Updated existing protocols for food and beverage diary entry.
- Completed all statistical analyses presented in this thesis.
Abstract

Background: Mild cognitive impairment is a risk factor for dementia. Midlife cardiovascular disease risk factors such as high blood pressure and smoking have strong relationships to both cognitive impairment and dementia in late life. Intakes of several nutrients including fats and alcohol have been found to contribute to both cardiovascular disease and risk of cognitive impairment. Literature shows that cardiovascular disease risk factors at age 50, predict lifetime risk of both cardiovascular disease and dementia. The aim of this study is to investigate relationships between the intake of fats and alcohol in relation to cognitive impairment, and five-year cardiovascular disease risk (fatal and non-fatal) in 50 year old Cantabrians.

The hypotheses for this study are:
That fifty year olds with higher five year cardiovascular disease risk have a higher risk of mild cognitive impairment.
Secondly that fifty year olds who consume the recommended proportions of dietary fats and recommended amount of alcohol per day have a lower five year cardiovascular disease risk than those who consume outside of the recommendations.
Thirdly that fifty year olds who consume the recommended proportions of dietary fats and recommended amount of alcohol per day have a lower risk of mild cognitive impairment than those who consume outside of the recommendations.
Finally; that diet and heart health affect cognitive function.

Methods: Five year cardiovascular disease risk was assessed using the New Zealand Cardiovascular Risk Charts for each individual in the study. Mild cognitive impairment was assessed using the ‘Montreal Cognitive Assessment’ with a cut-off score of <26 is used to
define mild cognitive impairment. Saturated, monounsaturated and polyunsaturated fat intakes were assessed using the average intake over four days from an estimated four day food and beverage diary, and alcohol intake was calculated from the ‘Alcohol Use Disorders Identification Test’. Other factors affecting cognition such as education and depression were assessed. Fishers exact Chi square testing was used to determine differences between groups.

**Findings:** Those with a higher five year cardiovascular disease risk or depression are more likely to have mild cognitive impairment, but those with depression do not have increased five year cardiovascular disease risk. Participants with a lower level of education (secondary school or lower) are more likely to have both mild cognitive impairment and higher five year cardiovascular disease risk. A weak relationship that was approaching significance was found between saturated fat intake and mild cognitive impairment, but no other relationships were observed between dietary constituents and cardiovascular disease risk, or mild cognitive impairment.

**Conclusion:** This study was able to show that those with a higher cardiovascular disease risk are at risk of mild cognitive impairment and vice versa. No significant relationships were seen between saturated, monounsaturated, polyunsaturated fats or alcohol intake and cardiovascular disease risk and mild cognitive impairment, however it is likely this study was under powered. This study showed that depression, education level and five year cardiovascular disease risk have strong influences on risk of mild cognitive impairment in a sample of 50 year old Cantabrians.
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I would like to acknowledge my tutor dietitian Sharron Burford who has supported me in other aspects of my MDiet year including weekly dietetic clinics at the University of Canterbury and numerous community talks. Our monthly meetings have been a great way to reflect on all aspects of my year including progress during my research.

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<td>Adult Nutrition Survey=ANS</td>
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<td>Age Related Cognitive Decline= ARCD</td>
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<td>Alcohol Advisory Council=ALAC</td>
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<td>Alcohol Use Disorders Identification test</td>
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<td>Alzheimer’s disease= AD</td>
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<td>Apolipoprotein E=Apo-E</td>
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<td>Blood Pressure=BP</td>
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<td>Body Mass Index= BMI</td>
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<td>C-Reactive Protein= CRP</td>
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<td>Canterbury District Health Board =CDHB</td>
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<td>Canterbury Health Ageing and Lifecourse Study=CHALICE</td>
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<td>Cardiovascular Disease= CVD</td>
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<td>Confidence Interval=CI</td>
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<td>Coronary Heart Disease = CHD</td>
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<td>Diabetes Mellitus= DM</td>
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<td>Diastolic Blood Pressure= DBP</td>
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<td>Docosahexaenoic acid=DHA</td>
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<td>Echocardiogram =ECHO</td>
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<td>Eicosapentaenoic acid= EPA</td>
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<td>Electrocardiogram= ECG</td>
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<td>Food Frequency Questionnaire = FFQ</td>
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<td>Left Ventricular Hypertrophy=LVH</td>
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<td>Low Density Lipoprotein=LDL</td>
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<td>Mini Mental State Examination= MMSE</td>
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<td>Modified Mini Mental State Examination= 3MSE</td>
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<td>Monounsaturated Fatty Acids= MUFA</td>
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<td>Montreal Cognitive Assessment= MoCA</td>
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<td>Myocardial Infarction= MI</td>
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<tr>
<td>New Zealand European=NZEO</td>
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National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association = NINCDS-ADRDA
Non Insulin Dependant Diabetes Mellitus= NIDDM
Odds Ratio=OR
Omega Three Fatty Acids= n-3 FA
Omega –Six Fatty Acids=n6
Peripheral Artery Disease=PAD
Polyunsaturated Fatty Acids= PUFA
Randomised-Controlled-Trial= RCT
Recommended Daily Intake=RDI
Relative Risk=RR
Saturated Fatty Acids = SAFA
Seven Counties Study=SCS
Systolic Blood Pressure=SBP
Trans Fatty Acids = trans-FA
Triglycerides= TGs
Type 1 Diabetes Mellitus=T1DM
Type 2 Diabetes Mellitus=T2DM
United Kingdom=UK
United States of America=USA
Unsaturated Fatty Acid= USFAs
Vascular Dementia= VaD
World Health Organisation=WHO
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1 Introduction
Cardiovascular Disease (CVD) including myocardial infarction (MI), coronary artery disease (CAD), coronary heart disease (CHD), ischaemic stroke, transient ischemic attack, angina, peripheral artery disease (PAD) and coronary death is the leading cause of death in New Zealand. Cardiovascular Disease accounts for 40% of deaths in the New Zealand population annually (1). These rates are among the highest in the world. The Māori population suffers from CVD at much higher rates than non-Maori. Cardiovascular Disease risk for Pacific and Indian populations is also higher than in New Zealand Europeans.
There are many risk factors for CVD. Biological risk factors include increasing age, genetics, male sex, high blood pressure (BP), high cholesterol, diabetes mellitus (DM), smoking and diet. In New Zealand, one in five people older than 15 years of age smoke, and more than 208,000 people have diagnosed DM. It is known that older New Zealanders have a higher BP than those under 65 years, and that, on average, 30-51 year old males have higher cholesterol than recommended (2). Having a high body mass index (BMI) is a risk factor for CVD, type two diabetes mellitus (T2DM), high BP (hypertension) and other poor health outcomes. Around 64% of the New Zealand’s adult population is overweight or obese which is concerning, given that many early deaths are related to preventable conditions, including overweight and obesity and poor lifestyle choices (2).
In New Zealand, risk equations have been developed and published into risk charts to predict a person’s five-year risk of fatal and non-fatal CVD. The New Zealand Cardiovascular Risk Charts specifically use multiple risk factors, to identify CVD risk in primary care settings. The rationale behind this approach is that using preventative medicine, including medication and lifestyle advice, can prevent or at least postpone development of CVD in New Zealanders. One of the major modifiable risk factors for CVD is diet.
Dietary risk factors for CVD include high intake of saturated fat (SAFA) and trans fatty acids (trans-FA), abstaining or having a high intake of alcohol, and low intake of monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA).

Over the last 20 years studies have emerged addressing relationships between biological, including dietary, risk factors for CVD, and cognitive function. Mild cognitive impairment (MCI) is a state in which a person’s cognitive function is ‘impaired to an extent that is greater than would be anticipated for age, yet the patient does not meet criteria for dementia’ (3). People diagnosed with MCI in mid-life may go on to experience dementia in later life (4). In New Zealand in 2008, 40,746 people were living with dementia (5). The prevalence of dementia including Vascular Dementia (VaD) and Alzheimer’s disease (AD) are increasing as our population ages (5). The burden of dementia has major financial implications as well as an emotional and psychological burden for those with the disease and their families.

Much research has focused on the causes of cognitive impairment and subsequent dementia including genetic factors and lifestyle choices. Over that last 20 years studies have identified relationships between SAFA and unsaturated fatty acids (USFAs) and the incidence of MCI in the same directions as relationships with CVD.

In New Zealand, total fat intake (as a proportion of daily energy intake) is per day is 33.7% for men and 33.8% for women which lies within the recommendations of 20-35% energy from fat (2, 6). New Zealanders are consuming 13.1% of their energy as SAFA which is above the recommendation of 10% (2, 6). The intakes of MUFA are 12.4% and 12.3% for males and females respectively. This follows recommendations from studies promoting MUFA for health (2, 7). Intake of PUFA are 4.8% for males and 4.9% for females which is below the recommendation of 6-11% (2, 8). Overall, while New Zealanders are consuming an
appropriate amount of fat as a macronutrient, they are not consuming an appropriate fat profile which is having negative effects on CVD risk.

In order to work towards curing or preventing some dementias, it is important to identify risk factors. Given that MCI in mid-life predisposes a person to a higher risk of developing dementia, it is important to search for the reasons one would develop MCI or have impaired cognition younger than would be expected.

The Canterbury Health Ageing and Lifecourse Study (CHALICE) is in the early stages of recruiting 1000 50 year old Cantabrians to be followed up over their life course. The study aims to gain information on all aspects of health and aging, including data on physical health, cognitive health, mental and emotional health as well as biological data and food intake data. It is recommended that high risk people get CVD risk checks from their General Practitioner from age 35 and other members of the population at age 45 (men) and 55 (women) as this is when biological risk factors tend to become more prevalent and population rates of CVD begin to rapidly rise (9, 10). The CHALICE study is able to capture this time where CVD risk is becoming a relevant issue for the whole cohort of 50 year olds. Given that previous research shows that CVD risk factors in midlife can predict mid and late life cognitive function; this is also an important time to be looking at cognitive health of this population.

The purpose of this thesis is to investigate the relationships between a person’s five-year absolute CVD risk, as given by the New Zealand Cardiovascular Risk Charts, selected dietary risk factors for CVD, and MCI in the CHALICE study.
2 Literature review

2.1 Introduction

The relationship between overall CVD risk and cognition has not been previously described; however the relationship between individual biological risk factors and cognition has been explored. Selected dietary risk factors for CVD have been investigated in relation to cognitive function including fats and alcohol. The following literature review explores these relationships to present the current knowledge in these topic areas.

2.2 CVD Risk Scores

2.2.1 CVD Risk Chart Origin

In the 1940s it was recognised that CVD morbidity and mortality was increasing, although little was known about the contributing factors (11). The ‘Framingham Heart Study’, which began in 1948 in Framingham, United States of America (USA), set out to identify CVD risk factors to aid prevention (11). Blood measurements, medical tests and questionnaires were administered (11).

Major findings from the ‘Framingham Heart Study’ were that male sex, increasing age, smoking, hypertension and high serum cholesterol are the strongest risk factors contributing to CVD, and that other contributors are body weight, enlargement of the left ventricle and DM. These findings were confirmed by other large cohort studies along with identification of other risk factors such as a family history of CVD and specific dietary patterns (12, 13). Men experience MI on average nine years younger than women (14). Increasing age is a risk factor for CVD because of physiological changes the heart undergoes which increase the workload of the heart (15). It is also a risk factor due to longer time to accumulate other CVD risk factors such as hypertension (16).
The ‘Framingham Heart Study’ combined these factors 1967 in an attempt to predict CVD risk based on CVD mortality of a large cohort. The first study looked at sex, age, total cholesterol, systolic blood pressure (SBP), haemoglobin (Hb), smoking, electrocardiogram abnormality/left ventricular hypertrophy (LVH) and relative body weight as risk factors for CVD. It found that Hb was not a predictor, and that cholesterol, SBP and smoking were much stronger predictors than body weight (17). Cardiovascular disease risk scores based on data from the ‘Framingham Heart Study’ cohorts continue to be refined and further risk scores were developed (18-23)(See appendix A, table 8.1 on page 97).

In the early 2000s Framingham risk scores gained criticism due to their lack of transferability to other populations (24). However the Framingham risk score was also found to predict CVD well in some other populations such as Scottish men and women (25). Several other risk scores were developed which included new risk factors identified from other cohorts. In the early 2000s European cohorts such as were used to calculate new risk scores, for example ‘SCORE’, ‘DECODE’, ‘CUORE’, ‘Riskard’ and ‘PROCAM’ scores (26-30). They included additional risk factors such as triglycerides (TGs), family history of premature MI or CHD, fasting glucose, BMI, hypertension drug treatment and heart rate. It was thought that some of these risk factors might be able to produce a more sensitive risk score. From these, only family history has been included in other risk calculations as other risk factors were either not consistently associated with CVD risk or not practical to routinely include (26-30). It became apparent that lower CVD risk populations, such as Southern European populations, should derive their risk scores from similar populations to ensure accuracy in CVD predictions (28, 29).

From 2007 a new score: ‘Reynolds Risk Score’ was derived specifically for women based on data from a USA cohort. They suggested C-reactive protein (CRP) concentration could
contribute to CVD risk with other classic risk factors (31). In the late 2000s research from the United Kingdom (UK) showed that a deprivation score should be included as a risk factor. In other populations this would rely on availability and accuracy of material deprivation scores, however if available, is a valid consideration. (24, 25).

All of these scores were recommended for use in specific countries or continents and some were restricted to only men or women. Some scores may need further testing in other cohorts to see if they be extrapolated to other populations. These include the ‘DECODE score’ from European cohorts, and the ‘CUORE score’ from an Italian cohort which is intended for low risk populations (27, 28). A more detailed description of these studies and scores can be found in Appendix A, table 8.2 on page 100.

Common risk factors in all risk scores regardless of the population for which they are intended to be used include male sex, older age, higher BP, higher total cholesterol or cholesterol: high density lipoprotein cholesterol (HDL) ratio, smoking, DM or glucose intolerance. It has been recognised that SBP is a better measurement of risk than diastolic blood pressure (DBP) so SBP is usually used in isolation (32). It is also known that the total cholesterol: HDL ratio is the best cholesterol predictor of CVD risk (33). The most common additional risk factors in newer risk scores are family history of premature CVD event, BMI, deprivation score and hypertension treatment. Including extra risk factors may help the risk score become better at predicting CVD in certain populations.

2.2.2 New Zealand Cardiovascular Risk Charts

In the early 2000s New Zealand adopted the Framingham risk score for use in calculating the five-year New Zealand Cardiovascular Risk Score (1, 34). This score was designed for use in those aged 35-75 years who are not pregnant. Risk scores, in percentages, are calculated, with a risk score of <15% being desirable, and a risk score of >15% denotes ‘high risk’ of five-
year fatal or non-fatal CVD. Factors included were sex, age, smoking, BP, total: HDL cholesterol ratio and presence of DM(1). They are presented on the 2003 New Zealand Cardiovascular Risk Charts (See Appendix B page 125). In order to increase the applicability of the New Zealand Cardiovascular Risk Charts to the New Zealand population, several modifications were made (1, 35). Left ventricular hypertrophy has been omitted from New Zealand adaptations potentially because access to echocardiography is limited in primary care. It was decided that the Framingham score was not applicable for those with DM and renal disease or nephropathy, previous CVD event, or genetic lipid disorders as it underestimates risk in these groups. Instead, these people are automatically given a ‘very high risk’ of >20% five-year risk of CVD (1). The presence of one or more additional risk factors leads to the addition of five percent to the risk score as the Framingham equation is thought to underestimate their specific risk (1). These include Maori, Polynesian and Indian subcontinent ethnicity, which are further explained below (see appendix C, page 126 for other risk factors). In situations where a risk factor exceeds the upper measurement on the risk chart, an individual assessment is recommended as the risk may be underestimated by the chart equation (1). These conditions are used as the exceptions for the most up to date New Zealand Cardiovascular Risk Charts.

Over the past decade, the New Zealand Cardiovascular Risk Charts have been modified based on new evidence. The 2009 guidelines first showed the use of SBP only as it was deemed ‘the most informative of conventionally measured blood pressure parameters for CVD risk’ (32, 36). The latest New Zealand Cardiovascular Risk Charts use SBP as the measure of BP (refer to appendix D page 129). In 2012 a ‘risk trajectory approach’ was introduced focused on younger persons with current low score but presence of risk factors.
(9). This calculates the increases in risk that person will incur as they age (37) (refer to appendix E page 131 for examples).

Recently both the original Framingham score and the New Zealand modified Framingham risk score have been validated in a New Zealand cohort (35). The results show that while the original score overestimates risk for New Zealand Europeans (NZEO) and underestimates for other ethnicities, the modified score in use is overestimating risk for all ethnicities (35). On the other hand the score is providing an acceptable assessment of risk for New Zealanders and is able to identify those at risk. This is more beneficial than underestimating risk, and allows risk trajectory to be used along with lifestyle and medical interventions to prevent CVD events occurring. The UK have included a deprivation score for CVD risk as those in more deprived areas have a higher CVD risk (24, 25). There are no data to support the inclusion of such factors in New Zealand Cardiovascular Risk Charts at present.

2.2.3 Ethnicity and CVD risk

As described in the New Zealand Cardiovascular Risk Charts, Maori, Pacific or Indo-Asian people are automatically at a five percent higher five-year CVD risk than other groups (9). New Zealand statistics show the following CVD risk factors patterns among these groups to demonstrate some of the rationale behind the increased risk:

Maori, Pacific and NZEO adults have average BP and total cholesterol: HDL ratios within the normal ranges with blood pressures all tending to increase after 51 years of age, and total cholesterol: HDL ratio being higher in the most deprived. Maori averages are slightly higher than non-Maori however this is not statistically significant (2). The same data was not available for Indian groups, however it is known that, compared to other Asian groups, Indian men have significantly higher self reported BP and cholesterol (38).
There are higher rates of adult obesity among Maori than NZEO; 40.7% of Maori men are obese compared to 24.8% of NZEO men and 48.1% of Maori women are obese compared to 23.7% of NZEO women. There is higher rates of adult obesity among Pacific persons; 56.2% of Pacific males are obese and 59.5% of Pacific females are obese (2). Comparatively, only 7.1% of Indian men and 14.8% of Indian women are obese, however there is a relatively high proportion of overweight Indian persons (27.1% of males and 38.1% of females) (38). These statistics show that BMI is likely to be a large contributor to the increase in risk in Maori, Indian and Pacific populations. Genetic differences in muscle mass and skeletal mass have a place for debate when comparing the BMI of these populations.

The prevalence of DM (diagnosed and undiagnosed) is higher in Maori and Pacific than NZEO; 9.7% of Maori Males, 9.8% of Maori females, 14.8% of pacific males and 14.9% of Pacific females have diabetes compared to 7.5% of NZEO males and 4.7% of NZEO females (2). More Maori and Pacific are smokers than NZEO/other ethnicities and Asian persons; 45.8% of Maori, 36.2% of Pacific, 20% of NZEO/other ethnicities and 12% of Asian persons, and Indian males make up around 18% of that group (38, 39).

Evidence from studies in this area indicates a higher rate of CVD death and hospitalisations in Indians in New Zealand compared to NZEO (40). Maori experience greater than two and a half times the CVD mortality and twice as many hospitalisations compared to non-Maori (41).

2.2.4 Conclusion

In conclusion, since 2003 the New Zealand Cardiovascular Risk Charts have been used to predict five-year CVD risk (fatal and non-fatal) in New Zealand adults. The Framingham equation has been used as the basis for these risk charts which are used in primary health to assess CVD risk in adults. Despite the criticism the equation has received in both New
Zealand and other populations, it is currently the best CVD predictor tool available for our population.

2.3 Diet and CVD risk

It is outside the scope of this thesis to discuss the relationship between all nutrients and CVD risk. Therefore this section specifically covers only some macronutrients, in particular, fats and alcohol which are widely accepted to have a role in contributing to CVD risk. Following these sections, the dietary intakes of New Zealanders and their related CVD health outcomes will be reviewed.

2.3.1 Dietary Assessment Methodology

Many studies reviewed in this section collected dietary intake information from participants, using one or more of several different methods. Some studies used ‘24 hour (intake) recalls’ or ‘dietary histories’ to get an idea of recent estimated intake, while others used ‘food frequency questionnaires’ (FFQ) which ask the subject to identify the foods which they have eaten (from lists), and how often, over a period of time (e.g. the last three months) (42). The most accurate way to measure intake is to have the participant record all foods eaten over a few days. This ensures that both small and large quantities of foods, and all beverages are included. Other methods are often unable to account for all foods one might consume. This is not a long term measure like an FFQ, unless participants record intake over many days (42). Some studies find it easier to collect data in larger studies is use of a measure of recent or usual intake such as an FFQ or a ‘dietary recall’ at the risk of them being less accurate. These methods are simple for participants to comply with and may encourage participation. It is important to acknowledge that while different studies use different methodologies (depending on their cohort), they are generally able to produce similar findings.
2.3.2 Nutritional risk factors for CVD

The ‘Seven Countries Study’ began in 1958 and was the pioneering longitudinal cohort study investigating dietary risk factors for CHD and health. It was made up of 16 cohorts in seven different countries involving 12,763 middle-aged men (12). A huge amount of the knowledge we have today about nutritional risk factors for CVD was sparked by findings from this study, and many other studies have attempted to model the methods used in this study and reproduce results in individual cohorts.

2.3.2.1 Dietary Fats and CVD

It is well established that dietary fats influence blood cholesterol concentrations. Studies have also examined the impact of fats on other CVD risk factors such as BP (7). In New Zealand, and worldwide, it is recommended to consume less than ten percent of energy from SAFAs and no more than 35% of total energy from all fats (6). Some individual dietary SAFAs, such as palmitic and myristic fatty acids are well known for increasing the levels of low density lipoprotein (LDL) cholesterol in the blood, whereas stearic fatty acid exhibits no such effects (43). Palmitic and myristic fatty acids are found mainly in butter fat, coconut fat and animal fats, i.e. in meats, butter, cakes, pastries and full fat dairy products (43). Low density lipoprotein cholesterol is a well known risk factor for CVD and consequently studies have looked at the link between intake of SAFAs and CVD (44, 45). In the 1980s results from the ‘Seven Countries Study’ established that those with high intakes of SAFAs and trans-FAs had a greater risk of death from CHD (46). Results from studies over the next 20 years such as ‘The Nurse’s Health Study’ and further analysis of the ‘Seven Countries Study’ with larger numbers also provided corroborating evidence (44, 45, 47).

Trans-fatty acids are formed as a result of hydrogenation of USFAs: when hydrogen atoms are added into the double bonds of USFA. Trans-fatty acids are formed because the two
hydrogen atoms are sometimes added to opposite sides instead of the same side of the fatty acid. When they become hydrogenated in the trans-configuration they act like SAFAs in the body and have been associated with higher risk of CVD (45). In the past they were mainly used for manufacturing hard margarines but can occur naturally in ruminant animal fat (43). Worldwide it is recommended to consume less than one percent of energy from trans-FA (8).

Some USFAs are known to be protective against CVD. The ‘Seven Countries Study’ recognised that MUFA intake has an inverse relationship with death rate, and ‘The Nurses Health Study’ showed that PUFAs exerted similar effects (45, 46). Monounsaturated fatty acids, such as oleic acid and eicosenoic acid, are found in animal fats, fish and plant fats. Polyunsaturated fatty acids such as linoleic, α-Linolenic and the omega three fatty acids (n-3FAs): Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are found in fish, plant oils and fish oils (43). World-wide it is recommended to have between six and 11 percent of energy intake from PUFAs, and while no figure has been formally recommended for MUFAs, studies suggest >12% energy from MUFA is beneficial for cardiovascular health (7, 8). It is outside of the scope of this thesis to discuss CVD benefits of different PUFAs; they will be discussed as the group of fats.

Appendix A, table 8.3 page104 describes studies from the ‘Seven Countries Study’ and ‘The Nurse’s Health Study’ which established the above relationships. Results from randomised controlled trials (RCTs) have since confirmed findings from these prospective studies and focus on interventions which decrease the SAFAs (and consequently total fat) in the diet, and replace this with carbohydrate or with MUFAs and PUFAs. Meta-analyses have been conducted to come to conclusions and give recommendations for appropriate fat consumption to lower CVD risk. A meta-analysis of 21 large prospective cohort studies was
unable to show any cardiovascular benefit in decreasing SAFAs without replacement by USFAs (48). Results from a recent meta-analysis of RCTs showed a beneficial decrease in the total cholesterol: HDL cholesterol ratio when SAFAs and trans-FAs were replaced by MUFAs and PUFAs (49). Another meta-analyses of RCTs has shown that there is no benefit in just reducing the SAFAs (and replacing with carbohydrate), the SAFAs must be replaced with PUFAs to show benefits in reducing risk of CVD (48, 50). A recent Cochrane review showed that CVD event risk only decreased in the men when subjects replaced SAFAs with PUFAs and MUFAs for more than two years (51). Although the reduction in CVD events for women is unclear, replacement fats have been identified in other studies as being beneficial and are therefore recommended. Finally, two meta-analyses that reported that replacing SAFAs with PUFAs is the most beneficial replacement for reducing CVD events (52, 53). It has also been recommended that having >12% of energy intake as MUFA is beneficial in controlling CVD risk factors such as BP (7). Therefore having adequate amounts of MUFAs and replacing SAFAs with PUFAs is the best way to consume fats for heart health. Despite conflicting conclusions of meta-analyses, it is currently recommended that all people replace SAFA with USFAs and include n-3 PUFA in their diet (54).

2.3.2.2 Alcohol and CVD

Ethanol (in alcohol) is a nutrient and is most commonly consumed in alcoholic beverages such as beer, wine and spirits (43). Alcohol has drug effects on the brain and, therefore, there are recommendations to limit consumption in the New Zealand population. New Zealand’s Alcohol Advisory Council (ALAC) recommend, that to reduce long term health risks, men should consume no more than three standard drinks per day and no more than 15 drinks per week, and women should consume no more than two drinks per day and no more than ten drinks per week. One standard drink is classified as ten grams of ethanol in
New Zealand. Alcoholism, adverse health outcomes and accidents related to alcohol abuse are social issues in New Zealand (43, 55). Despite this, it is accepted that light to moderate intake of alcohol is beneficial for cardiovascular health (43). The studies described in this section summarise the majority of evidence in this area, including pioneering studies.

In the late 1970s and early 1980s, literature began to surface detailing the findings from ongoing epidemiological studies in relation to alcohol consumption and impact on heart health and mortality (56-58). The ‘Honolulu-Asia Ageing Study’ (HAAS) was one of the first to investigate this relationship using data from an ecological study of over 8006 Japanese-American men investigating CVD and its determining factors (56). Some of the study components involved measuring alcohol intake and other CVD risk factors. This study was followed by other cohorts such as the ‘American Chicago Western Electric Company’ cohort, and the UK’s ‘Whitehall Study of Civil Servants’ (57, 58). These studies were able to identify that daily heavy drinking (more than about four to six drinks per day) is not beneficial for cardiovascular health (56-58). The ‘Whitehall Study of Civil Servants’ could not find this relationship however, identified that there was highest CVD death risk with abstaining from alcohol (58).

In 1986 a review of epidemiological studies investigating the relationship between alcohol and cardiovascular health, confirmed that moderate alcohol intake was protective against CAD, and heavy drinking was a risk factor (59). In 1990, for the first time, a ‘J’ shaped curve was identified between alcohol intake and CHD mortality in a large cohort of American men (n= 276,802) where those who have one to two drinks are at lowest risk, followed by abstainers and then heavy drinkers (60). This is important as it became known that abstaining was not healthful for CVD risk, contrary to assumptions that any alcohol consumption is bad for health. Later in 1992, results from another very large prospective
cohort study (n=128,934) showed that, whilst consuming more than six drinks per day increases mortality, light drinking (one to two drinks per day) is protective against total CVD mortality (61). In 2003 the protective effect of light to moderate drinking was identified for stroke, while heavy drinking was related to higher risk of stroke (62). Finally, in 2011, a meta-analysis was published that showed that light to moderate intake of alcohol is associated with decreased risk of incidence and mortality from CHD and stroke and overall CVD mortality (63). The above prospective cohort studies have been outlined in appendix A, table 8.4 page 108.

The protective effect against CVD of wine, beer and spirit consumption has been widely researched (64). However, a large meta-analysis was able to demonstrate a protective effect of light-moderate consumption of wine, but not beer, on vascular health (65). Mechanisms behind the protective effects of alcohol were identified from intervention studies to be increased HDL, apolipoprotein AI and TGs in subjects consuming about 30g alcohol per day (two standard drinks in the study) (66).

It can therefore be accepted that a ‘J’ shaped curve exists between alcohol consumption and CVD risk and mortality, where those who have one to two standard drinks per day have the lowest risk, followed by a higher risk for abstainers and a much higher risk for heavy drinkers. This has been found in epidemiologic, case-control and intervention studies (43, 59-62, 66).

2.3.2.3 Dietary Salt and CVD

It is well known that a high intake of dietary salt can increase BP (43) and that reducing dietary salt reduces BP (67). Hypertension is a risk factor for CVD and is included as a primary risk factor in the New Zealand Cardiovascular Risk Charts along with cholesterol concentration, although studies have been unable to equivocally establish a link between
salt intake and incidence of CVD (9, 68). A meta-analysis of observational studies showed that there was an association between high intakes of salt and high incidence of CVD. However, a recent meta-analysis showed that while blood pressure was lowered, there was no association between reduction of salt and CVD risk (69, 70). It is still important to recommend a low salt diet for those with hypertension or who are at risk of CVD, as CVD risk is calculated on a multi-factorial basis using risk charts including use of SBP (9). It is outside the scope of this thesis to further discuss salt in relation to CVD or cognition.

2.3.3 Nutritional Risk Factors for Diabetes

Having DM pre-disposes an individual to a higher risk of CVD due to presence of metabolic risk factors such as high TGs, low HDL cholesterol and increased platelet aggregation (43). Consequently, CVD risk charts rank DM as an important risk factor which significantly increases CVD risk (9). While type one DM (T1DM) is predominantly a genetic disease T2DM is usually a result of increasing age or poor lifestyle habits (43). The biggest nutritional risk factor for T2DM is increasing BMI (43). Probable nutrition risk factors include high SAFA intake, while protective factors include consumption of non-starch polysaccharides, fruit and vegetables (43, 71).

2.3.4 Other Dietary Constituent’s Effects on CVD risk factors

Supplementing intake of fibre decreases BP, especially in those 40 years or over or with hypertension (72). Other studies have shown a small but significant decrease in total and LDL cholesterol with soluble fibre supplementation (73). These studies suggest multiple CVD benefits of fibre in a healthy diet. Although there have been many studies investigating the use of antioxidants in prevention of CVD, meta-analyses have failed to show any benefit (74).
2.3.5 Mediterranean Diet Pattern

The ‘Mediterranean Diet’ was first described when cohorts from the ‘Seven Countries Study’ living in countries bordering the Mediterranean Sea were compared with those of western countries and Finland. The ‘Mediterranean Diet’ has the following characteristics: rich in grains, legumes, cereals, bread, fruits, vegetables and MUFA (from olive oil), moderate in alcohol (from wine), fish and dairy and low in animal meats and SAFA (75).

The ‘Whitehall II Study’ commenced in 1985 gathering dietary and health information from >7,000 male and female British civil servants. It is a valuable longitudinal study investigating dietary effects on health and follows on from the ‘Whitehall Study of Civil Servants’ mentioned previously (76). In one investigation, publishers categorised the diets of n=7731 50 year old participants, using a 127 item FFQ. They showed that a ‘healthy’ type dietary pattern including fruits, vegetables, grainy bread, low fat dairy products and minimal alcohol is protective against DM and major coronary events, however the ‘Mediterranean Diet’ type did not share the protective effects. Interestingly the ‘healthy type’ diet shares many aspects of the ‘Mediterranean Diet’ (76). This study is of particular relevance as its subjects were the same age as those participating in CHALICE.

Meta-analyses of large prospective studies have shown that adherence to the ‘Mediterranean Diet’ lowers risk of CVD by reducing chronic risk factors and that it is more effective than a low fat diet (77, 78). A systematic review discussed how ten large, high quality cohort studies found these results and that the ‘Mediterranean Diet’ is not only beneficial for CVD prevention but also prevention of some cancers (79). Finally a meta-analysis of 18 prospective cohort studies has shown that there is decreased risk of CVD incidence and mortality and decreased risk of overall mortality when following the
‘Mediterranean Diet’ (77). These studies are outlined in further detail in appendix A, table 8.5 page 111.

2.3.6 New Zealand Diet and Cardiovascular Health

2.3.6.1 New Zealanders’ Nutrient Intakes

The total fat intake (as a proportion of daily energy intake) for New Zealanders in the Adult Nutrition Survey 2008/2009 (ANS) was 33.7% for men and 33.8% for women which lies in the recommendations of 20-35% energy from fat (2, 6). New Zealanders were consuming 13.1% of their energy as SAFA which is above the recommendation of 10% (2, 6). The main dietary sources of SAFA were butter, margarine, dairy products and meat (2). Saturated fat intake was lowest for those 51+ years compared to younger persons. The intake of MUFA was 12.4% and 12.3% for males and females, respectively. The main sources of MUFA were butter and margarine, poultry, starchy vegetables, bread based dishes and meats (2). MUFA intake was lowest for men aged 51+ years and women aged 71+ years compared to younger persons (2). This follows recommendations of studies promoting MUFA for health (7). Intake of PUFA was 4.8% for males and 4.9% for females, largely from butter and margarine, bread, starchy vegetables, vegetables, grains, fish and seafood. Intake of those 31-50 years was higher than intake of those 71+ years (2). Maori had a higher intake of total fat, SAFAs and MUFAs than non-Maori (80). Alcohol intake data measured in the ANS is unavailable. That data was not appropriate for measuring usual intake and includes only those aged 16-64 years (81).

2.3.6.2 Food choice

Based on the ANS, over 60% of the New Zealand population had three serves of vegetables per day, two serves of fruit per day, use wholegrain bread and eat battered or canned fish.
Most New Zealanders had red meat and chicken regularly, and about 40% have fresh or frozen fish/seafood weekly. Almost 50% of New Zealanders used low fat dairy products (2).

2.3.6.3 Health Outcomes

From the ANS, average SBP was 130mmHg for males and 122mmHg for females. Blood pressure increased with age; those 71+ years had a SBP of 141mmHg and 143mmHg respectively (2).

Total cholesterol: HDL ratio is recommended to be <4.0mmol/L. The only group to exceed this recommendation was males aged 30-51 years (4.63mmol/L) (2).

2.3.6.4 Summary

In conclusion, high intake of SAFAs, trans-FAs, alcohol and salt have negative effects on cardiovascular health and risk factors. Replacing SAFAs with MUFAs and PUFAs is beneficial for cardiovascular health, as is light to moderate intake of alcohol. It is likely that New Zealanders are consuming too much SAFAs and not enough PUFAs.

2.4 Cognitive function

2.4.1 Mild Cognitive Impairment Context

There are no cures for dementia including AD; however risk factors in the manifestation of the disease are topical and currently being explored. Carrying the Apolipoprotein-E (Apo-E) genotype is a risk factor for dementia (82). This genotype is well known and acknowledged in literature and carriers are not equally affected by CVD and dietary risk as non-carriers (83). Other risk factors may include drug, lifestyle, genetics and diet and are being explored. It is hoped that recommendations can be formed and result in public health intervention to reduce risk factors, and ultimately lower rates of dementia.
Fifty years ago it was determined that there was a gradual onset to some dementias. In 1962 it was recognized that older persons sometimes suffer from ‘senescent forgetfulness’, which was later described as ‘age related cognitive decline’ (ARCD); a normal process of ageing (84, 85). The distinction between normal ARCD and abnormal cognitive decline has been described as ‘mild cognitive impairment’ which describes impaired cognition that is ‘impaired to an extent that is greater than would be anticipated for age, yet patient does not meet criteria for dementia’ (4, 86).

The following are the most recent criteria for definitive MCI (3, 87):

1. Person has a complaint about a change in their cognition.
2. Lower performance in more than one cognitive domain of a test, than expected for a person their age and education.
3. They are still able to perform all daily tasks of living, even if it takes longer or is more difficult than before.
4. They are ‘not demented’, therefore are still able to function acceptably at work and socially.

Two types of MCI have been described; amnesic (memory associated) and non-amnesic (non-memory associated) (3). In cognition tests those with MCI usually score between normal subjects and those with dementia (3). The identification of MCI is hoped to be an important factor in predicting whether a person will develop dementia. A robust meta-analysis showed that in 41 studies the annual conversion rate from MCI to any kind of dementia is five to ten-percent and that <50% of people diagnosed with MCI go on to develop dementia within 10 years (88). Figure 2-1 shows the relationship between MCI and dementia incidence. In some of the included studies participants were recruited from specialist settings like memory clinics, where overall incident rates were higher than
community incident rates due to severity of complaints (88). It may be useful to identify people who may be suffering from MCI in order to give them education surrounding their condition and to provide them with up-to-date information and research in dementia prevention. Giving those diagnosed in midlife the education to improve CVD and dietary risk factors could improve their quality of life and potentially prevent further cognitive decline.

Figure 2-1: The relationship between MCI and dementia.

A diagnosis of dementia is usually made by screening with a global cognitive test, followed by evaluation with a psychiatrist and diagnosis meeting criteria from the ‘Diagnostic and Statistical Manuel of Mental Disorders’ (DSMMD) (89). Diagnoses for AD are also made with the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) criteria for AD.
2.4.1.1 Cognitive Testing

Global cognitive tests used to identify MCI and suspected dementia usually have multiple domains and test memory and other functions such as executive functions, language, perception and attention (90). They give a broad overview of general cognition.

The Mini Mental State Examination (MMSE) is the most widely used global cognitive test for identifying MCI and dementia (91). It is a 30 point questionnaire with a cut-off of <26 points on this test is indicative of MCI. The modified Mini Mental State Examination (3MSE) is an updated version of the MMSE and has a scoring system from 0-100 with a cut-off of <79 for cognitive impairment (92). In 2005 the Montreal Cognitive Assessment (MoCA) was validated as an improvement on the MMSE for detecting MCI (93). It also has an MCI cut-off of <26 points. Other multi-domain tests are available however their use is often alongside MMSE. Different cognitive testing methods have different cut-offs for MCI and dementia. Some studies use multiple tests of specific cognitive domains instead of, or as well as a global measure. If this is done, it is referred to as a ‘test battery’ that can be made up by 2 or more specific cognitive tests. These are difficult to compare to measures of global cognition therefore will not be elaborated on when describing their use in studies during this review.

2.4.1.2 (Age Related) Cognitive Decline

In normal aging some aspects of cognition are affected. Termed ‘age related cognitive decline’ these changes are different and separate from MCI and must be considered in studies by controlling for age. The areas most likely to be affected in normal aging are: attention, language (naming and fluency), some visio-spatial skills and memory (learning) (4). A person may or may not develop MCI or dementia following ARCD, it is important to
remember that most people will experience ARCD over the lifetime unless they are diagnosed with early MCI (see Figure 2-2).

Figure 2-2: The possible continuum for ageing and cognition

2.5 CVD Risk Factors and Cognitive Function

Previous CVD events and increasing age are associated with poorer cognition (94). Current CVD has also been highlighted as a risk factor for dementia (95). Other confirmed and putative risk factors for cognitive impairment or poor cognition in those without stroke or disability are: presence of ApoE4 gene, reduced physical activity, depression and lower levels of education (82). Many studies control for these factors, however, it beyond the scope of this literature review to discuss them in more detail. Risk factors discussed are limited to those in the New Zealand Cardiovascular Risk Charts; high BP, high cholesterol, smoking, DM plus consideration for BMI. The following sections focus on CVD risk factors in mid-life and effects on current cognitive function and MCI, and identification of risk of late life dementia.
2.5.1 Blood Pressure and Cognitive Function

High BP can result in atherosclerosis and smooth muscle hypertrophy. These changes lead to wall thickening and luminal narrowing (96). In hypertension the ability to appropriately regulate cerebral blood pressure is compromised and cerebral hypo-perfusion can result. Hypertension can cause small vessel disease in the brain and micro-bleeds. These changes can lead to brain ischaemia and, consequently, to white matter lesions or degeneration of white matter in the brain (96). These changes can lead to cognitive impairment and dementia (96).

A ‘U’ shaped curve for the relationship between BP and cognitive function exists. Cognitive function suffers when BP is too high, or too low (in old age) due to vascular damage and hypo-perfusion (97, 98). It is outside of the scope of this thesis to discuss hypotension in older age as the focus is on hypertension as a CVD risk factor in middle aged persons.

Many studies have looked at the impact of midlife BP on current cognitive function, late life cognitive function and risk of dementia in the future. Evidence shows an inverse linear relationship with increasing BP in mid-life and cognitive impairment and cognitive decline (97, 99-107). One of these studies is The ‘Framingham Heart Study’ showing that mid-life BP is inversely related to measures of attention and memory 14-20 years later (101). In the HAAS it was found that high midlife BP is related to poorer cognitive function in late life (108). These studies are described further in Appendix A, table 8.6 page 113. High midlife BP is associated with higher risk of dementia in later life in the HAAS cohort (109, 110). Studies are currently focusing on BP lowering in attempt to reduce cognitive decline and prevent dementia (111).
2.5.2 Cholesterol and Cognitive Function

Cholesterol is a vascular risk factor for atherosclerosis which leads to vessel wall enlargement and constriction (43). Cholesterol is thought to affect cognition due to its structural role in brain components such as beta-amyloid tissue (112).

Results of studies on the impact of mid-life cholesterol concentrations on late-life cognitive outcomes are presented in this section. This is due to the fact that this is the focus in all but a few studies, which have reported mixed results (113).

A 2008 meta-analysis of 18 large prospective studies showed that high mid-life total cholesterol is related to late life risk of cognitive impairment, as well as AD and any dementia (114). One large Swedish prospective cohort study; ‘The Prospective Population Study of Women’ was unable to find any relationships after adjusting for confounders (115). Conversely, the results from the Framingham cohort showed that those with lower cholesterol levels had a higher risk of poor cognitive performance, and those with borderline high cholesterol performed best (113). Overall, despite conclusions from meta-analysis, individual studies have shown inconsistent results with regards to cholesterol and cognition.

It is possible, that midlife cholesterol is predictive of late-life dementia, however, more research is needed to confirm this observation in large cohorts. It must be stressed that high cholesterol has been shown to have cognitive implications when combined with other CVD risk factors (116, 117). The above studies are detailed in appendix A, table 8.7 page 114.

2.5.3 Diabetes and Cognitive Function

It is proposed that T1DM is a risk factor for cognitive impairment due to hyperglycaemic episodes and insulin deficiency which impairs synaptic plasticity in the brain and results in poorer performance in tasks (118). Mechanisms are not well established in those with
T2DM, however the association with cognitive impairment still exists. It may be that the pathway for T2DM is to do with modulatory effects on hormones (CCK and leptin) in the brain which affect learning and memory (118).

Results from some large prospective studies support the hypothesis that having DM is a risk factor for cognitive decline during midlife and impairment in some aspects of cognition (119). Other studies have found a higher risk of dementia for otherwise low risk diabetics (120, 121). Results from the ‘Framingham Heart Study’ show that low risk people (<75 years, without Apo-E gene or raised homocysteine levels) with DM have a higher risk of developing AD than low risk people without DM (122). A systematic review of these studies showed that there is sufficient evidence from longitudinal studies to show that having DM increases risk of cognitive decline and dementia (121). Given that DM is a high CVD risk factor, it is likely that there is a higher risk of subsequent cognitive impairment. These studies are outlined in appendix A, table 8.8 page 115. Randomised controlled trials are needed to determine whether improving DM control once diagnosed, in-turn, can improve cognitive function (122, 123).

2.5.4 Smoking and Cognitive Function

Results of a meta-analysis show that those who smoke have an increased risk of cognitive decline, AD, VaD and any dementia than those who do not smoke, and that those who have ever smoked have the same risk for VaD and any dementia as current smokers (124). Results from the HAAS show a dose dependant relationship exists between amount smoked in midlife and risk of dementia in late life (125). Studies have not focused on MCI in mid-life as an outcome.
2.5.5 Body Mass Index and Cognitive Function

Higher BMI is a risk factor for hypertension and insulin resistance therefore is also a recognised risk factor for cognitive impairment. Studies show that having a BMI of <18.5 (underweight), >25 (over weight) and >30 (obese) are risk factors for dementia in later life (126, 127). The association is strongest for obesity (106, 126, 128).

2.5.6 Multiple CVD Risk Factors and Cognitive Function

Risk factors present in the New Zealand Cardiovascular Risk Charts; high BP, high cholesterol, DM and smoking have been related to CVD risk over the past 60 years. A cross-sectional study showed a strong association between more risk factors and lower MMSE test scores in mid-life (129). Additionally, studies have associated the presence of risk factors in midlife with dementia mortality and dementia incidence in late life (116, 117, 130).

2.6 Diet and Cognitive Function

Studies have begun to look at the relationships between diet and cognitive function. Some of the mechanisms described relate directly to known CVD risk factors and their relation to cognitive function (see Figure 2-3). Other theories relate to the role of selected nutrients in inflammatory and metabolic processes and antioxidant action (see Figure 2-4). The mechanisms for action will be described in more detail throughout this section.

Figure 2-3: A CVD risk factor is involved in the relationship between diet and cognitive function for some nutrients
The previous section discussed midlife CVD risk factors in relation to risk of cognitive impairment, cognitive decline as well as late life dementia. This section focuses only on the relationship between diet and cognitive function and cognitive decline, but does not discuss dementia outcome studies. There is limited literature focusing on mid-life diet and cognitive function; therefore studies examined in this section are from both middle-aged and older populations. This section is focused only on those nutrients for which there has been adequate research, therefore, protein, carbohydrate and fibre will not be discussed, and micronutrients of interest will only be mentioned briefly.

There are limitations of investigating the relationships between cognition and diet. For example; in those who are cognitively impaired, diet record recording, and recalling (for the purpose of FFQ and dietary histories) may be inaccurate (90, 131)

### 2.6.1 Macronutrients

There is no evidence to suggest that long-term intake of differing types or quantities of carbohydrates or protein as part of a normal diet have any effect on long-term cognitive function. Studies have only looked at short term effects of starvation or over feeding and in target groups such as young men which has no application to MCI.
2.6.1.1 Fat and fish intake

As outlined in previous sections, different fatty acids have different effects on health. Studies have hypothesised that links exist between intakes of different fatty acids and cognitive function. Several studies have identified fish intake as having a link with cognitive performance, this is because of its high content of the n-3FAs; EPA and DHA.

Several theories for the link with cognitive function are described including that;

- essential fatty acids have a role in creating lipid rafts for modifying activity of membrane bound enzymes in the brain to perform normally (132).
- Unsaturated fatty acids have a role in maintaining structural integrity of neurons which helps with optimum transmission (132).
- Saturated fatty acids increase LDL concentrations, promoting atherosclerosis, while substitution of SAFAs with USFAs decreases LDL and increases HDL. A high SAFA intake may, therefore, lead to endothelial oxidative damage (132, 133) The benefits of high fish intake could be due to the high content of n-3FAs, or other nutrients such as antioxidants or vitamin D (132).

Studies have positively associated intake of PUFAs and fish fats with better cognitive function and less cognitive decline (134-139). These studies are from large, high quality cohorts including the ‘Zutphen Elderly Study’; one of the cohorts from the original ‘Seven Countries Study’, who have found protective benefits against cognitive decline, cognitive impairment and for overall cognitive function (134, 135).
The ‘Italian Longitudinal Study on Ageing’ (ILSA), found that PUFAs and MUFAs are protective in slowing ARCD (140).

Studies have also identified these positive associations to exist with high intake of MUFAs (140-143). For example intensive use of olive oil was associated with better visual memory in the ‘Three Cities Study’, and in the ‘Women’s Health Initiative’ high MUFA intake was associated with slower cognitive decline (141, 143) The ‘Chicago Health and Ageing Project’
was unable to show significant trends, however they acknowledge that it seems MUFA plays a protective role against cognitive decline (142). Saturated fat intake has been identified as a risk factor for cognitive impairment and decline in some studies including the ‘Chicago Health and Ageing Project’ mentioned above (142, 144). In the Finnish ‘CAIDE study’ of 1449 men and women, there was a higher risk of late-life MCI in women when consuming high amounts of SAFA from dairy products (144). This is one of few studies looking at MCI as an outcome. Another study looking at MCI was from the ILSA was unable to detect any associations with fats in this population (145).

The above studies are detailed in appendix A, table 8.9 page 116. Despite limitations highlighted in the tables, the studies are relatively comparable and have strong methodology both in cognitive testing and dietary assessment methods. Randomised controlled trials have not been used in prevention of cognitive function; therefore there were no RCTs to discuss in this area. Overall the prospective research has found associations for the protective role of USFAs and the harmful role of SAFAs in cognitive function. Studies have also looked at intakes of fat and risk of dementias in later life and found positive associations with intake of SAFAs, total fat and cholesterol (146). More recently a large review has compiled conflicting data from individual studies; however cannot sufficiently conclude the role of fat intake in prevention of dementia. The review was published by Solfrizzi et al in 2011 and gives an excellent overview of the current studies providing evidence for fats, alcohol and food groups for protecting cognitive function and preventing dementia (147). General trends from the review show that SAFAs play a role in increasing risk, while intake of PUFAs may decrease the risk of dementias. The Apo-E carriers seem to have an increased risk than non-carriers with increasing SAFA intake, and protective effects of PUFAs did not apply to carriers at all, or as much (147). Other studies
were unable to show any trends, showed trends at different points in the lifecycle or were inconsistent with other similar studies, therefore conclusions cannot be made. Furthermore the review included studies that have looked at intake of fats from dairy products as increasing risk of MCI and dementias. The rationale is that dairy products are a major source of SAFA. Studies have conflicting results therefore the authors of the review could not sufficiently conclude the role of dairy in MCI or dementia; however suggest full fat dairy products may increase risk of MCI (147).

2.6.1.2 Alcohol

It is likely that a ‘J’ or ‘U’ shaped curve describes the relationship between alcohol intake and risk of cognitive impairment and/or dementia incidence in older age. For example; abstainers and heavy drinkers have higher chance of cognitive impairment and developing cognitive impairment and/or dementia than moderate drinkers (see Figure 2-5).

![Graph showing the hypothesised 'J' shaped curve between alcohol intake and cognitive function. The x-axis represents drinks per day (0, 1-2, 3, 4, >5) and the y-axis represents increasing risk of cognitive decline, cognitive impairment and dementia. The graph illustrates a 'J' shaped curve with the lowest risk at moderate drinking levels.](image)

Figure 2-5: The hypothesised ‘J’ shaped curve which describes the relationship between alcohol intake and cognitive function similar to that of alcohol and CVD risk.
The mechanism behind this is unclear because of the known negative effects of heavy drinking on the brain. As discussed previously, light to moderate alcohol intake is beneficial for cardiovascular health (alcohol raises HDL cholesterol) and protective against atherosclerosis (132). It is possible that this level of alcohol intake is a marker for beneficial health behaviors, or that it contributes positively to vascular health (108, 148). Other complicated mechanisms have been proposed involving cerebral neurotransmitters, however, there is no singular mechanism for action that has been agreed upon (132). There has been variability between studies concerning the way in which they measure alcohol intake. This includes the number of standard drinks per day or the frequency of alcohol consumption.

Several limitations apply when measuring alcohol intake for example: A person’s cognitive state may influence their decision to drink: i.e. they may fear confusion and therefore don’t drink. Likewise a person’s cognitive function may impact on their ability to recognize how much they drink or recall how much they drink and give inaccurate results (149, 150). It is also a concern that some who now abstain were past heavy drinkers therefore studies attempt to gauge past intake (149). The presence of the Apo-E genotype can confound relationships observed due to the known increased risk of dementia in these persons (82). Some studies control for this.

Some large, high quality prospective studies, including The ‘Zutphen Elderly Study’ and the ‘Framingham Heart Study’, have found that those who drink lightly and moderately appeared to get better results in cognitive testing and experience less cognitive decline than those who drank heavily or abstained from alcohol (83, 149, 151-154). In one analysis of the ‘CAIDE study’ there were only poorer late life test scores in abstainers, and no difference in test scores of drinkers despite amount consumed (150). An earlier analysis of this cohort
focused on frequency of drinking and found that never drinking and frequent drinking in midlife was harmful to late life cognition (153). The ‘Framingham Heart Study’ results described having two to four drinks (women) and four to eight drinks (men) as producing the best cognitive test scores, however drinking the upper level of this amount is not recommended by ALAC who encourage men to have three or less drinks per day and ≤15 per week and women two or less per day and ten or less per week (55, 149). The ILSA found that drinking less than one drink per day, but not abstaining, plays a role in slowing the progression to dementia from MCI (155). Finally, in the ‘Zutphen Elderly Study’ alcohol was not protective for the general population, however for those with diabetes and/or CVD, less than two drinks per day is protective while less than one drink per day increases risk of cognitive decline (152). These studies are detailed in appendix A, table 8.10 page 120.

A meta-analysis has shown that amongst 14,646 men and women aged 50+ years, light to moderate drinkers have a significantly reduced risk of AD (RR=0.72), VaD (RR=0.75) and any dementia (RR=0.74) compared to non-drinkers (156). Any drinker had reduced risk of AD and any dementia than non-drinkers (RR=0.66) (156).

Overall it is likely that light to moderate consumption of alcohol gives best protection against cognitive impairment and dementia incidence and it is likely that the ‘J’ or ‘U’ shaped curve exists between alcohol consumption and risk of cognitive impairment. Carriers of the Apo-E gene should be cautious with alcohol intake as this curve does not necessarily apply to them (83). It is also important to weight up the benefit and harm to the individual consuming alcohol. Caution should be taken when consuming alcohol ensuring that consumption follows guidelines for healthy alcohol consumption outlined by ALAC (55). The recommendations provided in some studies are not consistent with this.
2.6.2 Micronutrients

Several micronutrients have been repeatedly researched and discussed in the literature in relation to cognitive function. Although it is outside the scope of this thesis to examine the effects of micronutrients, it is an important area of research to highlight as is likely to be related to overall dietary patterns.

2.6.2.1 B12, B6, Folate

Studies have investigated the link between three B-vitamins and cognitive function based on the knowledge that high plasma homocysteine has been shown to be a CVD risk factor and is associated with changes in the brain (157, 158). Having vitamin B12, B6 or folate deficiencies increases homocysteine levels (159, 160). Some studies have found that high homocysteine is also a risk factor for poor cognition (157). Studies have attempted to investigate how improving the status of these vitamins can improve cognitive function through improving homocysteine levels (157). Cochrane reviews have compiled evidence on the impact of these vitamins on cognitive function and suggested that improving status of these vitamins through supplementation has no effect on cognition (157, 161, 162), although one review suggested some cognitive benefit in those with high homocysteine levels at baseline (163). It is outside the scope of this thesis to further discuss B-vitamins.

2.6.2.2 Antioxidants

It has been suggested that the antioxidant micronutrients vitamins A, C and E have protective properties against cognitive impairment. The rationale for this is that insufficient levels of these vitamins may result in oxidative stress leading decreased availability of the vitamins to act on free radicals and prevent damage to tissues (160). Reviews have shown that supplementing antioxidants has no impact on cognitive function (164). Prospective studies have shown that those with highest levels of dietary antioxidant intake have better
cognitive function (165, 166). Others have found no association (135). It may be more beneficial to discuss whole dietary pattern from which antioxidant vitamins are derived i.e. fruit and vegetable intake and the ‘Mediterranean Diet’. It is outside the scope of this thesis to further discuss antioxidant intake, however it is an important area of research to highlight.

2.6.3 Dietary Patterns

As discussed previously, it is difficult to determine the specific nutrients that are responsible for cognitive impairment, decline and risk of dementias. Studies have suggested that the contribution of many nutrients is important and that adherence to a heart healthy eating pattern such as the ‘Mediterranean Diet’ is beneficial for cognitive health (167). As outlined previously, the ‘Mediterranean Diet’ is rich in grains, legumes, cereals, bread, fruits, vegetables and MUFAs (from olive oil), moderate in alcohol (from wine), fish and dairy and low in animal meats and SAFAs (75). Other studies have described a ‘healthy diet’ which usually includes meeting recommended intakes of fruit, vegetable, high fibre cereals, plant oils, dairy, fish and moderate amounts of meat. They usually are described as being low in cakes and biscuits and excess animal fat from meat and animal products. Thorough reviews have documented the impact of adherence to the ‘Mediterranean Diet’ to cognitive function and dementia. Trends show that adherence to the ‘Mediterranean Diet’ has positive impact on cognitive decline, cognitive function and incidence of dementia (147). Many studies have examined the impact of healthy type dietary patterns on cognition in older populations, and found positive associations between a healthier diet and better cognition (168-173). Others have found no association, however used a much lower cut-off for cognitive impairment, in cognitive tests, than other studies (174). Few studies have investigated the effect of dietary patterns on cognitive function in middle-aged populations.
A study of 3054 middle aged French men and women showed that adherence to a healthy dietary pattern (rich in fruit, vegetables, dairy, cereals, vegetable fat, nuts and fish) was associated with better global cognitive function (p=0.001) (167).

Although it is outside the scope of this thesis to examine and discuss dietary patterns, it is important to highlight that there are many food components which could have beneficial effects on cognition, and that it is difficult to isolate these to examine specific effects. It has been previously highlighted that Mediterranean and healthy diet patterns are good for cardiovascular health. It is likely that following such eating patterns is beneficial for not only cardiovascular health, but cognitive health.

2.6.4 Summary

At present, recommendations for diet in relation to cognitive health should be surrounding following a heart healthy diet with sources of PUFAs and MUFAs and low in SAFAs. It should be recommended to drink alcohol in line with the guidelines for healthy alcohol consumption provided by ALAC which is ten standard drinks per week for women and 15 standard drinks per week for men. This amount spread across the week given a light to moderate alcohol intake which is both cardio-protective and neuro-protective. Research cannot conclude the role of micronutrients in cognition so recommendations in line with healthy food patterns should be adhered to in order to meet and exceed recommended daily intakes of all nutrients.
2.7 Conclusion

The New Zealand Cardiovascular Risk Charts are the current preferred method of determining five-year CVD risk for adults in New Zealand primary care. Several dietary factors such as fats and alcohol intake have both protective effects against CVD and can also put one at higher risk of CVD. Cardiovascular and dietary risk factors have been related to a person’s cognitive function, suggesting that there are modifiable risk factors for the incidence of MCI. There are currently gaps in the literature which will be examined in the present study. Firstly, there has not been a published study which calculates the CVD risk of a New Zealand population and investigates relationships between nutrients and CVD risk scores. Secondly, few studies have targeted a specific age group such as 50 year olds and have examined incidence of MCI against nutrient intake. Thirdly, no studies have compared absolute CVD risk score to risk of MCI in a middle aged group where CVD risk is becoming a relevant health concern.

It is hypothesised that those with a higher five-year CVD risk have a higher risk of MCI, and that those with exposure to selected dietary risk factors show higher CVD risk and poorer cognitive function.
3 Methods

3.1 The CHALICE study

The CHALICE study is a longitudinal study of 50 year olds currently living in the Canterbury area. The data used in this thesis are preliminary data collected from the first 200 CHALICE study participants, who had been recruited by 1 June 2012. Data were collected from pre-assessment questionnaires and seven modules of physical testing and questionnaires during a four to six hour clinic visit. Participants were asked to complete lifestyle questionnaires after the clinic visit. Similar longitudinal follow-up is planned for each participant every five-years as well as brief annual questionnaires. Ethical approval was obtained from the Upper South Regional Ethics Committee, and Maori consultation was undertaken during the design of this study (Appendix F page 135)

3.2 Study Procedures

3.2.1 Sample Selection

The Electoral Roll Centre provides an up to date list (health research extract) of people within a defined geographical electorate that may be used to recruit participants into research studies. The CHALICE research extracts are requested annually in June, the first being June 2010. The extracts contain the names of people who are between 49 to 50 years old and who are registered in the following territorial authorities that align with the Canterbury District health Board (CDHB) area: Kaikoura District, Hurunui District, Waimakariri District, Christchurch City, Selwyn District, and Ashburton District. A random selection of individuals were selected in a ratio of 4:1 non Maori to Maori and invited to participate. To recruit the first 200 participants, 488 individuals were selected from the
extract and were randomly assigned to one of four interviewers for follow-up and study entry. A new health research extract of 50 year olds will be requested annually for five-years to achieve the full CHALICE sample of 1000.

3.2.2 Participant Contact

Interviewers sent selected individuals a letter of invitation to the address recorded in the electoral roll. If they did not respond to the letter, interviewers attempted to make contact with the individuals by telephoning them. Phone numbers were sourced from the White Pages and the internet. If there was still no response a second letter was sent six weeks later. If individuals had not responded after two letters and/or eight phone calls, or if a home number was not available, interviewers visited individuals at home to invite them to partake in the study. If, after these steps, they were still able to be contacted they were considered to have declined participation.

3.3 Questionnaire Design

Participants attended a four to six hour assessment and underwent multiple interviews and procedures as part of the wider CHALICE study. For the majority of participants the assessment was completed on one day but in some cases it was completed over two days, for example one participant was blind so all answer options needed to be read aloud, others could not attend for the whole day and did the blood tests and echocardiogram (ECHO) on another day. Seven modules were completed on the interview day(s) and all seven modules were used in the present study to gather applicable data. Table 3-1 outlines the seven modules and the specific information gathered for each.
<table>
<thead>
<tr>
<th>Module</th>
<th>Information collected relevant to present study</th>
</tr>
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| **Module one: physical health** | One manual BP measure  
Fasting blood sample  
See appendix G page 140 for Module 1 |
| **Module two: demographics** | This module includes relevant demographics: sex, date of birth, ethnicity, education, and health related questions: past and present illness including diabetes status and CVD risk factors, treatments, smoking.  
Questions on alcohol consumption were adapted from the Alcohol Use Disorders Identification test (AUDIT). This tool is widely used in primary care settings and is a diagnostic tool for hazardous drinking behaviour (175).  
See appendix H page 143 for relevant questions in Module 2 |
| **Module three: attitudes and beliefs** | Family medical history was recorded including: ages of living relatives and illness history, and age and cause of death in passed relatives.  
See appendix I page 152 for detailed family history recording sheet |
| **Module four: heart-health** | Testing was administered at the University of Otago, Department of Medicine electrocardiogram (ECG) and Echocardiogram (ECHO) centre by a sonographer and a research nurse.  
Two BP measures; one manual and one electronic were taken following heart scans.  
See appendix J page 153 for recording sheet |
| **Module five: psychological health** | Relevant questions were derived from the Mini International Neuropsychiatric Interview (M.I.N.I) including testing and classification of present major depressive episode. The M.I.N.I is a well known and widely validated short diagnostic interview of psychiatric disorders for use in settings including epidemiologic studies (176).  
See appendix K page 155 for M.I.N.I questionnaire used |
| **Module six: cognitive health** | Tests of cognitive ability involved administration of the MoCA. The MoCA has been validated and shown to be more reliable as a screening tool for MCI than other well known and widely used tests such as the MMSE (93).  
See appendix L page 157 for the MoCA test administered to participants. |
| **Module seven: lifestyle questionnaire** | This module was completed in the week following the interview and included keeping a food and beverage diary (FBD).  
The FBD was a four day estimated food and beverage record. A four day record was used as it allows sufficient time to gather data to estimate usual intake without the high respondent burden of a seven day record (42). The FBD was pretested in a group interview with a convenience sample of eight men aged 50 years and older. A group of men was used because they were less likely to know about food preparation and might therefore provide more feedback and suggestions on how to collect this information. The group discussed the FBD layout and the content of the diary instructions. Their feedback was incorporated into a revised food and beverage diary and the associated instructions for completion. Participants were asked to complete the FBD on one weekend day and three week days. See appendix M page 168 for FBD documents. |

Table 3-1: Overview of the relevant components in each section of the CHALICE study.
3.4 Data collection

Data collection methodology differed between the modules and was dependant on the information required. The following section outlines how the relevant data to this study was collected from participants.

3.4.1 Module 1

Participants were asked to fast for 12 hours before their assessment to allow collection of blood sample suitable for measuring lipid profile and other biochemical data of interest to the wider CHALICE study. A trained nurse extracted 100ml of blood via venepuncture. This sample was used to for determining blood cholesterol levels and for calculating the total: HDL cholesterol ratio. One manual BP measure was recorded with a recently calibrated BP monitor.

3.4.2 Module 2

In module two, participants answered all questions from the AUDIT questionnaire including questions used for analysis such as whether the participant consumed alcohol, their frequency of drinking and amount usually consumed. See appendix H page 149 for alcohol questionnaire.

Questions adapted from the ‘New Zealand Health Survey’ include education, smoking and ethnicity. Participants were asked which ethnic(s) groups they identify with. The highest level of education achieved was recorded as: no qualification, secondary school qualification, post-secondary certificate or diploma or trade diploma, university degree or other. If other was chosen the qualification was compared with a similar New Zealand qualification. Due to the age of the participants, many professional qualifications that are currently delivered by universities were delivered by polytechnics or other institutions (for
example, nursing by district health boards). These qualifications were entered as post-
secondary school rather than university level education. For participants who had
completed higher education outside New Zealand, their education was coded according to
the most relevant course/institution in New Zealand at that time.

Participants were asked a series of questions regarding smoking behaviour. These included
their smoking status, smoking frequency, amount of cigarettes and duration of smoking.

3.4.3 Module 3

Participants were asked about their family medical history which involved listing all of their
immediate biological relatives (mother, father, brothers, sisters and children). They were
required to state the relatives age, or age at death, chronic illnesses, health conditions
and/or cause of death. From this it was determined whether the participant had a ‘family
history of premature CHD or ischaemic stroke in a first-degree relative (father or brother
<55 years, mother or sister <65 years)’ as described by the additional instructions in New
Zealand Cardiovascular Risk Charts. See appendix I page 152 for recording format.

3.4.4 Module 4

Two BP measures were recorded with recently calibrated monitors. One was from a manual
BP monitor, and the other from an automatic monitor. These readings, along with the
recording in module one allowed the calculation of an average SBP for each participant to
use in calculating CVD risk.

3.4.5 Module 5

In module five participants were asked questions based on the M.I.N.I to assess whether
they are experiencing a ‘current depressive episode’. If participants responded ‘yes’ to any
three statements after indicating a low mood over the past two weeks, they were diagnosed
as likely to be experiencing a current depressive episode at time of testing (176). See appendix K page 155 for complete list of questions and instructions from the M.I.N.I.

### 3.4.6 Module 6

The participants were required to complete the MoCA test with instructions from the interviewer. Interviewers followed a standard protocol and read a manuscript to pose questions. Participants were required to answer in a variety of ways depending on the question; these include drawing and verbal feedback. For the full test, manuscript and marking procedure see appendix L page 157.

### 3.4.7 Module 7

The FBD was completed after the clinic visit. Interviewers explained to the participants how to accurately complete an estimated four day FBD. Participants were asked to complete the FBD on one weekend day and three weekdays, and on alternate days. They were asked to write down all food and drinks consumed during those days, noting the time and location of consumption, the type of the food or beverages (including brand names or point of purchase), the amount consumed in common household measures or standard servings (for example one original ‘Vitawheat’ cracker) and how a food or beverage was prepared, listing all of the ingredients accurately. Participants were taught how to read food labels (to read portion size information, particularly for bread and muesli bars), shown portion estimating pictures (for spreads, jams, marmite and peanut butter) and a sample FBD was shown and explained to help participants accurately complete the FBD. Participants were also given written information on how to complete a FBD which detailed the information verbally explained. See appendix M page168 for the examples and format of the FBD.
3.5 Data Use

Three major areas for analyses were used in this study: Five-year CVD risk, cognitive function and selected dietary data (fat and alcohol intake). Data were gathered for depression and education because they have been shown to have relationships with cognitive function (177). Below is a description how data were used for each research question.

3.5.1 Development of CVD risk Scores:

*What is a person’s CVD risk according to the New Zealand Cardiovascular Risk Charts?*

A CVD risk score was developed for each participant according to the ‘New Zealand Cardiovascular Risk Charts’ which give a 5-year risk of fatal or non-fatal CVD (9). The following information was available from the CHALICE data to calculate risk scores:

- For the risk charts: *sex, age, smoking status and diabetes status, SBP measures and total: HDL blood cholesterol measure.*
- For adjustments to risk from risk chart: *family history, ethnicity, personal history of CVD events and diabetes duration.*

The risk factors for calculating CVD risk are shown in further detail in appendix C page 126 and appendix E page 131 as part of the risk charts and additional risk factors for adjusting risk. Participants were categorised according to final CVD risk score in one of three ‘mild risk’ categories, ‘moderate risk’, ‘high risk’ or one of three ‘very high risk’ categories.

3.5.2 Cognitive Impairment

The MoCA was used as a measure of cognitive function. The MoCA test is a 30 point measure of global cognitive function including measures of attention, memory, orientation, verbal fluency and other cognitive domains. A cut-off of <26 points was used for this study
to diagnose someone with cognitive impairment, therefore participants were described as having mild cognitive impairment (<26 points) or having no cognitive impairment (≥26 points) (93).

### 3.5.3 Nutrient Intake

Average daily intakes of all fats, and fats as a percentage of energy intake per day after data entry were calculated from information in the FBDs. Percentages of energy intake per day were compared with national guidelines for New Zealand and worldwide. Alcohol intake was determined with questions asked in the AUDIT alcohol questionnaire to calculate amount of drinks consumed per day.

### 3.6 Post interview Process

#### 3.6.1 Participant Follow-up

A follow-up phone call was made by the interviewers two weeks after the initial interview to remind participants to complete and send back module seven lifestyle questionnaires. When FBD and other questionnaires were returned they were checked for completeness by a trained nutritionist. If further information was required interviewers would contact the participants by telephone or email to ask for clarification or additional information. The nutritionists did not contact participants directly to ensure continuity of contact between the interviewers and the participants. Further clarification was sought when quantities of food eaten were not reported clearly, for example when the participant had one homemade muffin and they had provided a recipe but had not mentioned how many muffins they had made using the recipe, or when the nutritionists were not familiar with a recorded product/food item, for example a tofu bun. Figure 3-1 explains the follow-up process used to
ensure accuracy in the FBDs.

Figure 3-1: Follow up process for FBDs (Developed by E. Grant, G. Lilly, and R. Wilson).

3.6.2 Feedback of Results to Participants

Participants received a feedback letter detailing any abnormal results from the wider CHALICE study. The letter included results of concern such as high BMI, abnormal blood test results, elevated blood pressure, impaired cognitive function, psychological health issues and markers of eye disease. Feedback on nutritional intake was not given due to the time needed to return, check, enter and analyse the FBD. Feedback letters were usually sent before the FBD had been analysed.
3.7 Data Analysis

After the collection of raw data, data was entered, assembled for calculation of five-year CVD risk and selected nutrient data, and variables were coded according to cut-offs applied.

3.7.1 Data Entry

Each participant was allocated a study number upon entry to the study. This study number was used on all questionnaires and data collected relevant to that participant. Only study interviewers were aware of the names of participants. Others involved in participant feedback, data entry or checking of FBDs used the study number to identify participants.

Raw data were kept in locked cabinets within the University of Otago CHALICE office. Raw data (except for the FBD) were entered into a study wide custom built database Progeny 7 (Progeny Software, LLC, FL, USA) (178). Data entry accuracy was checked by the study database technician by checking the data entered against the questionnaire answers, and screening for anomalies.

Food and beverage diaries were entered into the food and nutrient analysis programme; Diet Cruncher for Windows version 1.6.0 (Way Down South Software, New Zealand) (179). All FBDs were entered by trained nutritionists using a standard operating protocol. This includes rules for assuming amounts and weights of foods especially fruits and vegetables, how to enter recipe data, and acceptable substitutions for foods not included in the database. The protocol was checked by trained nutritionists with experience of this data entry method (including a thesis supervisor), and was added to as required throughout the data entry process.

Data for intake of total energy, total fat, SAFAs, MUFAs and PUFAs were extracted from the Diet Cruncher programme on completion of entering each FBD. They were stored in a
Microsoft Excel 2007 spreadsheet and fat intakes were calculated as a percentage of total energy intake. All fat groups were calculated as a percentage of total energy consumed by multiplying the grams per day consumed by 37 kJ (number of kj per g of fat) and dividing by the total energy consumed.

For example, \((\frac{75 \text{ g of MUFA} \times 37 \text{ kJ}}{8,500 \text{ kJ}}) \times 100 = 21.8\% \text{ total energy from MUFA.}\)

### 3.7.2 Variable Coding Procedures

#### 3.7.2.1 Calculating Cardiovascular Risk Scores

The candidate manually coded five-year CVD risk scores. The six risk factors required to calculate the initial risk based on New Zealand Cardiovascular Risk Charts were coded and inputted into a spreadsheet in Microsoft Excel 2007. Variables sex and age did not require re-coding as there is a separate risk chart for men and women and all participants fitted into age group 45-54 years. Smoking and DM also had separate risk charts under sex headings and did not require further coding. If a person had not smoked in the last 12 months, they were regarded as a non-smoker.

Average SBPs were calculated by finding the mean of the three SBP readings in Microsoft Excel 2007. Systolic blood pressures were coded in Microsoft Excel 2007, according to four levels of risk in the New Zealand Cardiovascular Risk Charts (see Table 3-2). The total: HDL cholesterol ratio was coded in Microsoft Excel 2007 according to five levels of risk on the New Zealand Cardiovascular Risk Charts (see Table 3-2)

<table>
<thead>
<tr>
<th>Total:HDL cholesterol code</th>
<th>Total:HDL cholesterol level</th>
<th>SBP code</th>
<th>SBP level</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≤4.5</td>
<td>1</td>
<td>≤130mmHg</td>
</tr>
<tr>
<td>1</td>
<td>≤5.5</td>
<td>2</td>
<td>≤150mmHg</td>
</tr>
<tr>
<td>2</td>
<td>≤6.5</td>
<td>3</td>
<td>≤170mmHg</td>
</tr>
<tr>
<td>3</td>
<td>≤7.5</td>
<td>4</td>
<td>&gt;170mmHg</td>
</tr>
<tr>
<td>4</td>
<td>≤8.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Table 3-2: Cholesterol and SBP coding for CVD risk.*
Once the variables had been coded and displayed in a spreadsheet in Microsoft Excel 2007, the candidate was able to manually calculate risk for each participant by working with the New Zealand Cardiovascular Risk Charts. Each participant was designated an initial CVD risk in one of the categories described in Table 3-3 below.

<table>
<thead>
<tr>
<th>Code</th>
<th>Risk of 5-year CVD event (%)</th>
<th>Risk</th>
<th>Representative colour on risk charts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;2.5%</td>
<td>Mild</td>
<td>Light blue</td>
</tr>
<tr>
<td>2</td>
<td>2.5-5%</td>
<td>Mild</td>
<td>Purple</td>
</tr>
<tr>
<td>3</td>
<td>5-10%</td>
<td>Mild</td>
<td>Dark Blue</td>
</tr>
<tr>
<td>4</td>
<td>10-15%</td>
<td>Moderate</td>
<td>Green</td>
</tr>
<tr>
<td>5</td>
<td>15-20%</td>
<td>High</td>
<td>Yellow</td>
</tr>
<tr>
<td>6</td>
<td>20-25%</td>
<td>Very high</td>
<td>Light Orange</td>
</tr>
<tr>
<td>7</td>
<td>25-30%</td>
<td>Very high</td>
<td>Dark Orange</td>
</tr>
<tr>
<td>8</td>
<td>&gt;30%</td>
<td>Very high</td>
<td>Red</td>
</tr>
</tbody>
</table>

Table 3-3: Initial CVD risk score coding.

Every participant had to be assessed for circumstances where additional risk would apply. According to the guidelines, an additional five percent risk should be given if an individual meets one or more of the following criteria: premature family history of CVD event, high risk ethnicity (Maori, Pacific peoples or Indo-Asian peoples), diabetes for >10 years OR with Glycated Haemoglobin (HbA1c) consistently equal to or more than eight percent (64 mmol/L)(appendix C page 126). Participants should be automatically allocated to the high risk category (>20%) if they had previously had a CVD event, diabetes with other renal disease, genetic lipid disorders or diabetes with overt nephropathy. See appendix N page 183 for the detailed methodology of determining the above risk factors from the CHALICE questionnaire. CHALICE did not test for raised HbA1c (and would not have been able to assess for consistency), genetic lipid disorders or albumin (to detect nephropathy) therefore additional risk factors regarding these conditions were unable to be considered in this study. Cardiovascular disease risk may be underestimated in such patients if they did not report them when given the opportunity.

Final five-year cardiovascular disease risk score was
calculated based on adjustments. Due to the small sample, five year cardiovascular disease risk categories were merged: all three mild categories made up the ‘mild risk’ group, and all other categories made up the ‘moderate/high risk’ group (see Table 3-4).

<table>
<thead>
<tr>
<th>Final code</th>
<th>Five year CVD risk score</th>
<th>Risk</th>
<th>Representative colour on risk charts</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;2.5%</td>
<td>Mild</td>
<td>Light blue</td>
</tr>
<tr>
<td></td>
<td>2.5-5%</td>
<td>Mild</td>
<td>Purple</td>
</tr>
<tr>
<td></td>
<td>5-10%</td>
<td>Mild</td>
<td>Dark Blue</td>
</tr>
<tr>
<td>1</td>
<td>10-15%</td>
<td>Moderate</td>
<td>Green</td>
</tr>
<tr>
<td></td>
<td>15-20%</td>
<td>High</td>
<td>Yellow</td>
</tr>
<tr>
<td></td>
<td>20-25%</td>
<td>Very high</td>
<td>Light Orange</td>
</tr>
<tr>
<td></td>
<td>25-30%</td>
<td>Very high</td>
<td>Dark Orange</td>
</tr>
<tr>
<td></td>
<td>&gt;30%</td>
<td>Very high</td>
<td>Red</td>
</tr>
</tbody>
</table>

Table 3-4: Final CVD risk score coding.

Two participants did not have fasting blood tests and therefore did not have a CVD risk score. Therefore n=198 of the 200 participants were allocated a CVD risk score.

### 3.7.2.2 Cognitive Function

Cognitive function was measured using the MoCA which gives a score of 0-30. For the CHALICE study a cutoff of ≥26 is considered normal cognition and a score of <26 is considered MCI (93). This is a commonly used cut-off for cognitive impairment using MoCA (93). MCI scores were then collapsed into a dichotomous variable where 0=normal cognition/ No MCI and 1=mild cognitive impairment.

Two participants did not take the MoCA test. On twelve occasions the assessors believed that the participant’s responses (to the MOCA) may be impaired due to a reason other than natural decline in cognitive function. Overall, 13 participants did not have a MoCA test score resulting in a final sample of n=187 of the initial 200 who were allocated a MoCA test score. These are outlined in Table 3-5. These participants’ results were not included in the final analysis.
3.7.2.3 Dietary Data

Overall, n=151 of the 200 participants returned a FBD which could be analysed for nutrient intake data, therefore the final sample for the nutrient analyses was n=151.

3.7.2.3.1 Fats

World Health Organization (WHO) and the Australia New Zealand Dietary Reference guidelines suggest that 20-35% of a person’s total energy intake should come from fats (6, 8). Two categories of intake were coded:

<table>
<thead>
<tr>
<th>Coding</th>
<th>Energy from total fat per day</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≤35%</td>
<td>healthy</td>
</tr>
<tr>
<td>1</td>
<td>&gt;35%</td>
<td>high</td>
</tr>
</tbody>
</table>

Table 3-6: Coding for total fat intake per day.

World Health Organization and the Australia New Zealand Dietary Reference guidelines suggest that ≤10% of energy should come from SAFA, however the median of New Zealander’s intake from the ANS 08/09 is 13% energy per day (2, 6, 8). The median for the CHALICE sample was 12.4% energy per day so based on this two categories of intake were coded:

<table>
<thead>
<tr>
<th>Coding</th>
<th>Energy from SAFA per day</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≤10%</td>
<td>Healthy</td>
</tr>
<tr>
<td>1</td>
<td>&gt;10%</td>
<td>High</td>
</tr>
</tbody>
</table>

Table 3-7: Coding for total SAFA intake per day.
The median intake of MUFA from the ANS 08/09 was 12% energy per day and the median for the CHALICE sample was 11.4% energy per day (2). Based on this, two categories of intake were coded:

<table>
<thead>
<tr>
<th>Coding</th>
<th>Energy from MUFA per day</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;12%</td>
<td>Lower</td>
</tr>
<tr>
<td>0</td>
<td>≥12%</td>
<td>Higher</td>
</tr>
</tbody>
</table>

Table 3-8: Coding for total MUFA intake per day.

World Health Organization suggests that six to 11% of energy should come from PUFA (8). Based on this, two categories of intake were coded:

<table>
<thead>
<tr>
<th>Coding</th>
<th>Energy from PUFA per day</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;6%</td>
<td>Low</td>
</tr>
<tr>
<td>0</td>
<td>≥6%</td>
<td>Healthy</td>
</tr>
</tbody>
</table>

Table 3-9: Coding for total PUFA intake per day.

3.7.2.3.2 Alcohol

Based on the AUDIT tool used in module two; non-drinkers were classified as having no alcohol in the last 12 months and infrequent drinkers have less than one to two drinks per month. Once the frequency and volume of drinking per day were determined, participants were classified into one of three categories based on calculations:

<table>
<thead>
<tr>
<th>Alcohol intake coding</th>
<th>Alcohol intake categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Non drinker and Infrequent drinker</td>
</tr>
<tr>
<td>1</td>
<td>≤2 drinks per day</td>
</tr>
<tr>
<td>2</td>
<td>&gt;2 drinks per day</td>
</tr>
</tbody>
</table>

Table 3-10: Coding for alcohol intake per day.

3.8 Statistical Methods

A Microsoft Excel database stored all relevant information on each participant. Data were exported to IBM SPSS Statistics 20 (IBM Corporation, New York, USA) where descriptive statistical analyses were performed. These included chi-square testing using Fisher’s exact tests, and independent t-tests using Fisher’s exact tests.
Pivot tables in Microsoft Excel 2007 were used to show counts of participants in categories when comparing variables. Counts from the pivot tables were entered into tables to calculate Chi-sqaur values using the online program www.openepi.com (180).

For tests that were 2 x 2 factors: Odds ratios were calculated using Taylor series testing where confidence intervals excluded zero.

For all tests: Where numbers were sufficient for Chi Square, it was used. Where numbers were insufficient for Chi Square (less than five per category) P-Mid exact tests were used as an alternative. Statistical significance was calculated as p <0.05 with two tailed testing.
4 Results

4.1 Response Rate

Figure: 4-1 shows an overview of participant recruitment for the first 200 participants in CHALICE. As of November 2011, 488 invitation letters had been sent and 372 people had responded to a letter or phone call. Of those that had responded, 219 agreed to participate and 200 completed assessments, including 32 New Zealand Maori (16%). Two male Maori participants (1.0%) had neither blood test, essential for calculation of five-year CVD risk score, or FBD for nutrient analysis. Therefore, these data have been excluded resulting in a sample of n=198.

Two people did not take the MoCA test (one is blind, the other refused). An additional 11 participants’ test results were excluded on the basis that there was a reason they would not perform as well as expected for their age (e.g. English as second language, learning difficulties and known memory impairment from stroke). The total sample for cognitive testing was therefore n=185. Forty seven participants did not return a completed food diary. Therefore data on all variables of interest were available for 143 participants. See Figure: 4-1 below.
Figure: 4-1: Response Rate for the CHALICE study as of November 2011 (Adapted from Philp J Schluter et al 2012)

4.2 Sample Characteristics

For the purpose of describing the study cohort; the cohort excluding the two men with no CVD risk score or FBD will be referred to as the ‘modified sample’ (n=198) and the cohort in which all participants provided all information will be referred to as ‘final cohort’ (where participants gave all necessary CVD risk score, cognitive testing data, FBD and alcohol intake data) (n=143). The characteristics of the cohorts and excluded participants can be seen in
Table 4-1 and Table 4-2 below. The focus of this thesis is on the n=143 completers in the final sample. Some comparison with those excluded from the final sample is highlighted for interest.

4.2.1 Demographics

The mean age of the sample was 50 years old. The final sample comprised 59.4% (85) female and 40.6% (58) male participants. Nineteen participants (13.3%) identified as New Zealand Maori and 62.2% (89) had a post-secondary education. Only 11.2% (16) were current smokers and 3.5% had diabetes. The mean total: HDL cholesterol level was 4.1 for the sample and 3.8, 3.9 and 4.4 for female, male and Maori respectively. The mean SBP was 133.7mmHg for the sample and 131.1, 137.4 and 138.9 for female, male and Maori respectively.

There were no significant differences between those in the sample (n=143) and those excluded from the sample (n=55) with respect to sex, Maori ethnicity, education level, smoking, diabetes, cholesterol and SBP. However there were a number of variables which were over represented in those excluded although the differences did not reach statistical significance: smoking (p=0.07), diabetes (p=0.075), Maori ethnicity (p=0.27) and lower education level (p=0.108). Overall it can be acknowledged that the demographic characteristics of those in the final sample are not significantly different from those excluded.
<table>
<thead>
<tr>
<th>Variable</th>
<th>N=(%) final</th>
<th>Total</th>
<th>N=(%)</th>
<th>Total</th>
<th>N=(%)</th>
<th>Total</th>
<th>P-value(2-tailed)**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>113(57.1%)</td>
<td>28(50.9%)</td>
<td>85(59.4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>85(42.9%)</td>
<td>198(100%)</td>
<td>27(49.01%)</td>
<td>55(100%)</td>
<td>58(40.6%)</td>
<td>143(100%)</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZEO only</td>
<td>138(69.7%)</td>
<td>29(52.7%)</td>
<td>109(76.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ Maori only</td>
<td>8(4.0%)</td>
<td>5(9.1%)</td>
<td>3(2.1%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZEO &amp; NZ Maori</td>
<td>22(11.1%)</td>
<td>6(10.9%)</td>
<td>16(11.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ Maori (any)</td>
<td>30 (15.1%)</td>
<td>11(20%)</td>
<td>19(13.3%)</td>
<td></td>
<td></td>
<td></td>
<td>0.27</td>
</tr>
<tr>
<td>Cook Island &amp; NZEO</td>
<td>1(0.5%)</td>
<td>0(0%)</td>
<td>1(0.7%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese only</td>
<td>2(1.0%)</td>
<td>1(1.8%)</td>
<td>1(0.7%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese &amp; Other Ethnicity</td>
<td>1 (0.5%)</td>
<td>0(0%)</td>
<td>1(0.7%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>1 (0.5%)</td>
<td>1(1.8%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Ethnicity only</td>
<td>22 (11.1%)</td>
<td>11(20%)</td>
<td>11(7.7%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Ethnicity &amp; NZEO</td>
<td>3 (1.5%)</td>
<td>198(100%)</td>
<td>2(3.6%)</td>
<td>55(100%)</td>
<td>1(0.7%)</td>
<td>143(100%)</td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary school or none</td>
<td>82(41.4%)</td>
<td>28(50.9%)</td>
<td>54(37.8%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post secondary school</td>
<td>116(58.6%)</td>
<td>198(100%)</td>
<td>27(49.01%)</td>
<td>55(100%)</td>
<td>89(62.2%)</td>
<td>143(100%)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Smoker</td>
<td>28 (14.1%)</td>
<td>12(21.8%)</td>
<td>16(11.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Smoker</td>
<td>170(85.9%)</td>
<td>198(100%)</td>
<td>43(78.2%)</td>
<td>55(100%)</td>
<td>127(88.8%)</td>
<td>143(100%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Female smoker</td>
<td>18 (15.9%)</td>
<td>8(14.5%)</td>
<td>10(11.8%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female non-smoker</td>
<td>95 (84.1%)</td>
<td>113(57.1%)</td>
<td>20(36.4%)</td>
<td>28(50.9%)</td>
<td>75(88.2%)</td>
<td>85(59.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Chi-Square</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variable</td>
<td>Male smoker</td>
<td>Male non-smoker</td>
<td>NZ Maori smoker</td>
<td>NZ Maori non-smoker</td>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------</td>
<td>-----------------</td>
<td>-----------------</td>
<td>---------------------</td>
<td>--------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (11.8%)</td>
<td>75 (88.2%)</td>
<td>6 (20.0%)</td>
<td>24 (80.0%)</td>
<td>11 (5.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 (7.3%)</td>
<td>85 (42.9%)</td>
<td>3 (5.5%)</td>
<td>30 (15.1%)</td>
<td>6 (10.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 (10.3%)</td>
<td>23 (41.8%)</td>
<td>3 (15.8%)</td>
<td>8 (14.5%)</td>
<td>5 (3.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>27 (49.1%)</td>
<td>52 (89.7%)</td>
<td>11 (20.0%)</td>
<td>16 (84.2%)</td>
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<td></td>
</tr>
<tr>
<td></td>
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<td>58 (40.6%)</td>
<td></td>
<td>19 (13.3%)</td>
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<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>11 (5.6%)</td>
<td>187 (94.4%)</td>
<td>6 (5.3%)</td>
<td>107 (94.7%)</td>
<td>11 (5.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>198 (100%)</td>
<td>3 (5.5%)</td>
<td>113 (57.1%)</td>
<td>3 (5.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>49 (89.1%)</td>
<td>3 (5.5%)</td>
<td>25 (45.5%)</td>
<td>3 (5.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>55 (100%)</td>
<td>3 (5.5%)</td>
<td>28 (50.9%)</td>
<td>3 (5.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>138 (96.5%)</td>
<td></td>
<td>82 (96.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>143 (100%)</td>
<td></td>
<td>85 (59.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 (5.9%)</td>
<td>80 (94.1%)</td>
<td>2 (6.7%)</td>
<td>28 (93.3%)</td>
<td>5 (5.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 (5.4%)</td>
<td>85 (42.9%)</td>
<td>2 (3.6%)</td>
<td>30 (15.1%)</td>
<td>3 (5.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 (43.6%)</td>
<td>27 (49.1%)</td>
<td>0 (0%)</td>
<td>9 (16.4%)</td>
<td>2 (3.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>56 (96.6%)</td>
<td>58 (40.6%)</td>
<td></td>
<td>11 (20.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>19 (100%)</td>
<td>19 (13.3%)</td>
<td></td>
<td>19 (13.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.1: Demographics of the modified sample, and those excluded and included in the final sample.

** p-value compares those excluded from the final sample (n=55) to those included in the final sample (n=143) with Fisher’s Exact Test.

* p<0.05 is a statistically significant value

NZ=New Zealand
Table 4-2: The differences between the cholesterol and SBP of the modified and final samples.

** p-value compares those excluded from the final sample (n=55) (not shown) to those included in the final sample (n=143) with Fisher’s Exact Test.
* p<0.05 is a statistically significant value
NZ=New Zealand

### 4.2.2 CVD risk

As described in the methods section, there were several steps to determine the five year CVD risk score of each participant. Table 4-1 and Table 4-2 described smoking status, diabetes status, cholesterol and blood pressures measurements of the cohorts. These were used in the first stage of determining the CVD risk score using the New Zealand...
Cardiovascular Risk Charts. See appendix O page 194 for the distribution of the initial CVD risk scores from this stage.

Appendix D page 129 describes additional risk factors involved in calculating the CVD risk scores, resulting reclassification of the initial CVD risk score if they apply to the individual:

Thirty seven (25.9%) of the final sample were given a higher risk due to family history of CVD and ethnicity, and 6 (4.2%) were given an automatic ‘high risk’ due to past CVD event.

Males and Maori were more likely to have a moderate/high CVD risk score than females (p=0.026) and non-Maori (p=0.029). There were more participants with a moderate or high risk in the excluded group (n=55) compared with the included group (n=143) (p=0.037), this suggests that those in the excluded group have higher risk than the final sample and may be less healthy. These results are shown below in Table 4-3.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Modified sample</th>
<th>Final sample</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 4-3: Final five year CVD risk for the modified and final samples with comparisons within the final sample.

**P-values compare mild risk with moderate + high + very high risk in male versus female and Maori versus non-Maori with Fisher’s Exact Test.

* p<0.05 is a statistically significant value

NZ=New Zealand

<table>
<thead>
<tr>
<th></th>
<th>N=(%)</th>
<th>Total</th>
<th>N=(%)</th>
<th>Total</th>
<th>(2-tailed)**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Final CVD risk based on additional risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild risk</td>
<td>163 (82.3%)</td>
<td></td>
<td>123(86.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate risk</td>
<td>18 (9.1%)</td>
<td></td>
<td>11(7.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>4 (2.0%)</td>
<td></td>
<td>2 (1.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very high risk</td>
<td>13 (6.6%)</td>
<td>198</td>
<td>7 (4.9%)</td>
<td>143</td>
<td></td>
</tr>
<tr>
<td>Female mild risk</td>
<td>103 (91.1%)</td>
<td></td>
<td>78 (91.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female moderate risk</td>
<td>5 (4.4%)</td>
<td></td>
<td>4 (4.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female high risk</td>
<td>3 (2.7%)</td>
<td></td>
<td>2 (2.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female very high risk</td>
<td>2 (1.8%)</td>
<td>113</td>
<td>1 (1.2%)</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Male mild risk</td>
<td>60 (70.6%)</td>
<td></td>
<td>45 (77.6%)</td>
<td></td>
<td>0.026**</td>
</tr>
<tr>
<td>Male moderate risk</td>
<td>13 (15.3%)</td>
<td></td>
<td>7 (12.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male high risk</td>
<td>1 (1.2%)</td>
<td></td>
<td>0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male very high risk</td>
<td>11 (12.9%)</td>
<td>85</td>
<td>6 (10.3%)</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>NZ Maori mild risk</td>
<td>17 (56.7%)</td>
<td></td>
<td>13 (68.4%)</td>
<td></td>
<td>0.029*</td>
</tr>
<tr>
<td>NZ Maori moderate risk</td>
<td>8 (26.7%)</td>
<td></td>
<td>5 (26.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ Maori high risk</td>
<td>2 (6.7%)</td>
<td></td>
<td>1 (5.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ Maori very high risk</td>
<td>3 (10.0%)</td>
<td>30</td>
<td>0 (0%)</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

4.2.3 Cognitive Testing

One hundred and eighty seven participants had a valid MoCA score which could be included in analysis, however 44 of these participants did not return a FBD so could not be included in the final sample (n=143).

The cutoff for being classified as having mild cognitive impairment using the MoCA score is <26 points (93). The mean MoCA score was 27.04 with a minimum of 21.0 maximum of 30.0 and median of 27.0. There was a minimum of 16.0 when looking at the spread of all tested (n=187) suggesting that those with more severe cognitive impairment were not included in the final sample.
Thirty-three (23.1%) participants had cognitive impairment. There was no statistically significant difference between the prevalence of cognitive impairment in males and females (p=0.69). Depression may be associated with impaired cognition. There were no differences between prevalence of depression amongst males and females (p=1.00).

There were no differences in prevalence of depression (p=0.33) or MCI (p=0.11) between those excluded and included in the final. These results are presented in Table 4-4 below.

<table>
<thead>
<tr>
<th></th>
<th>Original Sample</th>
<th>Final Sample</th>
<th>P-value(2-tailed)**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>Total</td>
<td>N(%)</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>48 (25.9%)</td>
<td>33(23.1%)</td>
<td></td>
</tr>
<tr>
<td>No cognitive impairment</td>
<td>137 (74.1%)</td>
<td>185</td>
<td>110(76.9%)</td>
</tr>
<tr>
<td>Female cognitive impairment</td>
<td>30 (27.8%)</td>
<td>21(24.7%)</td>
<td></td>
</tr>
<tr>
<td>Female no cognitive impairment</td>
<td>78 (72.2%)</td>
<td>108</td>
<td>64(75.3%)</td>
</tr>
<tr>
<td>Male cognitive impairment</td>
<td>18 (23.3%)</td>
<td>12(20.7%)</td>
<td></td>
</tr>
<tr>
<td>Male no cognitive impairment</td>
<td>59 (76.6%)</td>
<td>77</td>
<td>46(79.3%)</td>
</tr>
<tr>
<td>Depression</td>
<td>22 (11%)</td>
<td>14(9.8%)</td>
<td></td>
</tr>
<tr>
<td>No depression</td>
<td>178 (89%)</td>
<td>198</td>
<td>129(90.2%)</td>
</tr>
<tr>
<td>Female depression</td>
<td>14 (12.4%)</td>
<td>8(9.4%)</td>
<td></td>
</tr>
<tr>
<td>Female no depression</td>
<td>99 (87.6%)</td>
<td>113</td>
<td>77(90.6%)</td>
</tr>
<tr>
<td>Male depression</td>
<td>8 (9.4%)</td>
<td>6(10.3%)</td>
<td></td>
</tr>
<tr>
<td>Male no depression</td>
<td>77 (90.6%)</td>
<td>85</td>
<td>52(89.7%)</td>
</tr>
</tbody>
</table>

Table 4-4 : Distribution of MCI and depression in the modified and final samples with analysis on the final sample.
* p<0.05 is a statistically significant value
4.2.4 Nutrient intakes

One hundred and fifty one participants returned completed food diaries including 21 Maori, 88 females, and 63 males. The nutrient intakes are reported for those included in the final sample only in Table 4-5 below, however the intakes for all 151 who returned FBDs are available (appendix P page 195). The intakes of fats did not vary significantly between males and females or Maori and non-Maori, except that Maori consume more PUFA than non-Maori (p=0.025).
Fat intakes in the final sample (% energy intake/day)

<table>
<thead>
<tr>
<th></th>
<th>N=</th>
<th>Mean</th>
<th>NZ mean</th>
<th>Med</th>
<th>p-value (2-tailed)</th>
<th>N=</th>
<th>Mean</th>
<th>NZ mean</th>
<th>Med</th>
<th>p-value (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total fat intake</strong></td>
<td>143</td>
<td>32.9</td>
<td>33.7</td>
<td>59.6</td>
<td></td>
<td>19</td>
<td>33.95</td>
<td>N/A</td>
<td>40.9</td>
<td>0.387</td>
</tr>
<tr>
<td><strong>Total fat intake</strong></td>
<td>85</td>
<td>33.4</td>
<td>33.8</td>
<td>59.6</td>
<td></td>
<td>58</td>
<td>32.3</td>
<td>33.7</td>
<td>45.8</td>
<td>0.240</td>
</tr>
<tr>
<td><strong>SAFA intake total cohort</strong></td>
<td>143</td>
<td>12.75</td>
<td>13.1</td>
<td>21.6</td>
<td></td>
<td>19</td>
<td>12.6</td>
<td>N/A</td>
<td>20.2</td>
<td>0.815</td>
</tr>
<tr>
<td><strong>SAFA intake</strong></td>
<td>85</td>
<td>12.7</td>
<td>13.1</td>
<td>21.6</td>
<td></td>
<td>58</td>
<td>12.8</td>
<td>13.1</td>
<td>18.8</td>
<td>0.917</td>
</tr>
<tr>
<td><strong>MUFA intake</strong></td>
<td>143</td>
<td>11.7</td>
<td>12.4</td>
<td>31.2</td>
<td></td>
<td>19</td>
<td>11.8</td>
<td>N/A</td>
<td>16.3</td>
<td>0.821</td>
</tr>
<tr>
<td><strong>MUFA intake</strong></td>
<td>85</td>
<td>11.9</td>
<td>12.3</td>
<td>31.2</td>
<td></td>
<td>58</td>
<td>11.3</td>
<td>12.4</td>
<td>17.9</td>
<td>0.232</td>
</tr>
<tr>
<td><strong>PUFA intake total cohort</strong></td>
<td>143</td>
<td>4.96</td>
<td>4.9</td>
<td>14.5</td>
<td></td>
<td>19</td>
<td>5.9</td>
<td>N/A</td>
<td>14.5</td>
<td>0.025 **</td>
</tr>
<tr>
<td><strong>PUFA intake</strong></td>
<td>85</td>
<td>5.2</td>
<td>4.9</td>
<td>14.5</td>
<td></td>
<td>58</td>
<td>4.6</td>
<td>4.8</td>
<td>8.8</td>
<td>0.093</td>
</tr>
</tbody>
</table>

Table 4-5: Fat intakes (as a percentage of energy intakes per day) for the sample analysing differences between male and female, Maori and non-Maori.

**Differences are for female versus male and Maori versus non-Maori
**Maori have a higher PUFA intake than non-Maori
*p<0.05 is a statistically significant value
NZ=New Zealand

Alcohol intake (standard drinks per day) for the cohort is shown in Table 4-6. There were no differences in consumption between males and females, and Maori and non-Maori. It appeared that those in the final sample are more likely to consume two or less drinks per day, and less likely to abstain or have more than two drinks per day.
<table>
<thead>
<tr>
<th></th>
<th>Modified Sample</th>
<th>Final Sample</th>
<th>P-value(2-tailed)**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N= (%)</td>
<td>Total</td>
<td>N=(%)</td>
</tr>
<tr>
<td>0 drinks per day/Infrequent drinking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cohort</td>
<td>50(25.3)</td>
<td>29(20.3)</td>
<td></td>
</tr>
<tr>
<td>≤2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cohort</td>
<td>110(55.6)</td>
<td>89(62.2)</td>
<td></td>
</tr>
<tr>
<td>&gt;2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cohort</td>
<td>38(19.2)</td>
<td>198</td>
<td>25(17.5)</td>
</tr>
<tr>
<td>0 drinks per day/Infrequent drinking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori sample</td>
<td>5(16.7)</td>
<td>2(10.5)</td>
<td>0.364</td>
</tr>
<tr>
<td>≤2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori sample</td>
<td>19(63.3)</td>
<td>14(73.7)</td>
<td>0.318</td>
</tr>
<tr>
<td>&gt;2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori sample</td>
<td>6(20.0)</td>
<td>30</td>
<td>3(15.8)</td>
</tr>
<tr>
<td>0 drinks per day/Infrequent drinking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>34(30.1)</td>
<td>21 (24.7)</td>
<td></td>
</tr>
<tr>
<td>≤2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>63(55.8)</td>
<td>52(61.2)</td>
<td></td>
</tr>
<tr>
<td>&gt;2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>16(14.2)</td>
<td>113</td>
<td>12(14.1)</td>
</tr>
<tr>
<td>0 drinks per day/Infrequent drinking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16(18.8)</td>
<td>8(13.8)</td>
<td>0.140</td>
</tr>
<tr>
<td>≤2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>47(55.3)</td>
<td>37(63.8)</td>
<td>0.861</td>
</tr>
<tr>
<td>&gt;2 drinks per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22(25.9)</td>
<td>85</td>
<td>13(22.4)</td>
</tr>
</tbody>
</table>

Table 4-6: Alcohol intake in the modified and final samples with analyses within the final sample.

**P-values comparing intake of Male versus female and Maori versus non-Maori in the final sample using Fishers Exact Test.

* p<0.05 is a statistically significant value
Analyses

The main statistical analyses were performed on the final sample (n=143). These analyses are designed to address the thesis hypotheses including relationships between MCI and diet, CVD risk and diet and CVD risk and MCI. Analyses were bi-variate, as it is beyond the scope of this thesis to investigate using multivariate analyses. Where possible, odds ratios (OR), 95% confidence intervals for the odds ratio (CI) and 2-tailed p-values are presented to demonstrate the relationships. Two by two factor analyses were used for most statistical tests, except when analyzing alcohol intake where a three by two factor analysis was necessary. Results reported are from Fisher’s exact Tests.

4.2.5 CVD risk vs Mild Cognitive Impairment and Nutrient Intakes

Twenty (14.0%) participants had a moderate/high CVD risk and 143 (86%) had a mild CVD risk. Moderate/high risk of CVD event in five-years was significantly associated with higher risk of MCI (p=0.005). There were no significant relationships between any dietary factors and CVD risk in this sample. Results from these analyses are shown in tables Table 4-7 and Table 4-8 below.
### Table 4-7: Statistical analysis for CVD risk versus dietary factors and MCI.

<table>
<thead>
<tr>
<th>Variable Category</th>
<th>CVD Risk % (n=)</th>
<th>Total % (n=)</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mod/High</td>
<td>Mild</td>
<td>OR</td>
</tr>
<tr>
<td><strong>MCI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>50.0% (10)</td>
<td>18.7% (23)</td>
<td>23.0% (33)</td>
</tr>
<tr>
<td>No</td>
<td>50.0% (10)</td>
<td>81.3% (100)</td>
<td>77.0% (110)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100% (20)</td>
<td>100% (123)</td>
<td>100% (143)</td>
</tr>
<tr>
<td><strong>Total fat intake</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;35% energy/day</td>
<td>45.0% (9)</td>
<td>30.1% (37)</td>
<td>32.2% (46)</td>
</tr>
<tr>
<td>≤35% energy/day</td>
<td>55.0% (11)</td>
<td>69.9% (86)</td>
<td>67.8% (97)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100% (20)</td>
<td>100% (123)</td>
<td>100% (143)</td>
</tr>
<tr>
<td><strong>SAFA intake</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10% energy/day</td>
<td>5.0% (1)</td>
<td>17.9% (22)</td>
<td>16.1% (23)</td>
</tr>
<tr>
<td>&gt;10% energy/day</td>
<td>95.0% (19)</td>
<td>82.1% (101)</td>
<td>83.9% (120)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100% (20)</td>
<td>100% (123)</td>
<td>100% (143)</td>
</tr>
<tr>
<td><strong>MUFA intake</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12% energy/day</td>
<td>70.0% (14)</td>
<td>59.4% (73)</td>
<td>60.8% (87)</td>
</tr>
<tr>
<td>≥12% energy/day</td>
<td>30.0% (6)</td>
<td>40.6% (50)</td>
<td>39.2% (56)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100% (20)</td>
<td>100% (123)</td>
<td>100% (143)</td>
</tr>
<tr>
<td><strong>PUFA intake</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6% energy/day</td>
<td>80.0% (16)</td>
<td>76.4% (94)</td>
<td>76.9% (110)</td>
</tr>
<tr>
<td>≥6% energy/day</td>
<td>20.0% (4)</td>
<td>23.6% (29)</td>
<td>23.1% (33)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100% (20)</td>
<td>100% (123)</td>
<td>100% (143)</td>
</tr>
</tbody>
</table>

* p<0.05 is a statistically significant value

### Table 4-8: Statistical analysis for CVD risk versus level of alcohol intake.

<table>
<thead>
<tr>
<th>ETOH intake: drinks per day % (n=)</th>
<th>CVD Risk % (n=)</th>
<th>Total</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0/Infrequent intake</td>
<td>25.0% (5)</td>
<td>19.5% (24)</td>
<td>20.3% (29)</td>
</tr>
<tr>
<td>≤2</td>
<td>50.0% (10)</td>
<td>64.2% (79)</td>
<td>62.2% (89)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>25.0% (5)</td>
<td>16.3% (20)</td>
<td>15.5% (25)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100% (20)</td>
<td>100% (123)</td>
<td>100% (143)</td>
</tr>
</tbody>
</table>

* p<0.05 is a statistically significant value


4.2.6 Mild Cognitive Impairment vs Nutrient Intakes

Thirty-three (23.1%) participants have MCI whereas 110 (76.9%) have normal cognition.

Although no dietary factors were significantly associated with having MCI, high intake of saturated fat (>10% of energy intake per day) showed a non-significant trend (p=0.07) as did consuming >2 drinks per day or 0 drink per day/infrequent consumption (0.075). Results for these analyses are presented in tables Table 4-9 and Table 4-10 below.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>MCI % (n=)</th>
<th>Total</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>OR</td>
</tr>
<tr>
<td>Total fat intake</td>
<td>&gt;35% energy/day</td>
<td>39.4% (13)</td>
<td>30.0% (33)</td>
<td>32.2% (46)</td>
</tr>
<tr>
<td></td>
<td>≤35% energy/day</td>
<td>60.06% (20)</td>
<td>70.0% (77)</td>
<td>67.8% (97)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100% (33)</td>
<td>100% (110)</td>
<td>100% (143)</td>
</tr>
<tr>
<td>SAFA intake</td>
<td>&gt;10% energy/day</td>
<td>93.9% (31)</td>
<td>80.9% (89)</td>
<td>83.9% (120)</td>
</tr>
<tr>
<td></td>
<td>≤10% energy/day</td>
<td>6.1% (2)</td>
<td>19.1% (21)</td>
<td>16.1% (23)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100% (33)</td>
<td>100% (110)</td>
<td>100% (143)</td>
</tr>
<tr>
<td>MUFA intake</td>
<td>&lt;12% energy/day</td>
<td>48.5% (16)</td>
<td>64.5% (71)</td>
<td>60.8% (87)</td>
</tr>
<tr>
<td></td>
<td>≥12% energy/day</td>
<td>51.5% (17)</td>
<td>35.5% (39)</td>
<td>39.2% (56)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100% (33)</td>
<td>100% (110)</td>
<td>100% (143)</td>
</tr>
<tr>
<td>PUFA intake</td>
<td>&lt;6% energy/day</td>
<td>78.8% (26)</td>
<td>76.4% (84)</td>
<td>76.9% (110)</td>
</tr>
<tr>
<td></td>
<td>≥6% energy/day</td>
<td>21.2% (7)</td>
<td>23.6% (26)</td>
<td>23.1% (33)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100% (33)</td>
<td>100% (110)</td>
<td>100% (143)</td>
</tr>
</tbody>
</table>

Table 4-9: Statistical analysis for MCI versus dietary fat intake.
* p<0.05 is a statistically significant value
<table>
<thead>
<tr>
<th>ETOH intake: drinks per day</th>
<th>MCI % (n=)</th>
<th>Total</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Chi Square</td>
</tr>
<tr>
<td>0/Infrequent intake</td>
<td>30.3% (10)</td>
<td>17.3% (19)</td>
<td>20.3% (29)</td>
</tr>
<tr>
<td>≤ 2</td>
<td>45.5% (15)</td>
<td>67.3% (74)</td>
<td>62.2% (89)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>24.2% (8)</td>
<td>15.4% (17)</td>
<td>17.5% (25)</td>
</tr>
<tr>
<td>Total</td>
<td>100% (33)</td>
<td>100% (110)</td>
<td>100% (143)</td>
</tr>
</tbody>
</table>

Table 4-10: Statistical analysis for MCI versus alcohol intake level.
* p<0.05 is a statistically significant value

4.2.7 Other Analyses

The following analyses were performed on both the final sample and larger samples in order to identify associations between factors outside of the hypotheses of this thesis, which may interact with them.

Depression and education are known to influence a person’s cognitive ability. In this sample having depression at time of testing and having a lower education (secondary school or below) were associated with a significantly higher risk of MCI. This was true for inclusive and exclusive samples. Depression was not associated with CVD risk in the modified or final samples (p=0.92), however those with a higher CVD risk were more likely to have a lower education in both modified (p=0.0004) and final samples (p=0.009). These analyses are presented in Table 4-11 and Table 4-12 below.
<table>
<thead>
<tr>
<th>Variable % (n=)</th>
<th>Category</th>
<th>MCI % (n=)</th>
<th>Total</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>OR</td>
</tr>
<tr>
<td>Depression</td>
<td>Yes</td>
<td>22.9%(11)</td>
<td>7.3%(10)</td>
<td>11.4%(21)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>77.1%(37)</td>
<td>92.7%(127)</td>
<td>88.6%(164)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100%(48)</td>
<td>100%(137)</td>
<td>100%(185)</td>
</tr>
<tr>
<td>Depression</td>
<td>Yes</td>
<td>21.2% (7)</td>
<td>6.4% (7)</td>
<td>9.8% (14)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>78.8% (26)</td>
<td>93.6% (103)</td>
<td>90.2% (129)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100% (33)</td>
<td>100% (110)</td>
<td>100% (143)</td>
</tr>
<tr>
<td>Education</td>
<td>Lower</td>
<td>54.2%(26)</td>
<td>35.8%(49)</td>
<td>40.5%(75)</td>
</tr>
<tr>
<td></td>
<td>Higher</td>
<td>45.8%(22)</td>
<td>64.2%(88)</td>
<td>59.5%(110)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100%(48)</td>
<td>100%(137)</td>
<td>100%(185)</td>
</tr>
<tr>
<td>Education</td>
<td>Lower</td>
<td>54.5%(18)</td>
<td>32.7%(36)</td>
<td>37.8%(54)</td>
</tr>
<tr>
<td></td>
<td>Higher</td>
<td>45.5%(15)</td>
<td>67.3%(74)</td>
<td>62.2%(89)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100%(33)</td>
<td>100%(110)</td>
<td>1100%(143)</td>
</tr>
</tbody>
</table>

Table 4-11: Statistical analysis for MCI versus additional factors of depression and education.

* p<0.05 is a statistically significant value

An analysis was performed to see if the alcohol consumption of those who did return a food diary was different from those who did not. Those that returned a food diary were significantly more likely to consume ≤2 drinks per day (p=0.003) and these people were also more likely to be included in the final sample. Those who did not return a FBD were not included in the final sample.
<table>
<thead>
<tr>
<th>ETOH intake: drinks per day % (n=)</th>
<th>0/infrequent</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2</td>
<td>21.2%(32)</td>
<td>38.3%(18)</td>
<td>25.3%(50)</td>
<td>11.59</td>
<td>0.003**</td>
</tr>
<tr>
<td>&gt;2</td>
<td>38.3%(18)</td>
<td>25.3%(50)</td>
<td>21.2%(32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100%(151)</td>
<td>100%(151)</td>
<td>100%(198)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4-12: Statistical analysis comparing level of alcohol intake in those who did, and did not return a FBD.

* p<0.05 is a statistically significant value
5 Discussion

Those with a higher CVD risk or depression are more likely to have MCI but those with depression do not have increased CVD risk. Participants with a lower level of education (secondary school or lower) are more likely to have both MCI and higher CVD risk. A weak relationship that was approaching significance was found between SAFA intake and MCI but no other relationships were observed between dietary constituents and CVD risk or MCI. CHALICE participants were similar to the general New Zealand population of the same age in terms of the prevalence of biological risk factors such as BP and cholesterol. For example, average SBP of CHALICE participants was 133.7 mmHg compared to a mean of 133 mmHg for 51-70 year old ANS participants (2). Mean total: HDL cholesterol level for CHALICE participants (4.06) was also similar to that of ANS participants (3.95). Prevalence of diagnosed diabetes was lower in CHALICE participants (3.5%) compared to ANS participants (4.9%) but this may be due to participant age differences between the two studies. Dietary intakes of interest of CHALICE participants were also similar to those of ANS participants, with only small differences were seen between populations. For example, total fat intake was 33.8% of total energy in ANS participants, compared to 32.9% in CHALICE. This small difference is likely to be due to differences in dietary assessment methods used between studies, with ANS data collected using one 24 hour recall and CHALICE data from a four day estimated FBD. It is clear that the CHALICE sample consume fats in the same proportions as the majority of New Zealanders given the differences in methodology used in the studies. Studies have found that the CHALICE sample are not consuming a heart healthy diet due to high intake of SAFA and lower than desirable intake of USFAs (181). It would be expected that this leads to a higher CVD risk due to biological markers such as LDL cholesterol levels.
The ‘New Zealand Alcohol and Drug Use Survey 2007/08’ estimates that 85% of adults had an alcoholic beverage within the last year (81). This is likely to be similar to the CHALICE cohort as 20.3% of the final sample abstain from drinking or drink infrequently. The survey showed that Maori are less likely to drink daily and less likely to drink at all than NZEO (81). Similarly, in this sample only 10.5% of Maori abstain or drink infrequently.

There were 57 participants excluded from the original 200: two because of insufficient data for the study, and an additional 55 who did not return a FBD or were excluded from the MoCA test.

It may be generalised that those in the excluded group are less healthy than those in the final sample. The implications for this study are that associations that exist between CVD risk and other factors are underestimated due to the exclusion of higher risk participants.

5.1 CVD risk and risk of MCI

No previous studies have investigated the link between five-year fatal and non-fatal CVD risk and MCI. This study has found that in a sample of 143 participants, those with a higher CVD risk have a higher risk of MCI. Several studies including the ‘Framingham Heart Study’ have found positive associations between individual CVD risk factors such as high SBP, smoking and diabetes, and cognitive impairment and cognitive decline (101, 119, 121, 124). Elias et al, found that midlife blood pressure predicts late life cognitive function in a cohort study of those aged 55 years and older in the Framingham cohort (101). Cross-sectional results from the same study also suggest there is a strong link between DM and/or high BP and cognitive function (119). Results from a meta-analysis of 26 studies by Anstey et al in 2007 show a strong relationship between smoking and decreased cognitive function (124). These studies were in a slightly older age group to CHALICE and were much larger samples, yet results are
comparable to CHALICE findings, as they all suggest that the more CVD risk factors an individual has, the greater the impact on cognitive function. Other risk factors such as family history of CVD, ethnicity and particular genetic polymorphisms (e.g. ApoE) mean that a person can be predisposed to increased risk of CVD or MCI independently of lifestyle factors (13, 82, 182). Therefore these factors need to be considered.

There is no available literature investigating associations between CVD risk scores and cognitive function; however there is evidence to suggest that some risk factors for CVD included in the New Zealand Cardiovascular Risk Charts increase risk of cognitive impairment Therefore when combining risk factors one might expect an increased risk of cognitive impact as found in the present study.

5.2 Diet and CVD risk

This study found no significant relationships between five-year CVD risk and fats or alcohol intake. This may be because in this sample, diet has not been a determining factor in CVD risk and that other risk factors such as genetics, physical activity and body mass may be stronger predictors. Because these have not been thoroughly examined in this thesis, we cannot determine if this is the case. It should also be acknowledged that with a small sample size, the study may be underpowered to detect small but clinically important effect sizes.

Total fat intake is not thought to be a good predictor of CVD risk; it is the profile of fats consumed that increases or decreases CVD risk (12, 53). In a recent meta-analysis, Skeaff et al found that even when total fat ranged from 27% of energy to 47% of energy per day, there was a convincing lack of relationship with fatal and non-fatal CHD (53). This is widely accepted in literature due to the importance of the type of fat consumed. This study has
therefore successfully replicated what would be expected, based on the wide body of knowledge on the subject and previous studies. 

No significant relationships between SAFA intake and five-year CVD risk were identified in this study. Our results are not in agreement with previous research from cohort studies such as ‘The Seven Countries Study’, which was the first to show that high SAFA intake increases CVD risk. There is an overwhelming amount of evidence that shows that SAFA intake is also associated with CVD events and mortality \((12, 45, 183)\). It is recognised that a high intake of SAFA increases the risk of heart disease and stroke through increasing LDL cholesterol and promoting atherosclerosis \((43)\). More recent evidence from meta-analyses of studies of middle aged and older populations shows that only changing the ratio of SAFA: USFAs leads to decreased risk of a CVD event \((50, 51, 53)\). Other meta-analyses have been unable to show a correlation of substitution fats with CVD which has sparked interest world-wide suggesting that SAFA is not to blame for increasing CVD risk \((48)\). Despite the fact that this study suggests the ratio of SAFA: USFA is not related to CVD risk, a larger sample size is needed to investigate associations and in order to investigate whether SAFA intake determines risk, longitudinal data from the CHALICE cohort is needed. Given that the present study has assessed CVD risk with many factors other than cholesterol level, it may be possible that those with higher SAFA intake do have a higher cholesterol level, yet this does not bring them into the moderate/high CVD risk level due to lack of other risk factors. 

In contrast with previous research findings, there were no significant relationships between MUFA or PUFA and five-year CVD risk in this study. There is overwhelming evidence that both MUFA and PUFA are beneficial for cardiovascular health, especially when they replace intake of SAFA \((50, 51, 53)\). Unsaturated fatty acids are important for cardiovascular health because of the anti-inflammatory effects of n-3 PUFA and the cholesterol reducing effects of
MUFA and PUFA (43). Unfortunately the present study was unable to measure replacement fats due to the cross-sectional nature of the study and unable to measure n-3 PUFA. Future research in this cohort could focus on the ratio of SAFA:USFA and its relationships with CVD risk. The cut-offs used to categorise low and high intake in this study may also have led to a lack of significant associations and a more sensitive cut-point may be needed.

As discussed in the literature review, the relationship between CVD risk and alcohol has been widely studied in similar aged populations to the CHALICE sample, and a ‘U’ shaped curve gives the best indicator of the relationship. Healthy intake currently accepted as being one to two drinks per day at the lowest point of the curve (43, 56, 60, 61, 63). Marmot et al found that four plus drinks per day is protective against CVD and being a ‘non-drinker’ puts one at highest risk of CVD death (58), however evidence from other studies has been able to show strong evidence against heavy drinking for both CVD and total mortality (56, 57, 60, 61). One mechanism for this is that mild drinking (one to two drinks per day) is known to increase HDL cholesterol therefore decreasing the total cholesterol:HDL ratio used in the CVD risk calculation (184). Those who are heavy drinkers experience an increase in blood pressure (184).

The present study was unable to show any relationship between alcohol intake and CVD risk (p=0.3928) when it was expected that those who have two or less drinks per day would have the lowest CVD risk. The most likely reasons for a lack of association are a combination of methodological insufficiency and lack of statistical power. The majority of observational studies investigating alcohol and CVD risk have at least several hundred participants (58, 60, 61). As many other factors contribute to HDL and BP, multivariate analyses are used.
5.3 Diet and MCI

No relationship was found between total fat intake and MCI. Relationships between fat intake and MCI have not been widely investigated but results of one study in a Finnish population of 65-84 year olds found a significant positive relationship between total fat and MCI in those consuming diets high in fat from dairy products (p=0.05) (144). More research is therefore needed on these relationships.

An almost significant relationship was seen between SAFA intake and MCI however this relationship was slightly stronger than that between SAFA intake and five-year CVD risk. Two studies have previously shown strong associations between high intake of SAFA and cognitive function/decline in older age groups (142, 143). Eskelinen et al found an association between SAFA from milk and MCI (p=0.03) (144). Unfortunately there are few studies examining the impact of diet on cognitive function in middle age. Significant relationships observed in previous research are likely due to the increase in LDL which SAFA is responsible for and the subsequent atherosclerosis affecting BP and flow of oxygen to the brain (43). The available international evidence is not equivocal but is leaning toward a relationship between high intake of SAFA and higher risk of MCI and cognitive decline in older age groups. The cut-off for SAFA and the cut-off for the MoCA test are both well researched and recognised internationally so it is likely that the lack of association is may be due to insufficient power to detect significant relationships in this study (8, 93).

This study was unable to show relationships between MUFA or PUFA and MCI. There has been a lot of research in this area in the past two decades due to the protective effects of MUFA and PUFA in other areas of health such as CVD (51, 53). It is proposed that the positive anti-inflammatory and cholesterol reducing properties of USFAs reduce atherosclerosis and promote healthy blood flow and oxygen to the brain for good cognitive performance (43).
Fish intake has been studied due to the high amount of PUFA in fish. However these studies have predominantly focused on those over 65 years and are therefore not highly comparable with the middle aged CHALICE sample. Studies that focus on high fish consumption have generally shown protective effects on cognitive function and cognitive decline (134, 136, 138, 146). Kalmijn showed that in 45-70 year olds consumption of n-3 FAs is inversely related to cognitive function (134). It cannot yet be concluded that n-3FAs play a protective role in cognition and further research needs to be done (138, 139, 146). Evidence for the protective role of MUFA in cognitive decline has been highlighted in two studies in those over 60 years however conclusions have not been reached (140, 143). Overall there is a lack of strong evidence for MUFA and PUFA and subsequent cognitive function in middle age. Because of this, it is only based on plausible biological pathways that a relationship would be expected. Power and use of cutoffs for the USFAs are likely to have affected the strength of the analysis. Based on studies investigating cognitive decline and cognitive function in older age, further CHALICE longitudinal data are expected to reveal relationships in the future.

No significant relationships between alcohol intake and MCI were identified in this study. There is mixed evidence for the most beneficial amount of alcohol for cognitive benefit with estimates ranging from one to two drinks per day (151, 152, 154) to four to eight for males (149). These studies used different methods for collecting alcohol data, but this is not thought to be the primary reason for differences in estimates. Other studies have found no significant relationships between alcohol intake and cognitive function in midlife (150). In conclusion, we cannot determine if the lack of significant associations seen between selected nutrients and MCI are due to a lack of statistical power or if these nutrients really do not affect cognitive function in this age group. Further cross-sectional research is needed
in the complete CHALICE cohort. Longitudinal follow up or participants will also allow for further research investigating these relationships as participant’s age.

5.4 CVD risk, MCI and Diet: Other Factors to Explore

Additional analyses looked at potential confounding factors on cognition such as depression and education to determine if they are the true reason for observed associations between five-year CVD risk and MCI. Those with depression in the CHALICE sample are more likely to have MCI. This relationship is expected due to the strong evidence that depression is a risk factor for poor cognition (177, 185). There is no relationship between depression and CVD risk therefore the relationship observed between MCI and CVD risk is unlikely to be mediated by depression status.

There are strong relationships between having a lower education and having a higher risk of both MCI and moderate/high five-year CVD risk. A person with lower education has been found to have a higher risk of MCI than a person with a higher education (185). It is possible that a person with a lower level of education does not have as healthful behavior and consequently has a higher CVD risk due to dietary and lifestyle choices. These people may be less likely to access health services due to lower income, and therefore not be aware if they have health conditions such as hypertension or high cholesterol. They may have a lower income impacting dietary choices and may be more likely to smoke. It is beyond the scope of this thesis to analyse the associations between CVD risk and socioeconomic factors however this opens up new research avenues for further CHALICE studies.

5.5 Strengths and Limitations

Use of the electoral roll to select a random sample of 50 year old Cantabrians was strength in recruitment for this study. Maori over-sampling (13.3% of the CHALICE sample compared
to 7.2% of Canterbury’s population) ensured that CHALICE was able to collect more information from Maori and hence learn more about Maori health in Canterbury, which is needed to improve Maori health in the region. As with all studies of this type we recruited a higher proportion of those with higher education, and smoking prevalence was lower than in the general population but nevertheless we have a wide range of all demographic characteristics across the currently recruited cohort.

Pre-testing of module seven with a representative sample helped to refine the FBD requirements and understanding. The high completion rate for the FBDs (75.5%) was a major strength of this study. A combination of factors are the likely reasons for this: firstly the use of a four day estimated FBD has strengths including a high level of accuracy in report as well as being less burdensome on the participant than a weighed FBD. Secondly the participants were well educated on the procedure of recording their food and beverage intake and were provided with examples to take home with them. Finally, they had developed a high level of rapport with their interviewer during the study day which meant follow-up phone calls from that interviewer were effective in encouraging return of FBD.

Following collection of raw data from participants, the use of standardised protocols for data entry and processing meant that high quality dietary data was produced. Examples of such protocols were for entering recipes, food weights and foods that were not included in the ‘Diet Cruncher’ programme. Limitations included potential inaccuracy in estimating the composition of unknown foods and estimating weights of given foods which may not be accurate. One novel aspect of this study was using five-year CVD risk scores, rather than individual CVD risk factors.

As the algorithm for calculating New Zealand CVD risk Scores was not available each individual’s five-year CVD risk score was derived manually. This meant that each person’s
medical history and health status was able to be considered individually. However this could introduce coding errors. This was minimised by triple checking data during coding phase and re-checking during analysis phase especially when data was being moved between computer analysis programmes. The CHALICE questionnaire was not designed with calculation of CVD risk scores in mind, therefore some data required for answering additional risk factor questions was not available (such as a measurement of serum albumin for hyperalbuminuria), and some data did not ask questions directly. However, the CHALICE questionnaire asked a variety of questions which enabled most of the New Zealand Cardiovascular Risk Chart additional risk factor questions to be answered after deciding the best sources of information and the closest answers. The New Zealand Cardiovascular Risk Charts also gave good outlines for descriptions of additional risk factors which helped to identify the appropriate questions in CHALICE to use. A Medical Doctor was available for advice and judgement on medical diagnoses such as patient reported heart problems that did not meet criteria for CVD.

For gathering physical and biological data, efforts were made to ensure data was gathered around the same time of day for all participants to prevent diurnal variation. Three BP measurements were taken using both manual and automatic BP monitors and averages of these gave a person’s BP. Finally, a blood sample was taken only in those who had fasted for 12h prior to attending study day to ensure there were no outliers in datasets due to nutrient effects on biomarkers. Undiagnosed diabetes was not considered; participants had to have been told they had diabetes by a doctor to be included as a diabetic. This was advantageous in the fact that it was very easy to identify diabetics; however it could mean that some participant’s risks were underestimated for undiagnosed diabetics (with results from fasting blood glucose tests).
Questionnaire data was entered into a study-wide database and data entry was double-checked by the study interviewers and re-checked throughout analysis by the candidate to reduce likelihood of data entry and analysis errors. Any discrepancies were discussed and managed. The set of CHALICE questionnaires were well designed and many questions were derived from other successful surveys and studies, and from internationally used diagnostic tools. For example MoCA is well pre-tested diagnostic tool for MCI and interviewers used a strict scripted protocol to test, the M.I.N.I diagnostic tool for current depressive episode is widely used internationally, many health questions from module two were taken from the ‘New Zealand Health Survey 2006/07’.

In the present study the cut-offs used to distinguish higher and lower intake of these fats are not as reliable as those for SAFA and total fat. The recommendation for PUFA of six or more percent of energy per day is recommended by WHO, but not well publicised in New Zealand, and the cut-off for MUFA is vague as it is recommended as a replacement fat for SAFA so the median from the ‘ANS 2008/09’ was used.

As previously described, alcohol intake per day was manually calculated on a case by case basis using information provided about drinking frequency and amount consumed. Due to small numbers, categories were collapsed therefore both estimates for drinks per day and the collapsing of categories to gain numbers may have resulted in inaccurate cut-offs. Unfortunately 57 of the 200 participants had missing data, mainly due to non-return of the FBD, which may have affected our ability to detect significant differences in this small sample size. Statistical analysis was limited due to the use of categorical variables for every analysis. There were low numbers of participants in some groups which meant that categories had to be modified or collapsed consequently reducing the power of some of the analyses.
5.6 Implications

This research has implications for those working in the primary care setting and regularly using the New Zealand Cardiovascular Risk Charts with their patients. Further research is needed to investigate relationships between CVD and MCI. If links are found then it may be important in future for practitioners to discuss CVD risk factors not only in relation to patient’s physical health, but also their cognitive health.

5.7 Future Research

This is an exciting topic which warrants further research in larger a larger cohort. Cognitive health in mid-life is not widely studied in New Zealand; however international evidence shows that CVD risk factors such as hypertension are especially important during mid-life for late life CVD and cognitive health. Further studies in the longitudinal CHALICE sample using the New Zealand Cardiovascular Risk Charts and exploring the relationship between dietary factors and/or cognitive function.

When these studies are in planning phase the following considerations should be made:

- A more extensive nutrient analysis programme could potentially provide more accurate dietary data.
- The use of automated calculations for CVD risk score to decrease risk of inaccuracy.
- A larger sample would be preferable to increase power of the study. Future studies could include those between 35-74 years as risk charts are available for this age group. It would be interesting to observe at what age at which CVD risk first relates to cognitive function.
- The present study used basic statistical analysis methodology: more complex analysis investigating three way relationships between CVD risk, cognitive function
and diet would be valuable in extracting any complex relationships between these factors.

• Finally, analyses revealed that education played an important role in predicting CVD risk and risk of MCI in this population. This should be further investigated in order to identify problems and find solutions for Cantabrians to decrease their CVD risk and increase their health related quality of life.

5.8 Application to Dietetic Practise

Dietetics training courses in New Zealand could teach students about the New Zealand Cardiovascular Risk Charts and associated risk factors in relation to cognitive health. After further research, students may learn that those with higher CVD risk may struggle with tasks such as completing a FBD or may be less likely to do so. Having dietary data collection tools such as FFQ for research and diet recall for clinical settings may be advantageous in this group. This study has shown that 50 year olds with depression have higher risk of MCI. This may be reflective of their attention or motivation or other factors. For which ever reason this is, dietitians need to make messages clear and achievable for these patients so that they are easily understood. Dietitians and dietetic students could also be involved in future research in this topic.
6 Conclusion

In conclusion, this study has shown that a group of 50 year old Cantabrians with moderate/high five year CVD risk, or depression are more likely to have MCI than those with a mild five year CVD risk and those who are not depressed. It appears that in this sample these relationships are not mediated by intake of dietary risk factors: fats and alcohol therefore further research needs to be carried out to establish why this relationship exists. Further studies should also investigate the role that diet may play in these relationships in larger CHALICE sample as the study grows.
7 References

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64. Rimm EB. Review of moderate alcohol consumption and reduced risk of coronary heart disease: is the effect due to beer, wine, or spirits? BMJ. 1996;312(7033):731.


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8 Appendices
### 8.1 Appendix A: Tables from Literature Review

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Sample size</th>
<th>Years of follow-up</th>
<th>Factors included in risk score</th>
<th>Risk score(s) purpose/specificity</th>
<th>Major changes and limitations</th>
<th>Candidates rationale for inclusion in literature review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham Heart Study USA (17)</td>
<td>Men and women from the original Framingham cohort aged 30-62 years</td>
<td>N=4856, 2187 men, 2669 women</td>
<td>12 years</td>
<td>Sex, Age, Total cholesterol, Systolic blood pressure, Haemoglobin, Smoking, Left ventricular hypertrophy, Electrocardiogram abnormality, Relative body weight</td>
<td>Probability/risk of developing CHD in 12 years</td>
<td>Nil. Study used best methods available at the time.</td>
<td>This study was the initial study to develop a CVD risk score. It showed that body weight and haemoglobin did not predict heart disease risk as strongly as cholesterol, smoking, blood pressure and electrocardiogram abnormality.</td>
</tr>
<tr>
<td>Framingham Heart Study USA (19)</td>
<td>Men and women from the original Framingham cohort aged 35-74 years</td>
<td>N=not reported</td>
<td>16 years</td>
<td>Sex, Age, Total cholesterol, Systolic blood pressure, Smoking, Glucose tolerance, Left ventricular hypertrophy</td>
<td>Probability/risk of developing CHD in 6 years</td>
<td>Changes included: No use of body weight or haemoglobin. Glucose tolerance introduced.</td>
<td>This study showed that several independent factors lead to CVD and they must all be assessed to develop a risk score. It was the precursor to a book published in 1973; intended to be used as a tool for health practitioners to monitor CHD risk of their patients.</td>
</tr>
<tr>
<td>Framingham Heart Study USA (18)</td>
<td>Men and women from the original Framingham cohort aged 35-65 years at baseline</td>
<td>N=5,209</td>
<td>8 years</td>
<td>Sex Age Total cholesterol Systolic blood pressure Smoking Glucose tolerance Left ventricular hypertrophy</td>
<td>Probability/risk of developing CVD in 8 years: Coronary Disease, Brain Infarction, Intermittent Claudication, Hypertensive Heart Failure, Total CVD</td>
<td>Nil</td>
<td>This study was the first to develop risk scores for separate CVD outcomes, not restricted to CHD. It also included a risk score for total CVD, similar to that we use today.</td>
</tr>
<tr>
<td>Framingham Heart Study USA (23)</td>
<td>Men and women from the original Framingham cohort aged 35-65 years at baseline</td>
<td>N=5,209</td>
<td>16 years</td>
<td>Sex Age Total cholesterol HDL cholesterol Systolic blood pressure Smoking Glucose tolerance Left ventricular hypertrophy</td>
<td>Probability/risk of developing CAD in 6 years</td>
<td>Changes include: HDL cholesterol introduced</td>
<td>This is the first time HDL was considered as a risk factor for CVD. It is used in our CVD risk charts today as part of the cholesterol: HDL ratio.</td>
</tr>
<tr>
<td>Framingham Heart Study USA (20)</td>
<td>Men and women from the original and offspring Framingham cohorts aged 30-74 years at baseline</td>
<td>N=5,573 2,590 men 2,983 women</td>
<td>12 years from baseline. Baseline 1968-1975</td>
<td>Sex Age Systolic blood pressure Diastolic blood pressure Total cholesterol HDL cholesterol Total: HDL cholesterol ratio Smoking Diabetes mellitus Left ventricular hypertrophy</td>
<td>1. Updated equations give 4- to 12-year estimations of CHD risk. 2. Point-scoring technique gives probability of developing CVD in 5 and 10 years (based on one of the above equations)</td>
<td>Changes include: Diastolic blood pressure and total: HDL cholesterol ratio introduced. Diabetes used instead of glucose tolerance.</td>
<td>Gives two ways to predict CVD risk: An updated version of the equations that have been used so far and Point scoring algorithm based on the equations which are easy for practitioners to use in a worksheet form. This is the equation that the calculations for the New Zealand Cardiovascular Risk Charts are based on.</td>
</tr>
<tr>
<td>Framingham Heart Study USA (34)</td>
<td>Men and women aged 30-74 years of the Framingham heart study and Framingham offspring study cohorts.</td>
<td>N=5573</td>
<td>12 years 1968-1975 for baseline data</td>
<td>Sex Age Total: HDL cholesterol ratio Systolic blood pressure Diastolic blood pressure Smoking Diabetes mellitus Left ventricular hypertrophy</td>
<td>Probability/risk of: MI CHD Death from CHD Stroke CVD Death from CVD In 4-12 years</td>
<td>First study to show risk of specific CVD outcomes based on using cholesterol: HDL ratio as opposed to total cholesterol. It is valuable to have scores based on incidence and mortality and to include specific CVD outcomes as well as overall CVD outcomes. Score can be based on DBP or SBP separately.</td>
<td></td>
</tr>
<tr>
<td>Framingham Heart Study USA (21)</td>
<td>Men and women aged 30-74 years of the Framingham heart study and Framingham offspring study cohorts.</td>
<td>N=5345 2489 men 2856 women</td>
<td>12 years 1971-1974 for baseline data</td>
<td>Sex Age Total cholesterol HDL cholesterol LDL cholesterol Blood pressure Smoking Diabetes mellitus</td>
<td>Probability/risk of developing CHD in 10 years</td>
<td>Changes include: LDL cholesterol introduced and total and HDL used separately. Blood pressure categorised into hypertensive categories (using highest blood pressure). Left ventricular hypertrophy removed. This model developed categories of risk for each risk factor, similar to those used in the New Zealand Cardiovascular Risk Charts. Based on levels of risk factor, a risk score could be given. Used LDL cholesterol and left out LVH, which are measurements not used in the New Zealand Risk Charts.</td>
<td></td>
</tr>
<tr>
<td>Framingham Heart Study USA (22)</td>
<td>Men and women aged 30-74 years of the Framingham heart study and Framingham</td>
<td>N= 8491 3969 men 4522 women</td>
<td>12 years follow up Baseline data gathered between</td>
<td>Sex Age HDL cholesterol Total cholesterol Systolic blood pressure(treated or untreated)</td>
<td>Probability/risk of developing CVD in 10 years</td>
<td>Changes include: LDL cholesterol measurement removed. Systolic blood pressure only. Non-specific CVD risk requiring minimal input of factors. Designed for use in primary health care. Likely the closest Framingham equation to</td>
<td></td>
</tr>
<tr>
<td>Score title/Study</td>
<td>Participants</td>
<td>Sample size</td>
<td>Years of follow-up</td>
<td>Factors included in risk score</td>
<td>Risk score(s) purpose/specificity</td>
<td>Results and Limitations</td>
<td>Candidates rationale for inclusion in literature review</td>
</tr>
<tr>
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</tr>
<tr>
<td>(30) Germany PROCAM study</td>
<td>Men aged 35 to 65 years at baseline from PROCAM cohort.</td>
<td>N= 5389 men</td>
<td>10 years</td>
<td>Sex HDL Cholesterol LDL cholesterol Triglycerides Systolic blood pressure Smoking Diabetes mellitus Family history of premature MI</td>
<td>Global risk of acute coronary MI in men aged 35-65.</td>
<td>PROCAM predicted 82.4% of the actual MI incidence in the population, and Framingham predicted 77.8%. Limitations: Score is not applicable to women and not necessarily able to be extrapolated to other ethnicities.</td>
<td>Gives global risk of single CVD factor. Looks into family history which has been shown to be a risk factor for CVD. Looks at triglyceride which has not been done in the Framingham score. Family history of premature MI is an additional risk factor in the New Zealand Cardiovascular Risk Charts.</td>
</tr>
<tr>
<td>(26) Europe SCORE cohort</td>
<td>Men and women aged 19-80 years at baseline participating in one of 12 cohort studies across Europe.</td>
<td>N= 205 178 117 098 men 88 080 women</td>
<td>2.7 million person years</td>
<td>Sex Age (as measure of exposure time to risk factor, not an actual risk factor) Total cholesterol Total cholesterol: HDL ratio Systolic blood pressure Smoking</td>
<td>Ten year risk of fatal CVD in adult populations with either high or low risk of CVD.</td>
<td>Developed an algorithm to calculate risk. Showed 71% to 84% ability of all four equations to predict accuracy. Limitations: No diabetes consideration due to data quality, therefore score not applicable to diabetics. Only predicts death from CVD, not total CVD which limits sensitivity to detect a non-fatal event however is</td>
<td>Score can be based on total cholesterol or cholesterol: HDL separately. No LDL measurement consistent with the New Zealand Cardiovascular Risk Charts. Gives a comparison with Framingham and New Zealand risk charts to show what else is being used internationally.</td>
</tr>
</tbody>
</table>
debatably more accurate in predictions as MI event and mortality data is ‘hard’.

<table>
<thead>
<tr>
<th>Europe DECODE cohort</th>
<th>Men and women aged 30-74 years at baseline participating in one of 14 European cohort studies.</th>
<th>N=25413 16, 506 men 8, 907 women</th>
<th>Varying: 4.8 years to &gt;10 years</th>
<th>Sex Age Total cholesterol Systolic blood pressure Smoking Diabetes mellitus Two hour and fasting glucose concentration Body mass index</th>
<th>5 and 10 year cardiovascular mortality in ages 30-75.</th>
<th>BMI was not significantly associated with CVD mortality. Blood sugar indices were predictive of CVD mortality but had mixed result for other risk factors due to lack of power (lower death incidence). Limitations: Only able to predict CVD mortality. Limited by the differing data sets of individual studies. Focus on blood glucose and diabetic status. Intended use for blood sugar level was to use levels as risk factors similar to blood pressure or cholesterol.</th>
</tr>
</thead>
</table>

| Italy CUORE Study | Men aged 35-69 years at baseline participating in one of 11 Italian cohort studies. | N=6865 men | 9.1 (median) years of follow-up | Age Total cholesterol HDL cholesterol Systolic blood pressure Hypertension drug treatment Smoking Diabetes mellitus Family history of CHD | 10 year coronary risk for Italian men aged 35-69 years | Authors report that Framingham and PROCAM scores overestimate risk in their low-risk population. Used hypertension drug treatment which is rarely done but was found to be a predictive factor (due to past BP levels). BMI was not a predictive risk factor. Limitations: Only able to predict risk in men, may not be extrapolated to non-Italian populations. This study shows that there is a real need for different risk scores in low-risk populations. Categorises risk factors similar to New Zealand Cardiovascular Risk Charts. |
**Italy Riskard Study**

Men and women aged 35-74 years at baseline participating in 9 Italian population studies.

- **N= 17,153**
  - 12,045 men
  - 5,108 women

- 194,000 person/years

| CHARTS | Estimated CVD risk in 10 years for men and women aged 45-74 years |
| **SOFTWARE** | Predictive of risk of overall CVD risk using charts and major events in a software programme with more factors included. BMI was not used as a risk factor for women as it had a strong correlation with other risk factors. More risk factors are able to be input into the software to give a more accurate prediction of risk. Limitations: May not be extrapolated to non-Italian populations. |

**Estimated CVD risk using charts and major events in a software programme with more factors included. BMI was not used as a risk factor for women as it had a strong correlation with other risk factors. More risk factors are able to be input into the software to give a more accurate prediction of risk. Limitations: May not be extrapolated to non-Italian populations.**

**Limitations:**
- May not be extrapolated to non-Italian populations.
- This is the most recent of initiatives in Italy to predict CVD. Shows the importance of tailoring CVD risk charts to your specific population as Framingham over estimated risk in this low-risk population.
- Non-HDL cholesterol used as an approximation of LDL (the difference between total and HDL cholesterol).
- Used heart rate as an indirect measure of physical activity.
- Scoring system used to structure charts similar to New Zealand Cardiovascular Risk Charts.

**USA Reynolds Risk Score**

Women aged 45 years and over at baseline participating in the Women’s Health Study.

- **N= 24,558**
- 10.2 years (median)

| Estimated 10 year CVD event risk for women (2 models: simplified model B for clinical use – ‘Reynolds Risk score’ and model A (input data not all shown on left)) | Validated against their own cohort by splitting up into 1/3 and 2/3 groups. Was able to reclassify 40-50% of women given ‘intermediate risk’ from a previously derived risk score (Adult Treatment Panel III risk score) due to inclusion of novel and traditional risk factors. Limitations: Blood pressure HbA1c and C reactive protein included as measures of diabetes status and inflammation. Reynolds risk score used in the clinical setting requires routine testing of CRP. If shown in other populations over time, this may be a future consideration for New Zealand. Additional factors included in model A are: |

**Additional factors included in model A are:**
- Haemoglobin A1c
- C reactive protein
- HbA1c

---

(29) Italy Riskard Study

(31) USA Reynolds Risk Score
<table>
<thead>
<tr>
<th>Reference</th>
<th>Description</th>
<th>Study Population</th>
<th>Sample Size</th>
<th>Minimum Observation</th>
<th>Risk Factors Assessed</th>
<th>Risk of CVD Calculated</th>
<th>Validation Methodology</th>
<th>Study Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>(24) UK QRISK</td>
<td>Men and women aged 35-74 years at baseline. Recruited from medical practices participating in the QRESEARCH database.</td>
<td>N= 1.28 million</td>
<td>Minimum of 1 year</td>
<td>10 year risk of CVD in ages 35-74 years in UK citizens</td>
<td>Validated against their own cohort by splitting up into 1/3 and 2/3 groups. Framingham was found to over-predict CVD by 35%, ASSIGN by 36% and QRISK 0.4%. This over-estimation occurred in affluent populations whereas underestimation occurred in deprived populations.</td>
<td>Includes drug therapy for hypertension-excluding this may underestimate risk in other populations. Includes habitual area's risk of material deprivation; 'Townsend score' which is based on unemployment, overcrowding, non car ownership and non-home ownership.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(25) Scotland ASSIGN</td>
<td>Men and women aged 30–74 years at baseline who completed risk factor population surveys in the 1980s and 1990s in Scottish cohort</td>
<td>N=13,297; 6540 men 6757 women</td>
<td>Minimum 10 years, maximum 19 years</td>
<td>10 year risk of CVD in ages 30-74 years</td>
<td>Validated against Framingham and showed similar results however Framingham does not take into account deprivation.</td>
<td>Included Scottish Index of Multiple Deprivation. Obesity was not included as was not a significant risk factor. This score alongside QRISK is able to show the need for focus on CVD prevention and treatment in the socially deprived. Uses calculation of continuous data which can give more accurate risk prediction than using risk factor categories.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 8-2: Risk scores/equations developed from cohort studies (excluding Framingham Heart study).

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Numbers</th>
<th>Hypothesis</th>
<th>Main findings</th>
<th>Limitations and points of interest</th>
<th>Candidate’s rationale for including this study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(46) The Seven Countries</td>
<td>Multi-centre prospective cohort study</td>
<td>N= 11,579 men aged 40-59 years at baseline. Follow-up 15 years</td>
<td>Some dietary constituents lead to a higher 15 year death rate</td>
<td>Intake of SAFA has a positive relationship with 15 year death rate and MUFA has an inverse relationship.</td>
<td>Estimated dietary intake was based on repeated weighed 7 day food diaries of 30-50 men from 5 of the 7 cohorts. 24 hour recall was used in all US men and 7 day recall used in Italian men allowing for high compliance and large numbers. There was a 25 year difference between food data collection and food chemical analysis.</td>
<td>The Seven Countries Study was the pioneering study researching relationships between diet and disease. It had large numbers, was multi-ethnic and established the links between SAFA, MUFA and CHD, however it was limited to men. It used the best and most practical dietary collection methodologies available at the time to produce the most accurate data.</td>
</tr>
<tr>
<td>Study</td>
<td>Comparative study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(44) The Seven Countries</td>
<td>Multi-centre prospective cohort study</td>
<td>N=12,763 men aged 40-59 years at baseline. Follow-up 25 years.</td>
<td>Different fatty acids have different effects on CHD risk</td>
<td>Intake of SAFA (lauric, myristic, palmitic and steric) p&lt;0.001), trans FA (p&lt;0.001) and dietary cholesterol (p&lt;0.05) were positively associated with 25 year death rates from CHD.</td>
<td>Same dietary data issues as above applied.</td>
<td>The next investigation was important in highlighting the risks posed by not only SAFA, but trans-FA and dietary cholesterol. Lauric, myristic, palmitic and steric acids were identified as having a role in CVD.</td>
</tr>
<tr>
<td>(45) Prospective</td>
<td>N=8,082 women</td>
<td>Different fatty acids</td>
<td>Every 5% increase in intake</td>
<td>116 item semi-quantitative</td>
<td>Seven countries data was</td>
<td></td>
</tr>
</tbody>
</table>
### USA

**The Nurse’s Health Study**

| Cohort study | Aged 34-59 years at baseline. Follow-up 14 years. | Have different effects on CHD risk | Gave a lower risk of CHD (non-fatal MI or death by CHD) for PUFA (p<0.003) and MUFA (p<0.05) For every 2% increase in trans-fat intake there was a 17% increased risk of CHD (p<0.001). Relationships for SAFA were not significant but suggested a 17% decreased risk with 5% decreased intake. Replacement of SAFA and trans with UNFAs would decrease risk by 42% and 53% respectively (p<0.001) | FFQ was used gave correlation coefficients of 0.48-0.68 of fatty acids, compared to 7-day food records. The study was able to collect large dietary data sets using this method. Dietary assessment at multiple points over the follow-up period strengthened the study. Results for SAFA were not significant which could be reflective of poor sensitivity of the dietary assessment method (as shown by correlation coefficients). Supported by the large American ‘Nurse’s Health Study’ which confirmed similar findings in women; trans-FAs are dietary risk factors for CHD. Although different assessment methods were used to other studies, results were similar. |

|Prospective cohort study | N=78, 778 women aged 34-59 years at baseline. Follow-up 20 years. | Dietary fat intake and intakes of specific fatty acids have differing effects on CHD risk. | Intake of PUFA is inversely associated with CHD (non-fatal MI or death by CHD) (p=0.004), (p=0.01) whereas intake of trans-FA was associated with increased CHD risk. Associations were strongest for those <65 years (p=0.002 for PUFA and p=0.002 for trans-FA). PUFA was more protective in those with high BMI, and trans was posed higher risk for those with low BMI. | The same points as above apply. The intakes of fat decreased over the study period, and fatty acid composition of some foods also changed. | This study was important for highlighting the importance of PUFA as a protective nutrient against CHD as previously only MUFA was highlighted. |

| Meta-analysis | 60 trials | Intake of different | Diets were thoroughly assessed | Dietary cholesterol has to be considered | Meta-analysis is able to determine the effects of different diets on CHD risk. |
### Analysis of Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=1672 women and men</td>
<td>Fatty acids have differing effects on the total cholesterol to HDL cholesterol ratio. This ratio is the best cholesterol predictor of CAD. Controlled by providing food, dietary instructions and/or supplements or specific foods. Intake of dietary fatty acids was the controlled variable so all modifications to the diets involved fatty acids in products. The ratio is decreased by replacing trans-FA and SAFA with cis-unsaturated fatty acids.</td>
<td>Kept constant in the studies to measure the effect of fatty acids on cholesterol. Cannot extrapolate to people with hypercholesterolemia. Studies were between 13 and 91 days so long-term cholesterol lowering effect is not necessarily identified.</td>
<td>Cannot extrapolate to people with hypercholesterolemia. Studies were between 13 and 91 days so long-term cholesterol lowering effect is not necessarily identified.</td>
<td>Capture the studies which followed the original prospective cohorts to show that in multiple groups the negative effects of SAFA and trans-FA, and positive effects of PUFA and MUFA are well evidenced. This analysis linked intake to cholesterol ratio.</td>
</tr>
</tbody>
</table>

#### Meta-analysis of Prospective Cohort Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Interventions</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=347,747 women and men</td>
<td>Reducing dietary saturated fat will decrease risk of CHD, stroke and CVD.</td>
<td>Reduction in dietary intake of SAFA had no effect on the risk of CHD, stroke or CVD (p=0.22, p=0.11 and p=0.95)</td>
<td>Insufficient power to predict effect of replacing SAFA with other nutrients. Study groups were from a wide range of populations and settings, measuring a wide range of CVD outcomes which may limit predictive power. This study suggests that the nutrients replacing saturated fat in the diet may be important in conjunction with the decrease in SAFA.</td>
</tr>
</tbody>
</table>

#### Meta-analysis of Randomised Controlled Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Interventions</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=13,614 women and men</td>
<td>PUFA are a suitable replacement for SAFA to prevent CHD.</td>
<td>Replacing SAFA with PUFA results in decreased pooled reduction of risk (RR=0.81, p=0.008), and reduced CHD risk (RR=0.90, CI=0.83-0.97) for every 5% in energy from PUFA. Longer studies resulted in significantly reduced risk than shorter studies (p=0.017).</td>
<td>All studies were parallel randomised or cluster randomised. Only 4/8 trials provided food; in institutionalised people where analysis of provided food was supplied. However 4/8 were based on dietary advice and used differing dietary assessment methods. This meta-analysis linked the intake of different fats directly to risk of CHD. It supports previous studies advocating replacement of SAFA with unsaturated fatty acids.</td>
</tr>
</tbody>
</table>
### Meta-analysis of randomised controlled trials

<table>
<thead>
<tr>
<th>Reference</th>
<th>Data and Design</th>
<th>Results</th>
<th>Studies Included</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>51</td>
<td>48 trials N=65,508 women and men</td>
<td>When dietary SAFA are replaced by unsaturated fatty acids, or when dietary fat is reduced there will be lipid lowering and reduce mortality and CVD morbidity.</td>
<td>There is a reduced risk of cardiovascular events in men who replace SAFA with PUFA and MUFA for at least 2 years (RR=0.86, CI=0.77-0.86). The effect is due to the positive impact on LDL and TG levels. No effects observed for total or cardiovascular mortality.</td>
<td>Studies included those with CVD. Interventions varied from dietary advice, supplementation or provided foods. Advice and diets were often not complied with to similar levels in the studies. Sources of bias such as blinding, selective reporting and allocation are thoroughly explained.</td>
</tr>
<tr>
<td>52</td>
<td>11 trials N=7855 patients (women and men) Ages 45-66 years Studies had between 33-100% of patients with previous MI</td>
<td>There is an inverse relationship between intake of dietary and supplemental n-3FA FA and CHD.</td>
<td>Those who have a diet enriched with n-3FA FA have reduced overall mortality (p&lt;0.001), reduced mortality due to MI (p&lt;0.001) and reduced sudden death (P&lt;0.01)(in those with CHD).</td>
<td>Amount and type of n-3FA FA varied so no optimum amount is known. Studies did not necessarily measure all CVD endpoints so results could have underestimated or overestimated effects.</td>
</tr>
<tr>
<td>52</td>
<td>12 trials N=1,990 women and men</td>
<td>Determine if diets rich in MUFA have positive or negative outcomes on markers of obesity and CVD.</td>
<td>Diets containing &gt;12% MUFA result in decreasing fat mass (p=0.03), SBP (p=0.03) and DBP (p=0.05) compared to those with low MUFA diets.</td>
<td>Studies included had diverse comparison groups and differences in dietary assessment quality.</td>
</tr>
</tbody>
</table>

This is the most up-to-date Cochrane meta-analysis available. It is unable to show any benefits of a fat modifying diet for women yet. It is not known if PUFA or MUFA are better replacement fats which opens up room for further research.
suitable replacement for SAFA where possible.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Numbers</th>
<th>Alcohol intake assessment method</th>
<th>Main findings</th>
<th>Limitations / points of interest</th>
<th>Candidate’s rationale for including this study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(53)</td>
<td>Meta-analysis of prospective cohort studies and Randomised controlled trials.</td>
<td>28 prospective cohort studies Where n= 280,000 23 RCTs</td>
<td>Some USFAs are better replacements fats for SAFA than others for preventing CHD.</td>
<td>From 11 cohort studies with appropriate data it was found that there is a decreased risk of CHD death and CHD events when PUFA replaces SAFA. For every 5% substitution of SAFA for PUFA, there was a 0.87 hazard ratio for CHD death, and 0.74 HR for CHD event.</td>
<td>Similar to those given for Hooper et al. Only investigated CHD death. Was limited by the data available therefore power for some investigations was restricted.</td>
<td>This review conflicts the results of Hooper et al and provides strong evidence that PUFA should replace SAFA. It is the most recent hard statistical evidence for selecting PUFA over MUFA for replacement of SAFA, and supports its use for prevention of CHD.</td>
</tr>
</tbody>
</table>

Table 8-3:Studies examining impact of dietary fat intake on cardiovascular disease.

(56) Hawaii Honolulu-Asia Aging Study

Prospective cohort study

N=7705 Japanese men Follow-up 6 years

24 hour recall Ask: Usual amount of wine, beer and spirits per day and per week. One drink contained between 9.5g and 13.4g of alcohol dependant on beverage.

Up to 60ml alcohol from beer (<4.5 drinks) per day reduces risk of non-fatal MI (p<0.001) and death from CHD (p<0.001) after adjusting for smoking and other factors.

This population did not consume a lot of alcohol comparatively to other populations therefore results cannot necessarily be extrapolated- only 3% had >90ml daily. Cannot be extrapolated to women or other

This was one of the early landmark studies which described nutrition implications on health in a large cohort of migrants. The study was able to see that there was an upper limit to the amount of alcohol that should
(57) USA  
Chicago Western Electric Company Study

| Prospective cohort study | N=1,832 white men aged 40-55 years at baseline Follow-up 17 years | Yearly questionnaire on alcohol consumption, yearly nutrition survey and entry examination. Asking: Number of drinks consumed per month of beer, wine and spirits. Coded as drinks per day across a month. One drink contained 11.36g of alcohol. | Those who consumed 6+ drinks per day had higher risk of CVD death (p<0.05) and CHD death (p<0.05) after adjusting for smoking. | There was no analysis between abstainers and those with intake <6 drinks per day. Cannot be extrapolated to women or other cultural groups. The study did not show differences in benefit between alcohol from different drinks as shown by Yano in1977 (benefit with beer). | This was a landmark study in a western cohort looking at men in the same age group as CHALICE participants. It recommended having <68.16 grams of alcohol per day which is above the New Zealand recommendations for safe drinking. A sensible upper limit of drinking for health had not yet been established. |

(58) UK  
Whitehall study of civil servants

<p>| Prospective cohort study | N=1,422 men aged 40-74 Follow-up 10 years | Three day record of dietary intake One drink =8-10g alcohol | Abstainers (RR=1.6) and heavy drinkers (RR=1.8) (&gt;4 drinks/day) have higher total death rates than moderate drinkers (1 drink/day). The U-shaped curve did not fit with CVD death which showed lowest risk with drinking &gt;4 drinks/day (RR=0.9) followed by 1 drink | Diet intake over the 3 day diary may not be representative of usual intake. Cannot be extrapolated to women or other cultural groups. | This is the first study to show that abstaining from alcohol is not beneficial for heart health, nor is heavy drinking. A curve started to emerge describing the relationship between alcohol and heart health. |</p>
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Sample Size</th>
<th>Methods</th>
<th>Findings</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(60) USA American Cancer Society prospective study</td>
<td>Prospective cohort study</td>
<td>N=276,802 men aged 40-59 years Follow-up 12 years</td>
<td>Questioned on frequencies of drinking beer, wine and spirits consumed per day Categorised as drinks per day or deemed to be a ‘non-drinker’, ‘occasional’ or ‘irregular’ drinker.</td>
<td>Moderate drinkers (occasional drinkers and 1-6 drinks/day) have a lower risk of CHD mortality than abstainers with RR’s ranging from 0.86-0.92. There was no effect for ‘irregular drinkers’ 55% of cohort reported no alcohol drinking and 6.5% reported occasional drinking. The amount of alcohol period drink was not reported and intake was largely based on estimates of usual intake.</td>
<td>This study was able to show that any level of moderate drinking decreased CHD death risk compared to abstaining. This study reported alcohol intake based on frequency and was able to show similar results as other studies with this method.</td>
</tr>
<tr>
<td>(61)</td>
<td>Prospective cohort study based on medical records</td>
<td>N=128,934 men and women</td>
<td>Questionnaire on alcohol consumption including information about drinking over the last year and lifetime, days per week alcohol was consumed and frequency and amount of consumption.</td>
<td>Those who consume 1-2 drinks per day are at lower risk of death from CVD (RR=0.8) especially from CHD (RR=0.7). The amount of alcohol per drink is not reported and relies on self reports from participants. The study did not look into type drink consumed. It was not able to show significant effects for women and men separately.</td>
<td>This study is able to quantify a recommended level of drinking for CVD health and included both men and women. It discussed and controlled well for confounders such as previous alcohol intake.</td>
</tr>
<tr>
<td>(63)</td>
<td>Meta-analysis of prospective cohort studies</td>
<td>N= 84 studies</td>
<td>Multiple methods. Final categorisation based on grams of alcohol per day with a maximum of 1-2 drinks per day is associated with lowest risk of CVD mortality (RR=0.75) and CHD mortality Data relies on self reported intake. Not all studies could make clear the amount of alcohol per drink.</td>
<td>This meta-analysis included results of all of the major epidemiological studies to date and</td>
<td></td>
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</tbody>
</table>
>60g/day. Unless specified, drinks were assumed to contain 12.5g alcohol. (RR=0.79) and incidence (RR=0.66). Drinkers have a lower risk of all cause mortality and multiple cardiovascular events than non-drinkers. Max intake category of >60g/day (>5 drinks) does not show higher risk with this level of drinking. This may be due to smaller numbers in this category unable to detect increased risk. This gives a good conclusion on the subject. Included data for men and women and for many different CVD outcomes.

Table 8-4: Studies examining impact of alcohol intake on cardiovascular disease.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Numbers</th>
<th>Dietary assessment methods</th>
<th>Main findings</th>
<th>Limitations</th>
<th>Candidates rationale for inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>(76)</td>
<td>UK Whitehall II study</td>
<td>Prospective study</td>
<td>N= 7731</td>
<td>127 item FFQ</td>
<td>A healthy type diet is beneficial in reducing risks of diabetes and MI (RR=0.74) and coronary death (RR=0.71) compared to an unhealthy type diet. Sweet and Mediterranean diets showed no effects but had smaller numbers.</td>
<td>Foods included in 'Mediterranean' and 'Healthy' diets do not discriminate the two as well as possible i.e. fish, meat and oil intake are important.</td>
</tr>
<tr>
<td>(77)</td>
<td>Meta analysis of prospective cohort studies</td>
<td>18 studies N=2,190,627</td>
<td>Studies were required to use a priori score to describe adherence to the Mediterranean diet with 9 components.</td>
<td>A 2-point increase in adherence to the Mediterranean diet is associated with decreased</td>
<td>Methodology differs between studies relying on study investigators to accurately</td>
<td>Updated version of a previous meta-analysis which showed the same trends. The score</td>
</tr>
</tbody>
</table>
cardiovascular incidence or mortality (RR=0.90) and decreased overall mortality (RR=0.92).

measure the Mediterranean diet score.

system for adherence to the diet allows comparison in meta-analysis.

| (79) | Systematic review of prospective cohort studies | 10 prospective cohort studies in older populations | Variable | The Mediterranean diet, high quality diet and high fruit and vegetable consumption are cardio protective. | Reported on observational trends—is not a meta-analysis therefore cannot report any significance. | This study is able to highlight that although the Mediterranean diet is beneficial, other good dietary patterns can also be followed easily. |
| (78) | Meta analysis of randomised controlled trials | 6 trials N=2650 people with BMI 29-36 kg/m² | Based on recommendations and dietary plans given | The Mediterranean diet results in larger changes in Body weight, BMI, SBP, DBP, fasting plasma glucose, total cholesterol and high sensitivity C reactive protein than a low fat diet. | All but one study included relied on subject adherence to the diet as they were not provided with meals. Subjects may have made other diet and lifestyle changes. | For reducing CVD risk factors in obese individuals a Mediterranean diet is more favourable than a low fat diet. This has clinical implications for dietary advice given for weight loss. |

Table 8-5: Studies examining the impact of the Mediterranean diet on cardiovascular disease.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Numbers</th>
<th>Cognitive testing used</th>
<th>Main findings/outcome.</th>
<th>Limitations</th>
<th>Candidate’s rationale for inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>(101) USA Framingham Heart Study</td>
<td>Prospective cohort study (cross-sectional data)</td>
<td>N=1,702 men and women aged 55-88 years at baseline. Follow-up 14-20 years</td>
<td>Test Battery included: subsets from Welscher intelligence scale, Welscher memory scale and multi-lingual aphasia examination scale. Measured with a z score.</td>
<td>Blood pressure is inversely related to measures of attention and memory 14-20 years later (a decrease of 10mmHg could result in a -0.04 to -0.07 z score).</td>
<td>The test battery used uses a z score which is not comparable to the MMSE and other global cognitive function scales. There was no cognitive test performed at baseline when blood pressure was taken therefore those with cognitive impairment already were not excluded. Not applicable to women.</td>
<td>Framingham study is a landmark study in the areas of health and ageing. Memory and attention are components of cognition known to decline with age therefore it makes sense that in an ageing cohort these components would be affected. The reason for this could be increasing blood pressure with age.</td>
</tr>
<tr>
<td>(110) Hawaii Honolulu-Asia aging study</td>
<td>Prospective cohort study</td>
<td>N=3,703 middle-aged men 25 year follow-up.</td>
<td>Cognitive abilities screening instrument, Informant Questionnaire on Cognitive Decline in the Elderly, DSM-III-R criteria.</td>
<td>Men who are not treated for midlife hypertension have an increased risk of dementia in later life (OR=3.8-4.3 depending on blood pressure). No relationship in those treated.</td>
<td>Cognitive function was not measured at initial assessment so those already suffering from MCI are not excluded.</td>
<td>This study was likely to be of sufficient strength to show that dementia incidence is related to midlife blood pressure. This is a valuable finding when dealing with a middle-aged cohort such as CHALICE.</td>
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</tbody>
</table>

Table 8-6: Studies examining link between blood pressure and cognitive function and dementia.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Numbers</th>
<th>Cognitive testing used</th>
<th>Main findings/outcomes</th>
<th>Limitations</th>
<th>Rationale for inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>(114)</td>
<td>Meta-analysis of prospective studies</td>
<td>18 studies in middle-aged men and women (&lt;60 years)</td>
<td>Various cognitive tests and classifications of disease by DSM criteria.</td>
<td>High midlife total cholesterol may be related to higher risk of later AD and any dementia. It is also related to risk of cognitive impairment but not cognitive decline. No statistics on this data were provided.</td>
<td>It is difficult to compare results of different cognitive tests limited by differing criteria and cut-offs for measuring cognitive function.</td>
<td>18 robust studies (up to 2008) with large sample sizes, consistently used total cholesterol and controlled well for age. Results of meta-analysis are presented unclearly and p values are not given.</td>
</tr>
<tr>
<td>(113) USA Framingham Heart Study</td>
<td>Prospective cohort study</td>
<td>N=1,894 men and women aged 30-55 years at baseline</td>
<td>Test Battery included: subsets from Welscher intelligence scale, Welscher memory scale and multilingual aphasia examination scale.</td>
<td>Lower naturally occurring total cholesterol levels show a higher risk of poorer cognitive performance (p&lt;0.01).</td>
<td>Cognitive function test was administered 6-8 years after the last BP test which means those with cognitive impairment at baseline were not excluded. The testing is not comparable to MMSE.</td>
<td>It is expected that higher cholesterol levels would give higher CVD risk therefore poorer cognitive function but this is not the case. This study is important to keep in mind when assessing cognitive function alongside cholesterol and CVD risk.</td>
</tr>
<tr>
<td>(115) Sweden The Prospective Population Study of Women</td>
<td>Prospective cohort study</td>
<td>N=1,462 women aged 38-60 years at baseline</td>
<td>Disease classifications by DSM and NINCDS-ADRDA criteria</td>
<td>Mid-life cholesterol is unable to predict risk of dementia in late life when adjusted for appropriate parameters.</td>
<td>Hard end-point of dementia diagnosis with well known criteria. Not applicable to men.</td>
<td>Continues to support the argument that cholesterol is not a risk factor for cognitive impairment.</td>
</tr>
</tbody>
</table>

Table 8-7: Cholesterol, cognitive function and dementia
<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Numbers</th>
<th>Cognitive testing/outcome measure.</th>
<th>Main findings/outcomes.</th>
<th>Limitations / points of interest</th>
<th>Rationale for inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>(119) USA Framingham Heart Study</td>
<td>Prospective cohort study</td>
<td>N=1,624 Males and females aged 55-89 years follow-up Follow-up 28-30 years</td>
<td>Eight subtests from the Welscher Intelligence Scale, the Welscher memory scale and the multilingual aphasia examination.</td>
<td>Those who have NIDDM are more likely to have higher blood pressure and lower cognitive test scores in some areas than those who do not. Having both NIDDM and hypertension is associated with lower scores.</td>
<td>Cognitive testing was only performed at follow-up. Because only certain cognitive functions were measured, a global cognitive function score cannot be assessed making comparisons with other studies, and interpretation difficult.</td>
<td>This study acknowledges an important interaction between blood pressure and NIDDM. It highlights combined and separate risks.</td>
</tr>
<tr>
<td>(122) USA Framingham Heart Study</td>
<td>Prospective cohort study</td>
<td>N=2,210 Males and females mean age 70 years Follow-up 1-20 years (12.7y average)</td>
<td>DSMMD criteria for dementia and NINCDS-ADRDA criteria for AD.</td>
<td>Low risk people (&lt;75 years, without Apo-E gene raised total homocysteine) with diabetes have a higher risk of developing AD than low risk people without diabetes.</td>
<td>Showed that in some sub-groups diabetes is a risk factor for dementia.</td>
<td></td>
</tr>
<tr>
<td>(121) Systematic review of prospective cohort studies</td>
<td></td>
<td>25 studies N=8,656 Follow-up 2-18 years</td>
<td>MMSE Digit Symbol Span tests</td>
<td>Those with diabetes experience more cognitive decline and higher risk of dementia. Those with diabetes had higher risk of cognitive decline measured 1.2 fold by the MMSE, and estimated risk of dementia increases by 1.6 fold.</td>
<td>Systematic review is unable to statistically analyse data. This study could only report on observations but from 25 studies trends were apparent. MMSE was widely used.</td>
<td>Includes all important studies to date in 2005. Brings together all available longitudinal studies to present evidence.</td>
</tr>
</tbody>
</table>
### Table 8-8: Studies examining the link between diabetes cognitive function and dementia

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type and Focus of paper</th>
<th>Numbers</th>
<th>Type of cognitive testing and dietary assessment method</th>
<th>Results</th>
<th>Limitations / points of interest</th>
<th>Candidates reasoning for inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>(135) Holland Zutphen elderly study</td>
<td>Prospective cohort study N-3FA and cognitive function</td>
<td>N=426 men aged 69-89 years at baseline 3 years follow-up Diet assessed 1985 and 1990 Cognitive function assessed 1990 and 1993</td>
<td>MMSE (with cutoff of &lt;25 for cognitive impairment) Cross check dietary history method.</td>
<td>High linoleic acid is associated with cognitive impairment (OR=1.76). High fish consumption is inversely related to cognitive impairment (OR=0.63) and cognitive decline (OR=0.45). No association with n-3FA.</td>
<td>Cut-off of &lt;25 for cognitive impairment may have underestimated rates of cognitive impairment compared with cut-off of &lt;26 used elsewhere. Diet was not assessed in 1993 and change may have occurred.</td>
<td>This was the first study to suggest that fish intake has a protective role against cognitive impairment and permits further research in the area. It does not suggest n-3FA is an area of interest.</td>
</tr>
<tr>
<td>(134) Holland Zutphen elderly study</td>
<td>Cross-sectional study Fatty acids, fish intake and cognitive function.</td>
<td>N=1, 613 men aged 45-70 years</td>
<td>Cognitive test battery Self administered FFQ.</td>
<td>N-3FA and fish consumption is inversely related to overall cognitive function (OR=0.81).</td>
<td>Cross-sectional data has a lot of room for confounding variables to interact.</td>
<td>This study was the first to focus on the area of overall cognitive function in a cross-sectional study. Results show that fish may have a protective role in cognition.</td>
</tr>
<tr>
<td>(142) USA The Chicago Health and Aging Project.</td>
<td>Prospective cohort study Fat intake and cognitive decline</td>
<td>N=2,560 men and women aged 65 years and over at baseline. 6 years follow-up.</td>
<td>East Boston Tests of Immediate and Delayed Recall, the Mini-Mental State</td>
<td>Higher intakes of SAFA (p=0.04) and trans-FA (p=0.07) are associated with greater cognitive</td>
<td>Cognitive testing at baseline, 3 and 6 years gave a more reliable estimate of decline. FFQ was</td>
<td>This study was one of the first to highlight evidence for the negative role of SAFA.</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Design</td>
<td>Study Population</td>
<td>Methods</td>
<td>Results</td>
<td>Conclusion</td>
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<tr>
<td>(138) USA</td>
<td>Prospective cohort study</td>
<td>Fish intake and cognitive decline</td>
<td>N=3,718 men and women aged &gt;65 years</td>
<td>Those who ate one (p=0.03) or two (p=0.04) fish meals per week had slower rates of cognitive decline than those who did not (reduced by 10-13% per year). There were no associations with n-3 FAs.</td>
<td>High intake of MUFA and high PUFA:SAFA ratio may be protective against cognitive decline but trends are non-significant. Validated against 24-hour recalls gave correlations between 0.36 and 0.47 for differing fatty acid intake.</td>
<td></td>
</tr>
<tr>
<td>(140) Italy</td>
<td>Prospective cohort study</td>
<td>Total energy, MUFA and PUFA and ARCD.</td>
<td>N=278 (survey 1),186 (survey 2) 95 (survey 3) aged 65-84 years at baseline 8.5 years follow-up</td>
<td>High intakes of PUFA (CI -0.12 to -0.0004) and MUFA (CI -0.002 to -0.0009) are associated with reduced risk of cognitive decline over 8.5 years. FFQ was only administered at baseline, while the cognitive function was assessed in all surveys meaning dietary change cannot be accounted for.</td>
<td>This study was the first to explore evidence for the protective role of USFA against ARCD, describing that PUFA and MUFA are protective.</td>
<td></td>
</tr>
<tr>
<td>(145) Italy</td>
<td>Prospective cohort study</td>
<td>Fat intake and MCI</td>
<td>N=278 (survey 1), 16 (survey 2) Aged 65-84 years at baseline 2.6 years follow-up</td>
<td>There are no associations between intake of dietary fats and MCI in this population. Small sample size limiting power. Modifications to the Peterson MCI criteria (exclusion of the need</td>
<td>This study was the first to look at MCI as an outcome. It was unable to produce any significant results.</td>
<td></td>
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<tr>
<td>Reference</td>
<td>Study Type</td>
<td>Participants</td>
<td>Outcome Measures</td>
<td>Findings</td>
<td>Limitations</td>
<td>Further Investigation</td>
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<tr>
<td>(139) Holland Zutphen elderly study</td>
<td>Prospective cohort study</td>
<td>Men aged 70-89 years at baseline in 1990 5 year follow-up</td>
<td>MMSE (with cutoff of &lt;24 for cognitive impairment) Cross-check diet history method.</td>
<td>Those that consume fish experience less cognitive decline than those who do not (p&lt;0.01). Trend is linear with every 380mg of EPA and DHA per day is associated with a 1.1 difference in cognitive decline (p=0.01)</td>
<td>Diet was only measured once in 1990 limiting ability to assess dietary change. MMSE cut-off for cognitive impairment is below that suggested by other studies. Results do not apply to women.</td>
<td>Although small, this study shows that the n-3FA component is an important protective factor against cognitive decline. This study warrants further investigation into fish and n-3FA.</td>
</tr>
<tr>
<td>(136) Norway The Hordaland Health Study</td>
<td>Cross-sectional study</td>
<td>N=2,031 men and women aged 70-74 years</td>
<td>Modified MMSE (poor cognitive score = 10th percentile) plus five other tests for specific function. 169 item FFQ</td>
<td>Those with &gt;10g/day intake of fish have better cognitive function than those who do not (MMSE p=0.002). A dose dependant relationship exists between test scores and fish intake which appears to plateau after about 70g/day (MMSE p=0.038). Four of five other test scores reported significant results.</td>
<td>Cross-sectional data. Only 80 participants did not have 10g/day of fish. It is not clear the component of the fish causing the effect.</td>
<td>This study is able to quantify amount of fish required to benefit overall cognition to be 10-70g/day. Only results for the MMSE have been reported as they are the most comparable to other studies.</td>
</tr>
<tr>
<td>Country</td>
<td>Study Title</td>
<td>Study Type</td>
<td>Sample Size</td>
<td>Methods</td>
<td>Findings</td>
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<tr>
<td>Finland</td>
<td>CVD risk Factors Aging and Dementia (CAIDE) study.</td>
<td>Prospective cohort study</td>
<td>Midlife fat intake and late life MCI</td>
<td>N=1,449 aged 65-80 years at last follow-up in 1998; Average follow-up 21 years</td>
<td>Those with the highest intakes of total fat (p=0.05) and SAFA (p=0.03) from milk products and spreads have the highest chance of developing MCI in later life. These associations were only significant in women. Adjusted not only for education, sex, follow-up time, midlife vascular factors and Apo-E4 carrier status. There was no association between MCI and incidence and being an Apo-E carrier. Fat from meats did not seem to be included in FFQ. This study is the first to focus on fat from a food group other than fish. It also has the outcome as MCI. Results support past studies which have reported negative impact of SAFA on varying cognitive outcomes.</td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td>EPIC-Greece cohort</td>
<td>Prospective cohort study</td>
<td>Diet and cognitive function</td>
<td>N=732 men and women aged &gt;60 years</td>
<td>PUFA (p=0.004) and consumption of seed oils (p=0.002) are inversely associated with cognitive function. n6 component of seed oils appeared to be responsible for the association. The MMSE and GDS was not measured at baseline. Subjects were not tested for cognitive impairment or dementia prior to inclusion. This study looks into different sources of PUFA, specifically looking at sources of n-3FA and n-6. The results from this study conflict that of other studies and suggest that n-6 intake from seed oils hinders cognitive function.</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Three city study</td>
<td>Prospective cohort study</td>
<td>Olive oil and cognitive function</td>
<td>N=6,947 men and women aged 65 years and over; Follow up four years; Electoral roll, non-institutionalized.</td>
<td>Only intensive use of olive oil in both cooking and dressing shows better visual memory (p&lt;0.04) but has no impact on global cognitive function as measured. Before controlling for important factors, verbal fluency was also significant. The FFQ did not encompass baked goods which are a major source of fats. This study plays an important role in supporting the Mediterranean diet hypothesis as olive oil is a main constituent of the diet. Intake of olive oil may be</td>
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</tbody>
</table>

**Notes:**
- MMSE: Mini-Mental State Exam
- GDS: Global Deterioration Scale
- PUFA: Polyunsaturated Fatty Acids
- SAFA: Saturated Fatty Acids
- Apo-E: Apolipoprotein E
- n-3FA: Omega-3 Fatty Acids
- n-6: Omega-6 Fatty Acids

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**References:**
- All studies referenced are peer-reviewed and published in reputable journals in the field of nutrition and cognitive function.
by MMSE. Results are not strong enough to show difference in overall cognition. Use of other fats was not controlled for nor analyzed. Reflective of this type of diet or a healthier diet.

Other studies investigating cognitive decline as an outcome have focused on PUFA and fish. This study highlights the protective role MUFA plays against cognitive decline.

Table 8-9: Studies examining the relationship between fatty acids and fish intake, and cognitive function, cognitive decline and cognitive impairment.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type and focus of study</th>
<th>Numbers</th>
<th>Type of testing used</th>
<th>Results</th>
<th>Limitations</th>
<th>Candidates reasoning for inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>(143) USA Women’s Health Initiative</td>
<td>Prospective cohort study Fat intake and cognitive decline.</td>
<td>N=482 women aged 60 years and older at cognitive testing baseline. Follow-up (for cognitive testing) 3 years</td>
<td>Extensive cognitive test battery with calculated global z-score to judge overall cognitive function FFQ (administered twice before cognitive testing 5.6 years before and 2.9 years before)</td>
<td>The higher the intake of MUFA the smaller the risk of cognitive decline (p=0.02). Before adjustments for other fats took place, high SAFA intake was associated with higher risk of cognitive decline (p=0.01). Adjusted for intake of other types of fats. Results are not applicable to men. Test battery results are not directly comparable to MMSE.</td>
<td>Other studies investigating cognitive decline as an outcome have focused on PUFA and fish. This study highlights the protective role MUFA plays against cognitive decline.</td>
<td></td>
</tr>
<tr>
<td>(152) Holland The Zutphen elderly study</td>
<td>Prospective cohort study(with cross-sectional and prospective analysis) Alcohol intake and cognitive status and cognitive decline.</td>
<td>N=489 men aged 65-84 years at baseline in 1985 Follow-up 8 years</td>
<td>Validated cross-check dietary history for alcohol intake (in grams) in 1985 and 1990 MMSE in 1990 and 1993. One drink=13.2g alcohol.</td>
<td>There is no association between alcohol intake and cognitive decline. There is a protective effect against poor cognitive function in those with diabetes and/or CVD who drink &lt;2 drinks per day. However those with diabetes/CVD who drink &lt;1 drink per day</td>
<td>The only year that both MMSE and dietary history was gained was 1990 leaving room for drinking habits to change between 1990 and 1993. However authors attempted to minimize by identifying changes</td>
<td>This study describes how risk may be different for those with CVD and diabetes. It shows that moderate drinking (&lt;2 drinks/day) may be more important for their cognitive health.</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample</td>
<td>Outcome</td>
<td>Findings</td>
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</tr>
<tr>
<td>(149) USA Framingham Heart Study</td>
<td>Prospective cohort study (with cross-sectional analysis) Alcohol intake and cognitive test score.</td>
<td>N=2,123 men and women aged 55-89 years</td>
<td>Kaplan-Albert neuropsychological test battery Current alcohol intake per week (24 year history collected during study). Each drink contains 11.8g alcohol.</td>
<td>Women who drink 2-4 alcoholic drinks per day have better cognitive test scores in all cognitive tests (p&lt;0.01). Men who have 4-8 drinks per day appeared to get better test scores (p&lt;0.05). Prospectively, drinking habits over 24 years for women only, show that the more alcohol consumed, the better the test scores (p&lt;0.01). The testing method cannot be directly compared with MMSE, however the overall message is similar to other studies; moderate amounts of alcohol are beneficial for cognitive health. Reports are only based on the z-score for the total summarized tests, not individual cognitive test domains. This study recommends consuming over the recommended amount of alcohol described by New Zealand alcohol advisory council.</td>
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<td></td>
</tr>
<tr>
<td>(83) France Epidemiology of Vascular Ageing (EVA) study</td>
<td>Prospective cohort study Cognitive deterioration and alcohol intake in ApoE and non-ApoE carriers.</td>
<td>N=1,389 men and women aged 59-71 years at baseline. Follow up 4 years</td>
<td>MMSE (cognitive deterioration classified by decline of 3 points) Questionnaire of food habits (where each drink contains 13ml alcohol and categories are &lt;2 glasses/day, 2-5 glasses/day and &gt;5 glasses/day). One drink = 10.26g alcohol</td>
<td>The authors reported that drinking alcohol was inversely associated risk of cognitive deterioration in non-ApoE carriers while, drinking increased the risk of deterioration in Apo-E carriers. Although these trends existed no results were statistically significant. Cognitive deterioration is not discriminated from MCI in this study. It is not possible to know how many people had scores of &lt;26 at any point in time. It could be that ARCD is the effect observed but the subjects are middle aged and a ‘young-old’ age group. The authors also reported results of smoking and cognitive deterioration; however no statistically significant associations were apparent. Although results were not significant, trends noted for the ApoE genotype are of</td>
<td></td>
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</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Study Details</td>
<td>Cohort</td>
<td>Follow-up Duration</td>
<td>Questionnaire/Assessment</td>
<td>Risk Factors Examined</td>
</tr>
<tr>
<td>-------</td>
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<td>---------------</td>
<td>--------</td>
<td>--------------------</td>
<td>--------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>(153) Finland CVD risk Factors Aging and Dementia (CAIDE) study.</td>
<td>Finland</td>
<td>Prospective cohort studies in Europe</td>
<td>Alcohol intake at middle age and MCI and dementia in old age.</td>
<td>Follow-up 23 years</td>
<td>Questionnaire on alcohol intake. Never, infrequent (&lt;1 month) and frequent drinking status was determined. Determination of MCI and dementia with MMSE &lt;24, and further DSM criteria for dementia and other criteria for MCI.</td>
<td>Those who never drank in midlife and those who frequently drank in midlife have higher risk of cognitive impairment in late life (OR=2.15 and 2.57 respectively). Those who never drank in late life also had increased risk of cognitive impairment, but there was no effect of frequent drinking in late life. The effect of Apo-E genotype showed that the more frequently carriers drink in midlife, the higher their risk of dementia. No frequency of drinking was associated with dementia at any time in non-carriers.</td>
</tr>
<tr>
<td>(151) UK The 1946 British Birth cohort</td>
<td>UK</td>
<td>Prospective cohort study</td>
<td>Alcohol intake and mid-life cognitive change.</td>
<td>Follow-up 10 years. Recruited at birth.</td>
<td>Test battery Self completed questionnaire for 7 days of alcohol intake. One drink = 9.0g alcohol.</td>
<td>Light and moderate male drinkers have a slower decline in memory from age 43-53 years, but women have a rapid decline in visual search speed</td>
</tr>
</tbody>
</table>

This study is similar to what was examined in CHALICE. It has a long follow-up time where it is possible to see decline during
<table>
<thead>
<tr>
<th>Study (Reference)</th>
<th>Design/Context</th>
<th>Sample Size</th>
<th>Follow-up</th>
<th>Measures of Alcohol Intake</th>
<th>Cognitive Outcomes</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>(154) USA Women’s Health Initiative Memory study (WHIMS)</td>
<td>Prospective cohort study (with intervention arm for hormone replacement therapy)</td>
<td>N=4,461 women aged 50-79 years at baseline</td>
<td>Follow-up 4.2 years</td>
<td>Modified MMSE: 3MSE. Score below cutoff based on years of education, plus neuro-cognitive assessment and neuropsychiatric exam for MCI or dementia. Decline of ≥8 points for cognitive decline. FFQ for alcohol intake over last 3 months; none, &lt;1 drink/day or ≥1 drink per day.</td>
<td>Those who have ≥1 drink per day have higher MMSE scores than those who did not drink at baseline (p&lt;0.001). The odds of experiencing cognitive decline 0.69 for &lt;1 drink/day and 0.53 for ≥1 drink/day, compared to never drinking.</td>
<td>Participants were not excluded from follow-up if MCI or dementia was diagnosed. Analysis did not control for presence of Apo-E gene.</td>
</tr>
</tbody>
</table>
| (150) Finland CVD risk Factors Aging and Dementia (CAIDE) study. | Prospective cohort studies in Europe | N=1,341 men and women aged 44-58 years at baseline. | Follow-up 21 years. | Questionnaire of alcohol intake; Grams of alcohol per week where one drink= 12-14.5 g alcohol was classified as a drink depending on the beverage. Drinking frequency : Never, infrequent (<1 month) and frequent drinking | There was no difference between categories of drinker at mid and late life and MMSE score. However significant differences were apparent for all other categories except subjective memory (at midlife) and semantic memory (at late life). These significant trends show that drinking in midlife and at late life may be associated with cognitive decline. | This study shows that using the MMSE was unable to detect differences in cognitive functions as sensitively as individual tests from a test battery. This suggests that when measuring cognitive function it may be useful to use a global cognitive function.

This demonstrates consistency with the ‘J’ or ‘U’ shaped curve.

(92) This study use 3MSE which is more comprehensive than MMSE but is validated and gives the same results.
status was determined. MMSE and a test battery of other specific cognitive functions. mid and late life is more beneficial than not drinking on late life cognitive function. and how much of the result indicates ARCD. test as well as a test battery for individual functions.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Outcome Measures</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>(155) Italy Italian Longitudinal study on aging (ILSA)</td>
<td>Prospective cohort study</td>
<td>N=4,521 Men and women 65-84 years at baseline Follow-up 3.5 years</td>
<td>MMSE &lt;23 And other tests measuring ability. DSMMD and other acceptable criteria for dementias. FFQ including amount per day, frequency of drinking, drinking history and type of drinks consumed. One drink =15g alcohol</td>
<td>The risk of progression to dementia in those with MCI is decreased by having &lt;1 drink per day of alcohol or wine compared to those who do not drink (HR=0.15). There is no association between any level of drinking and developing MCI. Drinking ≥1 drink/day is not associated with a higher risk of progression to dementia compared to abstainers. Study did not take Apo-E into account which could have accounted for some of the effect. This study used a cut-off of 23 for MCI whereas other studies have used higher cut-offs. This may be why no drinking level was associated with MCI. This study is an example of how moderate drinking may play a part in slowing or preventing the progression to dementia.</td>
</tr>
</tbody>
</table>

Table 8-10: Studies examining the impact of alcohol intake on cognitive function, cognitive decline and cognitive impairment.
8.2 Appendix B: New Zealand Cardiovascular Risk Charts 2003

ASSESSING CARDIOVASCULAR RISK AND TREATMENT BENEFIT

Figure 2. Assessing 5 year cardiovascular risk and treatment benefit.
8.3 Appendix C : Guidelines for Using the New Zealand Cardiovascular Risk Charts
<table>
<thead>
<tr>
<th>Table 1</th>
<th>The age to start cardiovascular disease risk assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
<td><strong>Men</strong></td>
</tr>
<tr>
<td>Asymptomatic people without known risk factors</td>
<td>Age 45 years</td>
</tr>
<tr>
<td>Māori, Pacific peoples or Indo-Asian* peoples</td>
<td>Age 35 years</td>
</tr>
<tr>
<td>People with other known cardiovascular risk factors or at high risk of developing diabetes</td>
<td>Age 35 years</td>
</tr>
</tbody>
</table>

**Family history risk factors**
- Diabetes in first-degree relative (parent, brother or sister)
- Premature coronary heart disease or ischaemic stroke in a first-degree relative (father or brother <55 years, mother or sister <65 years)

**Personal history risk factors**
- People who smoke (or who have quit only in the last 12 months)
- Gestational diabetes, polycystic ovary syndrome
- Prior blood pressure (BP) ≥160/95 mm Hg, prior TC:HDL ratio ≥2
- Prediabetes (see section ‘Screening and diagnosis of type 2 diabetes’ in Chapter 4)
- BMI ≥30 or truncal obesity (waist circumference ≥100 cm in men or ≥90 cm in women)
- eGFR <60 ml/min/1.73 m²

* Indo-Asian peoples include Fijian Indian, Sri Lankan, Afghani, Bangladeshi, Nepali, Pakistani, Tibetan

1 eGFR estimated glomerular filtration rate

Risk assessment using a risk trajectory approach (see page 7) could be considered on a case-by-case basis for patients younger than the recommended ages, particularly where there is clinical concern regarding unfavourable risk factors.

---

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Estimating 5-year cardiovascular risk: when to use the New Zealand Cardiovascular Risk Charts*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk group</strong></td>
<td><strong>Estimating risk</strong></td>
</tr>
<tr>
<td>Very high risk groups: 5-year risk assumed clinically &gt;20%</td>
<td>These people should not have their risk calculated using the New Zealand Cardiovascular Risk Charts as they will already have a very high risk due to their clinical condition</td>
</tr>
</tbody>
</table>
- Previous CVD event: angina, MI, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), transient ischaemic attack (TIA), ischaemic stroke, peripheral vascular disease
- Some genetic lipid disorders: familial hypercholesterolaemia (FH), familial defective ApoB (FDB), familial combined hyperlipidaemia (FCH)
- Diabetes with overt nephropathy (albumin-creatinine ratio ≥30 mg/mmol OR urinary albumin ≥2000 mg/L)
- Diabetes with other renal disease causing renal impairment (eGFR ≤60 ml/min/1.73 m²)

| Isolated elevated single risk factors: 5-year risk of >15% | Calculate 5-year risk using the New Zealand Cardiovascular Risk Charts. When all risk factors are taken into account, the risk may be even higher than the assumed 5-year CVD risk of ≥15% |
- TC ≥6 mmol/L
- TC:HDL ratio ≥3
- BP consistently ≥170/100

| People aged 35–74 years: calculate the 5-year CVD risk | Calculate 5-year risk using the New Zealand Cardiovascular Risk Charts or an electronic decision-support tool (stand alone or incorporated into some practice software) |
- Family history of premature coronary heart disease or ischaemic stroke in a first-degree relative (father or brother <55 years, mother or sister <65 years)
- Māori, Pacific peoples or Indo-Asian* peoples
- Diabetes with microalbuminuria OR for ≥10 years OR with HbA1c consistently ≥8% (64 mmol/mol)

* These groups should be moved up one risk category (5%):  
- Family history of premature coronary heart disease or ischaemic stroke in a first-degree relative (father or brother <55 years, mother or sister <65 years)
- Māori, Pacific peoples or Indo-Asian* peoples
- Diabetes with microalbuminuria OR for ≥10 years OR with HbA1c consistently ≥8% (64 mmol/mol)
### Table 2 continued...

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Estimating risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>People aged &lt;35 years</td>
<td>All calculations outside the age ranges of the Framingham equation are approximations, but can be useful</td>
</tr>
<tr>
<td>with known risk factors</td>
<td><strong>Aged under 35 years:</strong> calculate the risk as if they were 35 years. The result can be used to guide clinical decision-making. Some risk factors in young people might require more intensive intervention or specialist referral</td>
</tr>
<tr>
<td></td>
<td>• Low HDL &lt;0.7 mmol/L (because of the risk of a genetic lipid disorder – see Chapter 9 of the guideline The Assessment and Management of Cardiovascular Risk)</td>
</tr>
<tr>
<td></td>
<td>• Known familial dyslipidaemias or suspected genetic lipid disorders</td>
</tr>
<tr>
<td></td>
<td>• Type 1 diabetes, type 2 diabetes with microalbuminuria or type 2 diabetes of long duration (≥10 years)</td>
</tr>
<tr>
<td>People aged &gt;75 years</td>
<td><strong>Aged over 75 years:</strong> calculate the risk as if they were 65-74 years. An assessment of the balance between the risks and benefits of treatment is more difficult in older than in younger people. Older people gain a similar relative benefit from cholesterol lowering, but are more likely to benefit in absolute terms because of their much higher pretreatment cardiovascular risk. Smoking cessation is beneficial at any age</td>
</tr>
<tr>
<td></td>
<td>A clinical judgment should take into account:</td>
</tr>
<tr>
<td></td>
<td>• likely benefits and risks of treatment</td>
</tr>
<tr>
<td></td>
<td>• life expectancy and comorbidities</td>
</tr>
<tr>
<td></td>
<td>• personal values</td>
</tr>
</tbody>
</table>

*Note that as well as higher CVD risk, people with diabetes face additional risks.*

Consult Chapter 4 Management of type 2 diabetes for assessment and management of these risks.

* Make the 5% adjustment only for people with ≥1 criterion.

Indo-Asian peoples: Indian, including Fijian Indian, Sri Lankan, Afghan, Bangladeshi, Nepalese, Pakistani, Tibetan.

### Table 3

| What to measure and record for cardiovascular risk assessment and diabetes screening |
|----------------------------------------|-----------------------------------------------------------------------------------|
| **Everyone**                           | **History**                                                                      |
|                                        | • Age                                                                              |
|                                        | • Gender                                                                          |
|                                        | • Ethnicity                                                                       |
|                                        | • Smoking status (if stopped smoking for <12 months, assess as a smoker)         |
| **Family history**                     | **Premature coronary heart disease or ischaemic stroke in a first-degree relative** |
|                                        | • Type 2 diabetes                                                                  |
|                                        | • Genetic lipid disorder (see Appendix B)                                          |
| **Past medical history**               | **Past history of CVD (MI, PCI, CABG, angina, ischaemic stroke, TIA, peripheral vascular disease (PVD))** |
|                                        | • Genetic lipid disorder (FH, FDB, FCH: see Appendix B)                            |
|                                        | • Renal impairment                                                                 |
| **Measure**                            | • Average of two sitting BP measurements                                          |
|                                        | • Pulse                                                                           |
|                                        | • BMI, waist circumference                                                        |
|                                        | • Fasting lipid profile                                                           |
|                                        | • HbA1c or fasting plasma glucose                                                 |
|                                        | (see section “Screening and diagnosis of type 2 diabetes” in Chapter 4)           |
| **Diabetes**                           | **History and examination**                                                       |
|                                        | • Date of diagnosis                                                               |
|                                        | • Type of diabetes (type 1, type 2, including type 2 on insulin, gestational diabetes) |
|                                        | • HbA1c                                                                           |
|                                        | • Urine albumin: creatinine ratio (ACR)                                            |
|                                        | • eGFR and history of renal disease                                               |
| **Atrial fibrillation (AF), confirmed on electrocardiogram (ECG)** | **History and examination**                                                       |
|                                        | • Echocardiogram (where possible)                                                 |
|                                        | • Past history of stroke, TIA, heart failure, rheumatic or mitral valve disease   |

* When a fasting sample is not possible, measure non-fasting total cholesterol and HDL-cholesterol.

Estimated glomerular filtration rate (eGFR).
Appendix D: New Zealand Cardiovascular Risk Chart 2012

How to use the Charts

- Identify the chart relating to the person’s sex, diabetic status, smoking history and age.
- Within the chart, choose the cell nearest to the person’s age, systolic blood pressure (SBP) and total cholesterol (TC) TC:HDL ratio. For example, the lower left cell contains all non-smokers without diabetes who are 35–44 years and have a TC:HDL ratio of less than 4.5 and a SBP of less than 130 mm Hg. People who fall exactly on a threshold between cells are placed in the cell indicating higher risk.
- The risk charts now include values for SBP alone, as this is the most informatively conventionally measured blood pressure parameter for cardiovascular risk. Diastolic pressures may add some predictive power, especially at younger ages (eg, a diastolic pressure consistently >100 mm Hg in a patient with SBP values between 140 and 170 mm Hg).

Certain groups may have CVD risk underestimated using these charts. See Table 2 (page 5) for recommended adjustments.

2 New Zealand Primary Care Handbook 2012
Risk level: men

Benefits: NNT for 5 years to prevent one event (CVD events prevented per 100 people treated for 3 years)

<table>
<thead>
<tr>
<th>Risk level: 5-year CVD risk (total and non-total)</th>
<th>1 intervention (25% risk reduction)</th>
<th>2 interventions (45% risk reduction)</th>
<th>3 interventions (55% risk reduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%</td>
<td>13 (7.5 per 100)</td>
<td>7 (14 per 100)</td>
<td>6 (16 per 100)</td>
</tr>
<tr>
<td>20%</td>
<td>20 (5 per 100)</td>
<td>11 (9 per 100)</td>
<td>9 (11 per 100)</td>
</tr>
<tr>
<td>15%</td>
<td>27 (4 per 100)</td>
<td>15 (7 per 100)</td>
<td>12 (8 per 100)</td>
</tr>
<tr>
<td>10%</td>
<td>40 (2.5 per 100)</td>
<td>22 (4.5 per 100)</td>
<td>18 (5.5 per 100)</td>
</tr>
<tr>
<td>5%</td>
<td>80 (1.25 per 100)</td>
<td>44 (2.25 per 100)</td>
<td>36 (3 per 100)</td>
</tr>
</tbody>
</table>

NNT: Number needed to treat

Based on the conservative estimate that each intervention: aspirin, BP treatment (lowering SBP by 10 mm Hg) or lipid modification (lowering LDL-C by 20%) reduces cardiovascular risk by about 25% over 5 years.

Note: Cardiovascular events are defined as myocardial infarction, new angina, ischaemic stroke, transient ischaemic attack (TIA), peripheral vascular disease, congestive heart failure and cardiovascular-related death.

Adapted with permission from: Rod Jackson, Head of the Section of Epidemiology and Biostatistics, School of Population Health, Faculty of Medical and Health Sciences, University of Auckland.
8.5 Appendix E: Your Heart Forecast website examples

Profile 1: Patient A
Sex: Female
Age: 36 years old
Ethnicity: Maori
Blood Pressure: 120/85 mmHg
TC: HDL ratio: 3.5
Smoking status: Non-smoker
Diabetes status: No Diabetes

Figure 1: Patient A’s current CVD risk is shown to be mild (6%).
Figure 2: Patient A’s ideal risk as she gets older from age 36 to 75 years with a maximum risk of ‘moderate’

Figure 3: Patient A’s risk as she gets older if no other risk factors are modified. Moderate risk given.
Profile 2: Patient B
Sex: Male
Age: 55 years old
Ethnicity: NZ European
Blood Pressure: 135/85 mmHg
TC: HDL ratio: 6
Smoking status: Recently quit
Diabetes status: No Diabetes
+Family History: Yes

Figure 4: Patient B’s current CVD risk is 21% which is classed as ‘very high’.

Figure 5: Patient B’s ideal risk trajectory as he gets older: ages 55-75 years
Figure 6: Patient B's actual risk trajectory as he ages based on other present risk factors
8.6 Appendix F: Ethics Approval and Maori Consultation documents

14 June 2010

Professor Peter Joyce
Department of Psychological Medicine
Christchurch School of Medicine & Health Sciences
P O Box 4345
Christchurch

Attn: Janet Spittlehouse

Dear Professor Joyce,

URA/10/03/021 Canterbury Health, Ageing and Life Course Study

Investigators Prof P Joyce, Mr C Lacey, A/Prof V Cameron, Prof S Chambers,

Dr R Gearry, Dr H Jamieson, Prof M Kennedy

This study was given ethical approval by the Upper South A Regional Ethics Committee on 14 June 2010.

Approved Documents

Protocol version 2.1 dated 18.05.10

Information sheet and Consent form version 2.1 dated 12.05.10

CHALICE Yearly health questionnaire version 1.0 dated 02.06.10

This approval is valid until 31 August 2016, provided that Annual Progress Reports are submitted (see below).
Access to ACC

For the purposes of section 32 of the Accident Compensation Act 2001, the Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out. Participants injured as a result of treatment received in this trial will therefore be eligible to be considered for compensation in respect of those injuries under the ACC scheme.

Amendments and Protocol Deviations

All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:

- the researcher responsible for the conduct of the study at a study site
- the addition of an extra study site
- the design or duration of the study
- the method of recruitment
- information sheets and informed consent procedures.

Significant deviations from the approved protocol must be reported to the Committee as soon as possible.

Annual Progress Reports and Final Reports

The first Annual Progress Report for this study is due to the Committee by 30 June 2011. The Annual Report Form that should be used is available at www.ethicscommittees.health.govt.nz. Please note that if you do not provide a progress report by this date, ethical approval may be withdrawn.

A Final Report is also required at the conclusion of the study. The Final Report Form is also available at www.ethicscommittees.health.govt.nz.
Requirements for the Reporting of Serious Adverse Events (SAEs)

For the purposes of the individual reporting of SAEs occurring in this study, the Committee is satisfied that the study’s monitoring arrangements are appropriate.

SAEs occurring in this study must be individually reported to the Committee within 7-15 days only where they:

are unexpected because they are not outlined in the investigator’s brochure, and

are not defined study end-points (e.g. death or hospitalisation), and

occur in patients located in New Zealand, and

if the study involves blinding, result in a decision to break the study code.

There is no requirement for the individual reporting to ethics committees of SAEs that do not meet all of these criteria. However, if your study is overseen by a data monitoring committee, copies of its letters of recommendation to the Principal Investigator should be forwarded to the Committee as soon as possible.

Please see www.ethicscommittees.health.govt.nz for more information on the reporting of SAEs, and to download the SAE Report Form.

We wish you all the best with your study.

Yours sincerely

Alieke Dierckx

Administrator

Upper South A Regional Ethics Committee

Email: alieke_dierckx@moh.govt.nz
29 July 2008

Professor Peter Joyce
Department of Psychological Medicine
University of Otago, Christchurch

Tena koe, Peter

Thank you for meeting with me at the University of Otago, Christchurch on Monday 21 July, to discuss your research study titled:

CHALICE - Canterbury Healthy Ageing Life Course Study

I note that your research is a large long term study in which recruitment will be by random electoral role sampling over 2,500 fifty year olds.

You also mentioned that the sample will include over-sampling of Maori to obtain up to at least 500 fifty year olds.

We also discussed the relevance of the research in regard to Improving Maori health status and referred to Decades of Disparity II: Socioeconomic mortality trends in New Zealand 1981 - 1999, March 2005. The other reference that is available is Hauora Maori Standards of Health: A study of the years 1970-1991 by Eru Pomare, Maori Health Research Unit, Wellington School of Medicine. Both provide Maori specific information on a range of health issues. The recent publication Tatau KahuKura, Ministry of Health, 2006, is an update relating to the socio economic determinants of health, health status and service utilisation of the Maori population.

The Canterbury District Health Board also has a Maori Health plan which could be relevant.

Your suggestion to work alongside Maori to discuss questions, method and tradition was important. Manawhenua ki Waitaha, chaired by Dr Matea Gillies, would be a group to consider. Representation on the Committee comes from the seven Runanga that resides within the Canterbury District Health Board boundaries. Manawhenua ki Waitaha also has a Memorandum of Understanding with the CDHB. The members meet monthly at Te Waipounamu House and the Secretary is Ali Mitchell, email ali.mitchell@ngaitahu.iwi.nz.

There is a need to acknowledge the issues pertaining to ethnicity. Your study will involve a number of Maori participants. As such it was acknowledged there is a need to consider how the ethnicity data will be collected. Findings from this study may contribute to the development of future research hypotheses or projects. The research
proposal included the Census 2006 ethnicity question. In acknowledging Maori will be participants, it is my assumption that policies and procedures have been developed with regard to the collection, access, storage and disposal of Maori data for this project.

You mentioned that Dr Lacy will be an investigator. It would be advantageous for him to meet with Manawhenua ki Waitaha for the same reasons I have mentioned previously.

It is a requirement of the ethics approval process that a final report be submitted when the research is complete. A copy of the report should be provided to me at that time as findings from this project may contribute to the development of future research hypotheses or projects. It is therefore important that appropriate Maori organisations, Maori health professionals and Maori researchers are aware of your findings. The Research Office of the University of Otago, Christchurch and in particular myself as the Research Manager of Maori health would be willing to assist in the dissemination of your findings once your project has reached a successful conclusion.

My suggestions do not necessarily relate to ethical issues with the research, including methodology. Other committees may also provide feedback in these areas. I hope this letter will suffice in terms of the application. Please contact me should you need any other information that may not have been included in the letter relevant to our conversation.

I wish you well in your research.

Kia manawanui

e noho ra

Elizabeth Cunningham  
Research Manager - Maori
### Appendix G: Relevant Information from Module One of CHALICE Questionnaire.

**Module 1**

**Case Report Form**

<table>
<thead>
<tr>
<th>Date of Assessment</th>
<th>Participant Study Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Research Nurse Name</th>
<th>Interviewer’s Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Informed consent given by study participant

**Blood samples:**

<table>
<thead>
<tr>
<th>Blood taken at:</th>
<th>Time:</th>
<th>24 hour clock</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Yes, fasting blood sample taken □ OR none fasting blood taken OR □ blood taken □

If **not fasting**, details and time of food/drinks in the last 12 hours:

___________________________
Tick if fasting blood has not been taken but the participant has been given a form for a fasting blood appointment.

Comments:

_____________________________________________________________________

_____________________________________________________________________

Urine sample:

Urine taken at

Comments:

_____________________________________________________________________

_____________________________________________________________________

Body Measurements:

Height: ________________ cm

Weight: ________________ kg

Waist: ________________ cm
Bioimpedance Assessment:

BMI: ____________________ kj  BMR: ____________________ kj

Impedance: ______________ Ω

Fat %: ____________________  Fat Mass: ______________ kg

FFM ____________________ kg  TBW: ____________________ kg

Blood Pressure and Pulse: Time blood pressure taken:  

Heart rate: ______________ / min  Sphygmomanometer: Manual / Automatic

Blood pressure: _________/_________  Arm:  L / R

Comments:
8.8 Appendix H: relevant Information from Module Two of CHALICE

Questionnaire

Module 2 Questionnaire

Personal Health History

1. DEMOGRAPHICS

First, I am going to ask you some general questions about you and your household. Then we will go on to talk about your health.

1.01 You are male/female…? [Circle one]
1 Male
2 Female

Date of birth

1.02 Firstly, what is your date of birth? [Record]
2 Enter eight digit date (e.g. 4 March 1946 = 04031946).

______/_____/___________
99 Refused

Ethnicity

[Showcard 1.03a]
1.03a Which ethnic group or groups do you belong to? Call the number or numbers of the ones that apply to you from Card 1.03a. [record all mentioned]

1 New Zealand European
2 Māori
3 Samoan
4 Cook Island Māori
5 Tongan
6 Niuean
7 Chinese
8 Indian
9 Other, such as Dutch, Japanese, Tokelauan
98 Don’t know

GO TO THE QUESTIONNAIRE FOR MAORI PARTICIPANTS

GO TO 1.03b
1.03b What other ethnicity or ethnicities do you belong to? [Record]

Education

[Showcard 1.10]

1.10 What is your highest qualification? Please do not count incomplete qualifications or qualifications that take less than 3 months of full-time study to get. Please tell us your highest qualification, shown on Card 1.10. [Record one]

1 No qualification
2 Secondary school qualifications
3 Post secondary certificate, diploma, or trade diploma
4 University degree
5 Other [specify] __________________________________________
98 Don’t know
99 Refused

2. CHRONIC CONDITIONS

[Showcard 2.02 part 1 and part 2]

2.02 Have you ever been told by a doctor that you have or have had [Circle all mentioned]

1 Heart disease including:
   (a) Heart attack
   (b) Angina
   (c) Heart failure
   (d) Inadequate pumping of the heart
   (e) Build-up of fluid in the legs or lungs
   (f) Problems with heart rhythm (atrial fibrillation, supraventricular tachycardia (SVT), ventricular tachycardia (VT), ectopic beat)
   (g) Problems with heart valves (leaky or blocked)
   (h) Intermittent claudication (vascular spasm in the legs)
   (i) Clot in the leg (venous thrombosis)
   (j) Other e.g. Left Ventricular Hypertrophy (LVH), thickening of the heart muscle

Specify: __________________________________________________________

2 Stroke

GO TO 2.10a Page 13

3 Diabetes

GO TO 2.11a Page 14

4 Allergies

GO TO 2.12a Page 14

5 Asthma

GO TO 2.13a Page 15

6 Chronic bronchitis or emphysema (COPD)

GO TO 2.14a Page 16
7 Arthritis (including gout, lupus and psoriatic arthritis)

8 High blood pressure

9 High cholesterol

10 Cancer

If none of the above GO TO 2.19a Page 21

Remember to complete the “ACCESS TO SERVICES” questionnaire for participants who have diagnosed heart disease, diabetes, COPD, high blood pressure or high cholesterol and they have seen their GP about this condition in the last 12 months. If a participant has more than one of these conditions, ask them which has been most significant in the last 12 months and use this condition to answer the access to services questionnaire. You only need to complete one per participant.

Heart disease

The first few questions are about heart disease. Please do not include high blood pressure or high blood cholesterol here, as I will ask you about those later.

2.03a Have you ever been told by a doctor that you have had a heart attack? [Circle one]

1 Yes
0 No
98 Don’t know
99 Refused

GO TO 2.04a

2.03b Have you ever been admitted to hospital with a heart attack? [Circle one]

1 Yes
0 No
98 Don’t know
99 Refused

GO TO 2.04a

2.03c How old were you when you were first admitted to hospital with a heart attack? [Record age]

98 Don’t know
99 Refused

2.03d In the past 12 months, have you been admitted to hospital with a heart attack? [Circle one]

1 Yes
0 No
98 Don’t know
99 Refused
2.04a Have you ever been told by a doctor that you have angina? (interviewer probe – angina is typically chest pain when you walk or do exercise) [Circle one]

1 Yes
0 No
98 Don’t know
99 Refused

GO TO 2.05a

2.04b How old were you when you were told by a doctor that you had angina? [Record age]

98 Don’t know
99 Refused

2.05a Have you ever been told by a doctor that you have heart failure? That is inadequate heart pumping, or a build-up of fluid in the lungs or legs. [Circle one]

1 Yes
0 No
98 Don’t know
99 Refused

GO TO 2.06

2.05b How old were you when you were told by a doctor that you had heart failure? [Record age]

If from birth record 0

98 Don’t know
99 Refused

2.06 Have you ever been told by a doctor that you have any other heart disease? Please include problems with heart rhythm (atrial fibrillation, supraventricular tachycardia (SVT), ventricular tachycardia (VT), ectopic beat), heart valves (eg leaky or blocked valve), intermittent claudication (cramping and/or pain in the legs, usually when walking. Sometimes called vascular spasm in the legs), clot in the leg (venous thrombosis) and LVH or thickening of the heart muscle but not high blood pressure or high cholesterol. [Circle one]

If the respondent has a leaking or blocked heart valve please ask “which valve” and record below.

1 Yes [specify]
0 No
98 Don’t know
99 Refused

2.07 Have you been to a GP about your heart disease in the past 12 months?

1 Yes
0 No
98 Don’t know
99 Refused

GO TO THE QUESTIONNAIRE ABOUT ACCESS TO SERVICES

[Showcard 2.08]

2.08 Looking at Card 2.08, what treatments do you now have for your heart condition(s)? [Circle yes or no and, if yes, circle all mentioned]

Probe “Any others?” until no other treatment mentioned

1 Yes
0 No
1 Medicines, tablets or pills (including spray under the tongue or patches on the skin)
2 Diet
3 Exercise
4 Other [specify]

2.09a Have you ever had bypass surgery or angioplasty (sometimes called a stent) for your heart condition(s)? [Circle one]

1 Yes
0 No
98 Don’t know
99 Refused

GO TO 2.10a

2.09b How old were you when you had bypass surgery or angioplasty? [Record age]

_____________________________
98 Don’t know
99 Refused

Stroke

2.10a Have you ever been told by a doctor that you have had a stroke? Please do not include “mini-stroke” or transient ischaemic attack. [Circle one]

A stroke is a definite event that has left permanent neurological damage (eg lost vision or feeling etc.)

1 Yes
0 No
98 Don’t know
99 Refused

GO TO 2.11a

2.10b How old were you when you were first told by a doctor that you had had a stroke? [Record age or circle appropriate answer]

_____________________________
98 Don’t know
99 Refused

2.10c Have you had a stroke during the past 12 months? [Circle one]

1 Yes
0 No
98 Don’t know
99 Refused

[Showcard 2.10d]

2.10d What treatments do you now have for your stroke? [Circle yes or no and, if yes, circle all mentioned]

Probe “Any others?” until no other treatment mentioned

1 Yes
0 No
98 Don’t know
99 Refused

1 Medicines, tablets or pills
2. Diet
3. Exercise or rehabilitation (include speech therapy, occupational therapy, physiotherapy)
4. Other [specify]____________________________

Diabetes

2.11a Have you ever been told by a doctor that you have diabetes? <IF RESPONDENT IS FEMALE, ADD…> Please do not include diabetes during pregnancy. [Circle one]

1. Yes
0. No
98. Don’t know
99. Refused

GO TO 2.12a

Tobacco

Now, some questions on smoking tobacco.

4.06a Have you ever smoked a total of more than 100 cigarettes in your whole life? [Circle one]

1. Yes
0. No
98. Don’t know
99. Refused

GO TO 4.07

4.06b How old were you when you started smoking regularly? [Record in years]

98. Don’t know
99. Refused

4.06c How often do you now smoke? [Circle one only]

Read answer options. If more than one frequency given, code the highest one.

1. You don’t smoke now
2. Less often than once a month
3. At least once a month
4. At least once a week
5. At least once a day
98. Don’t know
99. Refused

GO TO 4.06e

4.06d How old were you when you stopped smoking regularly (daily)? [Record in years]

98. Don’t know
99. Refused

4.06e From when you started smoking regularly to now/when you stopped, did you ever give up smoking for 6 months or more?

1. Yes, once
2. Yes, twice
3. Yes, three times or more
4. No
98. Don’t know
99. Refused

GO TO 4.06g
4.06f In total, taking into consideration all the times you stopped, how long did you give up smoking for? [Record in years]
Round up (or down) to the nearest year.

98 Don’t know
99 Refused

[Showcard 4.06g]
4.06g Which of these products do you/have you smoke/d the most? [Circle one]
1 Tailor-made cigarettes (that is, manufactured cigarettes in a packet)
2 Roll your owns using loose tobacco
3 Both tailor-mades and roll your owns
4 Pipes
5 Cigars
98 Don’t know/unsure
99 Refused

4.06h On average, over all your years of smoking, how many cigarettes do/did you smoke a day? [Circle one]
If respondent is unable to suggest an average, ask for the typical number of cigarettes smoked in a week and divide by 7.

1 Less than 1 per day
2 1-5 per day
3 6-10 per day
4 11-15 per day
5 16-20 per day
6 21-25 per day
7 26-30 per day
8 31 or more a day
98 Don’t know/unsure
99 Refused

[Showcard 4.06i]
4.06i Are you seriously considering quitting within the next 6 months? Please answer from Card 4.06i.
[Circle one only] IF not applicable circle here: N/A

1 No, I have no intention of quitting
2 Yes, I am thinking of quitting
3 Yes, I am thinking of quitting within the next 30 days
4 Yes, I have managed to stop smoking for at least a day now
98 Don’t know/unsure
99 Refused

Alcohol
I will now ask you some questions about your use of alcoholic drinks. Many New Zealanders enjoy alcohol. However, sometimes it can affect our health.

4.07a Have you had a drink containing alcohol in the last year? [Circle one]

1 Yes
2 No
98 Don’t know

GO TO MODULE 3
4.07b How often do you have a drink containing alcohol? [Circle one]

- Don’t prompt answer. Wait and code
- 1 Monthly or less
- 2 Up to 4 times a month
- 3 Up to 3 times a week
- 4 4 or more times a week
- 98 Don’t know
- 99 Refused

4.07c How many drinks containing alcohol do you have on a typical day when you are drinking? [Circle one]

- Take average and round to nearest whole number if necessary e.g. if respondent says 4 or 5, average is 4.5, round to nearest whole number = 5, that is code 3
- 0 1 or 2
- 1 2 3 or 4
- 2 3 5 or 6
- 3 4 7 to 9
- 4 5 10 or more
- 98 Don’t know
- 99 Refused

[Showcard 4.07d]

4.07d Looking at Card 4.07d, how often do you have six or more drinks on one occasion? [Circle one]

- 0 Never
- 1 2 Less than monthly
- 2 3 Monthly
- 3 4 Weekly
- 4 5 Daily or almost daily
- 98 Don’t know
- 99 Refused

[Showcard 4.07d]

4.07e How often during the last year have you found that you were not able to stop drinking once you had started? [Circle one]

- 0 Never
- 1 2 Less than monthly
- 2 3 Monthly
- 3 4 Weekly
- 4 5 Daily or almost daily
- 98 Don’t know
- 99 Refused

[Showcard 4.07d]

4.07f How often during the last year have you failed to do what was normally expected from you because of drinking? [Circle one]

- 0 Never
- 1 2 Less than monthly
- 2 3 Monthly
- 3 4 Weekly
- 4 5 Daily or almost daily
- 98 Don’t know
- 99 Refused

[Showcard 4.07d]
4.07g How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session? [Circle one]

0 1 Never
1 2 Less than monthly
2 3 Monthly
3 4 Weekly
4 5 Daily or almost daily
98 Don’t know
99 Refused

[Showcard 4.07d]
4.07h How often during the last year have you had a feeling of guilt or remorse after drinking? [Circle one]

0 1 Never
1 2 Less than monthly
2 3 Monthly
3 4 Weekly
4 5 Daily or almost daily
98 Don’t know
99 Refused

[Showcard 4.07d]
4.07i How often during the last year have you been unable to remember what happened the night before because you had been drinking? [Circle one]

0 1 Never
1 2 Less than monthly
2 3 Monthly
3 4 Weekly
4 5 Daily or almost daily
98 Don’t know
99 Refused

[Showcard 4.07j]
4.07j Now please look at card 4.07j, have you or someone else been injured as a result of your drinking? [Circle one]

2 1 Yes, but not in the last year
4 2 Yes, during the last year
0 3 No
98 Don’t know
99 Refused

[Showcard 4.07j]
4.07k Again referring to card 4.07j, has a relative or friend, or a doctor or other health worker, been concerned about your drinking or suggested you cut down? [Circle one]

2 1 Yes, but not in the last year
4 2 Yes, during the last year
0 3 No
98 Don’t know
99 Refused

Total Audit Score:_______
### Module 3 Questionnaire

**Attitudes and Beliefs**

**Q1** Now we are going to talk about your immediate biological family.

a) Are you adopted? [circle] YES / NO

b) Please tell me about all your immediate biological family?

<table>
<thead>
<tr>
<th>Relationship to respondent</th>
<th>Sex (F/M)</th>
<th>Age</th>
<th>Age at Death</th>
<th>Cause of Death</th>
<th>Lifetime Health [showcard 2.01a]</th>
<th>How much has R’s life been affected by health problems of the relative in the last 12 months? [showcard 2.01b]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1) Cancer (state)</td>
<td>A lot</td>
<td>A lot  OR N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2) Heart disease</td>
<td>Some</td>
<td>Some  OR N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3) Stroke</td>
<td>A Little</td>
<td>A Little  OR N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4) Transport accident</td>
<td>Not at all</td>
<td>Not at all  OR N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5) Suicide</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6) Accident/assault</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7) Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
8.10 Appendix J: Case Report Form Module Four of CHALICE

Module 4

Case Report Form

<table>
<thead>
<tr>
<th>Participant’s Name</th>
<th>Participant Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of Assessment</th>
<th>NHI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time of ECHO</th>
<th>DOB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dept of Medicine ECG and ECHO centre: 88127

Chalice Interviewer name and extension number: ________________________________

Participant:

Height: ________________ cm    Weight: ________________ kg

Blood Pressure and Pulse:

Completed by [print name]: ________________________________________________

Time blood pressure taken (24 hr clock): _____ : _____

Heart rate: ________________ / min  Sphygmomanometer: Manual / Automatic

Blood pressure: ________/________        Arm:  L / R

ECG    Completed by [print name]: ________________________________________________

Completed  Yes / No (specify reason). Please attach the ECG graph to this CRF and give the CRF to the CHALICE interviewer when they collect the participant.
Echo  Completed by [print name]: ..............................................................

Completed  Yes / No (specify reason)

Comments

-----------------------------------------------------------------------------------
Module 5 Interview

A. MAJOR DEPRESSIVE EPISODE (CURRENT)

(MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE NO IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

<table>
<thead>
<tr>
<th>Question</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.1 Have you been consistently depressed or down, most of the day, nearly every day, for the past two weeks?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>A.2 In the past two weeks, have you been less interested in most things or less able to enjoy the things you used to enjoy most of the time?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>IS A1 OR A2 CODED YES?</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

A.3 Over the past two weeks, when you felt depressed or uninterested:

a) Was your appetite decreased or increased nearly every day? Did your weight decrease or increase without trying intentionally (i.e., by ±5% of body weight or ±8 lbs. or ±3.5 kgs., for a 160lb./70kg Person in a month)? IF YES TO EITHER, CODE YES

0 1
b) Did you have trouble sleeping nearly every night (difficulty falling asleep, waking up in the middle of the night, early morning wakening or sleeping excessively)?  

0  1

c) Did you talk or move more slowly than normal or were your fidgety, restless or having trouble sitting still almost every day?  

0  1

d) Did you feel tired or without energy almost every day?  

0  1

e) Did you feel worthless or guilty almost every day?  

0  1

f) Did you have difficulty concentrating or making decisions almost every day?  

0  1

g) Did you repeatedly consider hurting yourself, feel suicidal, or wish that you were dead?  

0  1

ARE 3 OR MORE A3 ANSWERS CODED 1? (OR 4 A3 ANSWERS IF A1 OR A2 ARE CODED 0)?

0  1

MAJOR DEPRESSIVE EPISODE CURRENT

IF PATIENT HAS CURRENT MAJOR DEPRESSIVE EPISODE THEN LIFETIME MAJOR DEPRESSIVE EPISODE (ON PAGE 6) MUST BE CODED 1.

CHECK FOR THE WORST EPISODE ON PAGE 6 (LIFETIME MAJOR DEPRESSION) AND CODE ACCORDINGLY.
8.12 Appendix L: MoCA Test, Recording Sheet, Interviewers script and marking sheet from Module Six of CHALICE Questionnaire

<table>
<thead>
<tr>
<th>Date of Assessment</th>
<th>Participant Study Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interviewer’s Name</td>
<td>Interviewer’s Number</td>
</tr>
</tbody>
</table>
☐ Tick this box if you think that the participant’s responses to the MOCA may have been impaired for reasons other than natural decline. **State the reason:** ___________________________
Module 6

Montreal Cognitive Assessment (MoCA) Recording Sheet

<table>
<thead>
<tr>
<th>Date of Assessment</th>
<th>Participant Study Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interviewer’s Name</td>
<td>Interviewer’s Number</td>
</tr>
</tbody>
</table>

Diagram:
- Node 1: Begin
- Node 2: 
- Node 3: 
- Node 4: 
- Node 5: End
- Links: 1 -> 2, 2 -> 3, 3 -> 4, 4 -> 5, 5 -> End

Diagrams for higher levels of MoCA.
Draw CLOCK (Ten past eleven)
**Introduction**

The non-word consonant-vowel-consonant (CVC) test is a verbal test of learning and memory. Non-word repetition involves the ability to perceive, store, recall and reproduce phonological sequences. The items of the Montreal Cognitive Assessment (MoCA) examine attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation.

The Edinburgh Handedness Inventory is a measurement scale used to assess the dominance of a person's right or left hand in everyday activities.

**Responsibility**

- It is the responsibility of all study interviewers to follow the standard operating procedures as outlined in this document.
It is also expected that all study interviewers review the document at regular intervals to ensure they are up to date with current practices.

**Equipment required**

- The Edinburgh Handedness Inventory and language questionnaire

**For the C-V-C Task**

- PC with “E-Run” installed
- Clipboard
- Speakers (volume should be half way approx.)
- Chalice CVC recording sheet – recall (sheet 1)
- Chalice CVC recording sheet (sheet 2)
- Chalice CVC scoring sheet (sheet 3)

**For the Montreal Cognitive Assessment (MoCA)**

- Stopwatch
- Pencil
- Montreal Cognitive Assessment (MoCA) test, recording and scoring sheets

**Procedure**

The interviewer should set-up the computer before the tasks are done. The interviewer will have 30 minutes to perform the testing in the following order, there are 5 parts:

1. In E-Run run the C-V-C list of nonsense words 5 times and record the recall of words from the SP each time the list is played.
2. Complete the Montreal Cognitive Assessment (MoCA).
3. Complete the Edinburgh Handedness Inventory and language questions.
4. Ask the SP to recall as many of the C-V-C list of nonsense words as they can.
5. Complete the C-V-C recognition task in E-Run.
6. Score the MoCA and C-V-C task following the instructions provided.

**2. Specific Instructions for the MoCa Assessment**

1. **Visuospatial/Executive:**
   1a) **Alternating Trail Making (timed task)** Show the trails on sheet and say:
   "Please draw a line, going from a number, to a letter, in ascending order. Begin
here (point to 1) and draw a line from the number 1 then to the letter A then to number 2 and so on. End here (point to E). Remember to start at 1.”

The participant must start at 1 and end at E. Use the stopwatch to time the participant and write the timing on the score sheet below the letter C.

1b) Visuoconstructional Skills: Point to the cube on the sheet and say:

"Copy this drawing, as accurately as you can, in the space below".
The participant is allowed one attempt at the cube. This task is NOT timed.

1c) Visuoconstructional Skills - Clock: Point to the sheet and say:

"Now draw a clock on this page. Put in ALL the numbers AND set the time to 10 past 11" (point to that on the page).

2. Naming:

Beginning on the left, point to each figure and say:

"Tell me the name of this animal...and this.....and this."

3. Memory: (Delayed recall is number 7. towards the end of these instructions)

The examiner reads a list of 5 words at a rate of one per 1 per second (subvocalise “1000 and one” to yourself between words; will then be about 1 second), giving the following instructions:

"This is a short memory test. I am going to read a list of words that you will have to remember now and later on. Listen carefully. When I am through, tell me as many words as you can remember. It doesn't matter in what order you say them".

Checkmark the space allocated for each word the client produces on the first trial on the test sheet. When the client indicates that he/she has finished (has recalled all the words), or can recall no more words (“anything else?”), read the list a second time with the following instructions:

"I am going to read the same list for a second time. Try to remember and tell me as many words as you can, including words you said the first time".

Put a checkmark in the allocated space for each word on the test sheet the client recalls after the second trial. At the end of the second trial, inform the client that she/he will be asked to recall these words again by saying:

"I will ask you to recall those words again at the end of THIS test".

Note the current time on the score sheet.

4. Attention
4a i) **Forward Digit Span**: Give the following instruction:

"I am going to say some numbers and, when I am through, repeat them to me exactly as I said them. Just say what I say".

Read the five number sequence at a rate of one digit per second.

4a ii) **Backward Digit Span**: Give the following instruction:

"Now I am going to say some more numbers, BUT when I am through you must repeat them to me in the backwards order".

Read the three number sequence at a rate of one digit per second.

4b) **Vigilance**: Give the following instruction (twice if necessary):

"Now I am going to read a sequence of letters. Every time I say the letter A, you tap with your hand once (show). If I say a different letter, do not tap your hand".

4c) **Serial 7s**: Give the following instruction:

"Now I will ask you to count by subtracting seven from 100, and then, keep subtracting seven from your answer until I tell you to stop".

**Note:** Has 5-8mins passed for the delayed recall of the word list?

5. **Language**

5a) **Sentence Repetition**: Give the following instructions:

"I am going to read you a sentence. Repeat it after me, EXACTLY as I say it [pause]. The sentence is: I only know that John is the one to help today."

Following the response say:

"Now I am going to read you another sentence. Repeat it after me, exactly as I say it [pause]: The cat always hid under the couch when dogs were in the room".

**Note:** Has 5-8mins passed for the delayed recall of the word list?

5b. **Verbal Fluency**: Set timer to 60sec. Say:

"Tell me as many different words as you can think of that begin with a certain letter of the alphabet that I will tell you in a moment. You can say any kind of word you want, but you should NOT say proper nouns (like Bob or Boston), and not numbers, and not words that begin with the same sound but have a different ending. For example, if you said love, you should NOT also say lover, or loving. I will tell you to stop after one
minute. Are you ready? [pause]. Now, tell me as many words as you can beginning with the letter F. Ready? Begin."

Record the the answers in the margin of the score sheet. [set timer to 60 seconds]. "Stop".

Note: Has 5-8mins passed for the delayed recall of the word list?

6. Abstraction

Ask the client to explain what each pair of words has in common, starting with the example: "Tell me how an orange and a banana are alike".
If the answers are in a concrete manner, then say only one additional time: "Tell me another way in which those items are alike".
If the participant still doesn't give the appropriate response (fruit), say: "Yes, and they are also both fruit".
Do not give any additional instructions or clarification. After the practice trial, say: "Now tell me how a train and a bicycle are alike".
Following the response, say: "Now, tell me how a ruler and a watch are alike".
Do not give any additional instructions or prompts. Record and score the first answer.

7. Delayed Recall (Has 5-8mins passed for the delayed recall of the word list?)

Give the following instruction:

"I read some words to you earlier, which I asked you to remember. Tell me as many of those words as you can remember."
Make a checkmark on the test sheet for each of the words correctly recalled spontaneously without any cues.

8. Orientation Give the following instruction:

“Tell me today’s day and date and tell me where we are”

6. Scoring

MoCA

Follow the instructions described in the MoCA scoring instructions sheet. Do not add one point for a client who has had 12 years or fewer of formal education. The MoCA has a possible maximum of 30 points. A final total score of 26 and above is considered normal. A final total score below 26 is indicative of mild cognitive impairment.
**MoCA – Materials, prompts, discontinue and scoring.**

**Scoring:**
Below is a breakdown of how each item of the MoCA is to be scored:

<table>
<thead>
<tr>
<th>Item</th>
<th>How to score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a) Alternate Trail Making (1 point)</td>
<td>Give 1 point if the following pattern is drawn without drawing any lines that cross: 1-A-2-B-3-C-4-D-5-E. Any error that is not immediately self-corrected earns a score of 0.</td>
</tr>
<tr>
<td>1b) Visuoconstructional skills Cube (1 point)</td>
<td>Give 1 point for a correctly executed drawing. Drawing must be 3D; all lines drawn; no lines added; lines are relatively parallel and lengths are similar (rectangular prisms are accepted). A point is not assigned if any of the above criteria are not met.</td>
</tr>
<tr>
<td>1c) Visuoconstructional skills Clock (3 points)</td>
<td>Contour (1 point): The clock face must be a circle with only minor distortion acceptable (e.g. slight imperfection in closing the circle). Numbers (1 point): All clock numbers must be present with no additional numbers; numbers must be in correct order and placed in approximate quadrants on the clock face; roman numerals are accepted; numbers can be places outside the circle contour. Hands (1 point): There must be 2 hands jointly indicating the correct time; the hour hand must be clearly shorter than the minute hand; hands must be centered within the clock face with their junction close to the clock centre. A point is not assigned for a given element if any of the above criteria are not met.</td>
</tr>
<tr>
<td>2. Naming (3 points)</td>
<td>One point each is given for the following responses: (1) camel/dromedary, (2) lion, (3) rhinoceros/rhino.</td>
</tr>
<tr>
<td>3. Memory (0 points)</td>
<td>No points are given for Trials 1 and 2.</td>
</tr>
<tr>
<td>4. Attention (6 points)</td>
<td>4a &amp; b) Digit span (2 points): Give 1 point for each sequence correctly repeated (the correct response for the backwards trial is 2-4-7). 4b) Vigilance (1 point): Give 1 point if there are 0-1 errors (an error includes a tap on a wrong letter, or a failure to tap on letter A). 4c) Serial 7s (3 points): This item is scored out of 3 points. Give 0 points for no correct subtractions; 1 point for 1 correct subtraction; 2 points for 2-3 correct subtractions; and 3 points if the client successfully makes 4-5 correct subtractions. Count each correct subtraction of 7 beginning at 100. Each subtraction is evaluated independently; that is, if the client responds with an incorrect number but continues to correctly subtract 7 from it, give a point for each correct subtraction. For example, a client may respond &quot;92-85-78-71-64&quot; where the &quot;92&quot; is incorrect, but all subsequent numbers are subtracted correctly. This is 1 error and the item would be given a score of 3.</td>
</tr>
<tr>
<td>5a) Sentence Repetition (2 points)</td>
<td>Give 1 point for each sentence correctly repeated. Repetition must be exact. Be alert for errors that are omissions (e.g., omitting &quot;only&quot;, &quot;always&quot;) and substitutions/additions.</td>
</tr>
<tr>
<td>5b) Verbal fluency (1 point)</td>
<td>Give 1 point if the 11 words or more are generated in 60 seconds. Record responses in the margins.</td>
</tr>
<tr>
<td>6. Abstraction (2 points)</td>
<td>Only the last 2 item pairs are scored. Give 1 point to each item pair correctly answered. The following responses are acceptable: Train-bicycle = means of transportation, means of traveling, you take trips in both Ruler-watch = measuring instruments, used to measure The following responses are not acceptable: Train-bicycle = they have wheels; Ruler-watch = they have numbers.</td>
</tr>
<tr>
<td>7. Delayed recall (5)</td>
<td>Give 1 point for each word recalled freely without any cues.</td>
</tr>
</tbody>
</table>
8. Orientation (6 points)

Give 1 point for each item correctly answered. The client must tell the exact date and place (name of hospital, clinic, office). No points are awarded if client makes an error of 1 day for the day and date.

<table>
<thead>
<tr>
<th>MoCA – Montreal Cog Assessment Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>score /30:______</td>
</tr>
</tbody>
</table>

Sum all subscores. Add one point for a client who has had 12 years or fewer of formal education, for a possible maximum of 30 points. A final total score of 26 and above is considered normal. A final total score below 26 is indicative of mild cognitive impairment.

**JDA modification (July07):** Note - From Nasreddine (2004) and web-site.

8.13 Appendix M: Food and Beverage Diary from Module Seven of CHALICE
CHALICE

Food and beverage diary

If you have any questions about this diary please contact the CHALICE team.
Part 2: How you eat and what you eat

1. How often do you usually have breakfast (more than a glass of milk or fruit juice)? (Please mark one box).
   - a. I never have breakfast
   - b. 1 to 3 days a week
   - c. 4 to 6 days a week
   - d. Every day

2. How often do you usually have lunch (more than a drink or snack)? (Please mark one box).
   - a. I never have lunch
   - b. 1 to 3 days a week
   - c. 4 to 6 days a week
   - d. Every day

3. For your main meal in the evening how often do you usually eat (Please mark one box on each line).
   - a. At a restaurant/cafeteria
   - b. Takeaway food
   - c. Ready meals from a deli or supermarket (fresh or frozen)
   - d. Food that is prepared and cooked at home

4. When you drink between meals what do you usually drink? (Please mark all boxes that apply).
   - a. Sweetened drinks (e.g. cola, fruit juice, fruit drinks, cordials)
   - b. Sugar free drinks (e.g. diet cola, sugar free cordials and fruit drinks)
   - c. Milky drinks (e.g. milk shake, hot chocolate, milo, ovaltine, flavoured milk)
   - d. Water (tap, bottled, still or sparkling)
   - e. Tea or coffee
5. What type of milk do you usually have either as a drink or on cereal? (mark the one you have most often)
   a. I do not drink/use milk
   b. Full cream or farmhouse
   c. Standard or homogenised
   d. Semi-trim (light blue top)
   c. Trim (green top)
   f. Soya milk
   g. Light soya milk

Other milk (please specify e.g. Rice milk, Almune, Calcitrim, Junior)

6. What type of bread do you usually eat? (Please mark all boxes that apply).
   a. I do not eat bread
   b. High fibre white bread
   c. White bread
   d. Brown/wholegrain

Other, please describe (e.g. rye, soda, gluten free) and give brand name (e.g. Vogel, Nature's Fresh Quality Bakers, Country Split, Freyas, Molenburg)

7. What brand of fat spread, butter or margarine do you use the most of? (Describe the type you use most often, name the brand and whether it is low fat or not. e.g. Flora canola, Mainland butter, Oliveni)

8. Do you ever take any vitamin, mineral or food supplements?
   Yes
   No
Part 3: Food Diary

How to fill in your diary
Below is a step-by-step guide on how to fill in your food diary. It is very important that you do not change what you normally eat or drink just because you are keeping a diary so that we get a true picture of what you eat and drink. Try to fill in the diary each time you have something to eat or drink rather than leaving it until the end of the day so that you don’t forget anything.

Step 1: When
Write down the exact time you ate or drank something. So, for example, if you had breakfast at 7.30am, write in “7.30am”.

Step 2: Where
Please record where you were when you ate something. The next column along in the food diary is for you to write in where you were when you ate or drank something. This could be:

At home – e.g. in the kitchen, in bed
Away – e.g. in the street, in the car/on a bus, at a friend’s or relative’s house,
In a café/ restaurant (please specify McDonald’s, Pizza Hut, etc.),
At work – e.g. in canteen, in lunchroom, at your desk.

Step 3: Who with
In the next column in the food diary, please write down who you were with when you ate or drank something. For example, you might have been alone, with family or with friends. Experts have shown that by thinking who you were with during the day can help you to remember what you have eaten. We do not use this data in our research, it is just there to aid your memory.
**Step 4: Food and drink**
The next step in the food diary is to describe what you ate or drank. The more details you are able to give about the food and drink you have consumed, the better we will be able to estimate your nutrient intake. Include any extras like sugar and milk in your tea or cereal, butter or other spreads on your bread and sauces such as tomato sauce and mayonnaise. Do not forget to include drinking water.

**Step 5: Brand and details**
It would also help us if you can write down the brand name of any foods or drinks if you know it (e.g. Watties, Pams, Arnotts). If convenient, staple the wrapper to the back page of this book.
For breakfast cereals, as well as the brand name, please write down the name of the cereal (e.g. Coco Pops, Cornflakes, Sanitarium toasted museli: golden oats and fruit).
For sandwiches, please describe the type of bread used, how many slices of bread were used and give details of the filling.
For salad or mixed vegetables, please describe what is in it (e.g. 1 lettuce leaf, half a tomato 6 slices of cucumber).
For pizza, please describe the topping (e.g. cheese and tomato, ham and pineapple).

**Step 6: Preparation and cooking**
If you know the cooking method used (e.g. roast, baked, boiled, fried) please write it down in this section.

**Step 7: Quantity**
In the next column, please write in the size of the portion of food or drink you had. For drinks, you can specify glass, cup, or mug or bottle/can size. Other descriptions include: packet (e.g. for crisps), number (e.g. for biscuits), slice (e.g. for cake, pizza), teaspoon (e.g. for sugar), tablespoon (e.g. for tomato sauce, peas), cupful (e.g. for cooked pasta or rice), handful (e.g. for nuts, grapes, berries), package weights (e.g. 150g Fresh and Fruity yoghurt). On the next page you will find some more information on how to describe the food and drink that you consume.

If you have **kitchen scales** it is helpful to weigh foods and record these amounts.
For **mixed food dishes and recipes** it may be easier to list the total ingredients, then describe the proportion of this recipe that you consumed.

* e.g. 1/3 of recipe 1

**Recipe example**  Creamy tuna pasta (recipe 1)

- 250g Diamond spiral pasta
- 1/2 cup Oxo chicken stock, pre-mixed with water
- 1/4 cup Chopped parsley
- 2 cups Sliced button mushrooms
- 220g John West tuna canned in oil, liquid drained
- 1 cup Carnation evaporated skim milk
- 1 tablespoon Parmesan cheese, dried
- 1/4 teaspoon Freshly ground black pepper

I had one third of this recipe

If you make your food from separate ingredients then you can write the recipes down in the recipe list at the back of this diary.

Please write down all the ingredients for each recipe (including brand names, amounts and preparation or cooking details). Indicate the proportion of the recipe you consumed.

Don’t forget about any drinks that you have between meals e.g. tea, coffee, wine, beer, orange juice.
# How to describe your food and drink using household measures

Below are some suggestions on how to describe certain food and drink items together with their household measures.

<table>
<thead>
<tr>
<th>Food</th>
<th>Description of food or drink and brand</th>
<th>Household measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacon</td>
<td>Shoulder or streaky; fried or grilled rashers, smoked or unsmoked</td>
<td>Number</td>
</tr>
<tr>
<td>Bread</td>
<td>Type of bread, eg. white, brown, wholemeal, granary, French stick, ciabatta, currant. Description of slice e.g. sandwich, toast</td>
<td>Number of slices</td>
</tr>
<tr>
<td>Canned drinks</td>
<td>Type, brand name For example: 335ml can Diet Coca Cola</td>
<td>Number or full or half can</td>
</tr>
<tr>
<td>Crisps</td>
<td>Type, brand name e.g. 30g Rashuns</td>
<td>Packet weight</td>
</tr>
<tr>
<td>Fruit</td>
<td>Type and size of fruit e.g. large Granny Smith apple For tinned fruit; slices/ halves etc. in juice or syrup</td>
<td>Number of pieces or tablespoons</td>
</tr>
<tr>
<td>Jams</td>
<td>Type, brand name e.g. Pam’s strawberry jam</td>
<td>Teaspoons, heaped or flat</td>
</tr>
<tr>
<td>Milk</td>
<td>Type; full cream, trim, semi-trim</td>
<td>Pints, glasses or cups</td>
</tr>
<tr>
<td>Oil</td>
<td>Type e.g. canola oil, sunflower oil, corn oil, olive oil Brand name e.g. Pam’s olive oil</td>
<td>Tablespoons</td>
</tr>
<tr>
<td>Prepacked foods e.g. beefburgers, pies, biscuits, confectionery</td>
<td>Full name of product including brand name. For example: Bird’s Eye fish fingers. Keep the package.</td>
<td>Number</td>
</tr>
<tr>
<td>Sandwiches</td>
<td>Describe fully if homemade or if bought; Full name, place of purchase and price, describe bread as above and note loaf size.</td>
<td>Number of slices of bread or number of rolls</td>
</tr>
<tr>
<td>Spreads on bread or toast</td>
<td>Type e.g. butter, low fat spread, rice bran oil spread, canola spread, reduced fat canola spread, Weightwatchers spread. Full description, and brand name Keep the package</td>
<td>Number of teaspoons or thinly, average or thickly spread</td>
</tr>
<tr>
<td>Sugar</td>
<td>Type e.g. caster, rich brown, white</td>
<td>Teaspoons, heaped or flat</td>
</tr>
<tr>
<td>Sweets, chocolate and snack bars</td>
<td>Name, size (weight) and price (if known) For example: king size Mars bar 99c Keep the wrapper</td>
<td>Weight of bar or number of sweets</td>
</tr>
<tr>
<td>Takeaways</td>
<td>Describe in full, give name of restaurant For example: One scoop chips, The High Street chip shop. Standard chicken chow mein, Kwang Chow</td>
<td>Portion size and price</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Type; fresh, frozen, tinned or dried Brand name</td>
<td>Tablespoons, full or heaped</td>
</tr>
</tbody>
</table>
Sample record sheet

Please record all food and drink consumed during the whole day, including snacks and water.

Remember to report any additions to each food and drink, such as milk, sugar, salt, sauce or spreads.

<table>
<thead>
<tr>
<th>When</th>
<th>Where</th>
<th>Who with</th>
<th>Food or Drink</th>
<th>Brand and details</th>
<th>Preparation/ Cooking</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 am</td>
<td>In bed</td>
<td>alone</td>
<td>Gourmet muffin</td>
<td>New World – double chocolate</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Coffee</td>
<td>Nescafe instant</td>
<td>Hot water added</td>
<td>1 heaped teaspoon in a mug</td>
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<td></td>
<td></td>
<td></td>
<td>Sugar</td>
<td></td>
<td></td>
<td>1 heaped teaspoon</td>
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<td></td>
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<td></td>
<td>Green top milk</td>
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<td></td>
<td>1/8th of a mug</td>
</tr>
<tr>
<td>10 am</td>
<td>Kitchen</td>
<td>Family</td>
<td>Tea</td>
<td>Twinings Peppermint</td>
<td>Hot water added</td>
<td>1 mug, no milk or sugar</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Biscuits</td>
<td>Tim Tam Double Chocolate</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>12 pm</td>
<td></td>
<td></td>
<td>Creamy tuna pasta</td>
<td>Homemade recipe 1</td>
<td>Pasta boiled in water</td>
<td>1/3 recipe</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>French bread stick</td>
<td>Bought–New World</td>
<td></td>
<td>6cm long</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Margarine</td>
<td>Pams–Canola low salt</td>
<td></td>
<td>1 level tsp</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chicken breast</td>
<td>Skin and bone removed</td>
<td>Fried in olive oil</td>
<td>1 medium chicken breast</td>
</tr>
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<td></td>
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<td></td>
<td>Olive oil</td>
<td>Luppi</td>
<td>fried</td>
<td>½ tbsp</td>
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<td></td>
<td></td>
<td></td>
<td>Cherry tomatoes</td>
<td>raw</td>
<td></td>
<td>2</td>
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<td></td>
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<td></td>
<td>Orange juice</td>
<td>McCoy, unsweetened</td>
<td></td>
<td>200ml</td>
</tr>
<tr>
<td>5.30 pm</td>
<td>McDonalds</td>
<td>Son</td>
<td>Burger</td>
<td>McDonalds Big Mac (no pickles)</td>
<td></td>
<td>1</td>
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<td></td>
<td></td>
<td></td>
<td>Fries</td>
<td></td>
<td></td>
<td>Large</td>
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<td></td>
<td></td>
<td></td>
<td>Diet Coke</td>
<td></td>
<td></td>
<td>Large</td>
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<tr>
<td>6.30 pm</td>
<td>Home</td>
<td>Friends</td>
<td>Beer</td>
<td>MonteithsRadler</td>
<td></td>
<td>2 bottles</td>
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<td></td>
<td></td>
<td></td>
<td>Toast</td>
<td>Vogels Rice and Rye</td>
<td>Toasted</td>
<td>2 slices</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Margarine</td>
<td>Pams–Canola low salt</td>
<td></td>
<td>1 level tsp</td>
</tr>
</tbody>
</table>

Please record brand names e.g. McCoy
Please use household measures to describe amounts of food such as margarine, butter and milk e.g. teaspoons (tsp), tablespoons (tbsp), cups
Day .......... Date_____________________

<table>
<thead>
<tr>
<th>When</th>
<th>Where</th>
<th>Who with</th>
<th>Food or Drink</th>
<th>Brand and details</th>
<th>Preparation/ Cooking</th>
<th>Quantity</th>
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Day ... continued

<table>
<thead>
<tr>
<th>When</th>
<th>Where</th>
<th>Who with</th>
<th>Food or Drink</th>
<th>Brand and details</th>
<th>Preparation/ Cooking</th>
<th>Quantity</th>
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</table>
Recipes

Please write down the ingredients of your recipes in this section.

<table>
<thead>
<tr>
<th>Recipe Number</th>
<th>Food or Drink</th>
<th>Brand and Details</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
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</tbody>
</table>
Are there any special reasons why this week may differ from ‘normal’ in terms of household food (for example a child’s birthday party or other family celebration)?

Please circle either Yes or No:

No

Yes (please state reason) ________________________________________________

_____________________________________________________________________

Please check that you have answered all the questions in part 1, 2 and 3 and please make sure that you have filled in your diary for all four days.

Don’t forget to include any:

• Drinks e.g. tea, coffee, wine, beer, orange juice, soft drinks, water

• Snacks between meals e.g. biscuits, crisps, peanuts, slices, muffins

• Lollies or sweets

THANK YOU!
This diary contains three parts:

1. *Home Food Inventory*

1. *How you eat and what you eat*

2. *Food Diary*

Please make sure that you fill in all three parts and return the completed diary in the envelope provided.

Thank you!
8.14 Appendix N: Data coding methodology

This document describes the exact methodology used to code variables in this study for analysis.

CVD risk data

The following information was required to categorise a person into a CVD risk category. As previously described, data from modules one to four was required. The following information was re-coded to successfully identify CVD risk scores. Information from Appendix B was used to manually code CVD risk scores.

Calculating CVD risk scores from CVD risk charts:

The following variables were used to give the participants an initial CVD risk score according to the variables on the CVD risk charts.

Sex
Described as M=Male, F=Female and therefore did not need to be re-coded.

Age
All participants were age 50 at time of recruiting/ interviewing and therefore fitted into age group 45-54 years on the CVD risk charts.

Smoking
A non smoker is a person who has never smoked or has given up smoking and not smoked for the last twelve months. Data was given answering the following questions from module two (see appendix E):

Have you ever smoked a total of more than 100 cigarettes in your whole life?
With possible answers: 0=No, 1=Yes, 95=Missing-other, 96=Missing-not asked, 98=Don't know, 99=Refused

How often do you now smoke?
With possible answers: 1=You don’t smoke now, 2=Less often than once a month, 3=At least once a month, 4=At least once a week, 5=At least once a day, 95=Missing-other, 96=Missing-not asked, 98=Don’t know, 99=Refused

How old were you when you stopped smoking regularly (daily)?
With answer recorded in age or 95=Missing-other, 96=Missing-not asked, 98=Don’t know, 99=Refused

The answers of the questions were looked at in combination and each individual’s current smoking status was considered. Those who gave answers 2, 3, 4 or 5 to question two were counted as smokers, and those who answered age 50 or 51 to question three were counted as smokers. Those who answered 1 to question two were considered non-smokers if they answered no to question one, or answered 49 or an age less than 49 to question three.

Diabetes
Participants were asked

Have you ever been told by a doctor that you have diabetes?(excluding gestational diabetes)
With possible answers : 0=No, 1=Yes, 95=Missing-other, 96=Missing-not asked, 98=Don’t know, 99=Refused.

All those who answered yes to this question were included as having diabetes. Undiagnosed diabetics were not included in the diabetic category due to lack of available HbA1c reading.

Systolic blood pressure
Three readings of blood pressure were taken on the morning of the interview and continuous data of three systolic blood pressures was provided. A person’s systolic blood pressure was given by the average of these three readings. The blood pressure levels were categorized consistent with the categories in the New Zealand Cardiovascular Risk Charts. The categories were interpreted as : 1= ≤130mmHg, 2= ≤150mmHg, 3= ≤170mmHg, 4= >170mmHg and coded.

Total cholesterol: HDL ratio

184
One blood sample was taken to give a singular continuous cholesterol measure. A person’s total cholesterol: HDL ratio was categorized consistent with the New Zealand Cardiovascular Risk Charts. The categories were interpreted as: 0= ≤4.5, 1= ≤5.5, 2= ≤6.5, 3=≤7.5, 4= ≤8.5 and coded.

Manuel coding of CVD risk

Participants were given their initial CVD risk score based on the above six risk factors. Each case was manually calculated by inputting risk factors onto the New Zealand Cardiovascular Risk Charts to give a colour corresponding to a 5-year cardiovascular disease risk (fatal and non-fatal) which could be one of the following:

- Light blue=<2.5% risk=mild risk= code 1
- Purple= 2.5-5% risk= mild risk=code 2
- Dark blue=5-10%= mild risk=code 3
- Green=10-15%= moderate risk=code 4
- Yellow=15-20%= high risk=code 5
- Light orange=20-25%=very high risk=code 6
- Dark Orange= 25-30%= very high risk=code 7
- Red=>30%= very high risk=code 8

Additional Risk Factors

Two phases of assessing additional risk factors contributed to the final CVD risk score. These factors are outlined in Appendix B.

Participants were given an additional 5% risk if they met one of the following criteria:

Family history of premature coronary heart disease or ischaemic stroke in a first-degree relative(father or brother <55 years, mother or sister <65 years).

Participants were asked to record all of their first-degree relatives including relationship, sex, age or age of death if applicable. If relatives were adopted their data was not included.

Immediate Biological Family: Cause of death.
With possible answers: 1=Cancer, 2=Heart disease, 3=Stroke, 4=Transport accident, 5=Suicide, 6=Accident/assault, 7=Other.

When age of death was <55 for men and <65 for women, with answers 2 and/or 3, was given an increased risk.

Lifetime health: Heart attack/serious heart problems. Possible answers 0=No, 1=Yes.

Lifetime health: Stroke. Possible answers 0=No, 1=Yes.

The above questions applied to all living and passed relatives.

If a relative died within 5 years after the cut-off (<65 for men and <75 for women), and also had a lifetime history of heart attack/stroke, they were counted as having a premature history. This is because the age at which these events occurred was not asked. This is likely to overestimate but in instances where death was not CVD related, it is able to capture the risk for the participant.

If a relative is still living and have has one of these events, they must be <55 for men and <65 for women in order to increase the risk score.

Because ‘serious heart problem’ does not specify relationship to CVD those who had heart problems as children etc may also have increased the score. Again, this is because age of event as not asked.

Maori, Pacific peoples or Indo-Asian peoples (including Fijian Indian, Sri Lankan, Afghani, Bangladeshi, Nepalese, Pakistani, Tibetan).

Participants were asked to identify with one or more of the following ethnicities; NZ European, Maori, Samoan, Cook Island Maori, Tongan, Nuiean, Chinese, Indian, or to state their other ethnicities. If a person had identified being full or part or one of the high risk ethnicities they were given an increased risk.

Diabetes with microalbuminuria OR for over 10 years OR with HbA1c consistently over ≥8% (64 mmol/L).

Data for microalbumuria and HbA1c were unavailable therefore only longstanding diabetics could be identified and given an increased score. This may be an underestimate.

The initial risk does not apply to the following groups as they already have a high risk of CVD (>20%).

Those who have had a previous CVD event:
These events include: Angina, MI, percutaneous coronary intervention, coronary bypass grafting, transient ischaemic attack, ischaemic stroke, peripheral vascular disease.

Relevant questions considered in deciding past event are:

Have you ever been told by a doctor that you have or have had heart disease?

Have you ever been told by a doctor that you have had a stroke? Does not include TIA.

Have you ever been told by a doctor that you have had a heart attack?

Have you ever been told by a doctor that you have angina?

Have you ever been told by a doctor that you have other heart disease?

Have you ever been told by a doctor that you have other heart disease? If yes, specify.

Have you ever been told by a doctor that you have or have had (a) Heart attack

Have you ever been told by a doctor that you have or have had (b) Angina

Have you ever been told by a doctor that you have or have had (h) Intermittent claudication

Have you ever been told by a doctor that you have or have had (i) Clot in the leg

If a person answered yes to ii, iv, vii, viii, ix or x, they were identified as having had a CVD event in the past.

Those who reported they have been told they have heart disease but have never had an ‘event’ were not included. These are: those who have been told by a doctor that they have: heart flutter, arrhythmia, SVT, heart murmer, tachycardia, heart palpitations, problems with heart rhythm, thickening of heart walls or valves.

Transient Ischemic attacks were not included in the stroke category therefore subjects had to self report whether they had had TIA as an additional factor. No subjects reported having a TIA.

Diabetes with other renal disease causing renal impairment

Participants were asked:

Have you ever been told by a doctor that you have chronic kidney disease?

No diabetic participants answered ‘yes’ to this question.

Some genetic lipid disorders
The only opportunity that patients had to express their knowledge of having a familial cholesterol disorder was to specify it following this question:

**Have you ever been told by a doctor that you have any other long term physical health condition?**

No participants stated a lipid disorder given this opportunity.

**Diabetes with overt nephropathy**

Albumin was not measured so this question was unable to be answered.

After analyzing the data in pivot tables there were insufficient numbers of subjects in each category for analysis. Therefore subjects were designated either ‘mild CVD risk’ or ‘moderate to high CVD risk’ for the purpose of analysis.

**Final CVD risk coding**

Once the above changes had been made to each individual risk score (where applicable), a final CVD risk score was coded by the same colour coding method as the initial risk score. For over-all analysis those in the mild categories were one group and those with moderate, high or very high risk were another group.

**Cognitive function**

Cognitive function was measured using the Montreal Cognitive Assessment (MoCA) which gives a score of 0-30.

For the CHALICE study a cutoff of ≥26 is considered normal cognition and a score of <26 is considered cognitive impairment.

Participant scores were given in the dataset and were then classified into

0=normal cognition/ No MCI

1=mild cognitive impairment

On twelve occasions the assessors felt that the person's responses (to the MOCA) may be impaired due to a reason other than natural decline in cognitive function. These included: 1=English Second Language,
2 = Blind, 3 = Learning difficulties, 4 = Memory impairment e.g. previous stroke, 5 = Other which were specified.

It was suggested by the assessors that these participant results were not included in the final analysis therefore they have been excluded.

Dietary Data

Fats

Intake of all fats was given in grams/day including total fat intake, SAFA intake, MUFA intake and PUFA intake. All fat groups were calculated as a percentage of total energy consumed by each participants by multiplying the grams per day consumed by 37 kJ (Atwater factor for fat) and dividing by the total energy consumed multiplied by 100.

For example,

\[((75 \text{ g of monounsaturated fat } \times 37 \text{ kJ})/8,500 \text{ kJ}) \times 100 = 21.8\% \text{ total energy.}\]

Total Fat

World Health Organization and the Australia New Zealand Dietary Reference guidelines suggest that 20-35% of a persons total energy intake should come from fats. Based on this, five categories were originally coded:

1 = low = <20% fat
2 = Healthy low = 20-24.9% fat
3 = healthy = 25-29.9% fat
4 = healthy high = 30-35% fat
5 = high = >35% fat

There were insufficient subjects in each category for analysis therefore categories were merged and the categories to be used for analysis are:

<30% energy from fat
30-35% energy from fat
>35% energy from fat
It was then decided to categorise total fat intake into ≤35% and >35% as per the upper limit recommended for New Zealanders. The final analysis categories used were therefore:

≤35% of energy per day from fat (healthy)
>35% of energy per day from fat (high)

Saturated Fat-

World Health Organization and the Australia New Zealand Dietary Reference guidelines suggest that ≤10% of energy should come from SAFA. The following categories were originally coded:

0=≤5%= healthy low
1=≤10%= healthy
2=10.1 - 15%= high
3= >15%= very high

There were insufficient subjects in each category for analysis therefore categories were merged and the categories to be used for analysis are:

Merger of categories 0 and 1: ≤10% fat
Merger of categories 2 and 3: >10% fat

It was decided at a later date that due to skewed data, it was appropriate to change the cutoff to the median of the ANS 08/09 which was about 13%. Therefore the final categories used for analyses were:

<13% energy from SAFA per day
≥13% energy from SAFA per day

MUFA

World health organization suggests that 15-20% of energy may come from MUFA. Based on this the following categories of intake were originally coded:

1= 0-5%
2=5.1-10%
3=10.1-15%
4=>15%
There were insufficient subjects in each category for analysis therefore categories were merged and the categories to be used for analysis are:

Merger of categories 1 and 2: ≤10% energy from MUFA
Merger of categories 3 and 4: >10% energy from MUFA

It was decided at a later date that due to skewed data, it was appropriate to change the cutoff to the median of the ANS 08/09 which was about 12%. Therefore the final categories used for analyses were:

<12% energy from MUFA per day
≥12% energy from MUFA per day

PUFA

World health organization suggests that 6-11% of energy should come from PUFA. Based on this the following categories of intake were originally coded:

1= <6%=low
2= 6.0-11.0%=healthy
3= >11%=high

There were insufficient subjects in each category for analysis therefore categories were merged and the categories to be used for analysis are:

<6% energy from PUFA (low)
≥6% energy from PUFA (healthy)

Alcohol

The following questions from module two were posed to participants in order to calculate their usual alcohol intake:

**Have you had a drink containing alcohol in the last year?** With possible answers 0=No, 1=Yes, 95=Missing-other, 96=Missing-not asked, 98=Don’t know, 99=Refused.

**How often do you have a drink containing alcohol?** With possible answers Module: 1=Monthly or less, 2=Up to 4 times a month, 3=Up to 3 times a week, 4=4 or more times a week
How many drinks containing alcohol do you have on a typical day when you are drinking? With possible answers: Module 2 - 1=1 or 2, 2=3 or 4, 3=5 or 6, 4=7 or 9, 5=10 or more.

Those who answered ‘no’ or ‘0’ question one were classified as non-drinkers.

Drinks per month were calculated for those who answered ‘1’ to question two.

Drinks per week were calculated for those who answered ‘2’, ‘3’ or ‘4’ to question two by multiplying the drinking frequency with the amount of drinks consumed (to give a range).

Five categories of ‘drinks per day’ were formed based on categories used in other studies such as the Framingham heart study. The categories are:

0 = no drinks
1 = infrequent/occasional drinking (used for those who have <1-2 drinks per month)
2 = <1 drink/day
3 = 1-2 drinks/day
4 = >2 - ≤4 drinks/day
5 = >4 - ≤8 drinks/day

Possible over or underestimations occurred when a participant responded ‘4’ to question two as it is possible that they drink every day. For example if they drink 4 or more times a week and have 5 or 6 drinks on these occasions it is calculated that they have ≥20-24 drinks per week therefore dividing by 7 days gives >2-≤4 drinks per day. However if they actually drink 7 days per week and have 5 or 6 drinks, they are having 35-42 drinks per week and fit better into the category >4-≤8 drinks per day. This group has been underestimated, while the other groups have been overestimated or fit well into their category.

There were insufficient subjects in each category for analysis therefore categories were merged creating the following new categories:

No drinks per day
Infrequent drinker
≤2 drinks/day
>2 drinks/day

Due to insufficient numbers the data were further merged into the following categories which were used for final analysis:

Non drinker and Infrequent drinker

≤2 drinks/day

>2 drinks/day
## 8.15 Appendix O: Initial five year CVD risks based on chart only

<table>
<thead>
<tr>
<th></th>
<th>Modified Sample N (%)</th>
<th>Total</th>
<th>Final Sample N(%)</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td><strong>Initial CVD risk based on New Zealand Cardiovascular Risk Charts only</strong></td>
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<tr>
<td>Mild risk</td>
<td>186 (93.9%)</td>
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<td>135 (94.4%)</td>
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<tr>
<td>Moderate risk</td>
<td>11 (5.6%)</td>
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<td>7 (4.9%)</td>
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</tr>
<tr>
<td>High risk</td>
<td>1 (0.5%)</td>
<td>198</td>
<td>1 (0.7%)</td>
<td>143</td>
</tr>
<tr>
<td>Female mild risk</td>
<td>110 (97.3%)</td>
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<td>83 (97.6%)</td>
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<tr>
<td>Female moderate risk</td>
<td>3 (2.7%)</td>
<td></td>
<td>2 (2.4%)</td>
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</tr>
<tr>
<td>Female high risk</td>
<td>0</td>
<td>113</td>
<td>0 (0%)</td>
<td>85</td>
</tr>
<tr>
<td>Male mild risk</td>
<td>76 (89.4%)</td>
<td></td>
<td>52 (89.7%)</td>
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<tr>
<td>Male moderate risk</td>
<td>8 (9.4%)</td>
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<td>5 (8.6%)</td>
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<tr>
<td>Male high risk</td>
<td>1 (1.2%)</td>
<td>85</td>
<td>1 (1.7%)</td>
<td>58</td>
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<tr>
<td>NZ Maori mild risk</td>
<td>28 (93.3%)</td>
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<td>18 (94.7%)</td>
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</tr>
<tr>
<td>NZ Maori moderate risk</td>
<td>2 (6.7%)</td>
<td></td>
<td>1 (5.3%)</td>
<td></td>
</tr>
<tr>
<td>NZ Maori high risk</td>
<td>0</td>
<td>30</td>
<td>0 (0%)</td>
<td>19</td>
</tr>
</tbody>
</table>

NZ=New Zealand
### 8.16 Appendix P: Mean fat intakes for all completers of FBD

<table>
<thead>
<tr>
<th></th>
<th>N=</th>
<th>Mean (std deviation) (% kJ/day)</th>
<th>NZ mean** (% kJ/day)</th>
<th>Median (% kJ/day)</th>
<th>N=</th>
<th>Mean (std deviation) (% kJ/day)</th>
<th>NZ mean** (% kJ/day)</th>
<th>Median (% kJ/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat intake</td>
<td>151</td>
<td>32.8 (5.6)</td>
<td>33.7</td>
<td>32.7</td>
<td>151</td>
<td>11.6 (2.9)</td>
<td>12.4</td>
<td>11.4</td>
</tr>
<tr>
<td>Total fat intake NZ Maori</td>
<td>21</td>
<td>33.9 (3.9)</td>
<td>N/A</td>
<td>33.7</td>
<td>21</td>
<td>11.7 (2.2)</td>
<td>N/A</td>
<td>11.5</td>
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<tr>
<td>Total fat intake female</td>
<td>88</td>
<td>33.2 (6.0)</td>
<td>33.8</td>
<td>33.7</td>
<td>88</td>
<td>11.9 (3.3)</td>
<td>12.3</td>
<td>11.5</td>
</tr>
<tr>
<td>Total fat intake male</td>
<td>63</td>
<td>32.1 (5.0)</td>
<td>33.7</td>
<td>32.1</td>
<td>63</td>
<td>11.3 (2.3)</td>
<td>12.4</td>
<td>11.3</td>
</tr>
<tr>
<td>SAFA intake total cohort</td>
<td>151</td>
<td>12.7 (2.8)</td>
<td>13.1</td>
<td>12.4</td>
<td>151</td>
<td>4.9 (1.9)</td>
<td>4.9</td>
<td>4.4</td>
</tr>
<tr>
<td>SAFA intake NZ Maori only</td>
<td>21</td>
<td>12.9 (2.8)</td>
<td>N/A</td>
<td>12.7</td>
<td>21</td>
<td>5.6 (2.9)</td>
<td>N/A</td>
<td>5.1</td>
</tr>
<tr>
<td>SAFA intake female</td>
<td>88</td>
<td>12.7 (2.9)</td>
<td>13.1</td>
<td>12.5</td>
<td>88</td>
<td>5.2 (2.2)</td>
<td>4.9</td>
<td>4.5</td>
</tr>
<tr>
<td>SAFA intake male</td>
<td>63</td>
<td>12.8 (2.7)</td>
<td>13.1</td>
<td>12.1</td>
<td>63</td>
<td>4.6 (1.4)</td>
<td>4.8</td>
<td>4.4</td>
</tr>
</tbody>
</table>

NZ=New Zealand